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C-01

Traumatic Brain Injury-Induced Neuroendocrine Changes

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Traumatic brain injury which is a growing public health problem worldwide has recently been recognized as one of the most common causes of hypopituitarism. The causes of TBI-induced pituitary dysfunction are car accidents, falls, violence and war accidents including blast-related brain injuries. Neuroendocrine abnormalities were also reported in athletes dealing with contact sports including boxing and kickboxing. Boxing and kickboxing are characterized by chronic repetitive head trauma and they are accepted as mild traumatic brain injury. The prevalence of hypopituitarism after TBI is about 30%. GH is the most common hormone lost. The mechanisms underlying the hypopituitarism are still unclear; however, recent studies have demonstrated that genetic predisposition, neuroinflammation and autoimmunity may be responsible for the development pituitary dysfunction. The frequency of hypopituitarism is significantly lower in TBI victims with APO E3/E3 than in victims without APO E3/E3 genotype. The positivity of anti-pituitary and anti-hypothalamic antibodies is also a significant risk factor. Altered expression of miR-126-3p and miR-3610 may play an important role in the occurrence of hypopituitarism after TBI. Treatment of hypopituitarism with appropriate replacement therapies is beneficial in the improvement of manifestations caused by insufficient hormones.

C-02

A Body Weight Homeostat That Regulates Fat Mass in Rats and Mice

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Subjects spending much time sitting have increased risk of obesity but the mechanism for the antiobesity effect of standing is unknown. It is known that osteocytes can sense changes in bone strain, opening for the possibility that osteocytes of the weight bearing bones could sense changes in the body weight as well. We hypothesized that there is a homeostatic regulation of body weight, which can be influenced by posture.

To test this hypothesis, we implanted capsules that weighed 15% of the body weight into the abdomen of adult Sprague-Dawley rats and C57BL6 mice with diet induced obesity (Load). Control animals were implanted with an empty capsule of equal size (3% of the body weight). The body weight was recorded throughout the experiment and at the end fat pads and skeletal muscle was dissected and weighed. The glucose tolerance and leptin levels were checked in mice. We also unloaded some animals by exchanging the heavy capsule to light capsule after a couple of weeks.

We demonstrated that increased loading of rodents, reversibly decreases the biological body weight via reduced food intake. Importantly, loading relieved diet induced obesity and improved glucose tolerance. However, the body weight-reducing effect of increased loading was lost in mice depleted of osteocytes. We propose that increased body weight activates a sensor dependent on osteocytes of the weight bearing bones. This induces an afferent signal, which reduces body weight. These findings demonstrate a novel leptin-independent body weight homeostat (“gravitostat”) that regulates fat mass.
C-03

Hypothalamic Appetite Pathways Examined in a PWS Mouse Model

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Prader-Willi Syndrome (PWS) is a neurodevelopmental disorder characterized by childhood obesity and social deficits. Several genes including, MAGEL2 have been described to be inactivated in PWS. MAGEL2 is also abundantly expressed in hypothalamic appetite regulating neurons. We hypothesized that loss of MAGEL2 in key hypothalamic circuits may underlie or contribute to some of the metabolic phenotypes seen in PWS. Using cell type specific approach, we characterized impact of Magel2 deletion on AGRP and POMC-neuron activity and behavioural function focusing on appetite. We observed alteration in POMC-neuron activity as well as behavioural function whereas AGRP neurons appear to function relatively normal.

C-04

Neuroendocrine Regulation of Energy Homeostasis and Hypothalamic Obesity in Children

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Energy balance in humans is regulated by a complex neuroendocrine system centred in the hypothalamus. The key hypothalamic areas of energy regulation are the ARC (arcuate nucleus), the VMH (ventromedial hypothalamus), the PVN (paraventricular nuclei) and the LHA (lateral hypothalamic area). The mechanical or functional disruption of the hypothalamic network that regulates energy homeostasis causes intractable weight gain, which is named “Hypothalamic Obesity (HyOb)”. Although, understanding of mechanisms for the role of hypothalamus in energy homeostasis took many years, especially recent studies shed light on how the hypothalamus regulates appetite and satiety. The disruptions causing HyOb can result from brain tumours, neurosurgery, cranial radiotherapy, and genetic defects. Rapid weight gain and severe obesity are the most striking features of HyOb and caused by hyperphagia, reduced basal metabolic rate (BMR) and decreased physical activity. Currently, attempts at controlling of HyOb through diet, exercise or pharmacological treatment are not satisfactory. However, new treatment opportunities in genetic obesity and the application of bariatric surgery hold promise for the treatment of HyOb. This talk will summarize hypothalamic appetite regulation, and the pathophysiology, metabolic features, aetiology, clinical characteristics, and treatment modalities for hypothalamic obesity in children and adolescents.

C-05

A Time to Feast and a Time to Fast: The Influence of Feeding Patterns on Endocrine, Growth and Metabolic Outcomes

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The physiological impact of temporal feeding patterns remains a major unanswered question in nutritional science. We used a CLAMS-based automated feeding station with automated blood sampling to assess the impact of contemporary feeding patterns on growth and hormone profiles.

Grazing (GR; 1/24th of the daily consumption of ad libitum (AL)-fed rats provided every 30 mins during the dark phase), or meal-feeding (MF; 3x 1 hr AL meals at the beginning, middle and end of the dark phase) with a standard rodent chow (StRC) reduced caloric intake in male rats by 20% (vs AL-fed controls). GR reduced weight gain by 14%, nose-anus length and femoral length by 3% and tibial epiphyseal plate width (tEPW) by 15%, all of which were unaffected in MF rats. When fed a high fat (AFE 45% Fat) diet, abdominal fat storage efficiency was elevated in GR and MF rats by 52% and 37% respectively.

Although these feeding patterns had no effect on growth in StRC-fed male wild type (WT) mice, MF reduced tEPW by 15–16% in ghrelin−/− littermates.

Rats receiving StRC in either GR or MF patterns displayed a large pre-prandial ghrelin surge with a sharp feeding-induced decline. Despite continued feeding, circulating ghrelin increased progressively across the dark phase in GR rats, while MF rats produced a large surge in ghrelin before the last dark phase meal. GR aligned individual growth hormone (GH) profiles without altering total secretion or pulse parameters. In contrast, MF induced a 166% increase in overall GH secretion due principally to the appearance of two additional GH pulses per day.

Despite reducing caloric intake, meal feeding preserved skeletal growth by a ghrelin-dependent augmentation of pulsatile GH secretion, while grazing promoted fat storage. Thus, the contemporary shift from regular meals to more continuous feeding may switch nutrient partitioning from skeletal growth to fat storage.

C-06

The Potential Role of Neuronal Structure and Function Underlying Cognitive Brain Aging

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Normal aging is accompanied by a range of biological changes that diminish the quality of life. Understanding the alterations contributing to memory decline is important for developing strategies to prevent or lessen cognitive problems. What are the specific changes that take place during aging which lead to decrements in neural function? What are the intrinsic biological determinants of
C-07
Restoring Function to Inactivating GPCR Mutations in the HPG Axis
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Inactivating mutations in G-protein coupled receptors (GPCRs) at all levels of the HPG axis give rise to incomplete reproductive development and adult infertility. The majority of the mutations in GPCRs cause misfolding of the receptor and a failure to traffic to the cell surface. We have therefore sought for cell permeant small molecules which can bind orthosterically or allosterically to stabilize the nascent GPCR in the endoplasmic reticulum and chaperone the mutant GPCR to the cell membrane.

We have successfully ‘rescued’ many GnRH mutant receptors using small molecule antagonists which bind orthostERICALLY. After removal of the antagonists the mutant GnRH receptors demonstrate good cell surface expression. Michael Conn’s laboratory has since demonstrated that such receptor rescue can restore reproductive competence in mice harbouring an inactivating GnRH receptor mutation.

We have also demonstrated rescue of cell surface expression and signalling in a substantial number of LH receptor mutations causing infertility in humans using a cell permeant allosteric agonist.

Most recently we have rescued function of NKB receptor inactivating mutations with cell permeant small molecules.

These discoveries represent an advance towards personalized medicine for GPCR deficiencies in the human HPG axis.

C-08
Role of Amygdala Kisspeptin in Reproduction and Behaviour
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The neuropeptide kisspeptin is a potent stimulator of gonadotropin-releasing hormone (GnRH) secretion and essential regulator of reproduction. Mutations in the genes for kisspeptin or its receptor results in hypogonadotropic hypogonadism and failure to enter puberty. In addition to the well-studied kisspeptin neurones located in the hypothalamic arcuate nucleus and preoptic area, that are key to GnRH pulse and surge generation, they are present in several extra-hypothalamic loci, most notably the posterodorsal subnucleus of the medial amygdala (MePD). Although the medial amygdala has a long history of involvement in gonadotrophic hormone secretion, puberty and behaviour, we have recently shown using neuropharmaceutical techniques, and selective optogenetic and chemogenetic activation of MePD kisspeptin, their involvement in the regulation of hypothalamic GnRH pulse generator frequency, pubertal timing and behaviours including social and sexual behaviour, and anxiety.

C-09
Neuroprotective and Restorative Effects of Melatonin: In Molecular Aspect
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Melatonin is a powerful free radical scavenger with the desirable characteristics of a clinically-reliable antioxidant. So far, the neuroprotective effect of melatonin has been linked mainly to its direct free radical scavenging and indirect antioxidant activities. In recent years, we have focused on the signal transduction mechanisms of melatonin’s neuroprotective, therapeutic and plasticity-promoting effects against acute and post-acute brain injury. Melatonin regulates cellular signaling pathways through receptor-dependent and independent mechanisms. We have provided evidence that the neuroprotective effects of melatonin appear to be mediated through a mechanism independent of Gi protein-coupled metabotropic membrane receptors MT1, MT2. Our observations suggest that melatonin acts through the PI3K/Akt pathway to inhibit p53 phosphorylation which results in increased neuronal survival. Molecular and proteomics analysis indicate that nighttime Ischemic/Reperfusion injury results in less severe neuronal damage, with increased neuronal survival, increased levels of survival kinases and circadian clock proteins, and also alters the circadian-related proteins.

Besides its neuroprotective activity, post-acute administration of melatonin coordinates both ipsilesional and contralesional recovery processes on stroke-damaged brain tissue reflected by in-
creased neurogenesis and decreased reactive astrogliosis that resulted in reduced scar formation. Moreover, melatonin improves motor coordination and exploration behaviour and changes expression of plasticity-and angiogenesis-related genes and proteins suggesting an improvement in neurogenesis and angiogenesis in both hemispheres in a different manner. Melatonin triggers considerable changes in the expression of inflammation-related genes, many with distinct temporal and spatial patterns in different phases of poststroke recovery.

In the aspect of our previous- and present studies, the neurohormon melatonin, being well tolerated and having minimal side effects, is a promising candidate by its neuroprotective and restorative effect for the treatment of stroke patients either as a monotherapy or an add-on to the thrombolytic therapy.

**OC-001**

The Role of Physiological and Pharmacological Concentration of Melatonin on Protection of Remote Preconditioning in Myocardial Ischemia Reperfusion-Induced Inflammatory Mediator Nuclear Factor-Kappa B

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Ischemic heart disease is the leading cause of morbidity and mortality in developed nations. In recent years, it has been found that remote organ/limb temporary ischemia that renamed remote ischemic conditioning (RIC) can provide protection as an obstacle to the formation of lethal ischemic outcomes. The finding of this phenomenon can remove the requirement for direct cardiac intervention in cardiac protection. It has been shown that the cardioprotective effects of conditioning in aging and comorbidities are impaired. With aging, decreased melatonin synthesis in the pineal gland suggests that it is important in the pathogenesis of aging and aged-related cardiovascular diseases. In this study, effects of remote ischemic preconditioning (RIPerC) and melatonin on the inflammatory mediator nuclear factor-kappa B (NfkB) were investigated using an in vivo model of myocardial ischemia/reperfusion (I/R) injury.

Sprague-Dawley rats were divided into first two groups as non-pinealectomized (Non-Px) and pinealectomized (Px) groups, and then (i) Control; (ii) I/R (30 min ischemia, 120 min reperfusion caused by left coronary artery ligation); (iii) I/R+RIPerC (when myocardial ischemia initiated, 3 cycles of 5 min occlusion followed by 5 min reperfusion); (iv) I/R+Mel (10 days 10 mg/kg); (v) Px; (vi) Px+I/R; (vii) Px+I/R+RIPerC; (viii) Px+I/R+RIPerC+Mel groups. Hemodynamic parameters including ECG, blood pressure, heart rate were evaluated. NfkB was analyzed by qRT-PCR.

NfkB level was increased in the Non-Px+I/R group (2.2 ± 0.3; 1.0 ± 0.3; respectively) when compared with control. However, it was decreased with RIPerC and melatonin (0.4 ± 0.2; 0.5 ± 0.2; respectively). Compared with Px, NfkB level was increased in the Px+I/R group (1.2 ± 0.2; 2.3 ± 0.3; respectively). RIPerC applied to Px group was decreased NfkB level (1.1 ± 0.4), but its expression was reduced more when melatonin was administered before RIPerC (0.5 ± 0.1).

The physiological and pharmacological concentrations of melatonin may be important in I/R-induced inflammation. These results suggest that myocardial conditionings and melatonin are protective with similar so melatonin may be an agent which leads to pharmacological conditioning.

**Acknowledgement:** This study is supported by TUBITAK (Project No: 115S323).

**OC-002**

Novel Methods for Three-Dimensional Microscopic Imaging of Neuroendocrine Tissues: Whole Organ Clearing and Light Sheet Microscopy

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To visualize neuroendocrine tissues microscopically uninterrupted at high resolution, novel sampling and microscopy techniques are being developed. The aim of this study is clearing of various neuroendocrine tissues by CLARITY and 3DISCO, observe tissues in 3D to compare with conventional methods in terms of visualization of morphological and functional properties.

C57 adult mice (n = 10) were used to obtain tissues (brain, cerebellum, hypophysis, adrenal gland, pancreas, ovary, testis) of varying thickness (10, 40, 400, 1000 μm).

For thin sections, tissues were perfused with 4% PFA, removed, post-fixed with PFA; followed by sucrose-processing, cryo-sectioning, immunofluorescent labelling.

For CLARITY, mice were perfused with hydrogel monomer (HM) solution. Tissues were then incubated with HM, placed in clearing solution, primary/secondary antibodies were administered for 2 days.

For 3DISCO, tissues were perfused with 4% PFA with fluorescent-conjugated antibodies. Following post-fixation in PFA; tetrahydrofuran and dibenzylether were administered. As primary/primary conjugated antibodies, beta-III tubulin, MAP2 Neu-N, FITC-dextran, ASMA, 3bhydroxysteroid dehydrogenase, cytokeratin were used, and Alexa 488-594 were used as secondary antibodies. Tissues were imaged under Leica dmi8-SP8 confocal/LS and Leica dm6 MP microscope, with 488 nm, 552 nm and titanium-sapphire laser (920 nm).

CLARITY samples were successful for 1000 μm z-depth imaging. 3DISCO is faster for preparation, and gave good results at 400–600 μm with MP. 3DISCO samples were effective with conventional confocal microscope at 200 μm z-depth. 10–40 μm sections showed a resolution of 100–150 nm at x-y, structural integrity was not good for z.

Tissues were dissected and fixed in 4% paraformaldehyde (PFA) for 2 days.

Acknowledgement: This study is supported by TUBITAK (Project No: 115S323).
CLARITY and 3DISCO methods can effectively be used for imaging of neuroendocrine tissues at z-axis with high resolution.

Acknowledgement: This study has been conducted at KUTTAM.

OC-003

Acute REM Sleep Deprivation Induced Learning and Memory Impairments Ameliorated by Long Term Mild Treadmill Exercise

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It is clearly explained from the molecular to the phenomenological levels that sleep greatly contributes to the processes of memory and learning. Sleep problems are very common from infancy to adolescence and frequently elicit learning and memory impairment. Environmental enrichments like social interactions and exercise can adverse the diminished effects of stress on learning/memory and behaviour. Therefore, we aimed to investigate the effects of chronic mild treadmill exercise on learning and memory on sleep deprived rats.

Male Wistar rats (n = 28) 3 weeks old were randomly divided into; control (C), control + exercise (CE), sleep deprivation (SD), sleep deprivation + exercise (SE). Rats were deprived from sleep by placing into Plexiglas tanks. Animals for the SD, exercise/SD groups were remained on the tank for 48 hours after the exercise protocol. The running time in exercise groups were increased progressively through 4 weeks (15 min, 30 min, 45 min, 60 min and speed 10 m/min respectively). For define learning and memory of rats, we used Morris Water Maze test (MWMT). Results were analysed by SPSS 11.5 statistic software.

In MWMT, compare to the C (32.33 ± 6.13), CE (35.14 ± 6.65), SD (34.52 ± 8.77) groups; sleep deprived rats spent less time in the target quadrant (21.86 ± 6.21) (p < 0.05).

According to the MWMT, long-term mild treadmill exercise ameliorated the diminished learning and memory that caused from acute sleep deprivation. In Rajizahed study, they demonstrated the voluntary exercise impacts on learning and memory and found that exercise ameliorated the SD induced learning and memory impairments. A recent review from the literature suggests that forced exercise and voluntary exercise have different effects on brain neurochemistry and behaviour. Taken together, both types of exercise can be powerful application to rehabilitate the various stress conditions like sleep deprivation.

OC-004

Effects of Noopept on Hippocampal NGF and BDNF Levels and Cognitive Functions of Prepubertal Rats with Streptozotocin-Induced Diabetes

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Insulin resistance and long-term hyperinsulinemia impair blood-brain barrier functions and insulin activity in pubertal type 1 diabetes mellitus (T1DM) patients. Hyperinsulinemia causes neuronal degeneration leading to non-reversible cognitive disorders. NGF and BDNF are important proteins in neuronal regeneration, their tissue levels have been shown to decrease in diabetes and cognitive impairment. Noopept is a nootropic dipeptide that is used as a cognitive regulator. Noopept studies have suggested it to have anti-neuronal degeneration and anti-diabetic properties. In our study, we tried to determine the effects of noopept on hippocampal NGF & BDNF levels and cognitive functions in prepuberal DM rats.

In this study 60 prepubertal, posnatal 28th-day, male Sprague Dawley rats were divided into 6 randomized groups. i) control, ii) DM control, iii) noopept control, iv) DM-noopept, v) DM-insulin, vi) DM-insulin-noopept. On postnatal 28th day diabetes model was created by applying 50 mg / kg streptozotocin. 0.5 mg / kg noopept, one unit insulin was intraperitoneally administered for 14 days in the required groups. Cognitive assessment was done with Morris Water Maze test in postnatal 41–45th days. The research ended on postnatal 46th day. NGF and BDNF were assessed by ELISA test from hippocampal homogenate.

There was no statistically significant difference between NGF and BDNF values. There was no statistically significant difference in Morris Water Maze test.

By looking at references, we think that our research’s time limitation of two weeks, has affected the results. Measuring the levels of NGF and BDNF at the pro-protein and mRNA levels may provide more comprehensive results.

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OC-005

Galectin-3 Expression in Brain Tissue in the Rats Administered with Adriamycin

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Experimental studies have shown that adriamycin (ADR) affects lipid peroxidation in the neurons, thereby causing sensory neuropathy. Galectin-3 is novel marker with a potential role in inflammation and fibrosis as well as tumour progression. In this study, we aimed to investigate the effects of ADR on galectin-3 expression in brain tissue in rats administered with ADR.

A total of 14 adult male Wistar Albino rats were used for the experiment. The rats were divided into two groups as (I) experimental and (II) control groups. The experimental group was administered single-dose intraperitoneal ADR 10 mg/kg and the control group received no treatment. The experiment was performed over a period of 14 days. After the experiment, all the rats were decapitated under anaesthesia and the brain tissues were removed promptly. The tissues were embedded into paraffin blocks for histological analysis. Indirect immunohistochemical staining was performed with paraffin-embedded sections to determine galectin-3 immunoreactivity. In the evaluation of immunohistochemical staining, a histoscore was calculated based on the diffuseness and intensity of staining.

The results indicated that the galectin-3 expression in rat brain was significantly increased in the rats administered with ADR compared to control rats (p < 0.05).

The increase in galectin-3 immunoreactivity induced by ADR suggests that galectin-3 may have a role in the pathophysiology of the neurotoxicity caused by ADR.

OC-006

Anaesthesia Management of a Morbid Obese Woman Undergoing Transsphenoidal Hypophysectomy

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Anterior pituitary tumours account for nearly 18% of all intracranial tumours. Pituitary adenomas that cause hypersecretion of hormones lead to some diseases in patients. We present a surgical case under general anaesthesia of a woman suffering from visual disturbance caused by pituitary adenoma.

A 56-year-old, 129 kg, 161 cm, body mass index: 50 kg/m², ASA physical status III, presented 8 months after suffering a head injury, severe fatigue and defect of vision. Macroadenoma (pituitary adenoma) revealed in the suprasellar region as a dimension of 26x22 cm extending into the sphenoid sinus, and causing stalk left deviation was diagnosed on MR imaging. His medical history was diabetes mellitus, hypertension, asthma, hypothyroidism and phthisis. His past surgical history included cataract surgery 2 years before and it was learned that the problem was not encountered. His medications included metformin, levothyroxine and valsartan + hydrochlorothiazide. The rest of the physical examination was notable for oedema and puckers in the feet. Free T4: 0.85 ng/dl, TSH:0.59 μIU/ml, FSH:4.82 mIU/ml, prolactin:13.7 ng/ml and HbA1C: %5.6 were in her laboratory review. His vital signs were heart rate, 90; blood pressure, 160/70; and respiratory rate, 18. The patient was pretreated with 2 mg midazolam iv. On arrival to the operating room, routine monitors were placed, and invasive arterial cannulation additionally. Anaesthesia induction was achieved with propofol, fentanyl and rocuronium, and intubation was completed intraorally, successfully. Transsphenoidal hypophysectomy surgery took nearly 3 hours, and patient was extubated uneventfully. Bleeding 100 cc occurred during surgery and no blood transfusion was applied. After 3 days the patient was discharged without any problems.

Consequently, various comorbidities may develop depending on the changes in the hormones in patients with pituitary adenoma. These may also impair anaesthesia management. Anaesthesia management should be planned considering the physiological characteristics of the patient.

OC-007

Effects of Two Boron Containing Compounds and Melatonin in Aβ1-42 Toxicity

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Boron is a very important micronutrient for plant, animal and human health and metabolism. Melatonin has well-known neuroprotective effects. The presence of amyloid beta plaques is one of the neuropathological hallmarks of neurodegeneration. The aim of this study is to investigate the possible effects of two boron containing compounds, borax and boric acid, and melatonin in amyloid beta (Aβ) toxicity model.

In this study, SH-SY5Y cells were used. Cells are seeded into 6-well plates for 250,000 cells/well, 10 μM Aβ1-42 was used as a most effective toxic dose. Borax, boric acid (200 μg/ml) and melatonin (100 μM) were used before and after Aβ1-42 application Lactate dehydrogenase (LDH), Total Antioxidant (TAS) and Total Oxidant (TOS) levels were measured colorimetrically from cell culture media. Total protein isolation was done and the changes in the expression levels of pro-survival proteins (SIRT1, GSK-3β) and Akt were investigated by western blotting technique. All data were statistically evaluated by one-way ANOVA test.

LDH analysis showed that cellular toxicity increased in 10 μM Aβ1-42 (p < 0.001). Aβ1-42 toxicity decreased when borax, boric acid and melatonin were added before and after Aβ1-42 applica-
tion (p < 0.001). Melatonin increased TAS levels whereas it decreased TOS levels (p < 0.001). Western blotting exhibited that levels of SIRT1 and p-GSK-3β increased when boric acid was applied after Aβ1-42. The level of p-Akt elevated when borax was used after Aβ1-42 (p < 0.05). Melatonin increased SIRT1, p-GSK-3β and p-Akt when it was added before and after Aβ1-42 application (p < 0.05).

Our data indicated for the first time that the expression of SIRT1 was increased by boron containing compounds. These compounds decreased Aβ1-42 toxicity by elevating p-Akt ve p-GSK-3β levels. In conclusion, boron as a strategic mineral has been shown to have positive effects which are similar with melatonin on cell metabolism.

Prader-Willi Syndrome (PWS) is a neurodevelopmental disorder causing social and learning deficits, impaired satiety and severe childhood obesity. Genetic underpinning of PWS involves deletion of a chromosomal region with several genes, including Magel2, which is abundantly expressed in the hypothalamus of appetite regulating hypothalamic cell types, both AGRP and POMC-expressing neurons contain Magel2 transcripts but the functional impact of its deletion on these cells has not been fully characterized. Here, we investigated these key neurons in Magel2-null mice in terms of the activity levels at different energy states as well as their behavioural function.

Using cell type specific ex vivo electrophysiological recordings and in vivo chemogenetic activation approaches, we evaluated impact of Magel2 deletion on AGRP and POMC-neuron induced changes in appetite. To achieve this, Agrp-cre, Agrp-cre::Magel2m/-p, Pomc-cre and Pomc-cre::Magel2m/-p mice were transduced with rAAV2/8-FLEX-GFP virus for ex vivo electrophysiological recordings or rAAV2/1EF1a-DIO-hM3D(Gq)-mCherry virus for food intake study. Florence guided loose-seal recordings were performed from both sated and food deprived Agrp-cre and Agrp-cre::Magel2m/-p mice.

We found that under ad libitum and food deprived feeding conditions, baseline firing rates of AGRP neurons were similar in Agrp-cre or Agrp-cre::Magel2m/-p mice. We then compared POMC neuron firing rates under fed state, which was significantly lower in Pomc-cre::Magel2m/-p mice compared to Pomc-cre littermates. A closer examination of firing patterns showed that, POMC neurons from Magel2 null mice had significantly lower instantaneous firing rates. Chemogenetic activation approaches revealed that food intake and body weight changes were comparable in Agrp-cre or Agrpcre::Magel2m/-p mice. However, the extent of appetite suppression was much weaker in Pomc-cre::Magel2m/-p mice compared to Pomc-cre littermates.

Our results suggest that POMC neuron activity profile as well as its communication with downstream targets is significantly compromised while AGRP neuron function is relatively unaffected in Magel2 deficiency.

**OC-009**

**Effect of Captopril on Pentylenetetrazole-Induced Epileptic Seizure and Post Seizure Hippocampal Neuronal Damage in Mice**

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Recent studies show that angiotensin converting enzyme (ACE) inhibitors have positive effects on nervous system. The aim of this study was to investigate the effect of captopril, an ACE inhibitor, on pentylenetetrazole (PTZ)-induced seizures and post seizure hippocampal damage. We used 35 male 30–33 g Balb-C mice. Animals were divided into five groups as control, saline (PTZ; 1 ml/kg serum physiological), positive control (200 mg/kg valproic acid), captopril (25 mg/kg/day for 7 days) and captopril (50 mg/kg/day for 7 days). Thirty min after drugs administration at the indicated doses, PTZ was administered 60 mg/kg to induce epileptic seizure. The animals were observed for 20 min. Seizure stages (according to the Racine Scale), first myoclonic jerk times (FMJ) and first generalized tonic-clonic seizure (GTCS) times were recorded. Four hours after PTZ injection, brain tissues were removed. After routine histological process, serial sections from brain tissues were stained with toluidine blue to determine neuronal damage. The hippocampal cornu ammonis (CA) 1, CA2, CA3 and dentate gyrus regions were evaluated histopathologically. Statistical evaluation of the data was performed by one-way ANOVA and multiple comparisons were determined by the Tukey test. Statistical significance was defined at p < 0.05.

Obtained data suggest that in terms of epileptic evaluation, 25 mg/kg captopril decreased seizure stages and increased FMJ and GTCS compared to PTZ group (p < 0.05). However, 50 mg/kg captopril did not change seizure stages, FMJ and GTCS compared to PTZ group. In terms of histopathology, both 25 mg/kg captopril and 50 mg/kg captopril reduced neuronal damage in hippocampal CA1, CA2, CA3 and DG regions compared to PTZ group (p < 0.05).

In conclusion, we suggest that captopril has positive effects on epileptic seizure and post seizure hippocampal neuronal damage.
Potential Effect of 2-Isopropyl-5-Methylphenol (Thymol) Alone and in Combination with Selenium on Apoptosis, Intracellular Calcium, Caspase 3 and 9 Levels Through Activation of TRPV1 Channel

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In the current study, we investigated the protective effects of Selenium (Sel) on apoptosis and oxidative stress through Thymol induced TRPV1 channels activation in SHSY-5Y neuroblastoma cell line.

The cells were divided into 7 groups as control, Thymol, Thymol+Capsazepine, Thymol+Sel, Thymol+Sel+ Capsazepine, Sel, Sel+ Capsazepine and all groups were stimulated by TRPV1 Channel agonist which is Capsaicin before or during related analysis.

Results of the study demonstrated that thymol efficiently increased free cytosolic Ca2+ concentration and reactive oxygen species, caspase 3 and Caspase 9, mitochondrial depolarization and apoptosis levels through induction of TRPV1 Channels. However, increased apoptosis and other values in the cells were decreased by Sel treatments in Thymol+Sel group but, apoptosis, ROS, mitochondrial depolarization, caspase 3 & 9 values were increased in the Selenium group compared with the control group.

In conclusion, thymol could be used as a potent drug against several cancers types such as neuroblastoma through the regulation effect of Sel on Thymol induced-excessive TRPV1 channel activation.

Melanin Concentrating Hormone Neurons Regulate Reward Seeking Independent of Post-Ingestive Actions

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Evolutionarily, our brains drive great enthusiasm towards palatable nutrients. Craving and consuming palatable foods with high fat or sugar content often overcome homeostatic feeding. Even though certain brain regions are known to control physiological fed and fasted states along with hedonic and homeostatic feeding, neural populations that regulate hedonic feeding through predominating physiological needs remain unidentified. Earlier genetic studies have implicated a role for melanin concentrating hormone (MCH) neurons of lateral hypothalamic area (LHA) in food reward.

In this study, we aimed to use acute neuronal activity manipulation tools to functionally characterize MCH neurons in terms of appetite and reward. For this purpose, using DREADD technology, we remotely and reversibly manipulated MCH neurons to reveal their involvement in acute and chronic food intake control as well as glucose and insulin sensitivity. We also investigated rewarding capacity of MCH neuronal stimulation alone by optogenetic activation. We conducted nose poke assay, lever press assay and real time place preference assay to assess reward value of MCH neurons.

Our results suggest that MCH neurons are neither necessary nor sufficient to acutely change food intake but can alter blood glucose levels. Chemogenetic or optogenetic activation of MCH neurons does not regulate homeostatic feeding. Surprisingly, close loop self-stimulation experiments, along with nose poke and lever press assays have shown that MCH-neuron activation alone was sufficient to drive reward seeking.

Collectively, these experiments show a connection between MCH neurons and reward seeking, which takes place independent of homeostatic post-ingestive actions.

The Effects of Sitagliptin on Anxiety-Like Behaviour and GLP-1 in Streptozotocin-Induced Diabetic Rats

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Glucagon-like peptide-1 (GLP-1) is an incretin that is secreted mostly in the terminal ileum and increases glucose-induced insulin synthesis and secretion, decreases glucagon secretion and blocks beta-cell apoptosis. GLP-1 is inactivated by the dipeptidyl-peptidase 4 (DPP-4) enzyme in the plasma. GLP-1 receptor agonists and DPP-4 enzyme inhibitors have been widely used in the treatment of diabetes. It is known that diabetics have higher anxiety levels. The effect of GLP-1 on anxiety is unclear. The aim of this study was to investigate the effects of sitagliptin on anxiety-like behavior and GLP-1 in diabetic rats.

There were four groups in the study; control, control+sitagliptin (a DPP-4 enzyme inhibitor), diabetes and diabetes+sitagliptin. Diabetes was induced by streptozotocin (single 40 mg/kg, intraperitoneally). After 48 hours rats with blood glucose levels higher than 250 mg/dL were considered as diabetic. Sitagliptin was given 20 mg/kg (PO) for 21 days. Anxiety levels were evaluated with open field and elevated plus maze tests. GLP-1 and GLP-1 receptor levels in ileum, prefrontal cortex (PFC) tissues and plasma were measured with ELISA.

Diabetic rats exhibited greater anxiety-like behaviour in the elevated plus maze test (p < 0.05). GLP-1 receptor levels in PFC
were decreased in diabetic rats (p < 0.05). Both GLP-1 and GLP-1 receptor levels in ileum were decreased in diabetic rats (p < 0.05). Sitagliptin didn’t affect anxiety-like behavior, didn’t change ileum and PFC GLP-1 receptor levels; but decreased ileum GLP-1 levels and failed to lower blood glucose levels in diabetic rats (p < 0.05). In non-diabetic animals, sitagliptin increased anxiety levels, decreased both GLP-1 and GLP-1 receptor levels in PFC and decreased plasma GLP-1 levels (p < 0.05). Also, there was a moderate positive correlation between anxiety and PFC GLP-1 receptor levels (r = 0.63, p < 0.01).

These results indicate that GLP-1 was related with anxiety, whereas our sitagliptin dose may not be enough for the change of anxiety, GLP-1 and GLP-1 receptor levels in diabetic rats.

**OC-013**

**Investigation of a Catecholaminergic Circuit for Feeding between Hindbrain and Hypothalamus**

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Nucleus of solitary tract (NTS) is a structure that plays a critical role in homeostasis. It contains a variety of neuronal subtypes, each playing important roles in diverse aspects of physiology such as stress, blood glucose and energy expenditure. Ascending appetite related signals to hypothalamus have been poorly investigated. We have studied the role of NTS to paraventricular hypothalamic (PVH) connection in feeding behaviour with an emphasis on catecholaminergic [tyrosine hydroxylase (TH+)] neurons.

We used optogenetics and patch clamp electrophysiology to selectively activate NTSTH axons over PVH and evaluated cellular response. For this, we transduced NTS region of Th-cre mice with rAAV-FlexChR2 viral vectors and performed patch clamp recordings from acutely prepared PVH slices. Nearly half of the cells did not respond to the NTSTH axonal stimulation and the remaining neurons responded equally with increasing or decreasing activity.

Our results suggest a heterogeneous response profile among PVH neurons upon optogenetic stimulation of NTSTH axons.

**OC-014**

**Chronic Manipulation of Arcuate Kisspeptin Neurons in Aβ42 Induced Mouse Model of Alzheimer’s Disease**

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Alzheimer’s Disease (AD) is a progressive neurodegenerative disease which begins with insidious deterioration of cognitive functions and progresses to severe dementia, confusion, behavioural and personality changes. AD is microscopically characterized by several neuropathological lesions including formation of β-amyloid plaques and neurofibrillary tangles. Kisspeptin receptor GPR54 is expressed in extra-hypothalamic tissues like hippocampus and cortex. In this study, possible role of kisspeptinGPR54 system in AD mouse model and effects on catecholamine levels were investigated.

In this study, the AH mouse model was generated by injection of Aβ1–42 into the Dentate Gyrus (DG) region of Kiss1-CreGFP transgenic mice. Hypothalamic injection of CRE-dependent virus (AAV-FlexhM3D (Gq) -mCherry / -hM3D (Gq) -mCherry) was performed by stereotoxic surgery into the hypothalamic Arcuate (ARC) region for pharmacogenetic manipulations of the kisspeptin neurons. The AH model was behaviorally evaluated using the Morris Water Maze (MWM) test. Experimental groups were given intraperitoneal clozapine-N-oxide (CNO) injection for 1 month to enable chronic activation/inhibition of the kisspeptin neurons. MWM test was performed again after chronic manipulation. Brain fluid from cerebral ventricles were collected using brain microdialysis perfusion probe. Seven samples were collected at intervals of 20 min and CNO injection was performed after the second sample. Catecholamine levels (noradrenaline, dihydroxyphenylglycol, dopamine, dihydroxyphenyl acetic acid) were determined by HPLC method from collected samples. LH serum levels were determined by ELISA method in blood samples collected after decapitation. Coronal cross sections of 50 μm were taken with vibratome to determine the injection sites by confocal microscopy.

A significant difference was found when the escape latencies were compared in the MWM test (One-Way ANOVA, p < 0.05). As a result of the MWM test performed after chronic manipulation, it was seen that the activation group was significantly different from the other groups (p < 0.05). Catecholamine levels were altered after CNO injection. There was no significant difference in serum levels of LH.

In the MWM test after chronic activation of the kisspeptin neurons of the AH mouse model, the finding of the platform earlier
shows a positive effect of the kisspeptin on learning and memory despite the hippocampal injury.

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**OC-015**

**Synaptic Pharmacology of Orexigenic Arcagrpf → PVN Connection**

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Agouti related peptide (AGRP) expressing neurons in the arcuate nucleus of hypothalamus (ARC), has a central role in regulating appetite and metabolism. It has been shown that activity changes in these neurons are necessary and sufficient to acutely regulate feeding behaviour. AGRP neurons send dense intrahypothalamic axonal projections and make synaptic connections to paraventricular nucleus (PVH), which have been shown to be the key downstream target region.

Since ARCAGRP → PVN synaptic connection play a pivotal role in feeding, neuromodulators controlling the strength of this connection are also likely to be critical for appetite regulation. In this study we aimed to test the pharmacological properties of the ARCAGRP → PVN connection. For this purpose, we tested the effect of norepinephrine, serotonin and other key appetite regulating neuromodulators on the synaptic properties of this connection.

We used a combination of optogenetic and electrophysiology to study ARCAGRP → PVN synapses. For this we used channel rhodopsin assisted circuit mapping approach to isolate AGRP axon evoked synaptic currents from PVH neurons and evaluated impact of various neuromodulators.

Our preliminary results suggest that application of antagonists for norepinephrine and serotonin receptors work in opposite fashion to potentiate and inhibit ARCAGRP → PVN synapses respectively. We also showed that ghrelin and NPY have limited impact on this connection.

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**OC-016**

**Endoscopic Endonasal Transsphenoidal Surgical Resection for Microadenomas: Clinical Experience and Surgical Results of 30 Pituitary Microadenomas Treated in a Single Centre**

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Microadenomas are privileged group of hypophyseal tumours and pose significant surgical difficulties. The recent advances in endoscopic systems and surgical techniques, understanding the sellar anatomy facilitate endoscopic surgeries and improved surgical outcomes. However, there is still lack of adequate information about surgical results of microadenomas depending on case series. The aim of this retrospective study was to evaluate the results of pure transsphenoidal endoscopic surgery in a series of patients with microadenomas.

Thirty-one patients with hormone secreting microadenoma who underwent pure transsphenoidal endoscopic surgery at the Department of Neurosurgery of Ankara University in Turkey, between January 2014- March 2018 were retrospectively analysed in our study. Tumours were classified according to the types of hormone they secreted. All patients were followed up for at least 1 year. The disease control was analysed for each patient clinically and radiologically.

During the study period, 30 patients underwent pure endoscopic transsphenoidal surgery for treatment of microadenomas. There were 19 growth hormone-secreting, 1 prolactin-secreting, 8 adrenocorticotropin hormone secreting, 1 FSH-LH secreting and 1 thyroid-stimulating hormone-secreting adenomas. Gross total removal was achieved in 96.6% of the cases after a median follow-up of 15.6 months. The remission results for patients with secreting microadenomas was 83% and for functioning microadenomas, 89.47% for GH hormone-secreting, 100% for prolactin hormone-secreting, 75% for ACTH hormone-secreting, 100% for FSH-LH hormone-secreting and 100% for TSH hormone-secreting.

Endoscopic transsphenoidal surgery is an effective treatment option for patients with hypophyseal microadenomas. Although a small number of complications and unsuccessful interventions are some of the disadvantages of this approach and reported in recent literature, high disease control rates can be achieved even in this small size and deep-located tumours. Given the results of transphenoidal approaches in literature, endoscopic approach is significantly superior to microsurgery in terms of introducing wide operative field and surgical freedom. Simultaneous use of navigation systems with endoscopic instruments will improve the patient outcomes.

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**OC-017**

**TRPM2 Immunoreactivity in Cerebellar Purkinje Cell of Ovariectomised Rats**

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It is known that sex steroids affect neurological functions in normal and pathophysiological conditions. Purkinje cells are large neuronal cells in the cortex of the cerebellum that play a fundamental role in motor control. In this study we aimed to investigate the immunoreactivity of Transient Receptor Potential Melastatin2 (TRPM2) in cerebellar Purkinje cells of experimental ovariectomized rats.

In our study, 14 female Wistar albino rats with regular cycles were divided into 2 equal groups, control and ovariectomy. For the
control group, no procedure was performed during the experiment period of 30 days. The rats in the ovariectomy group were admitted to the operation table in the supine position and the abdomen was inserted with midline incision. Both ovaries were ligated from the mesothelium region and the cornu-uterine junctions, and the ovaries were excised and taken out.

At the end of the experiment, cerebellum tissues of decapitated rats were rapidly removed. Cerebellar tissues were embedded in paraffin blocks after routine histologic follow-up. The sections from paraffin blocks were treated with avidin-biotin-peroxidase method for TRPM2 immunoreactivity. In the evaluation of immunohistochemical staining; based on the prevalence and severity of immunoreactivity, histoscore was established.

At the end of the evaluation of the prepared immunohistochemical staining under the light microscopy, in the ovariectomized group the TRPM2 immunoreactivity in Purkinje cells was increased significantly compared with the control group.

It is concluded that TRPM2 may play a role in the development of neuronal changes that may occur due to experimental menopause.

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**OC-018**

**Visfatin Immunoreactivity in Rat Brain Tissues of Experimental Ischemia-Reperfusion**

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In ischemia, the brain does not use glucose for itself as a primary energy source and is exposed to anaerobic metabolism. Recently, the views on the hormonal regulation of metabolism have changed markedly. Adipokines have been described as the result of studies on adipose tissue, which provides the relationship between adipose tissue and brain. Visfatin was found when searching for new cytokine-like molecules released from lymphocytes. Studies have shown that visfatin levels may be associated with endothelial dysfunction and increased inflammation. In this study, it was aimed to investigate visfatin expression which is known to be related to energy metabolism in brain tissue of rats with brain ischemia-reperfusion model.

In our study, 14 adult male Wistar albino rats were used. Experimental animals were divided into two groups as control and ischemia-reperfusion (IR) group. Nothing was done to the control group during the experiment. For the IR group, surgical bilateral carotid communis arteries were uncovered, followed by clipping with aneurysm clips for 60 minutes followed by opening of the clips and reperfusion for 120 minutes. At the end of the experiment, rats were decapitated under anaesthesia and brain tissues were rapidly removed. Brain tissues were embedded in paraffin blocks after histological procedures. Sections taken from paraffin blocks were subjected to avidin-biotinperoxidase method for visfatin immunoreactivity. In the evaluation of immunohistochemical staining; a histoscore was established based on the prevalence and severity of immunoreactivity.

As a result of immunohistochemical staining, visfatin immunoreactivity was found to be statistically significant in the IR group when compared to control group (p < 0.05).

It has been concluded that visfatin may play a role in the pathogenesis of central nervous system changes that may occur due to ischemia-reperfusion.

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**OC-019**

**Adropin and Immune-Reactivity of NUCB2/Nesfatin-1 in Brain Tissue of the Rats with Experimentally Induced Diabetes Mellitus**

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Diabetes mellitus has an impact on each organ or system including the nervous system and brain. NUCB2/Nesfatin-1 first discovered in the hypothalamus, as well as adropin, a modulator of glucose homeostasis has not been previously assessed with regards to the change in their expression in the brain tissue during diabetes. Here it was aimed to evaluate the immune reactivity of NUCB2/Nesfatin1 and adropin in the brain tissue of the rats with experimentally induced diabetes.

In this study 14 male Wistar albino rats were either assigned to control or diabetic groups. During the study no intervention was performed for the rats in the control group. To induce diabetes, 60 mg/kg of streptozotocin was intraperitoneally injected to the rats. At the end of the study, rats were rapidly decapitated. Brain tissues were embedded into paraffin blocks following a routine histological screening. Avidin-biotin-peroxidase method was performed for the layers of paraffin blocks in order to obtain NUCB2/Nesfatin-1 and adropin immunoreactivity. While evaluating the degree of staining with immunohistochemical stains, histoscores were measured with regards to the extent and severity of immune-reactivity.

The staining of adropin and NUCB2/Nesfatin-1 immunoreactivity in rat brain tissue was evaluated under the light microscopy. The values obtained with adropin and NUCB2/Nesfatin-1 immunoreactivities were found to be increased both (p < 0.001).

It has been demonstrated that adropin and NUCB2/Nesfatin-1 molecules may play a role in the pathophysiology of structural, electrophysiological and cognitive dysfunctions that may occur in the central nervous system due to chronic hyperglycaemia and increased in the diabetic rat brain compared with the control group. It has been concluded that more extensive and detailed studies should be done in the future in order to find out whether adropin and NUCB2/nesfatin-1 can be used in central nervous system problems caused by clinically prolonged hyperglycaemia.
**OC-020**

**N-Cadherin Expression in Cushing’s Disease: Is It a Prognostic Marker?**

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Cadherins are Ca2+-dependent adhesion molecules. During tumour progression, the expression profile of them change resulting in a highly motile and invasive phenotype. N- (neural) cadherin (NCAD) promotes tumour cell survival, migration and invasion, and is associated with poor prognosis. Cushing’s disease (CD) is associated with significant morbidity and however the markers to predict the prognosis and recurrence are limited. NCAD was found to be expressed in growth hormone and prolactin secreting pituitary adenomas. Therefore, we aimed to evaluate NCAD expression in pituitary adenoma tissues of the patients with CD and the relationship with prognosis.

This retrospective evaluation included 72 patients with the diagnosis of CD. All patients had complete confirmatory data for CD and appropriate pathologic sections. NCAD were evaluated by immunohistochemical method, pituitary tumour size, invasiveness and histopathology features such as p53 and Ki-67 staining and postoperative disease activity were noted.

NCAD was expressed in 29 (32%) patients, gender distribution and the mean age were similar in NCAD+ and NCAD- patients. The tumour size and preoperative cortisol levels were higher in NCAD+ patients (p: 0.022 and p: 0.023) also p53 positivity and higher Ki67 expression were correlated with higher NCAD staining grade (p: 0.001 and p: 0.048). However, disease remission and recurrence rate were not different among NCAD+ and NCAD-groups. Also radiologic tumour invasion was similar between groups.

NCAD was expressed in 32% of CD adenoma but this rate is lower than anticipated in growth hormone and prolactin secreting pituitary adenomas. NCAD expression was related with higher tumour size but other radiologic features were similar with NCAD-cases. Also atypical adenomas (p53+ and >2% Ki-67 staining) had higher grade of NCAD staining then non atypical adenomas, that might be attributable as a prognostic role. However, more evidence is needed to confirm this hypothesis.

**OC-021**

**Effects of Alpha Lipoic Acid on Oxidative Damage in Central Nervous System in Experimentally Induced Diabetic Rats**

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Diabetes mellitus (DM) is a metabolic disease characterized by developing hyperglycaemia related with the disruption in insulin secretion or activity. Recent studies revealed that DM is generating functional disruption in CNS. Alpha lipoic acid (ALA) is a cofactor for mitochondrial enzymes which have a role in energy production and metabolism and can be naturally synthesized in the body. Malondialdehyde (MDA) is an end product of lipid peroxidation and used for demonstration of the level of oxidative damage. Superoxide dismutase (SOD), catalase and glutathione peroxidase (GSH-Px) are antioxidant enzymes. While glutathione (GSH) resists damaging caused by radicals, it has a role as a substrate for antioxidant enzymes and acts as a radical holder.

In this experiment we used a total of 28 rats. 14 rats were given 180 mg/kg streptozotocin (STZ) dissolved by single intraperitoneal (i.p.) injection. According to measurement results, the ones with blood glucose >250 mg/dL are considered as diabetics. Rats are divided into 4 groups; Control (group I), DM (group II), ALA (group III) and DM+ALA (group IV). MDA, SOD, CAT, GSH-Px and GSH values were measured in each group.

Our study suggested that ALA causes a decrease in MDA level while causing an increase in CAT, GPx, and SOD level and prevents the disturbances caused by oxidative stress. This study suggests that ALA has a neuroprotective effect, which prevents oxidative damage thereby decreasing oxidative stress in brain tissues.

**OC-022**

**Investigation of the Protective Effects of Vitamin E on Changes in Tacrolimus Applied to the Rat Brain**

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Tacrolimus is an immunosuppressive agent and is used to prevent tissue rejection after kidney, liver and heart transplantations. Tacrolimus is known to cause harmful effects on myocardium, kidney, bowel and liver. It has also been reported to have side effects such as neurotoxicity, hypertension, impaired glucose metabolism, gastrointestinal disturbances and a tendency to infection, increasing oxidative stress and reducing antioxidant status. Vitamin E forms the first line of defense against lipid peroxidation by protecting the free radical scavenger activity in the biomembrane from the free radical effect of polyunsaturated fatty acids present in the resulting cell membrane phospholipids. The aim of this study was to investigate the protective effects of vitamin E on changes in rat brain tissue induced by administration of tacrolimus.

Twenty-one male Wistar Albino rats were used in our study; Control, tacrolimus and tacrolimus + vitamin E. 0.8 mg / kg / day for tacrolimus group, 0.8 mg / kg / day for tacrolimus, 0.8 mg / kg / day for tacrolimus + vitamin E Group Vitamin E together with tacrolimus was orally administered at 500 mg / kg / day. At the end of 3 weeks of experiment, all groups were decapitated, Bax immunoreactivity was assessed by TUNEL staining and avidin-biotin peroxidase method on sections taken from paraffin blocks. When compared with the control group, Bax immunoreactivity and TUNEL positive cells were significantly increased in the tacrolimus group. Compared with the tacrolimus group, Bax immunoreactivity and TUNEL positive cells in the tacrolimus + vitamin E group were significantly decreased.
Depending on the application of tacrolimus, apoptosis has increased in rat brain tissue. Therefore, it has been concluded that the application of antioxidants with tacrolimus would be beneficial.

**OC-023**

**Response of Vagal Afferent Neurons to Macronutrients**

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The aim of this study is to investigate the responses of the vagal afferent endings to nutrients. Vagal afferents are the longest central nerves that innervate many visceral organs including intestines. They transmit information from the intestines to the brain and vice versa providing a two-way communication. The cell bodies of vagal afferents are within the nodose ganglia. Vagal afferents extend to the intestinal epithelium; but though they go into the villi they do not penetrate them they have no contact with the luminal content. In this study, neurons of nodose ganglia were cultured and the electrical response of neurons to various nutrients was analysed.

Nodose ganglia of young adult mice were removed and neuron culture was performed. The culture is kept in Hank’s salt solution. Also this solution was used for control group. The cells were loaded with voltage-sensitive dye Dibac-4. Spinning disc microscopy recorded the changing fluorescent brightness for 3 minutes while adding nutrients. Changing brightness was measured with Image J programme. One-way ANOVA and Posthoc Tukey tests were performed for statistical analysis. Nutrients were lipid mix, alanine, phenylalanine, glutamine, histidine, leucine, methionine, cysteine, threonine, galactose and glucose.

The neurons responded to nutrients differently. Seven amino acids out of eight responded electrically and this was usually depolarization. There was no response to glucose while galactose caused hyperpolarisation in general it led to depolarization in a subset of neurons. The response of nodose ganglia cells to lipids was inhibition.

This study indicates that vagal afferent neurons are influenced directly by numerous varied nutrients, which may be excitation or inhibition. These results challenge the currently accepted model suggesting that these afferents respond only indirectly to a few neuromediators released from intestinal epithelial cells.

**OC-024**

**The Effect of Pinealectomy and Melatonin Application on Metallothionin, ZnT3 and ZIP2 Levels in Rat Brain Tissue**

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The aim of this project was to investigate the relation among the metallothionin, ZnT3 and ZIP2 levels which is the basic mechanism in the regulation of zinc pool in the brain tissue parts of rats with pinealectomized and melatonin treatment.

Study was performed on total 36 male rats:

- **Group 1. (n:6) Control:** The group with no intervention and fed with normal diet.
- **Group 2. (n = 10) Melatonin:** The group with subcutaneous melatonin application with a dose of 5 mg/kg for four weeks.
- **Group 3. (n = 10) Pinealectomy:** The group with pinealectomy and fed with normal diet.
- **Group 4. (n = 10) Pinealectomy+ Melatonin:** The group with pinealectomy and subcutaneous melatonin application with a dose of 5 mg/kg for four weeks after pinealectomy.

Brain cortex, hippocampus and hypothalamus samples were analysed for ZnT3, ZIP2, and metallothionein by immunohistochemistry.

Pinealectomy caused significant decreases in metallothionin, ZnT3 levels in brain cortex and hippocampus (p < 0.05). Melatonin supplementation increased mentioned parameters in groups 2 and 3 (p < 0.05). Although pinealectomy did not cause any significant difference in ZIP2 levels in brain cortex and hypothalamus compared with the control group; melatonin application caused significant difference in ZIP2 levels in brain cortex, hypothalamus and hippocampus (p < 0.05).

The results of present study show that pineal gland is closely related with the regulation of ZnT3 and metallothionins in brain tissue. We can conclude that our findings especially indicating the relation between pineal gland and ZnT3 regulation in brain cortex, hypothalamus and hippocampus are the first and original findings when considering medline scanning.
OC-025
The Effect of Pinealectomy and Melatonin Supplementation on Serum Melatonin, Nesfatin-1 and Ghrelin Levels in Rats
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There is scarcely any study examining the relationship between the pineal gland and ghrelin and nesfatin-1 hormones, which are significantly involved in the regulation of diet. A few animal studies, although they have contradictory results, point out that there may be a relation between the pineal gland, and ghrelin and nesfatin-1. The present study aims to explore how ghrelin and nesfatin-1 hormones are affected in pinealectomized and melatonin-supplemented rats.

The study was conducted at the Experimental Medicine Research and Application Centre of Selcuk University and approved by local ethic committee. 36 Wistar male rats were used for experiments. Grouped designed as Group 1, Control group; Group 2, Melatonin-supplemented group; Group 3, Pinealectomized group; Group 4, Pinealectomized and melatonin-supplemented group. Blood samples collected from the animals which were decapitated at the end of the 4-weeks procedures were analysed by rat kits to determine melatonin (pg/ml), Nesfatin-1 (ng/ml) and ghrelin (pg/ml) levels according to ELISA method.

The lowest serum melatonin levels were found in the pinealectomized group 2, and the highest in the melatonin-supplemented group (group 4) (p < 0.01). A comparison of serum ghrelin levels between groups revealed that group 1 (control) and group 4 (melatonin supplementation) had the lowest, while Px group (group 2) had the highest levels (p < 0.01). As for nesfatin-1 levels, the lowest serum nesfatin1 levels were established in the pinealectomized group 2, and the highest levels were found in the melatonin-supplemented group (group 4) (p < 0.01).

An overall evaluation of study results suggests that the pineal gland and melatonin may have a substantial effect on the blood levels of ghrelin and nesfatin-1 hormones, which play critical roles in dietary behaviours. Melatonin supplementation has inhibitory effects on ghrelin levels and stimulatory effects on nesfatin-1 levels.

OC-026
Determination of Effective Mechanism of Melatonin in Hyperthermic Febrile Convulsion in Rats
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Melatonin is a neuropeptide that has anticonvulsant effects in neuroprotective and different experimental seizure models. In our previous study, melatonin has been shown to be anticonvulsant in the hyperthermic febrile seizure model. However, the mechanism of this effect at the receptor level is not clear. Our aim in this study is to investigate which melatonin receptors / receptors the anticonvulsant effect of melatonin shows in the hyperthermic febrile seizure model.

In our study, we used male Wistar Albino rats of 22 to 30 days, corresponding to 1.5–2 years of age in children. Groups were performed as Control; Etanol/saline; DMSO; Melatonin; Melatonin + Luzindole; Melatonin + K-185; Melatonin + Prazosin. The hyperthermic febrile seizure pattern was established by keeping the rats in 45°C water, and the latency, duration and severity of seizures were determined.

In our study, it was observed that melatonin shortened the duration of seizure, weakened the severity and did not affect latency (p < 0.001, p < 0.001 and p > 0.05, respectively) and that these effects were not completely blocked by receptor antagonists when compared to ethanol/saline group and DMSO groups.

In conclusion, the fact that the anticonvulsant effect of melatonin is not completely blocked by melatonin receptor antagonists in the present study suggests that a multimodal mechanism may be responsible for the effect of melatonin receptors alone on the anticonvulsant effect of melatonin. It will be useful to design new pharmacological studies to make the subject clear.
OC-027
Acetaminophen (Paracetamol): “Empathy-Killer” in a Dose-Response Relationship in Rats
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Empathy is the ability to understand and share someone else’s feelings, thoughts and behaviors; this is an important ability to survive and live together. Acetaminophen is affected cannabinoid 1 receptor that is located on empathy-related neuron’s pre-synaptic membrane such as oxytocin and vasopressin. The aim of this study is to investigate the effects of acetaminophen on empathy and empathy related neurohormones, oxytocin and vasopressin.

Twenty-eight adult outbred male Sprague Dawley rats were used in this study. Rats were harbored in the same environment 14 days, then all rats were trained for 12 days via Helping Behavior Test Equipment to rescue cagemate. After that all rats were divided into: (1) Control group (n = 7), (2) 100 mg/kg (n = 7), (3) 200-mg/kg (n = 7) and (4) 400-mg/kg acetaminophen group (n = 7). Each acetaminophen administration was one-time daily and given orally, empathy behavior evaluated 30 minutes later. A single dose and repeated dose of acetaminophen effect on empathy and anxiety was evaluated. Motor functions were assessed by Rotarod performance and open field tests. Blood samples were obtained. Brain tissues, thymus and adrenal glands were removed; amygdala and prefrontal cortex tissues were separated.

In Helping Behaviour Test Equipment, the mean opening door latency was found to be decreased in all animals (28±19.912, p < 0.0001). After single dose acetaminophen door opening time was found to be increased in only 400-mg/kg-acetaminophen group (p < 0.001). Repeated acetaminophen increased door opening time in both 200-mg/kg and 400 mg/kg-acetaminophen groups (p < 0.001). In Open field test; there was not any difference between all groups. There was not any difference about ambulation in open arms of elevated test equipment. There was no difference between the groups in the performance of the rotarod test. Prefrontal cortex oxytocin levels decreased in all acetaminophen-taking groups (p < 0.0001 for all). Prefrontal cortex vasopressin level decreased in only 200-mg/kg acetaminophen group (p < 0.0001). Oxytocin in amygdalae tissue decreased in both 100-mg/kg and 200-mg/kg-acetaminophen group (both of p < 0.05). Amygdala vasopressin levels decreased in all acetaminophen -taking groups (all of, p < 0.05).

These findings suggest that, acetaminophen decreased prefrontal cortex and amygdala oxytocin and vasopressin levels; reduces empathy both single high dose and repeated lower dose.

OC-028
Lipid Profile and Atherogenic Indices and their Association with Coronary Flow Reserve in Acromegaly Patients
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In this study, we aimed to investigate the atherogenic indices used in the detection of coronary microvascular disease in patients with acromegaly.

This prospective study included 54 patients with acromegaly and 31 healthy subjects. Patients consisted of active and remissioned according to GH (growth hormone) and IGF-I (insulin-like growth factor-1) levels. Lipid parameters (total cholesterol, triglyceride, low density lipoprotein cholesterol and high density lipoprotein cholesterol) levels of all patients and control groups were recorded. We also calculated atherogenic indices (plasma atherogenic index (PAI: logarithmTG / HDL), atherogenic coefficient (EC): nonHDL / HDL, Castalle risk indexes I: TG / HDL and II: LDL / HDL lipid parameters. Coronary flow reserve was measured using diprydamrole on the left anterior descending coronary artery using transthoracic Doppler echocardiography (TTDE).

There was no difference in biochemical parameters including lipid profile in patient and control group. Serum hs-CRP levels were high in the patient group but not statistically significant. The baseline diastolic flow rate measured from the left anterior descending coronary artery by the echocardiographic method was significantly higher in the patient group and the coronary flow reserve, expressed as the ratio of peak flow rate to basal flow rate, was significantly lower. In the correlation analysis; coronary flow reserve, Castelli index II, plasma atherogenic index, atherogenic coefficient were found to be negative correlations IGF-1, and age in the patients group. HDL cholesterol was positively correlated.

The use of plasma atherogenic indexes besides IGF-1 may be useful in the detection of coronary microvascular disease risk in patients with acromegaly.

OC-029
The Effect of Hexarelin on Pentylenetetrazole-Induced Epileptic Seizure and Hippocampal Neuronal Damage in Rat
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Recent studies have demonstrated that ghrelin receptors mediate antiepileptic effects. The aim of this study was to investigate the effect of ghrelin receptor agonist hexarelin on pentylenetetrazole (PTZ)-induced seizures and post seizure hippocampal damage.

In our study, we used 42 male 230–250 g Wistar Albino rats. Animals were divided into seven groups as control, saline (PTZ; 1 ml/kg serum physiologic), positive control (5 mg/kg diazepam),
50 μg/kg, 100 μg/kg, 200 μg/kg and 400 μg/kg hexarelin. 30 min after drugs administration at the indicated doses, PTZ was administered 45 mg/kg to induce epileptic seizure. The animals were observed for 30 min. Seizure stages (according to the Racine Scale) and first myoclonic jerk times (FMJ). 24 hours after PTZ injection, passive avoidance test was performed and then brain tissues were removed. After routine histological process, serial sections from brain tissues were stained with toluidine blue to determine neuronal damage. The hippocampal Cornu ammonis (CA)1, CA3 and dentate gyrus regions were evaluated histopathologically. Statistical evaluation of the data was performed by one way ANOVA and multiple comparisons were determined by the Tukey test. Statistical significance was defined at p < 0.05.

Obtained data suggest that 200 μg/kg and 400 μg/kg hexarelin decreased seizure stages and increased FMJ compared to PTZ group (p < 0.05). In addition, 200 μg/kg and 400 μg/kg hexarelin improved retention time in passive avoidance compared to PTZ group (p < 0.05). Furthermore, 200 μg/kg and 400 μg/kg hexarelin reduced neuronal damage in hippocampal CA1, CA3 and DG regions compared to PTZ group (p < 0.05). However, all these effects of hexarelin were not observed at 50 μg/kg and 100 μg/kg.

In conclusion, we suggest that hexarelin has protective effects on epileptic seizures and neuronal damage after PTZ dose-dependently.

**OC-030**

**The Role of Orexin_1_ and Orexin_2_ Receptors in Morphine Analgesia and Tolerance in Rats**

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Tolerance mechanism against morphine analgesia has not been clarified yet. The aim of this study was to investigate role of orexin_1_ and orexin_2_ receptor on morphine analgesia and tolerance in rats.

In our study, 90 Wistar Albino 230–250 g male rats were used. The animals were divided into fifteen groups as saline (serum physiologic 1 ml/kg; n = 6), orexinA (orexin_1_ receptor agonist; 10 μg/kg; n = 6), SB334867 (orexin_1_ receptor antagonist 1 mg/kg; n = 6), orexinB (orexin_2_ receptor agonist; 15 μg/kg; n = 6), TCS-OX229 (orexin_2_ receptor antagonist 0.5 mg/kg; n = 6), morphine (5 mg/kg; n = 6), orexinA + morphine (n = 6), SB-334867 + morphine (n = 6), orexinB + morphine (n = 6), TCS-OX229 + morphine (n = 6), morphine tolerance (n = 6), morphine tolerance + orexinA (n = 6), morphine tolerance + SB-334867 (n = 6), morphine tolerance + orexinB (n = 6) and morphine tolerance + TCS-OX229 (n = 6). In order to develop morphine tolerance, 10 mg/kg morphine was injected daily in the morning and evening for five days and tolerance was evaluated sixth days single dose of morphine. Analgesic effects were assessed by hot plate and tail flick analgesia tests. The resulting analgesic effect was measured and recorded at 0th, 30th, 60th, 90th and 120 minutes. Assessment of analgesic effect was formulated as % analgesia (MPE) (% analgesia = 100 x [postdrug latency-basal latency]/[cut off time-basal latency]). Statistical evaluation of the data was performed by two-way ANOVA and multiple comparisons were determined by the Tukey test. Statistical significance was defined at p < 0.05 level.

Obtained data suggest that orexinA and SB-334867 did not change morphine analgesia. SB334867 decreased tolerance development to morphine (p < 0.05). OrexinB reduced morphine analgesia (p < 0.05) but TCS-OX229 did not change morphine analgesia. OrexinA decreased tolerance development to morphine (p < 0.05).

In conclusion, we suggest orexin receptors may role in morphine analgesia and tolerance.

**OC-031**

**The Review of Thyroid Hormones Levels in Lithium Therapy Patients**

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Lithium toxicity or long-term lithium therapy have potential side effects for the thyroid. The aim of this study was to determine the effect of lithium on thyroid functions in euthymic patients with bipolar affective disorder, who have been on lithium monotherapy.

We collected laboratory data from the Clinical Chemistry department of the Turgut Ozal Medical Centre. Our study population included all patients who had at least one serum lithium measurement from November 1st 2000 to April 30th 2018. When the files were scanned, the results of sociodemographic data and thyroid function tests were recorded of the patients diagnosed with bipolar affective disorder taking lithium-monotherapy.

A total of sixty-three patients were included in this study and 34.9% of the patients (n = 22) were male and 65.1% (n = 41) were female. All patients were diagnosed with bipolar affective disorder. The mean age of the patients was 42 ± 13; 40 ± 12 years for females versus 42 ± 13 years for males. Free T4 (fT4) values of 76.2% (n = 48), free T3 (fT3) values of 93.1% (n = 54), TSH values of 95.2% (n = 59) of the patients were within the reference range.

According to the results of a study of patients using lithium, the ratio of the patients is in the reference range given as 95.3%, 95.3% and 84.4% respectively. These results were similar to the results of our study. The thyroid functions of the most patients were not affected by this drug. It is important to monitor the side effects of this drug, which has common endocrinological and haematological side effects, to evaluate the effectiveness of the treatment. More extensive studies are needed for better evaluation of the side effects of the disease.
OC-032
The Effect of the Application of Melatonin and Zinc in DMBA-Induced Mammary Carcinoma in Rats on Lipid Peroxidation and Element Metabolism
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In this study, it was aimed to investigate the effects of application of melatonin and zinc on lipid peroxidation and elemental metabolism in female rats with DMBA-induced mammary carcinoma. The study groups were composed of control, DMBA control and treatment (DMBA+ zinc, DMBA + melatonin and DMBA + zinc+melatonin) groups. Female rats (except the control group) were given a strong carcinogen DMBA. After tumour formation, zinc and melatonin were administered to the treatment groups at a dose of 5 mg/kg/day for 4 weeks. MDA as an indicator of tissue damage and GSH levels as an indicator of antioxidant activity in blood and breast tissue samples were determined by spectrophotometric method. Besides, some serum element levels (iron, magnesium, zinc and copper) were calculated.

The highest level of MDA found in plasma and breast tissue was obtained in the DMBA control group. Plasma MDA levels of the breast tissue were lower in the zinc group than in the melatonin group and significantly decreased in the zinc + melatonin group. Plasma MDA levels showed a significant decrease in the zinc + melatonin group, although there was no difference in the zinc and melatonin groups. The lowest GSH level found in erythrocytes and breast tissue was obtained in the DMBA control group. When zinc and melatonin groups were compared in the breast tissue, GSH level of zinc group was found to be higher than GSH level of melatonin group. Furthermore, the highest increase was found in the zinc + melatonin group. The highest levels of iron, magnesium and zinc were found in the zinc + melatonin group, and the highest level of copper was obtained in the DMBA control group.

The findings showed that the antioxidant activity suppressed by increased oxidative damage in rat mammary carcinoma was improved, but the administration of zinc + melatonin gave better results.

OC-033
Effects of Melatonin on Hepatic and Aortic Tissue STAT-3 Levels in Hypercholesterolemia Rats
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Hypercholesterolemia is recognized as a major risk factor for cardiovascular disease and has been reported that increase all-cause mortality in different epidemiological studies. It is characterized by nitric oxide bioavailability, lipid profile and oxidative stress changes. STAT-3 is an important transcription factor that upregulates a number of pro-inflammatory genes in endothelial cells, including cytokines, chemokines and adhesion molecules. In this study, it was aimed to investigate the effects of melatonin on hypercholesterolemia, STAT-3 levels in liver and aortic tissue.

Rats were divided into 5 groups (n:7). While control group was fed with normal diet, other groups were fed with 2% cholesterol and 0.5% cholic acid diet to develop hypercholesterolemia for 8 weeks.

Melatonin was administrated by i.p. injection both concurrently with cholesterol and only last 2 weeks. The tissue STAT-3 levels were detected by Western-Blot.

STAT-3 levels were increased with hypercholesteremia and decreased with melatonin administrations compared to hypercholesterolemia group. There was more reduction with the prophylactic melatonin administration than in the last two weeks.

Melatonin may protect against hepatic and vascular injury due to hypercholesterolemia via reduce the level of proinflammatory STAT-3. Life style changes such as protecting the level of endogenous melatonin may protect people from hypercholesterolemia-induced disorders.

OC-034
The Effect of Dopamin\(_2\) Receptor on Oxytocin-Induced Analgesia in Rats
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Recent studies have shown that oxytocin has analgesic activity. However, it has not yet been clarified by which way it has performed this analgesic activity. The aim of this study was to investigate the effect of dopamine\(_2\) on the oxytocin-induced analgesia.

In our study, 48 male 230–250 gr Wistar Albino rats were used. First, dose studies were performed with 100 \(\mu\)g/kg, 200 \(\mu\)g/kg and then animals were divided into nine groups as Saline, Cabergoline (D2 agonist;0.5 mg/kg), Sulproide (D2 antagonist;10 mg/kg), Cabergoline + Oxytocin and Sulproide + Oxytocin. Serum physiologic was given to the saline group and other drugs were administered intraperitoneally at
the indicated doses. Tail-flick and Hot-plate tests were used to measure analgesic effects. Analgesic tests were measured at 30 min-intervals (at 30th, 60th, 90th, and 120th minutes) and recorded in seconds. In order to evaluate the percentages of maximum antinociceptive effect (% MPE), the tail-flick and hot-plate latencies were converted to the percentage of anti-nociceptive effectiveness using this equation: % MPE = [(Post drug latency–Baseline latency)/(Cutoff value– Baseline latency)]×100. Statistical evaluation of the data was performed by two-way ANOVA and multiple comparisons were determined by the Tukey test. Statistical significance was defined at p < 0.05 level.

Obtained data suggest that the cabergoline produced analgesic activity alone (p < 0.05) and the combination with oxytocin increased the analgesic activity of oxytocin (p < 0.05). Sulpride did not produce analgesic activity alone, but the combination with oxytocin reduced the analgesic activity of oxytocin (p < 0.05).

In conclusion, we suggest that oxytocin may perform its analgesic activity with dopamine 2 receptors.

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**OC-035**

**Levels of Plasma NPY, Leptin and Nesfatin-1, and Their Relation to Zinc in Children with Obese and Metabolic Syndrome**

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The aim of the present study was to investigate the relation between zinc, a major trace element, and nesfatin-1, leptin, and NPY hormones, which are significantly involved in the regulation of food intake, in children diagnosed with metabolic syndrome and obesity.

The study registered 60 cases, of whom, 20 were boys and girls who presented at the Paediatric Endocrinology Polyclinic of Konya University Hospital with obesity and were diagnosed with metabolic syndrome [MeS(+)] obese], 20 were obese patients without metabolic syndrome criteria, and 20 were healthy control individuals. The sixty cases included in the study were allocated to six groups with an equal number of cases in each: Group 1, Boys with Metabolic Syndrome; Group 2, Girls with Metabolic Syndrome; Group 3, Obese Boys; Group 4, Obese Girls; Group 5, Control Boys; and Group 6, Control Girls. Plasma samples were analysed for NPY (ng/ml), Leptin (pg/ml) and Nesfatin1 (ng/ml) levels using ELISA method and serum zinc (μg/dl) levels determined after a minimum of 10 to 12 hours of fasting by atomic absorption method.

Leptin levels in boys and girls with metabolic syndrome were found significantly higher than those in obese and control boys and girls (p < 0.05). Nesfatin-1 and NPY levels in both control boys and girls, on the other hand, were higher than those in obese boys and girls (p < 0.05). Serum zinc levels were found higher in boys and girls with metabolic syndrome, in comparison to obese and control boys and girls (p < 0.05).

The results of the study demonstrated that metabolic syndrome and obesity alter the levels of leptin, nesfatin-1 and NPY, hormones which are involved in the regulation of food intake. These alterations may be associated with zinc levels, which are elevated in the metabolic syndrome.

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**OC-036**

**Effect of White Tea Consumption on Serum Leptin, TNF-α and Body Weight in Menopausal Model Rats**

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The postmenopausal period is associated with body weight gain in women. Body weight gain is also a common phenomenon in ovariectomized (Ovx) rats. In clinical and experimental studies, tea polyphenols have been reported to cause weight loss through thermogenesis and lipid peroxidation. However, the effect of white tea on Ovx-induced body weight changes is unknown. For this purpose, the role of long-term consumption of white tea (WT) on body weight gain in the menopausal model rats in the present study was examined.

In the study, 32 female rats were used in the range of 250–300 gr. Bilateral ovariectomy procedures were performed to sixteen rats. Then, the rats were grouped into sham, Ovx, white tea (WT) and Ovx+WT, respectively, as 8 in each group. WT was administered for 12 weeks with 0.5% drinking water. As a result of the experiment, body weight changes of rats, serum estradiol (E2), leptin and TNF-α levels were evaluated. Statistical analysis of body weights of groups used variance analysis in repeated measures. Data were analysed with one-way ANOVA.

There was significant difference between the body weights of Ovx and Ovx+WT group (p < 0.001). Body weight of the Ovx + WT group is lower than Ovx group. Serum E2 levels in Ovx group was found low compared to control group. Serum leptin levels in Ovx and WT groups were significantly decreased compared to control group (p < 0.01, p < 0.05, respectively). Serum TNF-α levels in Ovx group was significantly increased compared to control group (p < 0.01), but there was no significant in serum TNFα between control and WT groups.

The increase in body weight due to menopause can be limited by the addition of white tea to the diet. This effect can be regulated by both hormone and proinflammatory cytokine levels.

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OC-037
He Effects of Angiotensin II Receptor Blocker on Brain Oxidative Stress and Neurobehavioural Alterations in Ovariectomized Rats

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It is known that women are more susceptible to anxiety and depression in menopause. These disorders may occur due to increased oxidative stress. The renin-angiotensin system (RAS) components are produced within the CNS and related to mood disorders such as depression. Valsartan, a synthetic angiotensin II type 1 receptor antagonist, is a hypertensive agent. It was shown that valsartan (val) prevents Amiloid-β-related memory deficits in the Alzheimer disease model and anxiety/depressivelike behaviour in chronic mild stress model. The aim of this study was to investigate the effects of valsartan anxiety/depressivelike behaviour and oxidative stress in ovariectomized (ovx) female rats.

Thirty-two female rats were assigned to one of the following groups (n:8): control; control+val; Ovx and Ovx+val. Ovariectomy surgery was performed to remove both ovaries from the rats. Two weeks after surgery valsartan (40 mg/kg) administered orally by gavage for 14 days. Forced swimming test (FST) and open field test (OFT) was used to assess anxiety/depressivelike behaviour. The levels of malondialdehyde (MDA), a marker of lipid peroxidation, and reduced glutathione (GSH) was evaluated by spectrophotometrically in hippocampus and prefrontal cortex tissues. Arterial blood pressure was also measured. Differences between groups were evaluated with Kruskal-Wallis followed by a posthoc Bonferroni test to evaluate the differences with in the groups.

Our results have shown that ovariectomy significantly increased the immobility time in the FST and anxiety like behaviour in OFT. Ovariectomy also caused elevation of oxidative stress in hippocampus. Valsartan treatment significantly restored GSH levels and reduced MDA levels in hippocampus indicating attenuation of oxidative stress. In the prefrontal cortex, ovariectomy did not have any effect on oxidative stress parameters. Arterial blood pressure did not show any significant difference between groups.

The results of this study show that valsartan treatment diminish anxiety/depressivelike behaviour by reducing oxidative stress in hippocampal region in Ovx rat brain.

OC-038
ACTH and Amlodipine Effects on Neuroblastoma and Cortical Neurons

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Neuroblastoma (NB) is a type of cancer that occurs in certain types of nerve tissue. Cortex neuron have important role in central nervous system. Ectopic adrenocorticotropic hormone (ACTH) sedation is the cause of 10% -18% of Cushing’s syndrome cases. Ca2+ signalling is important for regulation of vital events for the cell such as contraction, motility, transmitter oscillation. Studies have shown that voltage-gated calcium channels are involved in many of the cancer features such as avoiding growth suppressors, resisting cell death, providing replicative immortality, stimulating angiogenesis and activating invasion and metastases and activating more.

In this study, it was aimed to determine the effects of amlodipine, a calcium channel blocker, and ACTH on human neuroblastomas and cortex cells by using different doses. The cytotoxicity assays were performed using the 3-(4,5-dimethylthiazol2-yl)-2,5-difeniltetrazolium-bromur (MTT) method depending on time and concentrations. After obtaining the confluence (up to 85% for SH-SY5Y) and sufficient branches (rat cortex neurons), the cells were treated with amlodipine (10 μM) and ACTH (25, 50 and 75 μg) at different concentrations for 24 hours. MTT assay, propidium iodide (PI) and Annexin V test were done according to the manufacturer’s protocol.

When the data were analysed, cell death was more than only ACTH application when amlodipine alone was applied. However, doses of amlodipine and ACTH co-administered neuroblastoma deaths were much higher (p < 0.05) than control group. Early apoptosis ratio in cortex neuron cell is the lowest in 25 μg dose of ACTH. These and similar studies are promising in the treatment of cancer.

OC-039
Relationship between Maximum Standardized Uptake Value Obtained with Ga68-Dotatate Positron Emission Tomography-Computerized Tomography (PET-CT) and Tumour Grade in Neuroendocrine Tumours

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Neuroendocrine tumours (NETs) are neoplasms that arise from cells of endocrine and nervous systems. The most common clinically encountered NETs are gastroenteropancreatic tumours, lung carcinoids, pheochromocytoma and medullary thyroid carcinoma.
Ga-68 DOTATATE Positron Emission Tomography (PET-CT) is more common gallium analogues used in the evaluation of NETs. Their mechanism of uptake in neuroendocrine cells is due to the increased expression of somatostatin receptor (SSTR) and is also the basis of imaging with somatostatin receptor scintigraphy. The maximum standardized uptake values (SUVmax) is a parameter used for the semiquantitative analysis of tumour metabolism. In our study, we investigated the association of SUVmax values obtained with PET-CT images with Ga-68 DOTATATE with NETs diagnosis or, of course, tumour grade.

The data of 16 patients with definite histologic diagnosis of NETs were selected. 68Ga-DOTA-NOC PETCT was performed on a dedicated dual modality PET-CT. A dose of 132 to 222 MBq of 68Ga-DOTATATE was injected intravenously. After 60-minute uptake period, the patients were taken for PET-CT. The tumour grade and SUVmax values of 16 patients with NETs were retrospectively compared.

An inverse relationship was found between SUVmax values obtained from tumour grade and Ga68 DOTATATE PET-CT images. The SUVmax values are decreasing as the number of mitoses and Ki67 score, which determine the Grade of tumours, increase.

According to the results obtained from Ga-68-DOTA PET-CT images, the expression of SSTR decreases as the NETs grade increases (poor differentiation). The results we obtained are similar to those of the literature.

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**OC-040**

**Very Unknown Neuroendocrine Features of Rubinstein-Taybi Syndrome in the Context of a Novel Identified Mutation**

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Rubinstein–Taybi syndrome (RSTS) is a rare, congenital, and neurodevelopmental disorder. One of the over 8,000 known rare diseases, RSTS affects males and females equally with a birth prevalence of 1:100,000 to 1:125,000. In addition to genetic polyclinic applications, these patients may sometimes perform their first application to the neurology, endocrine and psychiatry polyclinic. Neuroendocrine abnormalities seen in these patients; Arnold-Chiari malformation, cerebellar hypoplasia, syringomyelia, hypothyroidism, hypoplasia, growth hormone deficiency, pituitary hypoplasia, pituitary adenoma, parathyroid adenoma, pheochromocytoma and neuroendocrine tumours. Common behaviour problems in RSTS patients; short attention span, decreased tolerance for noise and crowds, autistic behaviours, impulsivity, and moodiness are frequently observed. Other abnormal behaviours included attention problems, hyperactivity, self-injurious behaviours, and aggressive behaviours.

We report the novel mutation in cAMP response elements binding protein (CREBBP) gene in two years old boy from Turkey who presented with developmental delay, intellectual disability, cerebellar hypoplasia, self-injurious behaviours, endocrine abnormalities and dysmorphic facial features. CREBBP sequencing analysis showed a novel mutation c.3233 C>T. It should be kept in mind that this disease, which is easily recognized by clinical geneticists with phenotypic characteristics, can be observed in any outpatient clinic with different findings.

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**OC-041**

**Comparison of Ga-68-Dotatate PET-CT and F-18 FDG PET-CT in Neuroendocrine Tumours; Pamukkale University’s First 3 Months of Experience**

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A group of neuroendocrine tumours (NETs) includes the somatostatin receptors (SSRs). In the evaluation of NET, Ga-68-DOTA PET-CT is frequently used and shows the SSR expression. In our study, we wanted to exhibit the Ga-68-DOTA PET-CT data.

In the study, F-18-FDG and Ga-68-DOTA PET-CT examinations of 12 patients with NET (7M;5F) were retrospectively investigated. After fasting for 6 h (blood glucose level was < 200 mg/dL), the patients received 259–407 MBq of F-18-FDG intravenously; on a different day, they received 148-296 MBq of Ga-68-DOTA intravenously. The patients were examined using a same dedicated PET/CT scanner (Gemini TF-TOF PET-CT).

Ga-68-DOTA and F-18-FDG uptake were concordant in 3 of 12 patients and discordant in 9 of 12 patients. Ga-68-DOTA and F-18-FDG uptake was positive in one patient (THoma). In 2 patients, Ga-68 DOTA and F-18-FDG uptake were not detected (colonicNET, thyroid papillary cancer). In 3 of 9 patients, Ga-68 DOTA uptake was observed in the lesions, while F-18-FDG uptake was not detected (two lung NET, one stomach NET (grade 1-2)). In 2 patients, F-18-FDG uptake was observed, while Ga-68-DOTA uptake was not observed (oesophagusNET+squamouscell carcinoma (grade 3), lung squamous cell carcinoma). Although Ga-68-DOTA and F-18-FDG uptake was observed in 2 patients, Ga-68-DOTA uptake was higher than F-18-FDG (paraganglioma, lung typical carcinoid tumour (grade 1)). In 2 patients, Ga-68-DOTA and F-18-FDG uptake showed heterogeneity (thyroid medullary cancer, lung atypical carcinoid tumour (grade 2)).

In our first 3-month Ga-68-DOTA PET-CT experience, it has been noticed that Ga-68-DOTA PET-CT in grade 1-2 tumours and F-18-FDG PET-CT in grade 3 tumours give more accurate results. Some of the grade 2 tumours showed heterogeneity due to the uptake of Ga-68-DOTA and F-18-FDG. These findings are consistent with the literature.
OC-042
Clinical Features and Risk Factors of Diabetic Polyneuropathy
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Diabetes mellitus is a serious chronic disease characterized by hyperglycaemia that results from insulin deficiency. Diabetic neuropathies manifest in several different forms, including sensory, motor, focal/multifocal and autonomic neuropathies. The most common type is diabetic distal symmetric polyneuropathy (DPN).

In this study, it was aimed to determine the polyneuropathy characteristics and risk factors in diabetic patients with neuropathic symptoms.

Thirty-five patients with diabetes who were referred to our clinic for neuropathy symptoms between 2016 and 2017 were included in the study. Detailed ophthalmological, physical and neurological examinations of all patients were performed. Total neuropathy scores of patients are calculated. Age, sex, duration of diabetes, duration of neuropathic symptoms, antidiabetic drugs used, additional diseases, haemoglobin A1c (HbA1c) levels were recorded.

The mean age of the patients was 61.6 ± 13.6 (range 37–78), for females 66.3 ± 11.3, for males 57.7 ± 14.5, p < 0.05) years. The mean duration of diabetes was 19.6 ± 14.0 (range 2–40) years. The mean duration of neuropathic symptoms was 6.6 ± 5.3 (range 1–15) years. The mean neuropathic symptoms duration was 9.6 ± 5.1 years for females and 4.1 ± 4.1 years for males (p < 0.05). The mean HbA1c level was 9.1 ± 1.8 and the mean total neuropathy score was 11.6 ± 6.7. The mean total neuropathy score was 16.0 ± 3.8 for females and 8.0 ± 6.6 for males (p < 0.05). The mean duration of neuropathic symptoms was 1.3 ± 0.5 years in patients without additional disease, and it was 8.5 ± 6.8 years in patients with additional disease (p < 0.05). The mean total neuropathy scores were 4.7 ± 3.3 in patients without additional disease, and it was 10.7 ± 7.7 in patients with additional disease (p < 0.05). Age, total neuropathy score, HbA1c level, duration of diabetes and duration of neuropathic symptoms were higher in the patients who were diagnosed as polyneuropathy during the neurological examination (p < 0.05).

DPN is diagnosed by the combination of neuropathic symptoms and abnormal electrophysiological findings and the total neuropathy score used in this study includes these parameters. In our study, total neuropathy score was higher in female patients, patients with comorbid diseases, and patients with polyneuropathy. In literature, it was reported that diabetic neuropathy is more common in males. In some studies, it was revealed that there was no difference in terms of sex. Unlike the literature, we found a significant relationship between female gender and total neuropathy score. HbA1c value, duration of diabetes and duration of neuropathic symptoms were higher in patients with polyneuropathy. As a result, duration of diabetes, duration of neuropathic symptoms, elevated HbA1c levels, additional diseases and female gender may be specified as risk factors for the development of DPN.

OC-043
Effects of Tacrolimus on Endothelin-1, Melatonin and Heat Shock Protein Levels in Experimental Brain Ischemia
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The aim of the present experiment to investigate the effects of tacrolimus on plasma endothelin-1, melatonin and brain Hsp-70 levels in experimental ischemic stroke.

Twenty-one male Wistar-Albino male rats were randomly divided into three groups which included seven rats. Animals in group 2 and group 3 were anesthetized and bilateral common carotid arteries were clamped with aneurysm clips for 10 minutes. Animals in group 1 were not clamped and were not given any treatment. Rats in group 2 received 1 ml saline and those in group 3 received 1 mg/kg tacrolimus intraperitoneally. Injections were applied 1st hour before ischemia and at 6th, 24th, 48th and 72nd hours post ischemia. All the animals were decapitated on the 4th day and plasma samples were obtained and brains were excised. Plasma endothelin-1 and melatonin levels were measured. Brain Hsp-70 immunostaining and neuronal cell death were scored semi-quantitatively.

The plasma endothelin-1 levels in group 3 were higher than group 2 and group 1, but were similar in group 1 and group 2. In group 1 plasma melatonin levels were lesser than group 2 and group 3. In group 2 plasma melatonin levels were higher than group 3. The mean neuronal death in group 3 was lesser than in group 2. The mean Hsp-70 immunostaining intensity in group 2 was greater than group 3 and group 1. In group 1 the mean Hsp-70 immunostaining intensity was lesser than group 3.

Tacrolimus administration in ischemic stroke reduces plasma melatonin and brain Hsp-70 levels and increases plasma endothelin-1 levels and has neuroprotective effect.

OC-044
Gastroenteropancreatic Neuroendocrine Grade 2 Neoplasms: Can We Define a Stricter Criterion
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Gastroenteropancreatic neuroendocrine tumours (GEP-NET) are a heterogeneous group of neoplasms derived from the gastrointestinal tract and the neuroendocrine section of the pancreas. The aim of this study was to evaluate Ki 67 proliferation index by histopathological analysis of GEP-NET G2 patients. Between 2011
and 2017, 15 patients with grade 2 neuroendocrine tumours originating from the gastroenteropancreatic system were studied retrospectively from the reports of Inonu University Medical Faculty Department of Pathology.

Histopathological and prognostic markers were compared with Ki-67 proliferation index. The median age at diagnosis was 51.55 (28–76) years. Seven of the patients (46.6%) were female and 8 (53.3%) were male. The most common localization was small bowel (36.7%). 2 of the patients (13.3%) had stomach, 5 (33.3%) had small intestine and 2 (13.3%) had colon NET. Pancreas-induced NET was present in four patients (26.6%). The mean tumour size was 4.5 cm (0.4–10 cm). The mean number of mitosis was 3.3 (1–10 number / 10BBA). Tumour necrosis was seen in 2 of the cases. Lymphovascular invasion was present in 7. Both had perineural invasion. Lymph node metastasis was present in 5 cases. The mean number of metastatic lymph nodes was 3.6 (1–7). The mean proliferation index with Ki67 was 6.9% (2% -20%). The mean number of metastatic lymph nodes was 3.6 (1–7). The mean proliferation index with Ki67 was 6.9% (2% -20%). The metastasis was observed in two cases.

We evaluated the histopathologic prognostic criteria differences, in the mitotic index range, and marked variability in Ki 67 ratios in the NETG2-diagnosed cases.

**OC-045**

**Regular Swimming Exercise in Rats Alleviates Gastric Ulcer-Induced Oxidative Stress by an Oxytocinmediated Mechanism**

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Oxytocin, a neuropeptide of the paraventricular nucleus, has anti-inflammatory actions. Regular exercise is known to reduce inflammation and exert protection on the gastrointestinal system. The aim was to investigate the role of endogenous oxytocin in potential anti-inflammatory effects of exercise on gastric ulcer healing.

Wistar albino rats (n = 56) were divided randomly as exercise (30 min/day swimming, 5 days/week for 6 weeks) or sedentary groups. On the 7th week, acetic acid (80%; ulcer) or saline (control) was applied on gastric serosa under anaesthesia. Starting at 4 days before ulcer induction and the following postsurgical 3 days, rats were injected intraperitoneally with oxytocin antagonist atosiban (0.1 mg/kg/day) or saline. On the 4th day of ulcer, following the measurement of gastric serosal blood flow, gastric tissue samples were obtained for the determination of 8-hydroxy-2'-deoxyguanosine (8OHDG) levels (ELISA); IL-6, IL-8, TNF-alpha levels, caspase-3 activity (Western Blot); myeloperoxidase activity, malondialdehyde, glutathione levels (spectrophotometric), luminol (chemiluminescence) and histopathologic analysis (hemotoxylin&eosin). Statistical analyses were made using ANOVA and Student’s t-test.

When compared with sedentary control groups, myeloperoxidase and caspase-3 activities, malondialdehyde, IL-6, IL-8, TNF-alpha, luminol and 8-OHDG levels showed significant increases in the sedentary ulcer groups, whilst glutathione levels and serosal blood flow were significantly decreased (p < 0.05–0.001). Compared with sedentary ulcer groups, regular exercise elevated serosal blood flow, reduced myeloperoxidase and malondialdehyde levels, and attenuated ulcer-induced gastric damage. Atosiban in exercised ulcer groups reversed exercise-induced alleviation of gastric damage and the reduction in malondialdehyde levels. Regular swimming exercise training accomplished prior to ulcer induction facilitated ulcer healing via alleviating ulcer-induced oxidative stress.

This anti-inflammatory effect of exercise appears to be mediated by an oxytocin-mediated mechanism.

**OC-046**

**Effects of Tobacco and Alpha Lipoic Acid Treatment on Puberty Parameters in Male Rats**

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In a wide range of countries, tobacco usage has become more common among adolescents. In the literature, several clinical and experimental studies investigated effects of tobacco on puberty, but alpha lipoic acid effects with tobacco using on puberty are not exactly known. Alpha lipoic acid (ALA) is a strong antioxidant and anti-inflammatory agent and important for gonadotrophin biosynthesis. In this study, we investigated ALA effects on puberty development on maternally tobacco-exposed female rats’ male offspring.

For the experimental studies, totally 28 female Sprague-Dawley rats were used. All animals were randomly divided into four groups [control (I), tobacco (II), tobacco+alpha lipoic acid (III) and alpha lipoic acid (IV)] and each group comprised of 7 rats. Female rats in group II and III were exposed to tobacco smoke (20 g/per day) twice a day for an hour during the experiment. Group III and group IV rats were received ALA (20 mg/kg) dissolved in saline by oral gavage in every other day. At the end of the eighth week, female rats in all groups were mated with male rats. Tobacco smoke inhaled by females was stopped at the 14th week of gestation. The effect of tobacco and ALA on puberty parameters was evaluated by vaginal smears and sexual hormones levels (LH, FSH, estradiol, progesterone, testosterone).

**Abstracts**
co smoke and alpha lipoic acid administration were continued throughout pregnancy. New-born male rats were selected for each group (n = 7). Then, puberty was determined by preputial separation. There was significantly delayed on puberty onset day group-III (57.44 ± 0.60) compared to control (51.87 ± 0.95), (p < 0.001). There was significantly increased difference in pubertal weight between control (153.3 ± 3.73, g) and group-IV (182.63 ± 4.24 g, p < 0.01). There was no any significant change in serum FSH levels. There was significant increase in serum LH level in all groups (II, III and IV) compared to control group (3.12 ± 0.05a, 3.00 ± 0.08b, 3.51 ± 0.104c and 2.60 ± 0.089, IU/mL, respectively, p < 0.01, p < 0.05, p < 0.001).

As a result, it was concluded that alpha lipoic acid and tobacco delayed puberty with together and LH increase was independent from alpha lipoic acid treatment.

OC-047
The Role of Bilateral Inferior Petrosal Sinus Sampling in Differential Diagnosis of Cushing Syndrome
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Bilateral inferior petrosal sinus sampling (IPSS) is the gold standard method in the differential diagnosis of Cushing Syndrome (CS) and has also been used in tumour lateralization. In this study, we aimed to evaluate the value of IPSS in differential diagnosis of CS, and diagnostic accuracy of IPSS in lateralizing the pituitary mass.

Twenty consecutive patients with CS and normal or suspicious magnetic resonance imaging (MRI) were assessed in the study. Four patients were not included in the study due to missing data. After selective catheterization of petrosal sinuses, the ratio of inferior petrosal sinus ACTH to peripheral blood ACTH (IPS:P), and the ratio of bilateral petrosal sinus ACTH levels to each other were measured at basal status and after intravenous (iv) corticotrophin releasing hormone (CRH) administration. Demographic, biochemical and clinical findings were retrospectively evaluated for each patient.

Of these patients, 14 were female (87.5%), and mean age were 38.19 (±11.095). Mean cortisol and ACTH levels were 24 ± 26 (range 1–89 μg / L) and 74.6 ± 123 (range 11.5–520 pg/ L) respectively. After IPSS with CRH, the diagnosis of Cushing’s disease was confirmed by IPS:P ratio of ≥2.0 at basal state and/or ≥3.0 after CRH administration in 11 of 16 patients (68.7%). Of these, the pituitary mass was lateralized to the right in 7 patients and to the left part of pituitary gland in 3 patients. The mass could not be lateralized in one patient. Except one (she refused surgery), all patients subsequently underwent to transsphenoidal exploration to evacuate the pituitary adenoma. Likewise; results of IPSS indicated peripheral location of tumors in 5 patients. Further evaluation of these patients pointed out adrenal Cushing syndrome in two patients (one had adrenal adenoma with co-secretion of catecholamine, the other bilateral adrenal hyperplasia). One patient was diagnosed as bronchial carcinoma located to the mediastinum. Tumours could not have been localized in other two patients. Of these five cases, two underwent to surrenalec tomy and in one case bronchial carcinoma was successfully resected.

IPSS using iv CRH is very helpful for differential diagnosis of CS and lateralization of tumour masses.

OC-048
RF9 Increases Intracellular Calcium Concentration by Protein Kinase C Activation in rHypoE-8 Cells
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RF9 is an antagonist of the RFamide-related peptide-3 (RFRP-3) receptor. RFRP-3 is accepted as the mammalian orthologue of avian gonadotropin-inhibitory hormone (GnIH). There are several studies that indicate a potential interaction between RF9 and kisspeptin neurons. However, mechanism of action of the RF9 as a kisspeptin agonist remains to be elucidated. Intracellular calcium ([Ca2+]i) signalling is an important mechanism involved in hormone secretion. For this aim, the role of RF9 on [Ca2+]i concentrations in rHypoE-8 cells, a model of kisspeptin neurons, were investigated by using in vitro calcium imaging system.

rHypoE-8 cells were plated on glass coverslip and loaded with 1 μM Fura-2 AM. RF9 was prepared at different doses (1–10 μM). Calpastatin C was used as a protein kinase C (PKC) inhibitor. [Ca2+]i analyses were performed in both normal and extracellular calcium-free conditions. Using the fura-2-based calcium imaging technique, [Ca2+]i responses were quantified by the changes in 340/380 ratio.

RF9 caused a significant increase in basal levels of [Ca2+]i after application at doses of 1 μM (n = 15, p < 0.05) and 10 μM (n = 15, p < 0.01). The stimulatory effect of RF9 (10 μM) on [Ca2+]i was persistent in extracellular Ca2+ free conditions (n = 15, p < 0.01). The changes in [Ca2+]i were significantly attenuated by pre-treatment with the PKC inhibitor.

Our results indicate that RF9 activates [Ca2+]i signaling through PKC mediated mechanism in the kisspeptin neurons.

OC-049
Effect of Different Doses of Corticosterone Administration on Brain Monoamine Levels in Male and Female Rats
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Stress causes various psychopathologies by acting on brain monoamine levels. However, relationship between glucocorticoids and monoamines is not well understood. The aim of this
study was to investigate effect of chronic corticosterone administration on norepinephrine and dopamine levels and turnover rates in critical brain regions at different doses and its differences according to gender. Female and male rats were injected with vehicle or 10, 20, 40 mg/kg corticosterone for 21 days. Norepinephrine, dopamine and their metabolites in hippocampus and striatum were analysed by high performance liquid chromatography. In male, hippocampus norepinephrine concentration was higher in the 40 mg group (16.34 ± 1.51) than control, 10 mg, 20 mg groups (7.95 ± 0.90; 6.33 ± 0.51; 10.61 ± 0.98, p < 0.05). Dopamine concentration (10.22 ± 1.28) in 40 mg group is higher than control (4.94 ± 0.58, p < 0.05). Norepinephrine turnover rate in 40 mg was lower than all other groups; DA turnover rate was lower in 20 mg (0.23 ± 0.02) and 40 mg (0.27 ± 0.02) groups compared to control (0.43 ± 0.06, p < 0.05). In female rats, hippocampus norepinephrine level was lower in 20 mg and 40 mg (1.77 ± 0.22; 1.18 ± 0.13) compared to the control and 10 mg (5.77 ± 0.91; 7.38 ± 0.55, p < 0.05). Dopamine concentrations were decreased in the 20 mg (3.97 ± 0.44) compared with control and 10 mg (6.25 ± 0.90; 6.18 ± 0.30, p < 0.05). Norepinephrine turnover rate was increased in 20 mg and 40 mg compared to the control and 10 mg. Dopamine turnover rate was higher in 20 mg than control and 10 mg (p < 0.05). In the 20 mg and 40 mg groups, the females had a lower concentration of norepinephrine and dopamine than the males (p < 0.001). In male, striatum norepinephrine and dopamine levels were lower in all corticosterone administration groups than control (p < 0.05). In female rats, norepinephrine, dopamine concentration and turnover rate did not differ between groups.

In conclusion, corticosterone administration caused opposite effects on norepinephrine and dopamine in the male and female hippocampus, but it affects only male in the striatum. Chronic corticosterone administration caused opposite effects in norepinephrine, dopamine and their metabolites in hippocampus and striatum in dose-dependent manner and these changes are quite different in males and females.

OC-050
Effects of Intracerebroventricular Administration of Salusin-β on Food Intake, Water Consumption and Body Weight in Male Rats
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Salusin-β is an endogenous parasympathomimetic peptide. This peptide is predominantly localized to the hypothalamus and posterior pituitary. Hypothalamus is controlling of feeding and drinking behaviour in a delicate balance. This study intends to clarify possible effects of the salusin-β on feeding and water intake behaviour in rats.

In this study, 250–270 g in weight of 40 male Wistar-Albino rats were used. Rats were evenly separated into four groups (n = 10). Osmotic mini-pumps were implanted to lateral ventricle and artificial cerebrospinal fluid (vehicle; sham group), 2 and 20 nmol/kg concentrations of salusin-β were infused for 7 days (10 μl/hour) to rats. Throughout the experimental period, the rats were kept in individual cages, and body weight, food and water consumption of the animals were daily recorded.

At the end of the seven-day infusion, all concentrations of salusin-β (2 and 20 nmol/kg) increased the daily food intake and body weight of the rats (p < 0.05). On the other hand, icv infusion of salusin-β decreased the daily water intake of the rats (p < 0.05). All these findings indicated that salusin-β increased the appetite in rats. Additionally, salusin-β increased body weight but decreased water consumption in rats. It is well known that many hormones such as leptin, neuropeptide Y (NPY), agouti-related peptide (AGRP), proopiomelanocortin (POMC) and cocaine and amphetamine regulated transcript (CART) take active roles in the interaction of the hypothalamic controlling of feeding behaviour in a delicate balance. The effects of salusin-β on hypothalamic orexigenic or an-orexigenic peptides should be investigated.

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OC-051
Effect of Pregnancy and Lactation Period on Depression Like Behaviour in Depressive Rats
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Sertraline is an antidepressant agent used for depression therapy. There is quite limited study with regards to effect of sertraline in experimental depression model in rats. Additionally, there is no detailed data regarding pregnancy and lactation period on behavioural status in depressive and sertraline treated rats. We aimed to investigate the effect of perinatal processes on depressive behaviour in animal model of depressive like behaviour.

Adult female pregnant Wistar rats were included in this study. Chronic light stress procedure was applied to animals for 21 days of pregnancy in order to establish depression model. Forced swimming test was used for evaluation of depression like behaviour condition of rats in 8th day of gestation. Sertraline was subcutaneously administered to the depressive and non-depressive groups at 10 mg/kg for 15 days through osmotic minipumps. Controls and depressive groups received saline via osmotic minipumps. Climbing time, swimming time, immobility time and mobility percent were determined by using animal behaviour monitoring and recording system. After weaning at 30th day of lactation, forced swimming test was applied to all animals for determining the behavioural condition.

Before antidepressant and vehicle treatments, depressive like behaviours were observed in depressive groups by analysing immobility, active swimming and climbing behaviours compared to control (p < 0.01, all). Although there is slightly decrease in climbing and swimming time and slightly increase in immobility in de-
pressive rat, there is no significant difference in depressive be-
aviours at 30th day of lactation.
Data from this study revealed that pregnancy and lactation pe-
riod may decrease depressive like behaviours in female rats. Anti-
depressant treatment in gestation period may have additive cura-
tive effect on depression.

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**OC-052**

**Investigation of the Effects of Mitochondrial-Derived Peptide (MOTS-c) on the Control of Feeding in Obese Rats**

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Obesity is a condition that is associated with having an excess of body fat, defined by genetic and environmental factors that are difficult to control when dieting. Many individuals are affected by obesity and are not aware of it. A novel bioactive peptide, mitochondrial-derived peptide (MOTS-c), has recently attracted attention as a potential prevention or therapeutic option for obesity and type 2 diabetes mellitus. MOTS-c is a potential regulator of metabolic homeostasis under conditions of high-energy supply. However, the effect of insulin resistance and obesity on plasma MOTS-c concentration in humans or rats is unknown. We hypothesize that MOTS-c may regulate the hypothalamic control of feeding system.

40 Wistar Albino male rats were used in the study. The rats were separated into 4 groups as the control, sham, 10 μM MOTS-c and 100 μM MOTS-c infusion (n = 10). The rats were fed with high-fat diet food as of the 21th day of birth for 12 weeks. After 12 weeks, it was determined that obesity occurred in the rats by scoring according to the Lee Index. Then, the rats were anesthetized (except for the control group), and osmotic mini pumps were placed in the lateral ventricle. With the help of the osmotic mini pumps, infusion of artificial cerebrospinal fluid (solvent) was performed to the sham group at a 120 μl volume (5 μl/hour) daily; and the infusion of 10 and 100 μM MOTS-c were performed to the study groups. Throughout the experimental period, the rats were kept in individual cages, and food consumption and body weight of the animals were daily recorded. After infusion period (14 day), the rats were decapitated, and the blood and brain tissue samples were collected. Serum ghrelin levels were measured by ELISA method in blood tissue. The NPY levels were determined using Western Blot method in hypothalamus tissue.

Chronic infusion of the MOTS-c caused to significantly in-
creases in food consumption (p < 0.05), but in the body weights of obese rats were not found any significantly difference. On the other hand, intracerebroventricular infusion of MOTS-c resulted in significant increases ghrelin and NPY levels (p < 0.05).

Our results show that MOTS-c may change feeding behaviour by affecting hypothalamic process in obese rats.

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**OC-053**

**MOTS-c Increases Food Consumption of Rats But Does Not Alter Body Weight**

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Obesity is one of the medical condition defined with an exces-
sive increase of the amount of body fat that causes a number of metabolic illnesses. Obesity adversely influences the individuals of health status, quality of life and reduces the lifetime. In accordance with the data of World Health Organization (WHO), obesi-

ty influences more than 300 million people worldwide and al-
most 1 billion individuals are overweight. The Mitochondrial-Der-
ived Peptide (MOTS-c) is one of the new hormones discovered in 2015. The first findings of the preliminary studies on the physio-
logical roles of MOTS-c suggest that it prevents the formation of insulin resistance. The study was designed to evaluate effects of chronic central infusion of MOTS-c on food intake and body weight in the rats.

In this study 40 male Wistar-Albino rats were used. Rats were evenly separated into four groups (n = 10). Osmotic mini-pumps were implanted to lateral ventricle and artificial cerebrospinal fluid (vehicle; sham group), 10 and 100 μM concentrations of MOTS-
c were infused for 14 days. Throughout the experimental period, the rats were kept in individual cages, and food consumption and body weight of the animals were daily recorded. At the end of the study, chronic infusion of both concentrations of the MOTS-c caused to significantly increases in food consumption (p < 0.05), but in the body weights of rats were not found any significantly difference.

The present results suggest that MOTS-c can play important roles in hypothalamus on regulation of feeding behavior and control of energy metabolism.

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Cannabinoid Type 2 Receptors Activation Improves Cognitive Dysfunction in a Okadaic Acid Induced Alzheimer Rat Model

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The Alzheimer’s disease (AD) is a neurodegenerative disease accompanied by changes in behaviours and neuropsychiatric symptoms and characterized by degeneration in cognitive skills and decrease in daily life activities. It has been shown in many experimental studies that tau hyperphosphorylation occurred in AD and memory formation was impaired. Neuroinflammation occurred in the brain and oxidative stress developed after intracerebroventricular (ICV) administration of okadaic acid (OKA). Expression of cannabinoid type 2 (CB2) receptors, which are found in many regions of the brain, are also found in the hippocampus. JWH-133 is a selective CB2 receptor agonist. In this study we investigated the role of JWH-133 on learning and memory in ICV OKA model of AD in rats.

In the present study, forty male Sprague-Dawley rats were randomly divided into four groups. Control, Sham: Rats were injected ICV with artificial cerebrospinal fluid (aCSF) and treated vehicle for 13 days, OKA: OKA was dissolved in aCSF and injected ICV (200 ng) in a volume of 5 μl bilaterally. OKA+JWH-133: Rats injected ICV with OKA and treated with JWH-133 intraperitoneally 0.2 mg/kg/day for 13 days. After 14 days of surgical operations and injections, Morris water maze test was performed. The parameters of latency to platform, distance moved to reach the platform and time spent in the target quadrant were evaluated.

The latency to platform and distance moved of OKA injected rats were increased in comparison to control, sham and OKA+JWH-133 groups. In the OKA+JWH-133 group, time latency to platform and distance moved were shorter than OKA group. In the OKA+JWH-133 group, time spent on target quadrant was more than OKA group.

OKA-treated rats showed significant impairments of spatial memory in Morris water maze test, which were largely reversed by administration of JWH-133.

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The Effect of Curcumin on Brain TRPM2 Channel Gene mRNA Expression Level in Experimental Alzheimer’s Rat Model Induced by Application of Intracerebroventricular Streptozotocin

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TRPM2 channel protein has a negative effect on Alzheimer pathology with intrinsic calcium influx into the neurons. It has been reported in recent studies that curcumin could inhibit induced TRPM2 channel protein in vitro. The aim of this study is to investigate the effect of curcumin on TRPM2 gene and Alzheimer pathology in in vivo Alzheimer rat model.

This study was carried out with 50 Wistar albino male rats. Analysis of experimental Alzheimer rat model performed by Morris water maze. Biochemical analyses including SOD, MDA, GSH in rat brain tissue accomplished by spectrophotometric methods. TRPM2 and MAPT gene expression levels performed by RT-PCR in rat hippocampus tissue. Hematoxylin-eosin staining was performed on brain tissues for histopathological analysis.

MDA levels increased in STZ group compared to STZ+curcumin. It was found that GSH levels decreased in STZ group while it increased STZ+curcumin group (p < 0.05). SOD activities were higher in STZ group than in STZ+curcumin group (p < 0.05). TRPM2 mRNA levels increased in STZ rats, but they were lower in STZ+curcumin group. Histopathologically, STZ group had neurodegeneration and STZ+curcumin had attenuated damage.

Oxidative stress, neurodegeneration and increased TRPM2 mRNA levels were shown in STZ induced Alzheimer rats. Curcumin caused a reduction in TRPM2 mRNA levels with positive effect on neurodegeneration.
Abstracts

**OC-056**

**Effects of Paroxetine, Bupropion or Agomelatine on Ovarian Tissue and Anti-Mullerian Hormone Levels in Female Rats**

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There is no almost study in the literature about the effects of antidepressants on gonads in female rats. Serum levels of anti-Mullerian hormone (AMH) may represent both the amount and property of the ovarian follicle pool and so could be a useful marker of ovarian reserve. The purpose of the present study is to evaluate the effects of paroxetine, bupropion and agomelatine; having different mechanism of action and used as antidepressant drugs, on histopathology of ovarian and AMH levels.

Female Sprague-Dawley rats (n = 40) were used. All animals were randomly divided into four groups (control, paroxetine, bupropion and agomelatine) and each group consisted of 10 rats. The animals started to receive daily oral paroxetine (3.6 mg/kg), bupropion (17 mg/kg) or agomelatine (10 mg/kg) from postnatal day 21 to minimum 90 days. The control group received only vehicle. The rats were decapitated under general anaesthesia on the first diestrus phase following 90th day. Afterwards, ovarian tissues were prepared for histological studies, and histopathological scores were performed. The changes were evaluated as non-existent (0), mild (1), moderate (2) or severe (3) according to histopathological status. Mean scores were calculated for each group. Also, serum AMH levels were measured by using ELISA method.

There was a significant difference in extreme vascular dilatation and congestion between control and paroxetine or agomelatine groups (p < 0.01). Agomelatine treatment significantly increased follicular degeneration (p < 0.001) and disruption of zone pellucida (p < 0.05) compared to control group. AMH levels were lower in the paroxetine and agomelatine groups compared to control group, but there was no statistical difference. However, there was a significant decrease in bupropion group (p < 0.001).

Our results showed that chronic peripheral treatment of paroxetine, bupropion or agomelatine adversely affected ovarian tissue and AMH levels. Thus, these antidepressants may cause reproductive system disruptions in females.

Paroxetine, bupropion, agomelatine, ovarian tissue, anti-Mullerian hormone, female rats.

Acknowledgement: This study was supported by TUBITAK (Project no: 113S193).

**OC-057**

**Role of TSH, fT3 and Anti-Thyroid Antibodies on Neurodegeneration of Streptozotocin-Induced Diabetic Rats**

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Diabetes Mellitus (DM) disrupts the pituitary-thyroid axis and leads to a higher prevalence of thyroid disease. Type 1 Diabetes Mellitus (DM1) and the dysfunction of thyroid are the most common endocrine diseases, which are interrelated with each other. The aim of this work was to carry out a comparative study on the thyroid functional state in streptozotocin (STZ)-induced diabetic rats.

Eight-weeks-old male Wistar albino rats were used in this experiment. Twenty rats were divided into two groups: control group and STZ group. A single ip injection of 50 mg/kg of STZ was given to the diabetic rats. Three days after the STZ injection, the animals that showed a fasting blood glucose level above 200 mg/dl were considered to have diabetes and were used in this study. The models of acute DM1 induced by high doses of STZ were used. After 6 months, all animals were decapitated and their blood samples were collected. Their brains were rapidly removed. After the serum was separated, it was immediately frosted and stored at –80°C. The levels of the serum thyroid-stimulating hormone (TSH), free triiodothyronine (fT3) and anti-thyroid antibodies (anti-TPO) were quantified by using ELISA. Transmission electron microscopy was used to examine the ultrastructural features of the neurons in the brains.

According to the results obtained from the diabetic rats with STZ, the levels of TSH (n: 10, in each; p < 0.005) and fT3 (n: 10, in each; p < 0.001) decreased significantly, while the TPO levels were the same with the control group. According to the histological findings, there was a significant difference in the degeneration of myelin between the STZ group and Control group.

These findings suggest that the decrease of the thyroid status and TSH levels in diabetic rats lead to neurodegeneration.
Examining the Effects of Agomelatine on Uterine Activity of Rats in Which Agomelatine Is Used during, before and in Various Stages of Pregnancy

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Agomelatine is a new anti-depressant shown as the best synthetic melatonergic medicine defined so far. It has agonist effects on MT1 and MT2 receptors, and antagonist effects on 5-HT2c receptors. Agomelatine is included in B Category for use during pregnancy. Melatonin, on the other hand, is a hormone known to have inhibitory effects on rat uterus, whether pregnant or not. In the light of these data, the possible effects of Agomelatine on rat uterine contractions were investigated in our study.

Seven Wistar Albino female rats were used in each of the 4 groups in the study. 1st Group: Diestrus; 2nd Group: Pregnant; 3rd Group: diestrus used chronic Agomelatine; 4th Group: pregnant group in which Agomelatine was used during all pregnancy stages as of the onset of the pregnancy. The uterine sections obtained from each group were placed in glass containers in isolated organ bath and Agomelatine was applied in non-cumulative dosage with 50, 100 and 200 μM doses; and isometric contractions were recorded. For the purpose of questioning the effect mechanism of Agomelatine, 2 μM dose luzindole was used.

When we compared each group within itself, was observed that Agomelatine caused inhibition in all groups at 200 μM; and caused 100% inhibition at 100 μM dose in Group 4. Statistically significant inhibition was detected at 100 μM dose in all groups in p-p, frequency and area values. In 50 μM dose, statistically significant inhibition was detected in the area values of all groups, and significant inhibition was detected in p-p values in Group 1 and 4. Also, significant inhibition was detected in frequency in Group 1, 3 and 4. When all groups were compared with the 1st Group, 200 μM, %100 inhibition was detected in all groups, and no statistically significant results were detected in all groups in 50 μM dose. In 100 μM dose, on the other hand, statistically significant inhibition was detected in Group 4 in p-p, frequency and area values, and there was no significance in other groups.

As a result, it was concluded that Agomelatine has an inhibitory effect on uterine contractions in rats, whether pregnant or not. However, the inhibition that was observed in the rats in which Agomelatine was used during pregnancy was at lower concentrations when compared with other groups. This effect being returned with luzindole, which is a melatonin MT1 and MT2 receptor antagonist, makes us consider that Agomelatine shows this effect through the mediation of melatonin MT1 and MT2 receptor.

Effects of Central Infusion of Irisin on the Energy Metabolism and Glucose Uptake in Rats

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Irisin is a myokine/adipokine mainly released by skeletal muscles during the exercise and it encourages browning of the white adipose tissue. It has been suggested that irisin regulates glucose and lipid homeostasis. The aim of this study was to investigate the possible changes in serum glucose and lipid levels and gene expression/protein levels of uncoupling proteins (UCPs) in muscle, white and brown adipose tissues after intracerebroventricularly irisin infusion.

The Wistar Albino male rats weighing 150–200 g were used in this study. The rats were divided into groups (n = 9 in each group). Two different doses of irisin were infused to all animals (except control and sham groups) as centrally for 14 days. The mRNA gene expression/protein levels of UCP1 (in brown and white adipose tissue), UCP3 (in skeletal muscle) and serum glucose levels and lipid profiles were determined.

The centrally infusion of irisin caused significant elevations in the UCP1 protein levels of white and brown adipose tissues (p < 0.05), but no significant alterations were determined UCP1 gene expression. The significant decreases were seen gene expression levels of UCP3 in muscle tissue (p < 0.05), but no significant changes were revealed in the UCP3 protein levels. It was demonstrated that irisin did not cause significant alterations in serum HDL, LDL, triglyceride, total cholesterol and serum glucose levels.

We found relationship between irisin infusion and the UCP1 and 3 in white and brown adipose tissues and we conclude that irisin may have effects on energy metabolism by affecting the UCPs.

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OC-060

Investigation of the Relationship between High Fructose Corn Syrup Consumption and Stress-Induced Behavioural Changes

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High fructose corn syrup (HFCS) is extensively used in a variety of commercial foods and soft drinks as a sweetener due to its low cost, high relative sweetness and long shelf life. Recent studies show that increasing the consumption of HFCS has been linked to increasing in the risk of diabetes, obesity and cardiovascular diseases. As fructose containing beverages cause slight increase in insulin levels and less satiating than glucose or other saccharides, people consume more food than normal and get more calories than needed and hence, cause obesity and similar metabolic diseases. Aim of the study was to investigate possible effects of different amounts HFCS consumption on depression- and anxiety-like behaviours besides known metabolic diseases.

A total of 32 Wistar male rats were randomly divided into four groups: control group receiving only tap water, Fructose 20 (F20) and Fructose 40 (F40) groups were given water sweetened with 20% and 40% HFCS solution, respectively. Stress group were exposed to stress. Following 14 consecutive days administration, animals were subjected to tail suspension test (TST), light/dark test (LDT) and open field test (OFT). After the behaviour tests, blood samples were collected.

There was no significant difference between groups in TST. LDT revealed that significant increase in the time spent in dark compartment in F20 (238.08 ± 8.38 sec), F40 (209.66 ± 11.35 sec) and stress (233.39 ± 8.94 sec) groups compared to control group (112.38 ± 12.99 sec; p < 0.01). The number of crossings were found significantly lower in stress group (112.38 ± 12.99 sec; p < 0.01). The number of crossings were found significantly lower in stress group (167.64 ± 5.68) compared to control (188.66 ± 9.64), F20 (173.66 ± 8.22) and F40 (180.40 ± 6.73) groups in OFT (p < 0.01). There was no significant difference in corticosterone levels of control (286.17 ± 18.20 ng/mL) and F20 (354.27 ± 17.91 ng/mL) groups, while F40 group (504.29 ± 40.96 ng/mL) had significantly higher corticosterone levels compared to stress group (412.51 ± 20.60 ng/mL; p < 0.01).

In conclusion, especially when the results of LDT and corticosterone levels were considered, our results supported the idea that different amounts of HFCS consumption may cause the anxiety- and depression-like behaviours like stress in rats.

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PC-002
Effects of Bee Bread on Apoptosis in Hypothalamus in Obese Rats
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Obesity, which is defined as the “New World Syndrome”, is one of the most important problems of the modern age. The treatment options, which are developed to cope with this disease that threatens the entire world including our country, substantially relate to dietary supplements. During this project, we examined the usability of bee bread, which is gaining importance each day with its rich nutrient content, as a dietary supplement.

The aim of this study was the determination of the effect of bee bread supplement in diets on apoptosis in obese rats.

In this study, 40 Sprague Dawley adult female rats, weighing 200–250 g was used. Rats were randomly divided into 5 separate groups (n = 8 for each group). For this study, the first step was to separate rats as the control group (n = 8) and the obesity group (n = 32). The rats, on which obesity formed, (n = 32) was fed with high fat content diet. The rats, on which obesity formed, was fed with this supplement for 4 weeks. Rats in the control group was fed with standard rat supplement during this period (n = 8). The rats, on which obesity formed, were separated into experiment groups with 8 members in each group (group 2, 3, 4, 5).

1st Group: Control: Group fed with standard rat supplement (n = 8)
2nd Group: Group fed with high fat diet (n = 8)
3rd Group: Group fed with 100 mg/kg/day bee bread (n = 8)
4rd Group: Group fed with 200 mg/kg/day bee bread (n = 8)
5th Group: Group administered with Metformin 300 mg/kg/day as positive control (n = 8).

When the experiment protocol is complete at the end of the four weeks feeding period, the rats were decapitated under ketamine-xylazine anaesthesia following collection hypothalamus tissues. Hypothalamus were fixed in formaldehyde and buried into paraffin blocks with the application of routine histologic tissue tracking methods. Apoptotic cell death with TUNEL is evaluated. TUNEL assays showed that the increase in the apoptotic cell number was statistically significant in fed with high fat diet group compared to control group (p < 0.05). The decrease in the apoptotic cell number was statistically significant in group 3,4 and 5 compared to high fat diet group (p < 0.05). Group 3, 4 and 5 showed close results when compared with the control group.

Our results have been shown that bee bread against obesity with a high-fat diet reduces and prevents apoptosis in the hypothalamus.

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PC-003
Effects of Melatonin and Metabolites on Hydrogen Peroxide Damage on Retinal Pigment Epithelium (ARPE-19)
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Melatonin, an endogenous neurohormone produced by the pineal gland and retina, is known to be a powerful antioxidant and free radical scavenger. Recently, circulating melatonin levels were significantly lower in Age-related macular degeneration (AMD) patients than age-matched controls. It is not known whether reduced melatonin levels play a role in the development of the disease in AMD patients. To determine the relationship between melatonin deficiency and RPE cell damage, it is important to investigate the protective effects of melatonin and its metabolites (N-acetyl serotonin and 6-Hydroxy melatonin) on RPE cells against oxidative stress.

This study aimed to evaluate the effects of melatonin and its metabolites in human retinal pigment epithelium cell (ARPE-19) culture model of oxidative stress. Control cells were cultured in the hydrogen peroxide (H2O2)-free medium. In H2O2 group ARPE-19 cells were exposed to 500 μM H2O2 alone for 16 h. In study groups, cells were preincubated with melatonin and its metabolites (0.000001–100 μM) for 4 h before H2O2 exposure. Cell viability was evaluated by MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide).

Incubation with 500 μM H2O2 alone for 16 h decreased cell viability by 33%. When the statistical results of melatonin were evaluated, it was found that the difference between control group and low concentration 0.000001 μM was statistically significant. In addition, the cell viability rate of 0.000001 μM was determined to be 47% (33% to 47%). However, further studies are required to evaluate the effects of melatonin and its metabolites in animal models of AMD.
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PC-004
Investigation of Adropin Levels in Experimental Myoglobinuric Acute Kidney Injury
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Myoglobinuric acute kidney injury (MAKI) is a uremic syndrome caused by intracellular elements getting into the circulation (rhabdomyolysis) due to traumatic or non-traumatic injury to striated muscle cells. It is reported that adropin expressed in brain, liver and kidney tissues is the regulator of energy homeostasis and metabolism in humans. However, the role of adropin in MAKI is still uncertain. The aim of this study is to evaluate serum and urine adropin levels, their relationship with urine microalbumin levels and their usefulness as biomarkers.

In our study, male Sprague-Dawley rats weighing 180–200 grams were divided into 2 groups (n = 8) as Control and MAKI. Both groups of rats which are anhydrous 24 hours before the procedure were injected in hind limb muscles. The rats in the control group were injected with saline whereas the rats in the MAKI group were injected with 50% glycerol solution at a dose of 8 ml/kg to induce MAKI. Rats were taken in metabolic cages 24 hours after the injections. After collecting the 24-hour urine, blood was taken under anaesthesia at 48 hours and the rats were euthanized.

Urine microalbuminuria and adropin levels were significantly higher in the MAKI group compared to the control group (p < 0.01). There is no significant difference in serum adropin levels between the groups. Urine adropin levels and microalbumin levels were positively correlated with a high correlation coefficient (r = 0.747, p = 0.001).

Adropin may potentially have a variety of metabolic effects in the pathophysiology of kidney injury. It can be considered as a new biomarker for kidney injury. Adropin should be investigated as a possible marker in assessing the time-dependent change in kidney injury.

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PC-005
The Effect of Ghrelin Receptor on Morphine Analgesia and Tolerance in Rats
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The tolerance mechanism against morphine analgesia has not yet been elucidated. The aim of this study was to investigate effects of ghrelin receptor on morphine analgesia and tolerance in rats. In our study, 54 Wistar Albino 230–250 g male rats were used.

The animals were divided into nine groups as saline (serum physiologic 1 ml/kg; n = 6), hexarelin (ghrelin receptor agonist 200 μg/kg; n = 6), GHRP-6 (ghrelin receptor antagonist 0.2 mg/kg; n = 6), morphine (5 mg/kg; n = 6), hexarelin+morphine (n = 6), GHRP-6+morphine (n = 6), morphine tolerance (n = 6), morphine tolerance+hexarelin (n = 6) and morphine tolerance+GHRP-6 (n = 6). Serum physiologic and GHRP-6 were administered intraperitoneally while hexarelin and morphine were administered subcutaneously at the indicated doses. In order to develop morphine tolerance, 10 mg/kg morphine was injected daily in the morning and evening for five days and tolerance was evaluated on sixth days single dose of morphine. Analgesic effects were assessed by hot plate and tail flick analgesia tests. The resulting analgesic effect was measured and recorded at 0th, 30th, 60th, 90th and 120th minutes. Assessment of analgesic effect was formulated as % analgesia (MPE) (% analgesia = 100 x [postdrug latency-basal latency]/[cut off time-basal latency]). Statistical evaluation of the data was performed by two-way ANOVA and multiple comparisons were determined by the Tukey test. Statistical significance was defined at p < 0.05 level.

Obtained data suggest that hexarelin increased morphine analgesic effect (p < 0.05) but GHRP-6 did not change morphine analgesic effect in analgesia tests. On the other hand, hexarelin decreased tolerance development to morphine (p < 0.05) but GHRP-6 did not change tolerance development to morphine in analgesia tests.

In conclusion, we suggest that ghrelin receptor may have important roles on morphine analgesia and tolerance.
Investigation of the Relation of Nesfatin-1 and Adropin with Blood Pressure in Experimental Hypertension Model

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Hypertension is the most common cardiovascular disease in terms of mortality, which increases the risk of developing myocardial infarction, stroke, heart failure and renal failure. Adropin and nesfatin-1 are peptides associated with energy homeostasis and metabolism. It is reported that the decrease in plasma adropin level may be associated with high blood pressure and brain nesfatin-1 signal plays a role in the regulation of cardiovascular response under stress. In our study, we aimed to investigate the relationship of nesfatin-1 and adropin with blood pressure levels in an experimental hypertension model induced by angiotensin II.

In our study, Sprague-Dawley rats weighing 240–260 grams were divided into control and hypertension groups (n = 8). With the osmotic mini-pump, angiotensin II solvent (0.01N acetic acid in saline) was administered to the control group and angiotensin II was given to the hypertension group for 7 days at a dose of 0.7 mg/kg/day. For both groups, blood pressures were measured by tail cuff plethysmography on days 1, 3, 5 and 7. After 24-hour urine collection, blood and tissue samples were taken under anaesthesia and the rats were euthanized.

There was no significant difference between renal tissue, serum and urine nesfatin-1 and adropin levels in control and hypertension groups. In the hypertension group; systolic, diastolic and mean blood pressure increased from the 1st day of the experiment, compared to the control group (p < 0.05).

We suggest that experimental hypertension models have a potential to investigate the relationship of nesfatin-1 and adropin levels with hypertension in molecular level at different time intervals and new studies are needed.

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Effects of Maternal Tobacco Smoke or Alpha Lipoic Acid on Puberty Onset, Estrous Cycle and Gonadotropin Levels in Female Rats

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Various environmental factors are known to affect puberty onset. However, there are few studies in literature about how maternal tobacco smoke (TS) or alpha lipoic acid (ALA) affect the hypothalamo-pituitary-gonadal axis at peripheral or central levels in rats. This study aimed to investigate effects of maternal tobacco smoke or alpha lipoic acid on puberty onset, estrous cycle and serum gonadotropin levels in female rats.

Adult female Spraque-Dawley rats were used. All animals were randomly divided into 4 groups (control, TS, TS+ALA and ALA) and each group consisted of 7 rats. All TS rats were exposed to TS (20 gram/day, for one hour twice a day) and all ALA rats received daily oral ALA (20 mg/kg) during 8 week. Afterwards all rats were impregnated, TS or ALA treatments continued during pregnancy. All treatments ended with birth and later new-born female rats were selected for each group (n = 7). Puberty onset was monitored by examination of vaginal opening in female rat pups. Subsequently, oestrous cycle was conducted daily for 15 days and determined by examination of the vaginal smear cytology. Also, serum FSH and LH levels were measured using Elisa method at the end of the experiment.

There was significantly advanced on puberty onset day for TS group (p < 0.05). There was a significantly increase in pubertal weight in ALA group compared to control group (p < 0.001). The mean total number of oestrous cycles and average duration of metestrus, diestrus, prooestrus or oestrus phases were not significantly different in all treatments groups compared to control. There was no any significant change in serum FSH levels, but serum LH levels were significantly increased in all treatment groups compared to control group (p < 0.05).

Present study showed that maternal tobacco smoke or alpha lipoic acid may differently affect hypothalamo-pituitary-gonadal axis in rats.
Changes in UCP2 and MicroRNA-139 Levels Due to Myocardial Ischemic Postconditioning and Melatonin Administration

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Ischemic postconditioning (PostC) is a strong endogenous cardioprotective phenomenon, which targets the increased tolerance of the myocardium against ischemia-reperfusion (I/R). It has been reported that protective effects of PostC decrease/disappear with age and chronic heart disease. Similarly, low serum melatonin levels have been reported in the same risk groups. UCP2 is a mitochondrial inner membrane protein which reduces mitochondrial reactive oxygen species formation. MicroRNAs have emerged as a group of important regulators via degradation or translational inhibition of their target mRNAs. Increasing evidences indicate that microRNAs are involved in the regulation of I/R injury. The aim of this study was to investigate the effects of PostC and physiological and pharmacological concentration of melatonin on I/R induced change of UCP2 and microRNA-139 levels using an in vivo model of myocardial I/R injury.

Rats were pinealectomized (Px) or sham-operated (non-Px) (control) 2 months before the I/R studies. 30 minutes of ischemia and 120 minutes of reperfusion were produced. PostC was induced by 3 cycles of R/I (10 s each) after the ischemia. Melatonin was administrated by ip injection last 10 days (10 mg/kg). UCP2 and microRNA-139 levels were analysed by using both qRT-PCR. UCP2 decreased with I/R and Px, increased by PostC and melatonin. PostC does not create significant effect in Px but protection was provided with melatonin. microRNA-139 decreased with Px and I/R, these changes have prevented with the treatment.

These results suggest that physiologic and pharmacological melatonin may be important in the protective effects of PostC. The protective effect of PostC disappeared when physiological melatonin decreased and this effect was seen to reverse with melatonin replacement. UCP2 and microRNA-139 may play an important role in cardioprotective mechanism of melatonin and PostC.

Functional Evaluation of Oxytocin Neuron Circuits in Magel2 Deficient Mice

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Prader-Willi syndrome (PWS) is a genetic disorder caused by disruption of a well-defined region on chromosome 15, which contains several paternally active genes including Magel2. PWS is associated with several physiological and behavioural problems including hyperphagia and social deficits. The chromosomal abnormalities that underlie PWS leads to inactivation of several genes, that is thought to cause hypothalamic dysfunction. Oxytocin is an important hypothalamic neuropeptide that has been implicated in both social and feeding behaviours. Since Magel2 is highly expressed in hypothalamus, we hypothesized that its deletion may cause oxytocinergic circuit defects that may contribute to PWS phenotype.

To understand full scope of oxytocinergic circuitry defects, we examined circuit properties of oxytocin neurons in normal and Magel2-deficient PWS mouse model. For this, we used patch-clamp electrophysiology technique to identify physiological properties of oxytocinergic information processing.

Electrophysiology results show that synaptic inputs to oxytocin neurons are dramatically altered, driving reduced activity in Magel2-deficient oxytocin neurons. Loss of Magel2 changes physiological properties of these neurons including the spontaneous activity, cell autonomous mechanism and synaptic input properties.

Our results suggest that Magel2 deletion leads to the disruption of oxytocin neurons circuits. Defects in satiety-circuits defined by oxytocin neurons may underlie the veracious appetite seen in PWS patients.

The Effect of Melatonin on Depressive Like Behaviour, Age and S100B Levels in Diabetic Rats

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In both human and animal models, diabetes is associated with pathological changes in the brain that lead to cognitive and affective deficits, and to an increased risk of depression and anxiety. Hyperglycaemia accompanied by an accelerated rate of advanced glycation end product (AGE) formation and accumulation. AGES play a role in diabetes-related depression and cognitive decline. The aim of the present study is to investigate the effects of melatonin on anxiety and depression-like behaviour and AGE and S100B, a calcium-binding protein secreted by astrocytes, levels in hippocampus and prefrontal cortex (PFC) in diabetic rats.

40 Wistar albino rats (6 months old) were divided in four experimental groups of 10 rats each: Normoglycemic control, Normoglycemic+melatonin treated group, diabetic control and Diabetic+melatonin treated group. Experimental diabetes was induced by a single intraperitoneal injection of streptozotocin (STZ) at the dose of 60 mg/kg. Melatonin (10 mg/kg, i.p) was administered once a day for 28 days. Anxiety and depression like behaviour was evaluated by Elevated plus maze (EPM) and Forced swimming test (FST), respectively. The concentrations of AGE and S100B in hippocampus and PFC were measured by ELISA. Differences between groups were evaluated with Kruskal-Wallis followed by a post-hoc Bonferroni test to evaluate the differences with in the groups.
The results showed that diabetic rats exhibited a significant behavioural deficit, including depression-like behaviour in FST and anxiety-like behaviour in EPM, along with a significant increase in AGE levels and decreased in S100B levels in hippocampus and PFC. Melatonin treatment prevented these behavioural abnormalities, decreased AGE levels and normalized S100B levels in these brain areas.

In conclusion, the present study revealed that melatonin exerts antidepressant-like and anxiolytic-like effects in STZ-induced diabetic rats, at least in part, through reducing AGE levels and preserving S100B levels in the hippocampus and PFC.

PC-011
The Interaction of SIRT1, TLR4 and IL7 in Human Dementia
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The growing association between neurodegeneration and inflammation has led researchers to investigate interaction of sirtuins with inflammation markers in neurodegenerative diseases. Herein, we analysed the contribution of SIRT1 to chronic inflammation associated with dementia through Toll like receptor 4 (TLR4) and interleukin-7 (IL7) for the first time. Furthermore, we investigated the association of three single nucleotide polymorphisms of SIRT1 gene including (rs7895833, rs7069102, rs2273773) with levels of SIRT1, TLR4 and IL7 expressions, as well as total antioxidant status (TAS), total oxidant status (TOS) with dementia in Turkish population.

We observed a significant increase in the SIRT1 level in dementia including Alzheimer’s Disease (AD). Interestingly, the level of TLR4 protein was significantly lower only in AD patients. There was a decrease in the level of IL7 between diseased- and healthy elderly subjects, however, it did not reach the accepted significance level. In the Pearson’s correlation test, we found a significant positive correlation between SIRT1 level and age in healthy elderly subjects whereas this correlation was disappeared in dementia patients. Also the positive correlation between IL7 and TLR4 in healthy elderly subjects was absent in dementia patients. However, there was no direct association between studied SNPs and dementia. According to logistic regression analysis, the superiority of AD risk 1.16 times increases due to an increase in the SIRT1 level and 24.23 times increases due to a decrease in the TLR4 level. Interestingly, a high level in the TAS increases the risk of AD approximately 33.32 times.

Taken together, the current study being the first for a much better molecular understanding of the interaction of the decreasing TLR4 levels and increasing SIRT1 levels in dementia and AD points the importance of epigenetics in several age-related diseases to provide a healthy aging by developing novel therapies to prevent or slow down the progression of AD.

PC-012
The Effects of Thymoquinone against Cisplatin-Induced Neurotoxicity Rat Model
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Cisplatin (CIS) is an effective broad-spectrum chemotherapeutic agent that is often associated with side effects such as neurotoxicity. Thymoquinone (TQ), one of the main components of Nigella sativa, exhibits various bioactive properties such as anti-inflammatory and antioxidant. We evaluated the neuroprotective effects of TQ in CIS-induced neurotoxicity by using biochemical and histopathological methods.

Rats were randomly assigned into four groups (n = 8). Control group; only solvent intraperitoneally. TQ group; 5 mg/kg on three consecutive days. CIS group; 7 mg/kg single dose of CIS. CIS+TQ group; 5 mg/kg TQ on three consecutive days after 7 mg/kg single dose of CIS. On day 4 of the study, the rats under anaesthesia were sacrificed. Brain tissue was assessed in all groups by histological, immunohistochemical (Image j) and biochemical means.

In the histological and immunohistochemical evaluations; the cerebral cortex was normal appearance in the control and TQ groups. In these groups, caspase-3 immunoreactivity was observed slightly. The CIS group exhibited histological changes such as congestion and neurodegeneration. It was found that the caspase-3 immunoreactivity significantly increased in the CIS group when compared with control group (p = 0.002). There was a marked attenuation in histological changes in the CIS+TQ group according to the CIS group. Additionally, caspase-3 immunoreactivity was detected to be milder in the CIS+TQ group compared with CIS group (p = 0.041). On the other hand, tau and neurofilament immunoreactivity were similar in all groups.

In the biochemical evaluations; malondialdehyde (MDA) level of CIS group was significantly higher than that of the control group (p = 0.017). But, MDA level of CIS+TQ group was similar to CIS group (p > 0.05). Glutathione (GSH) level and Superoxide dismutase (SOD) activity were similar in all groups (p > 0.05). All groups were similar in terms of SOD activity and MDA level.

Consequently, it is our thought that ISO has a therapeutic role against CIS-induced neurotoxicity.
PC-013

Weight Gain and Metabolic Changes Due to Olanzapine Treatment in Psychotic Patients

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It is known that olanzapine, an atypical antipsychotic, causes higher weight gain, blood glucose, lipid profile and adverse effects on liver enzymes. In this study, we aimed to determine the effect of olanzapine on body weight, serum lipid profile and liver enzymes in in psychotic patients.

A total of 30 patients between the ages of 18–65 who the onset of olanzapine treatment with the cause of psychotic symptoms in psychiatric clinic were included in this study. Blood levels of AST, ALT, LDL, HDL, TG, total cholesterol values, weight and waist circumference were measured at the beginning of the study (baseline) and 15th and 60th days of treatment.

It was determined that values of the weight and waist circumference of patients increased. While waist circumference increase was statistically significant in 15th day of treatment compared to baseline (p < 0.01), there was a decrease in this value at the 60th day of treatment compared to baseline (p < 0.01). SGOT and SGPT were elevated at a statistically significant level (p < 0.01) at 15th day of treatment, but they reduced at the 60th day of treatment. There was a significant increase in the lipid profile, LDL, triglyceride, total cholesterol values in both treatment groups compared to baseline (p < 0.01).

Olanzapine-induced liver enzyme elevation was evident in the early stages of treatment, but tended to decline as it progressed. This situation can be interpreted as the treatment should not be interrupted, even if the liver enzyme is elevated in the early period of treatment. Because elevation of olanzapine-induced blood lipid levels may cause in long-term serious consequences, it is important to take the necessary precautions in this regard and to regulate the treatment.

PC-014

Central Salusin-β Infusion Increase Serum Testosterone Levels in Male Rats

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Salusin-β, which is derived from preprosalusin, is a multifunctional bioactive peptide-based hormone. Salusin-β is predominantly localized to the hypothalamus. Hypothalamus is controlling of reproduction and drinking behaviour. The effects of this peptide on the reproductive system are not known. This study was undertaken to determine whether there is a relationship between salusin-β and serum testosterone level.

In this study, adult 40 adult male Wistar-Albino rats were used. The rats were separated into 4 groups as the control, sham, 2 nmol Salusin-β and 20 nmol Salusin-β (n = 10). All rats were anesthetized (except for the control group), and osmotic mini pumps (Alzet 2ML1) were placed in the right lateral ventricle. With the help of the osmotic mini pumps, infusion of artificial cerebrospinal fluid (solvent) was performed to the sham group at a 240 μl volume (10 μl/hour) daily; and the infusion of 20 and 20 nmol Salusin-β were performed to the study groups. After infusion period (7 day), the rats were decapitated, and the blood tissue samples were collected. Serum testosterone levels were measured by ELISA method in blood tissue.

Alzheimer’s disease (AD) generally covers 60% of mental disorders and is one of the most important neurodegenerative diseases. In our study, the human neuroblastoma cell line (SH-SY5Y) was transformed into neuron-like cells via introducing retinoic acid.

In the transformed cells, β-amyloid protein (200–0 μM) was applied for 24/48 hours at wide dose intervals to establish the Alzheimer’s environment and IC50 values were determined. Next, neuroprotective effect against toxicity generated by administration of leucomicine sesquiterpene in a wide spectrum doses (100 μg/ml) to β-amyloid administered cell culture was examined for 24 and 48 hours. 3-(4,5-dimethyl-thiazol-2-yl) 2,5-diphenyltetrazolium bromide (MTT) and lactate dehydrogenase (LDH) release tests were performed to determine cell viability rates in the in vitro Alzheimer model. Subsequently, the Annexin-V/PI study flow cytometry method was used to determine the type of death caused by toxicity in the cells. Apoptosis and nucleus integrities of the cells were examined under the microscope using the Hoechst 33258. Furthermore, leucomicine effects on acetylcholinesterase (AChE) activity, total antioxidative capacity (TAC) and total oxidative status (TOS) levels were determined.

According to the results, protective effect of leucomicine concentrations against β-amyloid for 24 hours and 48 hours was determined by cell viability tests. Flow-cytometry findings revealed
that leucomicine caused significant decrease in necrosis deaths in cells. It was further analyzed that the AchE activity, the TOS level and the TAC level decreased after leucomicine application.

**PC-016**

**Investigation the Effectiveness of Chronic Agomelatine on Foetal Number in before and Different Periods of Pregnancy in Rats**

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Agomelatine, an analogue of melatonin, is a new antidepressant approved by the European Union Pharmaceutical Agency in 2009 under the trade name valdoxan. Agomelatine has high affinity melatonergic (MT1 and MT2) receptor agonist and serotoninergic 5-HT2C receptor antagonist property at low sensitivity. Melatonin is an important molecule that regulates female reproductive cycle and has been detected at high concentration in preovulatory follicular fluid. Agomelatine is a derivative drug of melatonin and included in B category for use during pregnancy. For these reasons in our study we aimed to investigate the change of foetal number in rats using agomelatine at different periods of gestation.

In the study, 42 female Wistar-Albino rats were divided into 6 groups with 7 animals in each group:

Group 1: Pregnant.

Group 2: Pregnant group in which chronic agomelatine treatment was performed before pregnancy. Group 3: Pregnant group in which chronic agomelatine was used before and during the first 2 trimester of pregnancy.

Group 4: Pregnant group in which agomelatine was used during the first two trimester of pregnancy.

Group 5: Pregnant group in which agomelatine was used during all pregnancy stages.

Group 6: Pregnant group in which chronic agomelatine was used before and during all pregnancy stages.

One-way analysis of variance (ANOVA) test was used to assess the data and differences between groups.

As a result, mean foetal number values of the groups were calculated as 9.1, 10.7, 12, 11.7, 11.4 and 12.8 respectively. There was statistically significant difference between control and group 3 (p = 0.001), group 4 (p = 0.002), group 5 (p = 0.01), group 6 (p < 0.001), except group 2.

According to the result of this research, it is noticed that there is not enough study on this topic. In this study showed that agomelatine has foetal count enhancing activity in rats.

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**PC-017**

**Bipolar Affective Disorders Related to Vitamin B12 and Folic Acid Levels**

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Vitamin B12 and folic acid are vitamins that are necessary for the central nervous system function. Deficiency of these vitamins contributes to pathogenesis of several neuropsychiatric disorders such as mood disorders, cognitive changes and paranoid disorders. In this study, we investigated the levels of vitamin B12 and folic acid in patients with bipolar affective disorder who applied to our clinic.

We collected laboratory data from the clinical chemistry department of the Turgut Ozal Medical Center incorporating Malatya. Our study population included all patients who had at least one serum lithium measurement from November 1st 2000 to April 30th 2014 inclusive. When files were scanned, sociodemographic data including the patient’s identity and the results of B12 and folic acid tests were recorded.

In this study, a total of 222 patients were retrospectively screened. Although vitamin b12 levels results of all the patients could be reached, folic acid levels result of only 210 patients could be reached. Vitamin B12 levels of the % 72.5 (n = 161) patients were between the reference range, % 0.5 (n = 58) of patients were below the reference range, % 1.4 (n = 3) of patients were on the reference range. Folic acid levels of the % 96.2 (n = 202) of patient were between the reference range, % 0.5 (n = 1) of patient were below the reference range, % 3.3 (n = 7) of patient were on the reference range.

In our study, most of the patients’ vitamin B12 and folic acid levels were determined as normal. This retrospective study had significant limitations. First, this study was a retrospective patient file screening study. The second was drug use, frequency of exacerbations, and treatment response rates of patients with low levels of vitamin B12 and folic acid could not be evaluated. There is a need for more extensive work to address these limitations.
Protective Effect of $\text{Fe}_3\text{O}_4\text{-SiO}_2\text{-NH}_2$ Nanocomposite Functionalized with Boronophenylalanine on Glutamate Excitotoxicity in Primary Cortical Neuron Cell Culture

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Boron, an essential element, is involved in metabolic events such as cell membrane function, central nervous system function, hormonal metabolism and enzyme reactions. Boronophenylalanine (BPA) as boron compounds is preferred in the clinical treatment. Glutamate, the major stimulant neurotransmitter in the central nervous system, has functions in physiological events such as learning and perception. The aim of this study was to investigate the neuroprotective effect of magnetic $\text{Fe}_3\text{O}_4\text{-SiO}_2\text{-NH}_2$-BPA nanocomposite on glutamate toxicity in primary cortical neuron cultures.

In accordance with this purpose, firstly, the magnetic $\text{Fe}_3\text{O}_4\text{-SiO}_2\text{-NH}_2$-nanocomposite functionalized with BPA have been synthesized. While, the structure of the nanocomposite and chemical composition have been confirmed by TEM and FTIR methods, the boron content of $\text{Fe}_3\text{O}_4\text{-SiO}_2\text{-NH}_2$-BPA was determined as 1.47% by ICP/MS method. Afterwards, primary cortical neuron culture was prepared using new born Sprague-Dawley rats and glutamate excitotoxicity was induced by exposure to 6×10⁻⁵ M glutamate. The cells were incubated for 24 hours using different concentrations of BPA, $\text{Fe}_3\text{O}_4\text{-SiO}_2\text{-NH}_2$ and $\text{Fe}_3\text{O}_4\text{-SiO}_2\text{-NH}_2$-BPA (final concentrations in the well to be 10–250 μM). The proliferation inducing effect on cell viability was determined by using MTT assay. According to MTT assay, it was determined that cell viability was increased following BPA administration and observed that at 10–100 μM concentration of BPA, $\text{Fe}_3\text{O}_4\text{-SiO}_2\text{-NH}_2$ and $\text{Fe}_3\text{O}_4\text{-SiO}_2\text{-NH}_2$-BPA had a statistically significant protective effect on cell viability compared to glutamate control ($p < 0.01$). The most significant increase was observed following 10 μM BPA and $\text{Fe}_3\text{O}_4\text{-SiO}_2\text{-NH}_2$-BPA (equivalent to 10 μM BPA) administration ($p < 0.001$).

In this study, BPA and $\text{Fe}_3\text{O}_4\text{-SiO}_2\text{-NH}_2$-BPA at the low doses showed high neuroprotective effects in primary rat cortical neurons cultures against glutamate excitotoxicity. These results suggest that BPA and $\text{Fe}_3\text{O}_4\text{-SiO}_2\text{-NH}_2$-BPA can be used as a therapeutic agent against glutamate excitotoxicity, however, further studies are need clarify the mechanism of action of BPA.

The Role of Cholinergic Neurons in Arcuate Nucleus on Anxiety Behaviour

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Acetylcholine (ACh), which is known as a modulator in the central nervous system by affecting the presynaptic release of neurotransmitters has a relationship with anxiety and depression through basolateral amygdala and dorsal hippocampus. Arcuate nucleus (ARC) is the centre of appetite and regulates energy metabolism through its postsynaptic targets. The physiologic roles of newfound cholinergic (ChAT) population in the ARC are unknown. This new population has a possible relation between anxiety and eating habits. Here we intend that the ChAT in ARC have an anxiolytic effect on anxiety. This study aimed to reveal the anxiety relation of ARC-ChAT neurons.

To determine whether cholinergic signalling through the arcuate nucleus of the hypothalamus is associated with anxiety behaviour, we used ChAT-Cre transgenic mice expressing the Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) which are G-coupled channels to selectively stimulate ChAT neurons. Behavioural tests include elevated plus maze (EPM), open field (OF) and light-dark box tests. Pharmacogenetic activation group has a significant increase (independent Student T-test, $p < 0.05$) of the open arm duration in EPM compared to the control group. In contrast, results of OF and light dark box tests have no significance.

We have shown that the cholinergic neurons in ARC have an anxiolytic effect on anxiety in elevated plus maze.

Investigation of the Effects of Isorhamnetin on Motor Function, Sedation and Analgesia in the Diabetic Rats

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Flavonoids are phenolic compounds used in traditional Chinese medicine due to their high content of nutrients and their therapeutic effects. We aimed to investigate the effects of isorhamnetin (ISO), a compound in the flavonoid structure, on motor function, sedation, and analgesia in diabetic rats.
For this aim, 32 Wistar albino rats were divided into 4 groups (n = 8 in each group); Control group: We administered only 0.5 ml saline (SF) intraperitoneally (i.p.). STZ Group: 50 mg/kg streptozotocin (STZ) was dissolved in citrate buffer solution (pH: 4.5) to give single dose i.p. STZ + ISO Group: 50 mg / kg STZ i.p. 3 days after administration, 5 mg / kg ISO for 7 days single dose daily i.p. ISO + STZ Group: 5 mg / kg ISO for 7 days single dose i.p. after administration as a single dose 50 mg / kg STZ i.p.

The rats with a blood glucose level above 200 mg/dL at baseline 72 h after administrating a single dose of 50 mg/kg STZ were diabetic. All the rats were tested for rotarod and accelerod balance-motor coordination performance measurements, hot plate and tail-flick analgesimetry tests, and the effects of ISO on the nervous system and functions.

There were no significant results between the groups in the accelerod and tail flick tests. Nevertheless; In the rotarod test, it was tested that the starting time of 20 rpm was significantly lower in the control group than in the other groups. In the hot plate test, the end-of-test period of the STZ + ISO group was measured to be significantly reduced compared to the STZ and ISO + STZ groups.

In conclusion, the results of the present study demonstrated that ISO application after STZ injection lowered the pain threshold in the rats and also ISO application had a positive effect on motor functions.

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**Investigation of the Effects of Thalidomide Against Global Cerebral Ischemia-Reperfusion Injury in Rats**

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Stroke is the second most common cause of death worldwide and a common cause of morbidity in developing countries. Ischemia and subsequent reperfusion (I/R) causes severe damage to tissues and organs. Thalidomide (Th) reduces the destruction of inflammatory cascades on tissue cells by suppressing the production of Tumour Necrosis Factor-α, interleukins (IL-6, IL-10 and IL-12) and cytokines. Th has shown protective effects in different models of I/R damage. We aimed to investigate the effects of Th in global cerebral I/R injury in rats.

Rats were divided into 4 groups (n = 8). 1) Sham group: Only midline incision was performed. 2) I/R group: Twenty-four hours of reperfusion after 15 minutes cerebral ischemia after bilateral carotid artery occlusion. 3) Th+I/R group: 20 mg/kg Th was given 1 hour before the 15 minutes of ischemia then 24 hours of reperfusion 4) I/R+Th group: 20 mg/kg Th was given 1 hour after the 15 minutes of ischemia then 24 hours of reperfusion. At the end of the experimental procedure all rats were sacrificed and histological and biochemical analyses were run in the cerebral and cerebellar tissues.

Th also lowered the caspase-3 immunoreactivity in Th+I/R and I/R+Th groups by comparison to I/R group in the cerebrum. In the I/R+Th group, there was a significant decrease in the intensity of immunoreactivity compared to the I/R group (p = 0.01). Also, cerebellar cortex of I/R+Th group was observed in normal appearance. Superoxide dismutase and total glutathione levels in the cerebrum and cerebellum were found as increased whereas malondialdehyde production was found as decreased due to Th treatment when compared to the I/R group.

These findings have showed us Th has anti-apoptotic, anti-oxidant, and anti-inflammatory effects on neural tissues.

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