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Oral Communications

OC01

Blood Brain Barrier Dynamics and Antiepileptogenic Effects of Antiepileptic Drug-Bound Nanoparticle in Wag/Rij Rats as a Genetic Absence Epilepsy Model

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AIM: Epilepsy is a neurological disease that affects more than 65 million people worldwide. Absence epilepsy is seen in children and adolescents. The blood-brain barrier (BBB) constituted by the endothelial cells of the brain microvessels limits the passage of circulatory substances into the brain parenchyma. In this study, adult WAG/ Rij rats were used to show the effects of lacosamide (LCM) associated with gold nanoparticle (GNP) on seizures.
METHODS: All experimental animal procedures were performed after the approvement of the local ethics committee of Boğaziçi University and Koç University. One-way analysis of variance (ANOVA) followed by Tukey's HSD test was used to statistically evaluate the significance of four groups. To see the long-term effects of GNP on seizures, EEG recordings were obtained by electrodes placed in the right and left hippocampus, and an Elevated Plus Maze (EPM) test was performed. The presence of GNPs in the brain was determined by using Inductively Coupled Plasma Mass Spectrometry (ICP-MS) and electron microscopy. At the same time, hemogram analysis of the animals were performed at the end of the experiments.
RESULTS: Application of LCM with or without GNP caused significant decreases in amplitude, and seizure frequency values compared *with* baseline values ($p<0.01$). GNP+LCM injections significantly decreased anxiety levels as well ($p<0.01$). The findings obtained from in vivo imaging system (IVIS) showed that LCM reached higher levels of brain parenchyma in the presence of GNP ($p<0.01$). In ultrastructural examinations, GNPs were found in the neuronal structures after passing BBB endothelial cells. There were no significant changes in hemogram values.
CONCLUSIONS: Our results suggest that GNP is an effective transfer agent in terms of antiepileptogenic efficacy in the passage of LCM through the BBB, and more importantly, the application of low dose LCM as GNP+LCM strongly influences the amplitude, and frequency of seizures.

Keywords: Absence epilepsy, gold nanoparticle, electroencephalography, blood-brain barrier, lacosamide

OC02

The Effect of Resveratrol on Penicillin-Induced Epileptiform Activity

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AIM: Resveratrol (3,5,4'-tri-hydroxy stilbene; RESV) is *an* antioxidant polyphenolic compound. Studies have shown that resveratrol has neuron protective effects in various neurological diseases. The aim of this study was to investigate the effect of resveratrol on penicillin-induced epileptiform activity.
METHODS: Twenty-four male Wistar rats were used in our study (n: 6). Epileptiform activity was induced by administering 500 IU Penicillin-G to the cortex (intracortical) in a volume of 2.5 microliters with a Hamilton microinjector. Resveratrol was administered intraperitoneally at a dose of 25, 50, 100 mg/kg, respectively, after 30 minutes of penicillin injection. This study was approved by the Animal Experiments Local Ethics Committee (OMU HADYEK) and supported by OMU Project Office (PYO.TIP. 1904.17.019). One-way analysis of variance and Post Hoc Tukey tests were used for statistical analysis.

RESULTS: Compared *with* the control group, Resveratrol (50 mg/kg) reduces significantly in spike frequency in between 30-50 and 130-180 minutes ($p<0.05$). Resveratrol (25 mg/kg) significantly decreased spike frequency between 130-140 minutes and Resveratrol (100 mg/kg) significantly decreased spike frequency between 30 and 40 minutes ($p<0.05$). No statistically significant difference was found between the groups in terms of amplitude values ($p>0.05$).
CONCLUSION: Resveratrol showed anticonvulsant effect on penicillin-induced epileptic activity. Further studies are needed to explain the certain mechanism of anticonvulsant effect of resveratrol on epilepsy.

Keywords: Resveratrol, Epilepsy, Penicillin, Rat

OC03

Electroencephalographic Investigation of the Effects of *Ginkgo biloba* on Spike-Wave Discharges in Rats with Genetic Absence Epilepsy

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AIM: *Ginkgo biloba*, which is widely used in the treatment of some types of dementia and attention deficits, has been reported to cause epileptic seizures. The aim of the present study was to investigate the effects of chronic *Ginkgo biloba* extract (EGb 761) on absence seizures and locomotor behaviors in male WAG/Rij rats.

METHODS: 50, 100 and 200 or 400 mg/kg doses of EGb 761 were administered to male WAG/Rij rats with implanted EEG electrodes by oral gavage for 28 days. Absence seizures were evaluated on spike-wave discharges (SWDs) in EEG records that were obtained for 4 hours each week. The *number of*, mean duration and total duration of SWDs were determined for the analyzes. Electrophysiological data were analyzed by Wilcoxon test and locomotor data were analyzed by Mann-Whitney U test. The study was conducted with the permission of SBÜ Animal Experiments Local Ethics Committee 2017-1054.

RESULTS: In the group treated with 400 mg/kg EGb 761, the number and mean duration of SWD at the 1st and 7th doses and the total SWD duration at the 1st, 7th and 14th doses were significantly increased ($p < 0.05$). In *other* experimental groups treated with EGb 761 doses, there was no significant change in locomotor activity in the open field and the rotarod tests. CONCLUSION: *Ginkgo biloba* extract EGb 761 increased the epileptic SWDs parameters of WAG/Rij rats at high doses (400 mg/kg), causing a proconvulsant effect on absence seizures. It should be noted that *in epilepsy patients high-dose applications* of *Ginkgo biloba* extract EGb 761 may lead to an increase in neuronal excitability.

This study was supported by TÜBİTAK (Project no: 115S348).

Keywords: Absence epilepsy, EEG, {Ginkgo biloba}, spike-wave discharge, WAG/Rij rat

OC05

The Effect of Hemopressin Combined To CB1 Receptor Agonist and Antagonist on Epileptiform Activity in the Pentylenetetrazole Kindling Rat Model

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AIM: Hemopressin, α 9 amino acid nanopeptide derived from α chain of hemoglobin. However, it is not clear whatever hemopressin is agonist or antagonist of CB1 receptors. The aim of this study was examined its interaction between CB1 receptor agonist and antagonist in pentylenetetrazole kindling model.
METHOD: The animals were injected pentylenetetrazole (PTZ) sub-convulsive dose (35mg/kg/ i.p) for three days per week for a maximum 29 injections. Subsequently, combination injection of hemopressin (0.6 μg) + AM-251 (0.50 μg), AM-251 (0.50 μg) + hemopressin (0.6 μg) and, ACEA (7.5 μg) + hemopressin (0.6 μg) were administered. An ECoG recording was started when the PTZ injected and last for 30 minutes. The epileptiform activity frequency and amplitude were analyzed.

RESULTS: The administration of hemopressin (0.6 μg) + AM-251 (0.50 μg), significantly decreased the total number of spike wave discharges (SWDs), the number of spikes in each SWD and total SWDs time ($p<0.05$). While increased myoclonic jerk latency compared *with* the control group ($p<0.05$). The administration of AM-251 (0.50 μg) + hemopressin (0.6 μg), significantly increased the total number of SWDs and the number of spikes in each SWD ($p<0.05$), while no significant difference in total SWDs time, spike amplitude, seizure score and myoclonic jerk latency compared *with* the control group ($p>0.05$). The administration of ACEA (7.5 μg) + hemopressin (0.6 μg), significantly decreased the total SWDs, spike counts and total SWDs time ($p<0.05$), while significantly increased myoclonic jerk latency ($p<0.05$).

CONCLUSION: The hemopressin is acting as agonist of CB1 receptors in this model. When administered before the AM-251, homopressin decreased epileptiform activity, however when administered after AM-251 it increased epileptiform activity. When administrated with ACEA epileptiform activity was decreased suggesting that hemopressin acts as an agonist of CB1 receptor.

Keywords: Electrocorticography, Epilepsy, Hemopressin, AM-251, ACEA, pentylenetetrazole

OC06

Long-Term Dietary Probiotic Intake Ameliorates Pentylenetetrazole-Induced Epileptic Seizures by Reducing Oxidative Stress in Rats

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AIM: Pathophysiology of epilepsy isn't fully understood but the role of oxidative-stress in generation and progression of epilepsy is known. Intestinal microbiota modulates function of nervous system. A clinical case reported that fecal microbiota transplantation prevented epileptic seizures. This case reinforces hypothesis that microbiota may be protective in epilepsy. We investigated effects of long-term dietary probiotic-intake on seizures and oxidative-stress in pentylenetetrazole-induced seizure model in rats.
METHODS: Wistar male rat-weaners (30 days-old) were separated into 4 groups as control (n=7), probiotic (n=12), vehicle (n=12) and saline (n=12). Groups received 1ml/day saline, 109cfu/1ml/day probiotic mixture, 0,05mg/1ml/day inuline and 1ml/day saline by gavage for 60 days, respectively. 60 days later, except for control, groups received intraperitoneal injection of 50 mg/kg pentylenetetrazole and behaviors were videotaped for 30 min. Blood and brain samples were collected 24 hours after pentylenetetrazole injection. Seizures were assessed using Racine's scale. Oxidant (TOS, disulfide) and antioxidant (TAS, native and total thiol) parameters in plasma and brain samples were measured by automated-colorimetric method. Data were compared by Kruskal-wallis test.
RESULTS: In PTZ-treated groups, while 100% of rats in SF and vehicle groups entered generalized tonic-clonic seizure (stage-5), in probiotic group 91,6% of rats had generalized tonic-clonic seizure. Probiotic-intake extended onset-times of myoclonic-jerk and generalized tonic-clonic seizure (P=0,043; P=0,018), it shortened duration of generalized tonic-clonic seizure (P=0,009). Pentylenetetrazol increased plasma TOS and disulfide concentrations (P=0,001; P=0,007), it reduced native and total thiol concentrations (P=0,049; P=0,006), without changing TAS concentrations. Probiotic-intake decreased plasma TOS and disulfide concentrations (P=0,025; P=0,045), and it increased native and total thiol concentrations (P=0,035; P=0,046). Pentylenetetrazol increased brain TOS concentration (P=0,001) without changing TAS concentration. Probiotic-intake decreased brain TOS concentration (P=0,005).
CONCLUSION: When age-group of rats receiving probiotics is considered, long-term probiotic-intake from childhood demonstrated anticonvulsant effect on behavioral characteristics of epilepsy by improving epilepsy-impaired oxidant/antioxidant balance. Regular probiotic-intake from childhood may be a natural and effective approach for epilepsy prophylaxis. Grant-number: 2018.08.02.1370 (BAIBU-BAP).

Keywords: Epilepsy, microbiota, oxidative stress, probiotic

OC07

Effects of Selected Anti-epileptic Agents on Contractility of Gastric Fundus Strips Isolated from Control Wistar and Absence Epileptic WAG/Rij Rats

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AIM: Considering the high occurrence of gastrointestinal (GI) functional impairment including upper GI upset in epilepsy and GI-related side effects of anti-epileptic drugs, we aimed at investigating possible effects of valproic acid, levetiracetam and phenytoin on cholinergic agonist-induced contractions of gastric fundus isolated from healthy Wistar and absence epileptic Wistar Albino Glaxo/Rijswijk (WAG/Rij) rats.
METHODS: Fundus strips were mounted in organ bath containing Tyrode solution (pH=7.4, 95% O2 + 5% CO2 at 37°C), and contractile responses to cholinergic stimulation were tested with cumulatively-applied carbachol (CCh; 0.1, 0.3, 1 and 3 µM). In order to test the effects of anti-epileptics, valproate (100µM, 300µM, 1mM, 3mM), levetiracetam (100µM, 300µM, 1mM, 3mM) and phenytoin (10, 30, 100µM) were applied cumulatively on CCh (3µM)-induced contractions. Amplitude (mg) and area under the contraction curve (AUC) data were assessed as contraction parameters (AUC of 3µM CCh-induced contractions were regarded as 100% and drug effects were reported with reference to this). Data *were* analysed by using repeated measures ANOVA and Student's t-tests.

RESULTS: Mean amplitude (144.42%) and AUC values of contractions of fundus strips isolated from WAG/Rij rats were significantly higher than Wistars' ($n=21$, $p<0.05$). Considering the 3µM CCh-induced contractions; valproate [101±7, 82±12, 65±15, 53±16% (in Wistar group), 99±3, 103±5, 101±8, 97±11% (in WAG/Rij group)]; levetiracetam [96±5, 90±6, 83±6, 78±7% (Wistar), 104±4, 105±6, 105±7, 100±7% (WAG/Rij)] and phenytoin [87±4, 56±5, 28±8% (Wistar), 81±6, 56±6, 35±7% (WAG/Rij, n=7 for each subgroup)] exerted dose- and species-dependent effects. Phenytoin provided significant effects in both rat groups ($p<0.05$) and strongest relaxation effect ($p<0.05$).
CONCLUSION: The results from this *in vitro* study indicates that particularly phenytoin among the tested anti-epileptics agents caused relaxation of the fundus muscle. This effect may implicate impairment of gastric accommodation reflex and gastric emptying.
This study protocol was approved by Karadeniz Technical University Animal Research Ethics Committee.

Keywords: Antiepileptics, gastric fundus, gastric accommodation reflex, contractility, WAG/Rij rats

OC08

Effect of Thymoquinone on Ischemia/Reperfusion Injury in Isolated Hearts of Streptozotocin-Induced Diabetic Rats

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AIM: Diabetic patients have a high risk of cardiovascular diseases and cardiovascular complications which are the leading causes of morbidity and mortality. Thymoquinone, important bioactive component of black seed, has antioxidant and antidiabetic effects, and decreases blood glucose by increasing glucose use via increasing insulin secretion and preventing glyconeogenesis. This study was designed to investigate whether thymoqinone had protective effects against cardiac ischemia-reperfusion (IR) injury and oxidative stress in isolated hearts of diabetic rats.

METHODS: Thirty-five male Wistar albino rats (7 in each group) weighing 350-400 g were used. Animals were divided into control, IR, thymoquinone (10 mg/kg, 1 ml po, for 30 days), diabetes (streptozotocin 65 mg/kg, ip) and thymoquinone- or vehicle-treated diabetes+IR groups. After 20 minutes of stabilization; in control group 90 minutes perfusion, in IR groups 30 minutes ischemia and 60 minutes reperfusion were applied via Langendorff isolated heart system. Blood and heart tissue samples were taken for biochemical analysis and evaluated together with cardiodynamic parameters. The data were evaluated by Benforroni's multiple comparison test and $p<0.05$ was considered significant.

RESULT: Thymoquinone decreased blood glucose levels compared *with* diabetes group ($p <0.001$). End-diastolic pressure increased with ischemia, left ventricular developed pressure and max dp/dt decreased, thymoquinone treatment revealed a significant ($p <0.001$) return of all parameters compared to diabetic group. Thymoquinone also increased insulin levels, which decreased in diabetes ($p <0.01$). Diabetes increased cardiac injury markers CK-MB and NT-proBNP, inflammation markers CRP, TNF-α, IL-6 and IL-1β, endogenous antioxidants SOD and GSH, and these elevated levels were reduced by thymoquinone ($p <0.001$).

CONCLUSIONS: Diabetes activates inflammatory and oxidative mechanisms, causing cardiac damage and loss of function, thymoquinone has a positive impact on both glucose metabolism and cardiac performance, reducing the diabetes induced damage.

This project was supported by SRP unit of Bezmialem Vakıf University with the project number of 9.2017/8.

Keywords: Diabetes mellitus, heart, ischemia/reperfusion, oxidative damage, thymoquinone

OC09

Electrocardiographic and Histopathologic Evaluations on Possible Role of H3 Receptors in β-adrenergic Stimulation-Induced Myocardial Damage in Mice

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AIM: The present model deals with following questions: May the β-adrenergic stimulant "isoproterenol" leading to inflammatory/ischemic histopathologic changes in mice myocardium cause electrocardiographic alternations, as well? Additionally, may "isoproterenol" induced myocardial ischemia be prevented by H3 receptor (H3R) agonist "Imetit"?

METHODS: Four groups of Balb-c mice are *constituted* according to drugs given: Saline (SF), isoproterenol (ISO), Imetit (IMT), and a combination of IMT+ISO. Pre-condition lasted 7 days, for each days IMT and ISO+IMT groups were pretreated with oral 10 mg/kg Imetit. In both groups of ISO and ISO+IMT, 85 mg/kg isoproterenol was injected subcutaneously on the last two days to induce myocardial ischemia. At the end of pre-condition, two ECG leads are obtained (lead-I and "Z") under Na-Pentobarbital (75 mg/kg) + Fentanyl (0.2 mg/kg) anesthesia. Hearts were removed for histological evaluation: ventricular-wall sections were stained with Hematoxylin-Eosin (H&E) for morphological examination, and tissue level of inflammatory parameters IL-1β, TNF-alpha, MCP-1 were evaluated with indirect-immunoperoxidase staining. Data were compared with the t-test or Kruskal-Wallis test.

RESULTS: We found the J-wave area in lead-Z being a new ECG marker for ISO-induced myocardial ischemia. Both QJ interval and QRS duration increased due to ischemia (ISO), $p<0,001$ and $p<0,05$, respectively. H&E examination supported ECG findings, MCP-1 increased in ischemic myocardium ($p<0,001$) whereas IL-1β and TNF-α cytokines were unchanged. These ECG and histological alterations were not seen in pretreated animals with Imetit (IMT+ISO), except MCP-1. Imetit alone (IMT) decreased both atrial and ventricular conduction velocity therefore both PQ interval and QRS duration are increased, $p<0,05$, and $p<0,05$ respectively.

CONCLUSION: The J wave area in lead-Z seems to be sensitively correlated to the histological finding of ISO-induced myocardial ischemia in mice. We considered that H3 receptor might present on membranes myocardial cells, basing on increased PQ interval and increased QRS duration due to H3 agonist Imetit.

Keywords: ECG, fare, H3 receptor, imetit, isoproterenol, myocardial ischemia

OC10

Erythrocyte Derived Nitric Oxide Production in Pulmonary Arterial Hypertension

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AIM: Pulmonary arterial hypertension (PAH) is one of the rare fatal disease which is characterized by abnormally high blood pressure in the pulmonary artery. Major causes of the increased pulmonary artery pressure include decreased plasma NO (nitric oxide) levels due to decreased endothelial nitric oxide synthase (eNOS) enzyme activity in pulmonary artery endothelial cells. Erythrocytes have special importance that determining the vascular resistance in pulmonary circulation: NO released from endothelial cells in response to shear stress, that only occurs by the presence of erythrocytes. Erythrocytes constituently produce endothelial type NO under basal conditions and contribute to NO pool in the vascular system which has important roles on physiological systemic blood flow regulation. It is not known whether erythrocyte eNOS enzyme activation and NO production changes in PAH patients.

METHODS: Packed of erythrocytes were isolated from two different groups; healthy and PAH volunteers. Than packed were re-suspended in Hepes solution at a hematocrit of 0.01 l/l. Sampling protocols were approved by local ethical committees (06.02.2019/128). Intracellular NO, Ca+2 and ROS levels and eNOS activation measured by flow cytometry. Student-t test was used for evaluating the results. Statistical significance was $p<0.05$.

RESULTS: Intracellular NO and ROS levels decreased in PAH patients compared *with* healthy group ($p<0.001$; $p<0.01$). Phosphorylated eNOS level also diminished in PAH patients ($p<0.001$). However, there was no difference in intracellular Ca+2 levels between two groups.

CONCLUSIONS: The results of the study suggest that in PAH patients NO production in erythrocytes only diminished via eNOS phosphorylation decrement rather than intracellular Ca+2 changes.

Keywords: Erythrocyte, Hypertension, Nitric oxide, Pulmonary artery

OC11

The Effect of Heterochronic Parabiosis Model on Vascular Responses of Thoracic Aorta in Aged Mice

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AIMS: We aimed to determine effect of parabiosis model on vascular response of aged and young mice.

METHODS: In our study, young and old Balb/c mice were used and separated into 6 groups as isochronic old (IP-O), heterochronic old (HP-O), isochronic young (IP-Y), heterochronic young (HP-Y), control young (C-Y) and control old (C-O). While in the heterochronic parabiosis group, old and young animals were surgically combined through their skin, in the isochronic parabiosis groups, either young and young or old and old animals were combined too. After surgery, animals were sacrificed at 3rd, 5th, 7th and 9th weeks and then thoracic aortas were isolated. Vascular responses were determined by organ bath. To determine contraction responses, phenylephrine (10-9-3x10-5M) and potassium chloride Kkrebs (20 mM, 40mM and 80mM), and to determine vasodilation responses acetylcholine (10-9-3x10-5M), and sodium nitroprusside (10-9-3x10-4M) were used. While dose-response curves were evaluated by using repeated measure ANOVA, maximum contraction and relaxation responses were evaluated by using generalized linear model. LSD test was used as Post Hoc test. Data were shown as ±standard error and $p\leq0.05$ was obtained as significant difference.

RESULTS: Aging had a significantly lowering effect on maximum ACh relaxation responses ($p\leq0.01$). However, in the HP-Y group, the maximum ACh relaxation response at the 3rd weeks was significantly lower ($p\leq0.05$), but this significance disappeared at 9th weeks. Maximum ACh dilatation responses of groups; C-Y: 77,78±5,13, HP-Y; in 3rd week: 76,29±4,39, 5th week: 64,47 ±7,28, 7th week: 67,24 ±5,82, 9th week: 72,62 ±6,61, C-O: 60,79 ±6,25, HP-O; 3rdweek: 58,69±4,84, 5thweek: 57,14±2,98, 7th week: 60,19 ± 6,42, 9thweek: 73,28, IP-Y; 3rdweek: 70,48±7,16, 5thweek: 71,82±3,61, 7th week: 71,19±8,25, 9th: 76,62±5,61, IP-O; 3rdweek: 63,31±3,37, 5th week: 58,46±9,28, 7th week: 60,31±4,34, 9th week: 58,08±12. Maximum phenylephrine contraction responses were lower in the heterochronic parabiosis group ($p\leq0.05$).

CONCLUSION: The parabiosis model may have improving effect on endothelial disfunction.

Keywords: endothelium-dependent vasodilation, parabiosis, vascular tonus

OC12

Effects of Adropin and Spexin on Cardiac Inflammatory Markers; Chronic Renal Failure Model

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AIM: One of the most common cause of death in developed countries is cardiovascular diseases. Chronic renal failure (CRF) is an important risk factor for cardiovascular diseases such as pericarditis, hypertension, cardiomyopathy. In this study; the possible protective effects of newly identified spexin and adropin peptides on cardiovascular damage in adenine-induced chronic renal failure model were investigated.

METHODS: Wistar albino rats of both sexes divided as (180-220g, N=35) vehicle (5%CMC, 1 ml/kg, po) or CRF (adenine, 600 mg/kg, 5% CMC, 10 days/po) groups. CRF group was divided as saline (SF; 1 ml / kg, n = 7), adropin (2.1 g / kg / ml, n = 7), spexin (35 g/kg/ml, n=7) or adropin + spexin(n=7). Following the experimental procedure, rats were sacrificed at 4 weeks and serum and tissue samples were taken. Serum chemokines (eotaxin, group-alpha, IP-10, MCP-1, MCP-3, MCP-1a, MIP-2, rantes) and cytokines (G-CSF, IPN-g, IL- 2, IL-4, IL-5, IL-10, IL-12, IL-13 and IL-17α) were measured. Immunohistological staining was performed on aortic and cardiac tissues. Data were expressed as mean ± standard error, statistical analyzes were compared with ANOVA.

RESULTS: While eotaxin and rantes levels of chemokines increased in CRF (1247.0±130.2 vs 207.1±92.63; $p<0.05$) and spexin group (946.4±75.26; $p<0.05$), there was a decrease in Group-α levels (167.8±34.02 vs. 56.93±25.46; $p<0.05$). While MCP-1, MCP-2 and MIP-2 levels decreased in CRF group, it increased in adropin and adropin+spexin treated groups ($p<0.05$). In CRF group, G-CSF, IFN-γ, IL-4, IL-5, IL-10, IL-12 and IL-17α levels increased significantly (respectively: 20.15±1.86 vs 29.44±8.04; $p<0.05$, 20.15±1.86 vs 31.46±7.68, $p<0.05$, 7.46±2.71 to 14.41±5.03; $p<0.01$, 8.36±3.78 vs 13.96±2.02; $p<0.05$, 14.75±3.56 vs 26.73±7.45; $p<0.01$, 50.58±5.46 vs 90.77±31.95; $p<0.05$, 1.68±0.64 vs 5.75±3.45; $p<0.01$). G-CSF, IFN-g, IL-5 and IL-10 levels were decreased in the spexin and/or adropine groups ($p<0.01$).

CONCLUSION: In our study, therapeutic effects of adropin and spexin on some chemokines and cytokines in CRF-induced cardiac inflammation were demonstrated.

Keywords: Adropin, spexin, chronic kidney disease, cardiovascular, inflammation

OC13

The Effect of Different Doses Apelin 13 on Erythrocyte Deformability in Rats

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AIM: Apelin and apelin receptor (APJ) form a signaling pathway and are widely expressed in a variety of tissues including the heart, kidney and vessels. Apelin and APJ have various effects in many systems such as regulation of blood pressure and vascular tone, cardiac contractility, nociception, heart rate, apoptosis, inflammation. The fact that apelin can be used as a protective and therapeutic agent in the future will make important contributions both for human health and economically. Therefore, we aimed to investigate the effects of apelin-13 administration on erythrocyte deformability in rats.

METHODS: Thirty male Wistar Albino rats were randomly divided into 5 groups. Rats were identified as control, Apelin-25, Apelin-50, Apelin-100 and Apelin-200 groups. Apelin-13 was administered intraperitoneally at 25, 50, 100 and 200µg/kg. The same volume of saline was administered intraperitoneally to the control group. After the administration, intraperitoneal ketamine 100 mg / kg was administered to all rats and euthanasia was performed. Erythrocytes were obtained from heparinized whole blood samples. Deformability measurements were performed on erythrocyte suspensions in phosphate buffered saline. For the measurement of erythrocyte deformability, a constant flow filtrometer system was used and the relative resistance was calculated.

RESULTS: The erythrocyte deformability index was significantly different between the groups ($p=0.043$). Apelin application of 200 µg/kg was found to increase the relative resistance. The erythrocyte deformability index was significantly higher in the 200 µg/kg Apelin group compared to the control and 50 and 100 µg/kg Apelin groups ($p=0.030$, $p=0.027$, $p=0.011$, respectively). The deformability index of the control group and Apelin 25, 50 and 100 µg/kg groups were similar.

CONCLUSIONS: We did not find any studies about the effects of apelin on erythrocyte deformability in different doses in the literature. We found that high-dose apelin-13 administration adversely affected erythrocyte deformability. However, these findings should be supported by clinical and experimental studies in more detailed and large series.

Keywords: Apelin 13, erythrocyte deformability, rat

OC14

Determination of Hemorheological Parameters in Patients with Major Depression

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AIM: Cardiovascular disease (CVD) incidence is high in patients with major depression. CVD have been related to high blood viscosity. This study aimed to evaluate the determinants of blood viscosity, in patients with major depression.

METHODS: Patients diagnosed to have major depression (n=25) according to DSM-V criteria. The level of depression was determined by Beck Depression Inventory Hamilton Depression Scale. Depression duration was not determined. Recurrence rates of major depression episodes were recorded. Control group (n=30) received a psychiatric interview excluding major depression. All participants were between 18-65 years old. Individuals with CVD, hypertension, diabetes mellitus and smokers were excluded from both groups. Blood viscosity was evaluated through hemorheological parameters. Plasma viscosity was determined by cone-plate viscometer at 900 sec^{-1} (120rpm) shear rate. Erythrocyte deformability and aggregation were determined by LORCA (laser-assisted optical rotational cell analyzer). Measurements were made at 37°C. "t test" and "Mann Whitney U test" were used as statistical methods.

RESULTS: Compared with the controls, plasma viscosity of the patient group was higher (1.33±0.09 and 1.39±0.02 mPa.sec respectively) and erythrocyte deformability index at 0.53Pa shear stress was lower (0.065±0.002 and 0.059±0.002 respectively) ($p<0.05$). Erythrocyte aggregation parameters: AMP, AI, t½ and γIscmax revealed no statistically significant difference between groups. Complete Blood Count revealed no difference in erythrocyte count, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, red cell distribution width and leukocyte count between groups. Mean corpuscular hemoglobin concentration was lower in the patient group ($p<0.05$).

CONCLUSION: High plasma viscosity and low erythrocyte deformability in patients with major depression may contribute to the high risk for cardiovascular diseases. Further studies carrying out long-term follow-up of patients with major depression and relating the initial hemorheological findings to emerging cardiovascular problems are needed to clarify the link between depression and cardiovascular diseases.

Keywords: Erythrocyte Aggregation, Erythrocyte Deformability, Hematocrit, Hemorheology, Major Depression, Plasma Viscosity

OC15

Effects of Estrogen and Estrogen Receptor Agonists on Acetaminophen-Induced Hepatorenal Toxicity in Rats

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AIM: Acetaminophen (APAP) is the most widely used analgesic, and APAP-induced intoxication is most common among voluntarily taken drugs. When taken at above-treatment doses, APAP becomes toxic on liver and kidneys. Estrogen receptor (ER) subtypes have been reported to have antioxidant and anti-inflammatory effects. The aim was to investigate the role of sex in APAP toxicity and therapeutic effects of treatment with selective estrogen receptor agonists on this toxicity.

METHODS: Wistar albino female (n=56) and male (n=16) rats were used. Female rats underwent overiectomy (OVX) or sham-OVX under ketamine anesthesia. Forty days after OVX, rats were injected subcutaneously (each, 1mg/kg/day) with 17β-estradiol, ERα agonist propyl-pyrazol-triol (PPT), ERβ agonist diarylpropionitrile (DPN) or vehicle (oil), while male and sham-OVX rats were injected with vehicle for 10 days. On 49th day, rats were orogastrically given APAP (3g/kg) or saline (control) and decapitated 24 hours later. Renal and hepatic myeloperoxidase activity, antioxidant glutathione levels and luminol/lucigenin chemiluminescence levels, and serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN) and creatinine levels were measured. Histopathological examinations were performed. ANOVA and Mann Whitney-U tests were used for data analysis.

RESULTS: Compared to control group, serum AST, ALT, BUN and creatinine levels in the APAP-given male, OVX and sham-OVX groups were elevated, while hepatic histological damage scores, renal myeloperoxidase activity were increased, hepatic glutathione levels were depleted ($p<0.001$). However, hepatic MPO activity was increased only in male rats ($p<0.05$). PPT treatment reversed changes in both kidney and liver ($p<0.05$-0.001), while DPN and 17β-estradiol replenished glutathione levels in the liver and reduced renal MPO activity and creatinine levels ($p<0.05$-0.01).

CONCLUSIONS: Except an additional increase in hepatic neutrophil infiltration in males, acetaminophen-induced acute hepatorenal toxicity was similar in female/male sex or in menopause, while pretreatment with ER agonists provided protection by decreasing toxicity-induced oxidative damage.

Keywords: Acetaminophen, estrogen receptors, hepatorenal toxicity, antioxidant

OC16

Assessment of the Blood and Salivary Level of Oxidative Stress and Insulin Resistance Factors in Gestational Diabetes Mellitus

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AIM: Gestational diabetes mellitus (GDM) is a medical complication of pregnancy mirroring the prevalence of type 2 Diabates Mellitus (DM). Present study is aimed to investigate the plasma and salivary levels of malondialdehyde (MDA) and nitric oxide (NO) which are biomarkers of oxidative stress, sulfhydryl compounds (RSH) and thioredoxin reductase (TrxR) that have been implicated in antioxidant defense, and chemerin which plays a role in insulin sensitivity in normal pregnancy and GDM.

METHODS: Study group (n=51) which are systemically healthy, mean of ages Control=30,2±4,1, GDM=32,1±4,3 (p>0,05), and body mass index Control=24,2±2,9 and GDM=25,7±2,5 (p>0,05) were divided into two groups as control (n=29) and GDM groups (n=22) diagnosed by administering oral glucose tolerance test (50-100g). Saliva samples were collected without stimulation between 08.30-10.00 am. Then salivary and blood TrxR and chemerin levels were measured by Elisa method using commercial kits whereas saliva and plasma MDA, RSH and NO levels were determined by spectrophotometric analysis. The Ethical approval accession number:10.02.2014/78. Statistical analysis was performed by Shapiro Wilk, Mann Whitney U, Student's t test. Statistical significance was assumed when $p<0.05$. Since the data hasn't show normal distribution, non-parametric tests were used and the median values were compared.

RESULTS: High density lipoprotein levels were significantly lower in GDM ($p<0.05$). The plasma and salivary levels of chemerin, NO, RSH showed no significant difference in GDM ($p>0.05$). GDM groups had significantly lower median plasma TrxR ($p<0.05$) whereas salivary TrxR level was significantly higher ($p<0.001$). The median plasma levels of MDA showed no significant difference between control and GDM ($p>0.05$) whereas salivary MDA levels were found to be statistically significant higher in GDM ($p<0.001$).

CONCLUSION: A good glycemic control with diet in GDM may explain that insulin resistance and oxidative stress parameters are not different from control.

Keywords: Gestational diabetes mellitus, insulin resistance, oxidative stress

OC17

Intracerebroventricular MOTS-C Infusion Suppresses Thyroid Hormone Secretion in Rats

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AIM: Discovered in 2015, Mitochondrial-derived peptide (MOTS-c) is a peptide with 16 amino acids encoded by mitochondrial DNA. Studies have shown that MOTS-c decreases obesity and insulin resistance and plays an active role in cell metabolism. In our previous study, we reported that intracerebroventricular (ICV) MOTS-c infusion increases feed intake in rats but does not cause changes in body weight. All these findings suggest that peptide may play a role in metabolic rate and energy balance. This study was conducted to investigate the effects of ICV MOTS-c infusion on thyroid hormone secretion in rats.

METHODS: Forty male Wistar-Albino rats were used in the study. The rats were divided into 4 groups (n = 10) each with approximately body weights. Osmotic mini-pumps were attached to the brain infusion kits placed in the lateral ventricles of rats other than the control group and a volume of 5µl/h infusion were applied (yBOS in the sham group, 10 and 100 µM MOTS-c in the treatment groups) for 14 days. At the end of the infusion after the decapitation of rats, brain (hypothalamus) and blood samples were collected. TRH mRNA level was determined by using RT-PCR method from the hypothalamus tissue and serum TSH, T3 and T4 hormone levels were determined from blood samples by ELISA method.

RESULTS: In rats, MOTS-c infusion partially reduced TRH mRNA levels, but significantly decreased serum TSH, T3 and T4 hormone levels ($p <0.05$).

CONCLUSION: The results of the study show that MOTS-c can play important physiological roles in the hypothalamus-pituitary-thyroid axis. If the effect of MOTS-c on the HPT axis can be explained in more detail, a different approach will be obtained for the treatment of these axis-based diseases. This study was supported by TUBITAK (Project:116S744).

Keywords: MOTS-c, TRH, TSH, T3, T4

OC18

Vitamin D, Parathormone, Bone Weight and the Amount of Mineral in Pre- and Post-Menopausal Obese Women

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AIM: The fact that vitamin D is lower in obese compared to normal weight individuals suggests that vitamin D may play a role in obesity. Therefore, we aimed to determine the relationship between vitamin D, Parathormone (PTH), bone weight and the amount of mineral in pre- and post-menopausal obese women.

METHODS: 200 pre-menopausal and 200 post-menopausal obese women were included in our study (Ethics Committee Number: 2019/0212). Body composition was measured with bioelectrical impedance analyzer (TANITA-48M) and blood parameters were determined by biochemical tests. Student's t, Mann-Whitney U, Shapiro-Wilk, Spearman's rho and Pearson correlation tests were used and $p<0.05$ was considered statistically significant.

RESULTS: According to the obesity classification, 71 pre-menopausal women and 68 post-menopausal women were class I obese, 77 pre-menopausal women and 61 post-menopausal women were class II obese, 52 pre-menopausal women and 71 post-menopausal women were class III obese. The mean vitamin D levels were 16.91±13.17 in pre-menopausal women and 22.59±16.49 in post-menopausal women ($p<0.05$). While 83.75% of 400 obese women had vitamin D deficiency or insufficient, 16.25% (65) of obese women had normal vitamin D values (>30 ng/mL-150 ng/mL). Age, weight, height, vitamin D, calcium and phosphorus levels, bone density, muscle mass, lean mass, the amount of mineral and basal metabolic rate were significantly different in pre- and post-menopausal women, ($p<0.05$). PTH and mineral amounts were negatively correlated with vitamin D in pre-menopausal women, while there was a negative correlation between body mass index, weight, fat and PTH with vitamin D in post-menopausal women ($p<0.05$).

CONCLUSIONS: The prevalence of low vitamin D in obese women was found 83.75%. As vitamin D levels decreased both body weight and PTH increased in obese women while only mineral amount increased in pre-menopausal women. Our findings suggest that obesity may be related to vitamin D levels.

Keywords: Obese women, vitamin D, pre-menopausal, post-menopausal

OC19

The Effect of Ileal Interposition in Rats With Metabolic Syndrome

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AIM: Metabolic syndrome (MetS) is a cluster of metabolic abnormalities that includes hypertension, central obesity, insulin resistance, and atherogenic dyslipidemia. It includes abdominal obesity, insülin resistance, elevations of serum triglyceride, glucose, blood pressure, and reduced HDL cholesterol. The presence of three or more of these constitutes a clinical diagnosis. Our aim is to prevent the evolution of the parameters that define the MetS, with ileal interposition (IT) technique.

METHODS: IT is a surgical procedure involving the transposition of a distal ileum segment to the proximal jejunum in a properistaltic direction. MetS was induced in male Wistar rats by neonatal administration of monosodium glutamate (4g/mg body weight, BW) during the 0, 2, 4, 6, 8, 10th days. Control group received saline (0,01ml/g BW) during the 0, 2, 4, 6, 8, 10 days. At the 5 month, Mets rats were submitted to ileal interposition or sham surgery. A 15cm segment was transected from 25 to 10cm proximal to the ileocecal valve. The jejunum was transected 5cm distal to Ligament of Treitz. The previously transected 15cm ileum segment was then interposed in an isoperistaltic fashion. After 2 months; lipid levels (HDL, LDL, TG, T-chol), abdominal obesity (perigonadal-retroperitoneal fad pad weighing), oral glucose tolerance test (OGTT), Lee index (by dividing the cubed root of body weight, by the nose-to-anus length), insulin resistance (HOMA-IR scor) and secretion were evaluated. Continuous variables were expressed as mean ± standard deviation and categorical variables as number and percentage.

RESULTS: In IT rats; retroperitoneal (Mets: 6,708 ± 0,523, IT: 2,396 ± 0,768, $p<0,05$), perigonadal (Mets: 6,104 ± 0,787, IT: 2,381 ± 0,629, $p<0,05$) fat content and Lee index (Mets: 0,321±0,003, IT: 0,306±0,002, $p<0,05$) statistically significant decrease was observed. It was also observed that IT caused improvement in insulin resistance (Mets: 12,935 ± 2,763, IT: 6,314 ± 1,115, $p> 0.05$) and impaired lipid profile (TG: 1,86±0,189, IT: 0,874±0,125, $p<0,05$) in the Mets group.

CONCLUSION: The primary effect of GLP-1 is that it stimulates insulin secretion. The observed results in our study may be due to the increase in GLP-1 level after metabolic surgery.

Keywords: Ileal interposition, metabolic syndrome, rat

OC20

Salivary Cortisol Levels Were Higher in Women Than Men at the Noon and in the Mid-Night

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AIM: Cortisol, the end product of the hypothalamopituitary (HPA) axis, is secreted into the bloodstream from the adrenal gland. In blood, cortisol is either in free or protein bound form. As a small steroid hormone, free cortisol easily passes into the saliva and therefore salivary cortisol represents the free or effective cortisol. Nowadays, measurement of salivary cortisol is widely used to assess the activity of HPA axis non-invasively. Aim of the current study was to measure salivary cortisol levels in women and men throughout a day.

METHODS: Women (n=54) and men (n=62), 18-to-32-year-old, were participated to the current study following ethical consent from Malatya Clinical Research Ethics Committee, Turkey. Saliva was collected at the 30th min of awakening, at noon and in the mid-night before sleeping. They were stored frozen until analyses by ELISA. Data did not have a normal distribution and Kruskal Wallis test was used for statistical analyses. Data were presented as median (min-max) and p less than 0.05 were denoted as significant.

RESULTS: Awakening salivary cortisol levels did not differ between the women and men (11.4 vs.14.7 ng/ml, respectively, P=0.499). However, salivary cortisol levels were higher in women than men at noon (13.3 vs 10.3 ng/ml, respectively, P=0.016) and at mid-night (6.5 vs. 5.5 ng/ml, respectively, P=0.042). Mean salivary cortisol was not different between the women and men (12.3 vs. 11.2 ng/ml, respectively, P=0.228).

CONCLUSIONS: The results suggest that men and women have different diurnal stress reactivity. Moreover, it seems that this reactivity is stronger in women than man from noon till mid-night. The significance of this difference remains to be elucidated but suggests a sexually dimorphic HPA axis observed in rodents (Oyola and Handa, 2017). Oyola MG and Handa RJ (2017). Stress, 20:476-494. Supported by the Scientific Research Unit (BAP, TDK-2017-812), İnönü University, Malatya.

Keywords: Salivary cortisol, woman and men stress level, hypothalamo-pituitary (HPA) axis

OC21

mTOR Inhibition and Melatonin Treatment Reduces Glioblastoma Cell Viability in Vitro

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AIM: Glioblastoma multiforme (GBM), grade IV astrocytoma, is the most common primary brain tumor with high malignancy and poor prognosis. The standard therapy includes the resection of the tumor followed by the radiotherapy or radiotherapy and chemotherapy combination. The phosphatidylinositol 3-kinase (PI3K)/AKT/mechanistic target of rapamycin (mTOR) pathway is indicated to be frequently deregulated in GBM. Melatonin is an indolic hormone and its anticancer activity has extensively been studied in vitro and in vivo. However, studies investigating effects of melatonin on GBM are limited. Therefore, in this study, effect of melatonin and mTOR inhibition with rapamycin on GBM viability was investigated in vitro.

METHODS: The human GBM cell lines A172 and U87-MG were maintained in DMEM containing 10% FBS and 1% PSN at 37 °C under 5% CO2 humidified atmosphere. Cytotoxicity of Rapamycin and melatonin were determined by WST-1 colorimetric proliferation assay following treating the cells with rapamycin and melatonin alone or in combination for 24 and 48h in 96-well culture plates. Cell viability was measured. Statistical analysis was done by Two-way ANOVA.

RESULTS: Rapamycin and melatonin differentially decreases GBM cell viability as at 24 h, melatonin significantly decreased the cell viability at 100 and 400μM doses in U87-MG, but not A172 (U87-MG: $p<0.001$ vs. Control and U87-MG vs. A172: $p<0.001$), while rapamycin was more effective in A172 cells at 48h at 20 nM ($p<0.001$). On the other hand, 100 nM rapamycin + 400 μM melatonin treatment were found to be more effective in U87-MG compared to A172 cell line ($p<0.001$) at both time points.

CONCLUSIONS: Our in vitro findings suggest that combinatorial treatment with melatonin and rapamycin may be an option for treatment in GBM. However, one should note the importance of genetic background differences in GBM. In vivo studies are needed to elucidate effectiveness of rapamycin and melatonin on GBM.

Keywords: mTOR, Glioblastoma, melatonin, cell viability

OC22

Green Synthesis of Mgs Nanoparticles and Their Effects on Neuroblastoma Cells

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AIM: Magnesium Sulphur nanoparticles (MgS NPs) is one of the important nano metals that are being used effectively in drug delivery systems. Neuroblastoma, which is the most common extracranial tumor of childhood, is a cancer which is extremely difficult to treat. This study was conducted to determine the anticancer activity and oxidant-antioxidant properties of MgS NPs.

METHODS: Magnesium Sulphur nanoparticles have been synthesized by green synthesis, a cleaner method for toxic effects. Na_2S and Punica granatum plant extracts were used in green synthesis method. In cell culture, aseptic conditions SH-SY5Y was developed in suitable nutrient medium. Five different (10, 25, 50, 75 and 100 µg/mL) doses of MgS NPs were applied on the cell line for 24 hours. The analysis of the study, which was conducted in a positive and negative controlled manner, was performed with MTT cell viability test and total oxidant and total antioxidant tests.

RESULTS: As a result, application of 75 µg/mL MgS NP dose was found to reduce cancer cell viability by 51.56% compared with the control. It has been determined that the effects of MgS nanoparticles increase especially with increasing doses. In light of the data obtained, it was noted that the oxidant effects of MgS nanoparticles increased in cancer cells in a correlation with MTT analysis.

CONCLUSIONS: The efficacy of MgS nanoparticles on cancer cells was clearly demonstrated by the tests performed. It is clear that nanoparticles synthesized by green synthesis have antiproliferative effect on SH-SY5Y cells.

Keywords: MgS NPs, SH-SY5Y, cancer cell lines, green synthesis, neuroblastoma (NBL)

OC23

Mir663 Prevents Erythropoietin Inhibition Caused By TNF-Alpha in Normoxia and Hypoxia

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AIM: In chronic inflammatory diseases, pro-inflammatory cytokines such as Tumor necrosis factor-alpha (TNF-α) are present in high amounts in the circulation. Experimental studies have shown that TNF-α inhibits the synthesis of Erythropoietin (Epo), the main stimulant of hematopoiesis. Our aim was to figure out which micro-RNAs are involved in the Epo repression by TNF-α.

METHODS: First we determined the dose of TNF-α in HepG2 cells that has no cytotoxic effect by MTT and that inhibits Epo synthesis by qRT-PCR and ELISA. Then we performed the micro-RNA array study with TNF-α (20 ng/ml) treated cells and array results were confirmed by qRT-PCR. We transfected miR663 group with the miR663 mimics (30 pmol) for 24 hrs, other groups treated with transfection reagent, followed by treatment of TNF-α and miR663 groups with TNF-α for 24 hrs, control group incubated with normal medium. We analyzed Epo mRNA level by qRT-PCR. If miR663 mimic prevents the Epo-repression by TNF-α more Epo dependent UT-7 cells would survive. So, we co-cultured HepG2 cells with UT-7 cells. Percentage of apoptotic UT-7 cells were determined by TUNEL assays.

RESULTS: According to our array study, TNF-α significantly decreases miR663 expression. After transfection of miR663 mimics into HepG2 cells, TNF-alpha was unable to decrease Epo mRNA amounts. Furthermore, miR663 mimics transfection resulted in a lower apoptosis rate of UT-7 cells in co-culture experiments.

CONCLUSIONS: miR663 is involved in Epo mRNA production and that is able to prevent or reverse the inhibitory effect of TNF-α. In our co-culture study, transfecting HepG2 cells with miR663 mimics decreased apoptosis of UT-7 cells. This study is supported by The Scientific and Technological Research Council of Turkey (TUBITAK, no: 216S729), by the Eskisehir Osmangazi University Scientific Research Projects Committee (no: 2017-1635), Turkey and by Erwin-Riesch-Stiftung, Germany.

Keywords: Array, erythropoietin, inflammation, miRNA, TNF-α

OC24

Investigation of the Effect of Melatonin Administration on Calpain-1 Expression and Atrophic Morphology in Atrophy of Mouse Myoblast Cell Line Exposed to Hydrogen Peroxide

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It is known that oxidative stress is the main factor in the formation of disuse muscle atrophy, the most common type of muscle atrophy. The first important damage which is exerted by oxidative stress on proteases such as calpain-1 has been demonstrated in several studies. Treatment options include antioxidants, and in these groups mitochondrial targeting antioxidants such as melatonin have been shown to be more effective.

AIM: In this study, we aimed to determine the effect of melatonin treatment on oxidative stress-induced atrophy morphological change, calpain-1 expression and redox balance in C2C12 muscle cells.

METHOD: We have used H_2O_2 to generate oxidative stress. Four groups of C2C12 cells were created as K(Control), M(Melatonin), H(H_2O_2), M+H (Melatonin+ H_2O_2) groups. For morphological evaluation, measurement of myotube diameter with Image J Program was performed. In the second step, the amount of calpain-1 protein from total protein lysates was measured by western blot method. TAS and TOS kits were used to find out the antioxidant/oxidant statuses of the cells. Statistical analyzes were performed in SPSS program. The level of significance was set at $p < 0.05$.

RESULTS: There was a statistically significant decrease in the mean myotube diameters of the H group compared to the other groups (K, M, M+H) and statistically significant increase in mean myotube diameter of M group compared to K and H groups. The expression level of calpain-1 protein was increased in H, M and M+H groups compared with K group. TOS was higher in the H group than other groups. The highest mean TAS value was seen in the H group (rebound effect).

CONCLUSION: These results suggest that H_2O_2 produces muscle atrophy in C2C12 cells and that melatonin prevents morphological change and in addition to calpain-1 protein, other mechanisms can also take part in the prevention of disuse muscle atrophy. Functional studies need to be carried out to better explain this effect.

Keywords: Muscle atrophy, calpain 1, melatonin, mitochondria targeted antioxidants, redox balance

OC25

Acute Effects of Intermittent Exercise Performed at Anaerobic Threshold Level on Vascular Function in Healthy Young Men

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AIM: Although the effect of different intensity exercise is known, the intermittent exercise effects on vascular endothelial function is unknown. Vascular endothelial function of intermittent exercise which interspersed by short resting intervals performed at the anaerobic threshold levels were compared with continuous exercise.
METHODS: Peak oxygen consumption (VO_2 peak) was determined by analysis at breath by breath in physically active 18-24 years old healthy men (n=12). Intermittent exercise consisting of 1 minute long 8 loads and 75 second rest periods is described on the bicycle ergometer and the duration of the continuous exercise at the same workload was determined. After 2 exercise bouts with 1-week break in between, venous blood lactate levels were measured immediately. Brachial artery flow-mediated dilation (FMD) was measured at baseline and at 30 minutes after exercises. Endothelial nitric oxide synthase (eNOS), endothelin-1, adiponectin levels were measured by ELISA in serum obtained at 5 and 60 minutes after each exercise. Sample size was calculated according to differences of adiponectin in moderate intensity, intermittent and continuous exercise, with power analysis ($d=0.8$ and $\alpha=0.05$). Wilcoxon Signed Ranks Test was used for statistical comparisons.

RESULTS: Mean VO2peak (33.42 ± 5.9ml/min/kg) and anaerobic threshold levels (47.33±5.85%) of the participants were determined. Blood lactate levels of continuous exercise were found to be higher than intermittent exercise (27.76 ± 7.43mg/dl, 18.54 ± 4.87mg/dl; $p<0.05$, respectively). There was no difference in FMD response after both exercises (7.05±15.11%; 2.49±16.24%). Endothelin-1, eNOS activity, and adiponectin levels were not different before and after in intermittent and continuous exercises.

CONCLUSION: Considering the increase in blood lactate levels in continuous exercise, resting periods can be factor that facilitates adaptation for individuals who feel difficulty in exercising. However, we suggest that intermittent or continuous exercise at the anaerobic threshold level in healthy men does not produce a significant acute change in endothelial function.
The study was supported by TUBAP (2018/100). Ethical approval (05/22).

Keywords: Anaerobic threshold, intermittent exercise, FMD, vascular function

OC26

The Protective Effect of Weekend Warrior and Continuous Exercise Models on Depression Induced Cognitive Impairment

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AİM: Depression is an important physiopathological process that goes on with cognitive decline. Exercise improves depressive mood. Our aim was to show the role of weekend warrior and continuous exercise models on cognitive impairment in depression, to exhibit the possible underlying mechanisms.
METHODS: Male rats (n=36) were separated as; Sedentary (SED), weekend warrior (WW: moderate intensity swimming 75 min/day, 2 days/week) continuous exercise (CE: moderate intensity swimming 30 min/day, 5 days/week) groups. The groups were then divided into subgroups according to depression induction with chronic mild stress (CMS) procedure (n=6/group). CMS and exercise protocols continued for 6 weeks. Cognitive functions were evaluated by object recognition and fear conditioning, anhedonia by sucrose preference, anxiety like behavior by Porsolt, open field and elevated plus maze. Following decapitation, brain tissue glutathione (GSH) levels, superoxide dismutase (SOD), catalase (CAT), as an indicator of inflammatory response myeloperoxidase (MPO) activities, malondialdehyde (MDA) level were measured, tissue damage was evaluated. Data was analyzed by ANOVA, student's t tests, $p<0.05$ was significant.
RESULTS: Cognitive function, sucrose preference was decreased with CMS, increased in both CMS-induced exercise groups ($p<0.05$). Increased freezing time with CMS was decreased in CMS+WW group ($p<0.05$). Suppressed SOD, CAT activities in SED+CMS group and also GSH content were improved via both exercises ($p<0.05$). MPO activity, MDA levels was increased with CMS and reinstated back with both exercises ($p<0.05$). Latency in Fear Conditioning Test decreased with CMS ($p<0.05$) and increased with CE ($p<0.05$). The rearing number was decreased with CMS and improved with CE ($p<0.05$). Histopathological grade changes of damage in neurons was alleviated with both exercises. CMS-induced memory decline was improved by both exercise protocols via suppressing inflammatory process, anxiety level, by improving antioxidants.
CONCLUSION: WW had similar effect with CE on CMS-induced depression model by improving cognitive function, decreasing anxiety like behavior, anhedonia, repressing inflammatory process and improving antioxidant system.
Keywords: Cognitive function, depression, exercise, weekend warrior,

OC27

Comparative Evaluation of Effective Exercise Intensity Using Metabolic Equivalent and Anaerobic Threshold

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AIM: Metabolic Equivalent (MET) and anaerobic threshold (AT) are commonly used methods to determine exercise intensity levels. We aimed to evaluate effectiveness of MET and AT comparatively on determination of exercise intensity in young male subjects.

METHODS: Total of 31 male participated to this study (20.7±2.0 years, 72.1±9.6 kg, 179±8 cm). Each subject performed an incremental exercise test (15 W/min) to their maximal levels using a cycle ergometer. Ventilatory and pulmonary gas exchange parameters were measured by using metabolic gas analyzer and turbine volume transducer and evaluated breath-by-breath. AT was estimated using V-slope method. One MET is equal of 3.5 millilitres of O2 consumed per kilogram of body weight per minute (mL/kg/min). Pearson correlation analysis and paired-t test were used for statistical analyses ($p<0.05$).

RESULTS: The work rates (mean ± SD) at the AT and maximal exercise were found to be 135±19 W and 220±26 W, respectively. O2 uptakes at the AT and at maximal exercise were found to be 1.89±0.26 L/min and 3.02±0.35 L/min. MET at the AT was varied from 5.71 to 9.98 and averaged 7.59±1.2. AT occurred 62% of maximal oxygen uptake (minimum 53% and maximum72%). There was a low but significant correlation between percent of AT and MET values ($R=0.43497$, $p=0.01$).

CONCLUSION: Moderate exercise intensity based on MET parameter is generally varies between 3 to 6. In addition, AT that reflects the onset of metabolic acidosis, also indicates moderate exercise intensity. However, MET <6 observed in only 4 subjects (12%) at the AT reflecting moderate intensity and >6 observed in 27 subjects (88%) reflecting higher exercise intensity. Consequently, AT is a more accurate tool for determining exercise intensity compared with MET due to the variations in fitness status of each individual.

Keywords: Anaerobic threshold, metabolic equivalent, oxygen uptake

OC28

Determination of Time-Related Muscle Damage/ Regeneration and the Pathways Involved in Response to Swimming Exercise in Mice

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AIM: Maintaining muscle mass is important in quality of life. Although exercise is known to have beneficial effects on muscles, pathways involved and time-dependent muscle damage and regeneration processes in response to swimming exercise have not been elucidated. The aim of this study was to investigate early, late skeletal muscle damage, regeneration as well the pathways involved in response to acute, prolonged swimming exercises.

METHODS: 8-12 weeks old male mice were divided as control and swimming. After exercise groups were divided into acute and chronic, each group was further divided in terms of time (3, 24 hours) passed from the last exercise session till the end of the experiment. Acute exercise was applied as 30 min, one session, chronic group swam 5 days/week, 6 weeks, 30 min/day. Plasma creatine kinase (CK) activity was measured by a kit. Muscle damage, percentage of muscle damage, histological damage score (H-score) and leukocyte infiltration were determined using gastrocnemius-soleus muscles. Real-time PCR was used to validate whole-transcriptome results. Data were evaluated with Kruskal Wallis Analysis of Variance, Mann Whitney U test with Bonferroni Correction. $p<0.05$ was considered statistically significant. The study was approved by the ethics committee (PAUHADYEK-2017-17).

RESULTS: The percentage of muscle damage, H-score and leukocyte infiltration were higher in exercise groups compared to control. Increases in acute 3 hour, acute 24 hour, chronic 3 hours groups were statistically significant ($p<0.05$, $p<0.001$, respectively). No significant difference was observed in CK activity. Expression changes of skeletal muscle actin alpha-1 *acta1*, somatic cytochrome c *cycS*, skeletal fast 2 troponin I *tnni2* genes which demonstrated most dramatic expression changes in whole-transcriptome analysis were confirmed by real-time quantitative PCR.

CONCLUSION: Based on the findings and literature, the pathways involved in skeletal muscle damage and regeneration in response to swimming exercise were drawn. This study was supported by PAUBAP (2017SABE014).

Keywords: Swimming exercise, skeletal muscle regeneration, muscle damage, creatine kinase, real-time PCR

OC29

Effects of Nicotine Administration on Anxiety Tests in Nicotine Preferred Rat Lines

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AIM: Studies show that nicotine reduces anxiety and stress. This effect may contribute to development of addiction. In our laboratory, nicotine-preferring (NP) rat line is generated using selective breeding. This study aimed to reveal the regulatory effect of genetic background, which increases tendency to addiction, and chronic nicotine treatment on anxiety. Accordingly, we studied the changes in anxiety-like behavior observed before (basal) and after nicotine exposure in NP rat lines and their controls.

METHOD: This study involved 4 groups (n=12): Control-Males (CM), Control-Females (CF), NP-Males (NPM), NP-Females (NPF). In all groups, anxiety tests [open-field (OF), marbel-burying (MB), forced-swim (FS)] were performed during basal state. Anxiety tests were repeated during the last two weeks of forced oral nicotine (50 μg/ml) administration (seven-weeks).

RESULTS: In OF-test, nicotine decreased total distance traveled and speed (indices of locomotor activity) in all groups ($p\leq0.001$); NP-groups traveled less than controls. Number of line crosses in outer zones decreased in NP-groups ($p\leq0.001$), males ($p=0.029$) and with nicotine ($p<\neg0.002$). In NP-groups, time spent in outer zones was less than controls ($p=0.016$) which is reduced further by nicotine. There was a main effect of line on the number of line crosses (increased in NP-groups, $p=0.005$) and time spent in inner zones; NPM spent more time than controls ($p=0.001$).
In MB-test, burying behavior decreased in NP-groups ($p=0.005$) and females ($p=0.012$); nicotine exposure reduced marble burying in all groups ($p=0.002$). In FS-test, nicotine had no effect on immobility time. Diving ($p<0.001$) and struggling ($p<0.001$) were decreased with nicotine exposure, whereas swimming was increased ($p<0.001$).

CONCLUSION: All tests demonstrated that nicotine reduced anxiety in all groups. OF and MB tests showed that basal anxiety in NP-groups was lower than controls. However, OF-test showed that nicotine decreased anxiety-like behavior more in NP-groups. These findings indicate that the genetic background that plays a role in nicotine dependence is associated with anxiety.

(Research Fund Grant TYL-2018-20417 EÜHADYEK 2019-001).
Keywords: Nicotine, anxiety, nicotine preferred rat line

OC30

Effect of Oral Nicotine Administration on Expression of Neuropeptide Y and Neuropeptide Y2 Receptor in Rat Brain

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AIM: Neuropeptide-Y (NPY), one of the most common neuropeptides in brain, plays crucial role in many physiological processes including addiction. Nicotine is a compound causes addiction. It has been reported that withdrawal-induced stress and negative affect may be associated with NPY. Studies report anxiogenic effects of NPY through NPY-Y2 receptors. However, this subject is not studied comprehensively. The aim of our study is to investigate expressions of NPY and NPY-Y2 receptor in different brain regions after oral nicotine exposure and withdrawal.

METHODS: Forty adult, male Wistar rats were used for study. Rats were divided into four groups as Control (n=10), Nicotine (n=10), 24-hour withdrawal (24-W, n=10) and 48-hour withdrawal (48-W, n=10). Tap water was given to controls, while three other groups received forced oral nicotine (50µg/ml in tap water) for 12 weeks. After nicotine treatment, Control and Nicotine groups were decapitated 60 minutes, whereas 24-W and 48-W groups were decapitated 24 and 48 hours after removal of drinking bottles, respectively. Prefrontal cortex (PFC), hippocampus, nucleus accumbens, dorsal striatum, ventral tegmental area, medial hypothalamus, septum and amygdala were dissected. NPY/NPY-Y2 expressions were analyzed using qRT-PCR. SPSS v25 was used for statistical analyses.

RESULTS: NPY expressions were increased in PFC of 48-W compared with other groups ($p<0.001$) and in hippocampus of Nicotine group compared with control ($p=0.007$) and 24-W ($p=0.048$). There was an upregulation of NPY in amygdala of 24-W compared with control ($p=0.027$) and 48-W ($p=0.036$). NPY-Y2 expression was increased in PFC of 48-Y compared to control and Nicotine group ($p<0.001$).

CONCLUSION: We can suggest that regulation of NPY/NPY-Y2 receptor expression by nicotine withdrawal may be related to withdrawal-induced negative affect and contribute to development of addiction. This study was supported by Ege University Scientific Research Projects Commission (project numbers: 18-BAUM-001 and TYL-2019-20469) and approved by Institutional Animal Ethics Committee of Ege University (approval number:2017-101).

Keywords: Amygdala, hippocampus, neuropeptide Y, nicotine, NPY-Y2, prefrontal cortex

OC31

The Effect of CDP-Choline on Hippocampal tCAMKII, pCaMKII and pCREB Levels in REM-Sleep Deprived Rats

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AIM: The aim of this study was to investigate the effects of cytidine 5-diphosphocholine (CDP-choline) on learning, memory and long term potentiation (LTP) in REM sleep-deprived (SD) rats.

METHODS: Male Wistar albino rats (n=72, 200-300 g, 8-12 weeks old) were randomized to 12 groups and placed in appropriate cages. Sleep deprivation or environmental control was induced by placing rats on a platform with 6.5cm or 13cm diameter, respectively, for 4 days according to Flower pot method. Learning parameters were tested for 4 consecutive days and on the 5th day memory parameters were tested in Morris Water Maze (MWM). 30 minutes before the MWM, saline (S) or 100 µmol/kg (C100), 300 µmol/kg (C300), 600 µmol/kg (C600) doses of CDP-choline were administered intraperitoneally. After behavioral tests rats were decapitated and pCREB, tCaMKII and pCaMKII proteins were analyzed in hippocampus homogenates using Western-blot (WB) technique. The groups were compared using One-Way ANOVA and Student's t test.

RESULTS: Escape latencies decreased significantly in all groups ($p<0.001$). REM sleep deprivation impaired memory parameters ($p<0,001$) and latency of the first occurrence in platform area was significantly ($p<0,001$) shorter in rats receiving CDP-choline ($p<0.05$). WB analysis revealed that, tCaMKII ratio was unchanged while the pCaMKII ($p<0,05$) and pCREB ($p<0,01$) ratios were decreased as a result of sleep deprivation. Also, pCaMKII levels were greater in SD+C600 group compared to those receiving saline ($p<0,05$).

CONCLUSION: We observed that REMSD has no effect on learning but may impair memory and CDP-choline can reduce the impairment in memory parameters. We determined that the model used to generate REMSD may cause stress and escape latencies of REMSD rats were shorter on the first two days of the MWM, which is probably associated with exploratory behavior due to enhanced stress. Therefore, stress affects the learning, memory and CDP-choline may have positive effects on stress. We observed that sleep deprivation diminishes important proteins in LTP pathway.

Keywords: REM sleep deprivation, Morris water maze, learning, memory, CDP-choline

OC32

The Role of Sex in Maternal High Fat Diet Induced Changes in Autonomic Signaling

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AIM: Exposure to high fat diet (HFD) during perinatal age has been shown to induce neuroplastic changes in autonomic circuitry. Using rats exposed to maternal HFD, this study was designed to investigate the short and the long term changes in autonomic outputs and the role of sex in these changes.

METHODS: Pregnant rats were fed with HFD from prenatal day-14 to postnatal day-21. ECG was recorded and HRV was analyzed in 10- and 20-week age male and female offsprings. In anesthetized rats, (ketamine 60 mg/kg; xylazine 6 mg/kg, ip) muscarinic receptor blocker atropine (2 mg/kg, ip) or beta adrenergic receptor blocker propranolol (4 mg/kg, ip) was administered following a baseline recording, then drug-induced changes were recorded. Differences among the groups were analyzed by Mann Whitney-U test. Experimental protocols were approved by the Animal Ethical Committee of Akdeniz University (2017.09.005).

RESULTS: Compared to control rats, high frequency component (HF) was found to be lower in 10-week old male rats exposed to maternal HFD; low frequency component (LF) and LF:HF, an indicator of sympatho-vagal balance was found to be significantly ($p<0.05$) higher. These changes were restored in 20-week old male rats. In 20-week old female HFD rats, HF component was recovered, in contrast, LF component and LF: HF were measured significantly higher ($p<0.05$) compared to the control rats. Moreover, a desensitization of atropine- and propranolol-induced responses in heart rate and HRV components was detected in 20-week old female rats exposed to maternal HFD.

CONCLUSIONS: The present data indicate that perinatal HFD-induced alterations in autonomic signaling were restored in male rats, while, increased sympathetic tone exhibited a sustained pattern in female rats.

Keywords: Heart rate variability, high fat diet, sex, sympathetic tone

OC33

Effects of Angiotensin IV on Learning-Memory and Hippocampal Oxidative Stress in Diabetic Rats

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AIM: The angiotensin IV molecule and its receptors are one of the leading molecules in the brain renin-angiotensin system and have been associated with the regulation of cognitive functions. In this study, we aimed to investigate whether angiotensin IV has a protective effect on cognitive functions and oxidative stress in streptozotocin-induced diabetic rats.

METHODS: 32 male Wistar albino rats, 250-300 g, were used and divided into four groups of control, diabetes, angiotensin IV (5 µg/kg, sc, 21 days) and diabetes+angiotensin IV. Diabetes was induced by intraperitoneal administration of Streptozotocin (60 mg / kg) and blood glucose were measured. The Morris water maze test performed to determine the learning and memory levels of rats at 21st day. In addition, hippocampi were taken for biochemical analysis. Statistical analyzes were performed with the Instat Statistical Package Program at $p<0.05$ significance level. Comparison between groups performed with One-Way ANOVA or Kruskal Wallis tests. Post-hoc comparisons were performed with Bonferroni and Dunn tests.

RESULTS: Time spent in platform area in diabetes group was lower than the control group ($p<0.05$) and the Ang IV group was higher than the diabetes group ($p<0.001$). There was no significant difference between control and D+Ang IV group. Superoxide dismutase, glutathione peroxidase and malondialdehyde levels increased in diabetic group compared with control group ($p<0,01$) and decreased in Ang IV group compared with diabetes group ($p<0.001$). Brain-derived neurotrophic factor levels were lower in the diabetes group compared with the control group ($p<0.01$), but increased in the Ang IV and D+Ang IV groups compared with the diabetes group ($p<0.001$, $p<0,05$).

CONCLUSIONS: It is suggested that exogenous administration of angiotensin IV has a positive effect on impaired spatial learning and memory and hippocampal oxidative stress in diabetic rats. This project was supported by Istanbul University-Cerrahpasa Scientific Research Projects Unit.

Keywords: Diabetes mellitus, hippocampus, angiotensin IV, cognitive functions, oxidative damage

OC34

N-(P-Amylcinnamoyl) Anthranilic Acid Attenuates Remedial Effects of Memantine on Memory Deficits Following Intracerebroventricular Streptozotocin Administration in Rats

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AIM: Alzheimer's disease (AD), a neurodegenerative disease, accounts for great majority of dementias. Current drugs are not capable of halting the progression of AD. So, more effective novel agents are urgently needed. N–(p–amylcinnamoyl) anthranilic acid (ACA) is an antagonist of transient receptor potential melastatin–2 (TRPM2) which is a non–selective, Ca^{2+} –permeable cation channel. Oxidative stress is a substantial etiologic entity for AD pathogenesis. Cellular stress leads to ischemia and Ca^{2+} accumulation by activating TRPM2. Effect of ACA on memory impairment associated with AD has not been known. The aim of the study is to relief oxidative stress and improve spatial memory by administering ACA treatment.

METHODS: A total of 60 Wistar rats randomly divided into six groups; (1) control, (2) sham–operated, (3) intracerebroventricular (ICV)–STZ, (4) ICV–STZ + memantine (5 mg/kg ip), (5) ICV–STZ + ACA (25 mg/kg ip) and (6) ICV–STZ + ACA + memantine.

RESULTS: Only memantine (5 mg/kg) treatment exhibited a therapeutic efficacy in Morris water maze test. Western blot analyses in hippocampal tissues showed that TRPM2 protein expression was markedly suppressed in 3rd group ($p<0.001$). ACA, memantine or memantine + ACA treatments ameliorated that suppression ($p<0.05$, $p<0.01$, $p<0.01$).

CONCLUSION: Our findings showed for the first time that TRPM2 protein expression was significantly suppressed in the rat model of STZ–induced memory impairment while each of the ACA, memantine and ACA + memantine treatments reversed this suppression. However, ACA did not provide any improvement in spatial memory, instead it worsened the spatial memory.

Gaziantep Experimental Animals Local Ethics Committee Decision No: 2017/32

Keywords: Memantine, N–(p–amylcinnamoyl) anthranilic acid, TRPM2

OC35

Effect of Neurokinin 3 Receptor on Cognitive Behavior and Catecholaminergic System in a Rat Experimental Alzheimer Model

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AIM: Alzheimer's disease is considered to be a form of progressive/ irreversible dementia that creates serious health problems with increase of aging population. Cognitive impairment usually begins nearly with memory damage, progresses to loss of daily living activities. It is known that catecholaminergic systems are commonly affected in AD. Neurokinin B is tachykinins family hormone. Neurokinin 3, NKB receptor, is involved in learning/memory related processes. Activation of NK3R facilitate releasing of many neurotransmitters like dopamine and noradrenaline. Aim of project is to investigate role of NK3R agonism in cognitive functions and its effects on catecholaminergic system in AD.

METHODS: Experiment was performed on 50 adult male Wistar albino rats:1) Control 2) AH, 3) Control+NK3R agonist, 4) AH+NK3R agonist, 5) AH+NK3R agonist+antagonist groups. Experimental Alzheimer's model was established by applying amyloid beta 1-42 intracerebroventricularly. Following NK3R agonist/antagonist injections, Morris water maze test was performed for learning/memory assessment. At the end, animals were decapitated, tissues were collected. Catecholamine analysis was performed from brainstem tissue by HPLC method. SAS University Edition 9.4 was used for statistical analysis.

RESULTS: Distance moved on test stage of MWM was compared between groups and statistically significant difference was found ($p<0.05$). AH group had greatest distance between all groups. Distance covered by AHS group was significant when compared with AHSO/ KS groups ($p<0.05$). There was no significant difference in NA concentration between groups ($p>0.05$). NA was lower in AH group compared with other groups. It was found to be increased in AHS group compared to AH group. DA concentration was significantly different between groups ($p<0.0001$). DA was lower in AH group compared with other groups. In AHS group, DA level was increased.

CONCLUSION: Impaired learning/memory parameters were recovered with NK3R agonism in AD group. Activation of NK3R increased NA/DA in brainstem. Positive effects of NK3R on learning are likely to be catecholamine mediated. Further studies are needed to clarify action of NK3R on learning and memory in AD.

Keywords: Neurokinin 3, Alzheimer, behavior

OC37

The Effect of Hippocampal Replay-Induced During Wakefulness on Learning and Memory in Rats

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AIM: Hippocampus is essential for long-term memory. Daily experiences are reactivated in the hippocampus during slow wave sleep. We aimed to reveal the effects of hippocampal replay induction during wakefulness on learning and memory in rats.

METHODS: Spraque Dawley male rats weighing 300-350 g were used. Groups were designed as control group (n=12), sound-matched swimming group (SMS; n=12) and sound-matched swimming+replay group (SMSR; n=12). Morris water tank test was used to assess learning and memory. Control group had acquisition trials for four days, followed by probe trials on the 5th and 10th days. SMS rats received a 50-80 dB sound with ups and downs in 5-10 kHz frequency range during acquisition trials and SMSR received additionally two times a day for 4x90 s during wakefulness. Rats in the SMS and SMSR groups were randomly divided into two subgroups on the 5th day. The first subgroup received the sound for 4x90 s during wakefulness between days 5-10, to evaluate the effect of persistent reactivation on memory. The second subgroup received no sound and got the probe trial on the 10th day. One-way ANOVA test was used for statistical analysis.

RESULTS: Escape latency significantly shortened on the fourth day compared with the first day in all groups ($p<0,001$). Escape latencies of SMS group and SMSR groups were significantly shorter than that of control group on the second day ($p<0.05$). This difference disappeared in the following days. In the probe trial applied on the 5th day, the time spent in target quadrant in the SMSR group was significantly longer than that of the control group ($p<0.05$). None of the parameters assessed in the probe trials on the 5th and 10th days revealed any difference.

CONCLUSION: Our results suggest that exposure to sound during learning accelerates the learning process and replay induction increases the memory performance.

Keywords: Learning, memory, replay, hippocampus

OC38

Neuroprotective and Antioxidant Role of Astaxanthin Against Brain and Hippocampal Damage Caused by Methotrexate

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AIM: Methotrexate (MTX) is a chemotherapeutic agent widely used in the treatment of certain types of cancer. Chemotherapeutic agents may have toxic effects on different organs. In this study, we aimed to investigate the neuroprotective and antioxidant effects of astaxanthin (AST) against brain cortex and hippocampal injury caused by MTX.

METHODS: After approval of the Ethics Committee (12.12.2018/475), Twenty-four female Wistar Albino rats were randomly divided into three groups; Group I (control), Group II (study group - 20 mg/kg MTX, i.p, single dose, 2th day), Group III (treatment group – MTX+AST, 20 mg/kg MTX, i.p, single dose, 2th day + 100 mg/kg AST, by gavage, 7 days). The rats were sacrificed under anesthesia after the last AST application. The brain and hippocampus tissue samples were collected for biochemical, pathological and immunohistochemical analyzes. Total antioxidant capacity (TAS) and total oxidant capacity (TOS) were measured in brain cortex and hippocampus. Also, iNOS, caspase-3, G-CSF, growth regulated oncogene (GRO), and myelin basic protein (MBP) immune reactions were analyzed. One-Way ANOVA and post-hoc Tukey test were used for data analysis. $p<0.05$ was considered significant.

RESULTS: MTX; increased TOS levels in brain cortex and hippocampus ($p=0.001$), and decreased TAS levels. AST treatment brought these values closer to the control group. Histopathological examination revealed marked hyperemia and degeneration in some cells in the MTX group. Also, edema was observed in the brain. Hyperemia and edema decreased in AXA treated group. In MTX group, caspase-3, iNOS, GCSF and GRO immune reactions increased while MBP expression decreased in brain and hippocampus tissue samples ($p<0.001$). AST treatment reversed the MTX induced reactions in brain and hippocampus ($p<0.001$).

CONCLUSION: Results of the present study revealed that MTX induced both brain cortex and hippocampus cells damage. AST has ameliorative effects both biochemical and pathological findings in rats.

Keywords: Methotrexate, astaxanthin, brain, hippocampus, neurodegeneration.

OC39

Investigation of Ventilatory Long Term Facilitation Exposed to Intermittent and Sustained Hypoxia and Comparison of Its Effects on Brain Stem and Spinal Cord in Rats

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AIM: Exposing to intermittent hypoxia (IH) causes a permanent increase in amplitude of respiratory motor output which is known as long-term facilitation (LTF). Increased hypoxic ventilatory response during sustained hypoxia causes ventilatory acclimatization to hypoxia (VAH) and both give rise to ventilatory neural plasticity. The pathways that induce LTF activate serotonin (5-HT2A) and adenosine (A2A) receptor activation-dependent metabotropic receptors (Gq and Gs). Although LTF is mainly serotonin-dependent, it is thought that the adenosine-dependent pathway suppresses the serotonin pathway due to increased severity and/or duration of hypoxia. In our study, we hypothesized that A2A receptor activation, which causes acute intermittent isocapnic hypoxia (AAIH) induced ventilatory LTF (vLTF) plays a major role on VAH.

METHODS: Three experimental groups were used in the study. Normaxic group (n=10; FIO2=0.21) was kept in normaxia. For AIIH group (n=11) was performed 5 times 5 minutes hypercapnic hypoxic (FIO2=0.10 and FICO2=0.04) bursts interrupted normoxic gas fraction for 4 times 5 minutes. Whole body plethysmography (WBP) was used to measure V, fR and TV. CSH group (n=10; FIO2=0.10) was exposed to hypobaric hypoxia for one week. After tissues were perfused 5-HT2A, A2A receptors and BDNF pERK and pAkt proteins in 30µ thick transverse brainstem (NTS) and spinal cord (phrenic nerve) sections were labeled with immunofluorescence staining method. Statistical significance was accepted as $p<0.05$ for WBP measurements and immunoreactivity.

RESULTS: In this study interactions between signaling pathways and pathways causing LTF were investigated for VAH. For results, the Gq pathway that was activated after moderate AIIH caused LTF formation on NTS and phrenic motor neurons, but no evidence of vLTF formation was found according to WBP measurements. VAH was similar to that of plasticity due to A2AR activation.

CONCLUSION: It is thought that understanding these interactions specific to Gs and Gq proteins through defined cross-talk inhibition mechanisms within other systems including respiration will contribute to explaining the mechanisms of neural plasticity occurring in sensory and motor neurons.
Keywords: Adenosine, hypoxia, long term facilitation, serotonin, ventilatory acclimatization to hypoxia, ventilatory neural plasticity

OC40

The Roles of mTOR Pathway Substrates on the Regulation of Muscle Mass and Force Production in Skeletal Muscle Hypertrophy

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AIM: Although the protein synthesis and hypertrophy in skeletal muscle are known to be mediated by mammalian target of rapamycin (mTOR) pathway, recent studies have reported that the roles of different substrates of mTOR in muscle hypertrophy may vary due to differences in their sensitivity to rapamycin. The aim of this study was to investigate the roles of rapamycin-sensitive and insensitive components of mTOR on muscle mass and force production during exercise induced muscle hypertrophy.

METHODS: Skeletal muscle hypertrophy was induced by applying chronic resistance exercise. mTOR inhibitor rapamycin (1.5 mg/kg) or carrier was administered by intraperitoneal injection 3 days/week for 8 weeks. Muscle strength was recorded weekly. Hind leg wet muscles were weighed. Muscle cross-sectional area was determined by Hematoxylin-Eosin staining. Akt and S6K1 levels were measured by western-blot. One-way or two-way ANOVA was performed between the groups followed by Tukey-Kramer multiple comparison test.

RESULTS: Wet muscle weight and cross-sectional area decreased in the groups receiving rapamycin compared with control exercise group although resistance exercise has elevated muscle mass and fiber size values ($p<0.05$). Muscle strength was increased at the end of the exercise program in all groups receiving rapamycin or its carrier ($p <0.05$). S6K1 expression levels were not different among the groups. Akt expression level in exercise+rapamycin group decreased comparing to the other groups ($p<0.05$).

CONCLUSION: The results of our study showed that while rapamycin-sensitive mTOR pathway regulates muscle mass increase during skeletal muscle hypertrophy induced by resistance exercise, rapamycin-insensitive mTOR pathway could be necessary to provide force production. Since the main problem in skeletal muscle pathologies is the decrease in muscle strength, besides the alterations in muscle mass the mechanisms that regulates the force production needs to be better understood as well.

Keywords: Hypertrophy, mTOR, rapamycin, resistance exercise

OC41

The Effect of Adenosine 2A Receptor Agonist and Antagonist Administration on Hypoxic Ventilatory Response

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AIM: Changes in hypoxic ventilatory response (HVR) due to the intensity and severity of hypoxic stimulation are shown as examples of neuroplasticity, resulting in short-term effects that alter transient synaptic activity, such as increased neurotransmitter release. Increased severity and / or duration of hypoxia is known to increase adenosine release from central nervous system (CNS) neurons. The aim of this study was to show the effects of adenosine 2A receptor (A2AR) activation/inhibition due to increased amount of adenosine with hypoxia on HVR.

METHODS: In our study, there are four groups and each groups have 12 Sparaque-Dawley rats weighing 250-300 grams were used. Each group was kept in normoxic conditions for one week. Except for control group (Sham_CON), dimethyl sulfoxide (DMSO; Sham_DMSO), adenosine 2A receptor agonist (CGS21680; Sham_AG) and adenosine 2A receptor antagonist (MSX-3; Sham_ANT) groups were administered 1 mg/kg daily. Ventilation (V), respiratory frequency (f) and tidal volume (TV) measurements were measured by whole body plethysmography (WBP) to demonstrate the change of HVR at the end of one week. V, f and TV parameters were analyzed and $p<0.05$ significance level was accepted for statistical analysis.

RESULTS: According to the WBP measurement results, V, f and TV values were significantly increased in the Sham AG group HVR measurement compared with the other groups. When reoxygenation was achieved after HVR, there was no significant difference between V, f and TV values between the groups.

CONCLUSION: In this study, we aimed to determine the role of adenosine release which is considered necessary for plasticity in respiratory centers. Short-term continuous hypoxia exposure with A2AR agonist administration increased adenosine release. With this ongoing study, we think that the release of adenosine in plasticity is essential for the maintenance of the mechanism of ventilatory acclimatization to hypoxia (VAH) and for development of AH through chronic sustained hypoxia (CSH).

Keywords: Adenosine, hypoxic ventilatory response, neuroplasticity

OC42

Omega 3 (DHA) Treatment of Collagenase-Induced Achilles Tendinopathy in Rats: Analyses of Histopathological and Biomechanical Aspects

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AIM: Achilles tendon is the strongest tendon with the heaviest load carrying capacity in human body but is the most frequently traumatized and ruptured. Achilles tendinopathy (AT) is more frequent pathology in athletes. Docosahexaenoic acid (DHA, Omega-3) has anti-inflammatory, anti-nociceptive and analgesic effects and is emphasized to increase collagen synthesis. In this study, we aimed to investigate histopathological and biomechanical effects of DHA in induced AT model in rats and compare with collagen effectiveness.
METHODS: This study was approved by Ataturk University Local Ethics Committee for Experimental Animals. AT model was induced with application of type I collagenase to the left peritendinous area on rats. Groups are randomly divided into 4 groups (Group1: diseased control, Group2: DHA (150mg/kg), Group3: DHA (300mg/kg), and Group 4: collagen (7.2mg/kg). Duration oral treatment was 8 weeks. Right tendons of first group rats were used as healthy control. At the end of the experiment, rats were sacrificed under general anesthesia and Achilles tendons (with calceneus bones) were removed for biomechanical and histopathological testing.
RESULTS: Biomechanically, it was observed that maximum rupture strength and maximum strength values caused permanent damage on tendons are decreased statistically in first group ($p<0.05$) and increased in 2nd, 3rd and 4th groups ($p>0.05$) when compared with healthy controls. Histopathologically, in the first group, normal structure of tendon was disrupted, tendon cells were degenerated and inflammation cells were present, whereas no lesion was observed in healthy control group. In groups 2, 3, and 4, decreased degeneration and increased proliferation of dense connective tissue cells (fibrocytes and fibroblasts) with new capillary vascular formation was noted.
CONCLUSION: It was determined that DHA increased formation of fibroblasts and collagen synthesis histopathologically and tendon elasticity and breaking strength biomechanically. In this context, it was concluded that DHA may be an alternative compound that can be used easily in AT treatment. (Ataturk University Scientific Research Project No: THD-2019-7060).
Keywords: Omega 3, collagen, Achilles tendinopathy

OC43

Effect of Moderate Swimming Exercise on Learning-Memory and Investigation of Role of Sirtuin-1 on Elderly Rats

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AIM: The aim of this study is to investigate the effect of physical exercise on the essential protein of long-term potentiation (LTP) in the hippocampus, cyclic AMP-Responder Element Binding Protein (CREB) and Brain-Derived Neurotrophic Factor (BDNF) which were important in neuronal survival, growth, and synapse stabilization and their relations with Sirtuin-1(SIRT1) which is one of the important family of proteins in regulation of gene expressions related to aging.

METHODS: In the study 32 male Sprague-Dawley rats (300-500g) aged between 11-12 months and 15-16 months old were used. The study was randomly separated into four groups and 8 rats in each group. Groups; Control-1 (C1/11-12 months), Exercise-1 (E1/11-12 months), Control-2 (C2/15-16 months), Exercise-2 (E2/15-16 months). Exercise protocol was 30 minutes/per day, 5 days/week training period 8 weeks of moderate swimming. The animal was subjected to Morris Water Maze test 5 days before sacrifice. After sacrifice, the hippocampus was removed for histological analysis. One-way analysis of variance (One Way ANOVA) was used to compare the characteristics of the groups examined over time. Statistical significance was taken as $p<0.05$.

RESULTS: There was no statistical difference between the groups according to time in the platform finding parameter ($p>0.05$). There was a statistically significant difference between Exercise 1 and Exercise 2 in the platform zone input parameter and the number of entries increased ($p=0.026$). In the hippocampus tissue, it was found that each of SIRT1, BNDF, CREB immunoreactions increased in E1, K1 groups ($p=0.001$). In comparison with E2, K2 group, each of CREB and BDNF immunoreactions were increased ($p=0.001$). CONCLUSION: We foresee that SIRT1 is a signaling pathway activating BDNF that activates CREB and activates neuroplasticity. We think that this pathway activated by SIRT1 is an alternative route for enhancing effect of mild exercise on the plasticity on elderly rats and may be a new therapeutic target for dementia.

Acknowledgments: This study was supported by the 2018-6710 project of the Scientific Research Projects Coordination Unit of Süleyman Demirel University.

Keywords: BDNF, CREB, learning-memory, LTP, SIRT1

OC44

Investigation of the Role of Asprosin in Physiopathology of Experimental Hypertension Model

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AIM: Hypertension is one of the most common cardiovascular diseases and in more tahna 95% of cases its cause is unknown. Asprosin is a newly discovered hormone which white adipose tissue secretes. It is known that asprosin might be related to obesity and cardiovascular diseases due to its effects on glucose metabolism. The aim of our currently study was to evaluate the relationship between asprosin and blood pressure and renal functions.

METHODS: Ethics committee approval was received. 16 male Spraque Dawley rats weighing 260-310 grams were separated into two groups as Control (C) and Hypertension (HT). In terms of group HT, L-NAME at a dose of 400 mg/L was put in the rats' drinking water for 6 weeks. Blood pressure was measured each week by tail-cuff plethysmography. At the end of the sixth week, 24-hour urine was collected from the rats. Then, blood and kidneys were taken under anesthesia and euthanasia was performed. Mann-Whitney U test was used for statistical comparisons. $p<0.05$ was considered significant.

RESULTS: In the HT group, there was a significant increase in systolic, diastolic and mean blood pressure levels after 2 weeks ($p<0.05$). Serum urea, creatinine, calcium and magnesium levels were increased and serum asprosin levels were significantly decreased ($p<0.05$). Although the increase in urine asprosin levels and decrease in creatinine clearance were not significant, there was a significant increase in fractional $Na+$, $K+$, $Ca2+$ and $Mg2+$excretion ($p<0.05$).

CONCLUSION: Our results showed that asprosin is associated with renal glomerular and tubular dysfunction and may play a role in the pathogenesis of hypertension. We suggest that asprosin has a role in the pathophysiology of hypertension and its relationship with glomerular and tubular dysfunction should be further investigated.

This project was funded by TÜBİTAK (1919B011800461).

Keywords: Asprosin, kidney, hypertension, glomeruler function, tubuler function

OC45

Asymmetric Change of Some Memory-Related Mediators in Hippocampus in Spatial Memory Improvement Induced by Enriched Environment in Adolescent Rats

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AIM: Hippocampus, which is the critical brain region for learning/memory function, has been reported to be associated with optimal function of lateralization and right hippocampus is predominant in spatial memory. However, asymmetry of mediators which are critical for memory in hippocampus is unclear and effects of external factors have not been studied. In this study the effects of enriched environment (EE) in right and left hippocampus to neurotrophic factors (BDNF) and oxidative stress markers (postulated act as signal molecules) were investigated.

METHODS: Male adolescent rats were divided into two groups: Control and EE (n=11/group). EE group was placed in enriched cages 1h/day as differently than control. Four-weeks later, spatial memory was tested in Morris water maze. The right and left hippocampus were separated. BDNF, lipid-peroxidation product-malondialdehyde (MDA), protein-oxidation product-protein carbonyl (PCO) and antioxidant enzyme superoxide dismutase (SOD) were measured by ELISA. Results were compared with Two-Way ANOVA test.

RESULTS: EE improved spatial memory ($p<0.05$). The control group had left>right asymmetry for BDNF ($p<0.001$). BDNF in right and left hippocampus in EE group were higher compared to control ($p<0.001$) and although there was left>right asymmetry, similar to controls, level of asymmetry was lower ($p<0.05$). There was no right-left asymmetry for oxidative stress markers in control group. In EE group, PCO and SOD values were similar with control. Interestingly, MDA level in right hippocampus of EE group was higher than the right of control group ($p<0.01$) and right>left asymmetry ($p<0.001$) was seen.

CONCLUSION: Our findings suggest that BDNF is responsible for enhanced spatial memory in both halves of hippocampus (although left-dominance is maintained). Our original finding that spatial memory improvement with increased MDA in right hippocampus, supports the suggestion that oxidative stress products may act as signal molecule in spatial memory formation. Moreover, we suggest that this occurs predominantly in the right hippocampus.

Keywords: Enriched environment, hippocampal asymmetry, spatial memory, BDNF, malondialdehyde

OC46

Effects of Ginkgo Biloba Components and Calcium Channel Blockers on Cortical Neuron Excitability in WAG/Rij Rats with Absence Epilepsy: In Vitro Calcium Imaging Study

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AIM: There are clinical and experimental studies showing that Ginkgo biloba extract (EGb 761) causes epileptic seizures. Determining the proconvulsant mechanism of action of EGb 761 is important for clinical applications of this drug. The aim of the present study was to investigate the effects of EGb 761 active components and calcium channel blockers on the neuronal excitability in cortical neuron culture of WAG/Rij rats with genetically absence epilepsy by using calcium-imaging technique.
METHODS: Ethical committee permission was obtained, and cortical neuron culture obtained from WAG/Rij rats (P1-P4) was used in the study. Measurement of intracellular calcium levels were performed under confocal microscope using Fluo-4 calcium indicator dye. Neuronal excitability was induced by 30 mM KCl. The cultured cells were treated with the active ingredients of EGb 761, ginkgolide A, B, C and bilobalide concentrations of 1, 10 and 100 µM. Calcium channel blockers nicardipine (10 µM), mibefradil (10 µM) or dantrolene (10 µM) were administered together with the most effective component of EGb 761 to determine the ion channel responsible for calcium exchange. Calcium imaging values were expressed as relative fluorescence change ($\Delta F/F0$) after normalizing in percent. Experimental groups were compared using Mann-Whitney U test after Kruskal-Wallis analysis of variance. $p<0.05$ was considered statistically significant.
RESULTS: It was determined that 10 and 100 µM doses of Ginkgolide B caused a significant increase in intracellular calcium level ($p<0,001$). However, it was found that intracellular calcium increase due to ginkgolide B was inhibited by all three of calcium channel blockers nicardipine, mibefradil and dantrolene ($p<0,001$).
CONCLUSION: Ginkgolide B has been shown to increase the cortical neuron excitability in WAG/Rij rats. It was concluded that T-and L-type voltage-gated calcium channels and ryanodine receptors may be responsible for the increase of neuronal excitability due to ginkgolide B.
This study was supported by TUBITAK (Project No: 115S348)
Keywords: Ginkgo biloba, WAG/Rij, calcium imaging, absence epilepsy, neuronal excitability

OC47

The Role of 5-Hydroxytryptophan and 7-Nitroindazole on Absence Epilepsy

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AIM: Serotonergic and nitric oxide systems are known to be involved in neurological diseases including epilepsy. The aim of this study was to investigate the effect of serotonin precursor, 5-Hydroxytryptophan (5-HTP) and specific neuronal nitric oxide synthase inhibitor 7-Nitroindazole (7-NI) on absence epilepsy.

METHODS: Six-eight months aged male WAG/Rij rats weighting 200-300gr were used in this study. The experiments consisted of control group, 5-HTP group (50 mg / kg i.p), 7-NI group (40 mg / kg i.p) and 5-HTP + 7NI groups. Baseline ECG recordings taken for 3 hours at 10 am daily and 3hour ECO recordings after drug administration were analyzed and compared statistically. The OMU Animal Experiments Local Ethics Committee approved this study (OMU HADYEK).

RESULTS: Compared with baseline ECG recordings, 5HTP (50mg / kg) significantly increased the number and duration of spike waves ($p < 0.05$). The 7-NI (40 mg / kg) and 5-HTP + 7-NI groups did not significantly alter in terms of the number and duration of spike waves ($p > 0.05$).

CONCLUSION: 5-HTP increased epileptic activity in WAG / Rij rats and 7NI inhibited this effect. The role of antioxidants in this effect need to be clarified with further studies by using biochemical analyzing methods.

Keywords: 5-HTP, 7-NI, absence epilepsy, WAG/Rij

OC48

Investigation of the Interaction of Exenatide and Cannabinoid Receptors in Penicillin-Induced Epilepsy Model

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AIM: This study aims to investigate the interaction between exenatide, a glucagon-like peptide-1 receptor agonist, and cannabinoids on epileptiform activity in penicillin-induced cute epilepsy model.

METHODS: Our study is approved by ethics committee. Male Wistar rats (180-240 g) were divided into 11 groups (n=8). Intracortical penicillin-G (500 IU) injection was used to induce epileptic seizures (Control group). Intracerebroventricular (i.c.v.) exenatide (0.5, 1 and 5 μg/kg) was injected 30-min after penicillin to determine its effective dose. Other groups received i.c.v. injection of CB1 receptor agonist ACEA (7.5 μg/rat) or CB1 receptor antagonist AM-251 (0.25 μg/rat) with or without effective exenatide dose, 0.5 μg/kg exenatide (ineffective dose) and 2.5 μg/rat ACEA (ineffective dose) together or 1 μl dimethyl sulfoxide (solvent for ACEA and AM-251,) 30-min after penicillin injection. In addition, 2,5 μl physiological saline (solvent for penicillin) was injected into the somatomotor cortex. Three-hour electrocorticography recordings were obtained. One-way ANOVA test was used for statistical analysis.

RESULTS: Effective exenatide dose was 1 μg/kg and significantly reduced spike frequency between 60-180 minutes ($p<0.05$). ACEA (7.5 μg/rat) significantly decreased the spike frequency while AM-251 (0.25 μg/rat) increased ($p<0.05$). When exenatide (1 μg/kg) and ACEA (7.5 μg/rat) was given together, spike frequency significantly decreased but this effect was not different from their effects when applied alone. There was no significant change in spike frequency when exenatide (1 μg/kg) and AM-251 or the ineffective doses of exenatide and ACEA were given together, compared with the control group.

CONCLUSION: The finding that ACEA did not potentiate the effect of exenatide and no change in the frequency of epileptiform activity by co-administration of ineffective doses of exenatide and ACEA, shows that antiepileptic effects of exenatide and cannabinoids may involve different pathways. This study was supported by OMU (PYO.TIP.1904.18.007).

Keywords: Epilepsy, GLP-1, exenatide, rat, cannabinoid, penicillin

OC49

Investigation of Rumination and Distraction Emotion Regulation Strategies from a Neuro-Cognitive Point of View

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AIM: "Emotion regulation" term describes the ability to unconsciously manage the emotions in daily life. Since, this term can be considered as a sub-type of emotion-cognition interaction, researchers discuss how the neural systems underlying the particular emotion regulation strategy exist. The aim of this study is to show the relations between neuro-cortical spontaneous activities and emotion regulation strategies in terms of principal components extracted from EEG epochs in both eyes-opened (EO) and eyes-closed (EC) states.

METHODS: 64-channel surface EEG series, downloaded from publicly available dataset so called LEMON, were collected from females aged between 20-65 years old in EO and EC states. Principal Components (PCs) of EEG epochs of 2 s were estimated from both EC and EO recordings. Then, two groups who use two emotional strategies so named rumination and distraction with high scores and low scores were compared to each other in both statistical tests and deep learning classifications in terms of PCs.

RESULTS: Significant statistical differences ($p<0.5$) were obtained between two groups in both EO and EC states mostly at occipito-parietal regions. In particular, frontal (Fp2, F2, F6, FT8, AF8), central (C1, C3, C4, C6), parietal (CP2, CP5, P7, P8, PO9) differences were obtained in EO state ($p<0.5$), while both frontal (F3, F4, F5, F6, F7, AF3, AF4, AF7, FC4, FT7) and occipito-parietal (O2, O7, Oz, CP1, CP2, CP6, Pz, P2, P5, P6, PO4, PO7) differences were obtained for EC state ($p<0.5$) in groups. When the PCs estimated from EEG epochs in both EO and EC states were combined in a single feature set, the groups were classified by using deep learning algorithms with high accuracy of 96.84%.

CONCLUSION: Findings reveal that the regulation of emotion is controlled by interactions between regions within the amygdala–frontal neuronal circuitry. Probably, emotion regulation strategies can be determined by analysing EEG measurements in adults.

Keywords: Emotion regulation, EEG, rumination, distraction

OC50

Artificial Intelligence Assisted Tactile-Visual Substitution System

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AIM: In this study, we aimed to design a high yield-low cost artificial vision system, which will enable the sense of touch to be used as a sense of sight in blind individuals.

METHODS: The project consists of two parts as mechanical and electronic ones. In the mechanical part, a vest model is designed in three dimensions in computer environment and then the appropriate servo motors are mounted on the vest and connected to the electronic system. In the electronic part, a video camera was connected to a minicomputer (Raspberry Pi) and the image was processed using Python programming language and Tensorflow library. In this way, a device is designed to instantly process the image and to touch the appropriate places on the person's back at appropriate times. It was examined whether the appropriate pattern could be transferred to the model by showing the letters, objects and numbers to the designed device and the correct estimation rate hypothesis was examined by Pearson chi-square test.

RESULTS: The medical device was tested on a model and its success in recognizing snapshots was recorded. Before testing, the question was asked whether the accuracy of our device was 90% and attempts were made to investigate the accuracy of this hypothesis. Twenty random numbers and letters were determined, and they were shown to the machine provided and the correct pattern was drawn on the model. The accuracy of artificial vision device was 90% ($p<0.05$).

CONCLUSION: A system is designed to minimize the error and transfer letters, numbers and objects to the sense of touch by making image improvements with the help of artificial intelligence algorithms. We have got very accurate results in the model stage, and we have started the necessary studies to test this system in humans.

Keywords: Artificial intelligence, vision substitution, artificial vision, robophysiology

OC51

Effects of Ionotropic GABA Receptor Blockade in Septic Encephalopathy

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AIM: Sepsis induced encephalopathy which affects the central nervous system and the tissues coordinated with the CNS, has a higher mortality and morbidity rate. We aimed to investigate the effects of the ionotropic GABAA receptor antagonist Bicuculline on encephalopathy on brain tissue of rats with sepsis induced by lipopolysaccharides in the present study.

METHODS: The adult male Sprague Dawley rats were divided into 4 groups as the control (n.6), LPS (10 mg/kg i.p.) (n:8), Bicuculline (1.5 mg/kg s.c.) (n:8), and LPS+Bicuculline (n:8) (Ethics number: 2016/08) in the study. LPS were aDMİN applied 10 mg / kg i.p. as a single dose. Rats were decapitated 24 hours after injection. Rectal body temperatures were measured for monitoring the hemodynamic changes, and neurophysiologic changes were noninvasively recorded using the electroencephalography (EEG). The pro-inflammatory cytokine TNF-α, anti-inflammatory cytokine IL-10 and GABA levels in brain tissue were determined using ELISA, and MDA levels were determined using the spectrophotometric method for the lipid peroxidation analysis. The morphological analysis was performed by immunofluorescence staining method using Neun, S100-ß and synaptophysin antibodies. One-way variant analysis, and Tukey test were used for statistical analysis.

RESULTS: We found that the inflammation in the LPS group increased the inflammatory parameters and increased MDA and GABA levels in the brain tissue compared with the levels in the control group, and caused damage in tissue level ($p<0.05$). There was no significant difference between control, Bicuculline and LPS+Bicuculline groups ($p> 0.05$). In the electrophysiological recordings, activity compatible with acute non-focal seizures was observed in the LPS group, however, activity compatible with resting was detected in other experimental groups ($p<0.01$).

CONCLUSION: In conclusion, we suggest that a GABAA receptor antagonist-Bicuculline may be effective in treatment in septic encephalopathy.

Keywords: Sepsis, GABA, bicuculline, encephalopathy

UNPUBLISHED

OC52

The Role of Peroxisomes in the In Vivo Alzheimer's Disease Model Induced by Administration of Aβ 1-42 and the Effect of Taurine

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AIM: Oxidative stress is one of the major causes of Alzheimer's disease, a multifactorial disease that results in neurodegenerative dementia. In this study, we investigated the role of peroxisomes and taurine, a powerful antioxidant, in the Alzheimer's disease model induced by amyloid beta 1-42 (Aβ 1-42) neurotoxicity.

METHODS: In our study, old (28±4 months) Wistar albino male rats; were divided into 5 groups (n=6) as control, sham, Aβ 1-42, taurine, Aβ 1-42+taurine. Taurine was given to animals at dose of 1000 mg/kg/day for 6 weeks with drinking water. Following taurine administration, animals were injected intracerebroventricular (icv) Aβ 1-42 (into the lateral ventricles, 5 µl) by stereotaxic surgery. After 14 days, cerebral cortex and hippocampus tissues were isolated from the brain. MDA and GSH levels were measured spectrophotometrically. The expressions of peroxisomal PEX14 and PMP70 membrane proteins with CAT enzyme were demonstrated by Western blotting. Kruskal Wallis and Mann Whitney U test and Bonferroni correction were used for statistical analysis. $p<0.01$ was considered significant.

RESULTS: It was found that Aβ 1-42 injection decreased CAT expression in the cortex, PEX14 and PMP70 expressions and GSH levels in the hippocampus, and increased MDA levels in the cortex and hippocampus ($p<0.01$). Although taurine administration partially improved the adverse effects of Aβ 1-42 injection, a significant increase was found only in the hippocampus GSH level ($p<0.01$).

CONCLUSION: The decrease in peroxisomal proteins and antioxidant capacity in the brain with icv Aβ 1-42 injection in old rats showed that peroxisomes may play a role in the neurodegenerative and oxidative processes related to Alzheimer's disease. Taurine supplementation may have positive effects especially on increasing antioxidant capacity, but it did not have a significant effect on peroxisomal functions in the dose and duration used in our study.
This work was supported by the project GU-BAP-01/2017-30. Ethical approval: (G.Ü.ET-17.058).

Keywords: Alzheimer's disease, neurodegeneration, oxidative stress, peroxisome, taurine

OC53

The Role of Phosphatidylinositol-3 Kinase/Akt and ERK-1/2 Pathways in The Neuroprotective Activity of Lithium

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AIM: Lithium is commonly used as a mood stabilizer in bipolar disorders. Current studies show that lithium treatment results in neuroprotective effects on neurodegenerative diseases even its mechanism is not clearly understood. This study focuses on intracellular mechanism mediated by lithium after cerebral ischemic injury.

METHODS: Experiments were conducted with the approval of the local ethics committee (2019/28). 8-10 weeks old male Balb/c mice were divided in three sets. In the first set, mice were exposed 90 minutes middle cerebral artery occlusion model (MCAO) than 24 hours reperfusion. At the onset of reperfusion, animals were subjected to intraperitoneal lithium injection. The brains were sliced to evaluate infarct volume, oedema and blood-brain barrier impairment. 30 minutes MCAO followed by 72 hours reperfusion performed for the other set of experiment to assess apoptosis and apoptosis-related proteins by TUNEL staining and Western blot (WB) analyzes.

RESULTS: In the first set of experiments, the lithium treatment significantly decreased infarct volume and brain oedema compared with the control group after 90 minutes MCAO ($p=0.03$, $p=0.014$). In the second set, the lithium treatment significantly decreased the apoptotic cell number compared with the control group after 30 minutes MCAO ($p=0.238$). The effects of lithium on apoptosis related pathways after cerebral ischemia were assessed and the results showed that lithium increased the Akt and Erk1/2 protein levels after MCAO ($p=0.02$, $p=0.000$). Akt and ERK1/2 phosphorylations were suppressed with the use of inhibitors Wortmannin and PD98059 respectively. SPSS was used for statistical analysis. Statical significance was analyzed by one–way analysis of variance (ANOVA) followed LSD tests ($p<0.05$)

CONCLUSION: The increase of Akt phosphorylation with lithium treatment after MCAO were reversed with Wortmannin injection, besides any alteration with inhibition of ERK1/2. It was shown the neuroprotective mechanism of lithium mediated by Akt phosphorylation after ischemic injury.

Keywords: Ischemia, lithium, Akt, Erk

OC55

The Effect of Electromagnetic Field Exposure in The Prenatal Period on Behavior and Synaptic Proteins and The Role of Zinc Support

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AIM: We aimed to investigate the relationship between autism-like behaviors and EMF exposure as an environmental factor during the prenatal and postnatal periods, the role of synaptic proteins such as NLGN3 and SHANK3, gender differences and the effects of zinc supplementation.

METHODS: Rat pups born from four groups of pregnant rats were used: Control group (n=4), EMF group (n=6), Control+Zinc group (n=3), EMF+Zinc group (n=5). Zinc was administered orally to pregnant rats (5 mg/kg/day, 5 days/wk). Pregnant and pup rats were exposed to EMF using Helmholtz coil system (50 Hz, 3 mT, 5 days/wk, 4 h/day). EMF exposure of rat pups was initiated on the first day of pregnancy and continued until the 28th postnatal day. Social approach, open field, elevated plus maze and forced swim tests were performed on days 28 and 42. Blood and brain tissue samples were taken after the tests. Zinc levels in blood, NLGN3 and SHANK3 levels in prefrontal cortex, hippocampus, and amygdala tissues were measured by ELISA. Synaptic structures in amygdala were examined by electron microscopy. Differences between groups were evaluated by One-way ANOVA Post-hoc Bonferroni, and paired group comparisons by T-test. $p<0.05$ was considered significant.

RESULTS: Behavioral tests showed that EMF exposure had no effect on social behavior in offspring, but adversely affected activity and exploratory behavior and increased anxiety, while zinc supplementation had a partially positive effect on female offspring, but not on male offspring. SHANK3 and NLGN3 proteins were significantly lower in EMF groups and zinc supplementation was not found to have a positive effect.

CONCLUSION: Exposure to EMF may alter the levels of synaptic proteins in the developing brain, leading to behavioral changes with gender differences. Zinc supplementation, which can be used in different doses, might be useful for ameliorating EMF-related behavioral and structural effects.

Keywords: Behaviour, electromagnetic field, neuroligin3, SHANK3, synapsis, zinc

OC56

Investigation of the Effect of Different Intensity of Acute Stress on GLP-1, IGF-1 and MMP2 Levels of Hypothalamus and Intestine in Rats

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AIM: Glucagon-like peptid-1 (GLP-1) is a new important hormone for insulin metabolism, food intake and control of body weight. GLP-1 is also closely related with insulin-like growth factor-1 (IGF-1) and matrix metalloproteinase2 (MMP2) that are important for tissue homeostasis and health. The aim of this study was to investigate the effects of different intensity of acute stress on intestine and hypothalamus GLP-1, GLP-1 receptor levels, as well as IGF-1, MMP2 levels.

METHODS: After approval of Dokuz Eylul University School of Medicine Animal Care Committee, thirty adult outbred male Sprague Dawley rats were divided into three groups: 1-Control, 2-0.2mA foot-shock (low-intensity), 3-1.6mA foot-shock (high-intensity). Stress groups were exposed to electric foot-shocks for 160 ms duration with 20 min intervals. One hour later, blood sampling was completed under carbondioxide anesthesia. Hypothalamus and terminal ileum tissues were extracted. Serum corticosterone and tissue GLP-1, GLP-1 receptor, IGF-1, MMP2 levels were measured by ELISA protocol. Significant differences between groups were analyzed by one-way ANOVA and post-hoc Bonferroni test.

RESULTS: Both of low and high-intensity acute stress decreased intestinal GLP-1, IGF-1 and MMP2 levels (both stress groups compared with control, $p<0.0001$). Only high intensity stress decreased intestinal GLP-1 receptor levels (compared with control, $p<0.05$; compared with low-intensity stress, $p<0.002$). However, low-intensity acute stress increased GLP-1 levels ($p<0.0001$), high-intensity stress increased GLP-1 receptor levels ($p<0.05$) in hypothalamus. Stress did not change IGF-1 and MMP2 levels in the hypothalamus. Strong positive correlations were found between intestinal GLP-1 levels and IGF-1 levels ($r=0.757$, $p<0.0001$) and also between intestinal IGF-1 levels and MMP2 levels ($r=0.806$, $p<0.0001$).

CONCLUSION: Our results indicate that acute stress mainly affected intestinal GLP-1, IGF-1, and MMP2 levels; all of which were found to be decreased with differences in CNS and periphery. Further researches are needed to investigate the mechanisms of acute stress in different intensities; the role of dopaminergic system and other stress related pathways in acute stress.

Keywords: GLP-1, gut-brain-axis, hypothalamus, IGF-1, intestine, MMP2

OC57

Effects of Western Diet and Short-Chain Fatty Acids on Colonic Inflammation

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AIM: Western diet (WD) worsens inflammatory and metabolic events, which are improved by short-chain fatty acids (SCFA). Therapeutic effects of SCFA were studied in combination with WD in colonic inflammation induced by dextran sulfate sodium (DSS).
METHODS: Wistar-albino rats (n=40) were divided into five groups. Both control and DSS groups were fed with either normal diet (ND) or WD for 31 days or last 10 days by adding DSS (0.05%) to water. In half of ND- or WD-fed groups, SCFA (150mM/L-acetate, 50mL/L-propionate, 50mM/L-butyrate) was added to water. Body weight, serum glucose levels were measured. Hepatic functions and lipid profile were evaluated. IL-6, IL-10, TNF-alpha were measured in colon, while myeloperoxidase (MPO) activity, lipid peroxidation (MDA), glutathione, chemiluminescence levels were measured in colon and liver. Macroscopic scoring, histopathologic evaluation of colon tissue was performed. ANOVA and t-test were used for statistical analyses.
RESULTS: In ND-fed rats, DSS induced colonic inflammation (increased colon-MPO, $p<0.01$). Inflammation also observed histopathologically. In contrast to feeding with ND, WD reduced inflammatory parameters; colon MPO ($p<0.05$) and macroscopic scoring ($p<0.01$), while adding SCFA had no significant effect. Increased serum triglycerides ($p<0.01$), VLDL ($p<0.01$) and hepatic injury (elevated AST-ALT, $p<0.01$) were observed in WD groups, which were reversed by SCFA ($p<0.05$). Despite that DSS-alone did not affect hepatic functions significantly when given with WD, hepatic MPO ($p<0.05$) and luminol ($p<0.05$) levels were increased. Addition of SCFA in both ND and WD had no further effect on these parameters. DSS increased proinflammatory cytokines (IL-6, TNF-α) and reduced anti-inflammatory cytokine (IL-10) levels ($p<0.01$), while SCFA improved these alterations. However, adding WD had no significant impact on these cytokines.
CONCLUSION: Despite its beneficial effect against DSS-induced colonic inflammation, WD worsened serum lipid profile. Consumption of SCFA improved WD-induced lipid profile alteration but had no impact on colonic inflammation.

Keywords: Colonic inflammation, short chain fatty acids, western diet

OC58

P-Coumaric Acid Ameliorates Colitis by Means of Preventing Neutrophil Infiltration and Endogen Anti-Oxidant Depletion

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AIM: P-Coumaric acid (CA) is a hydroxycinnamic acid that is found in wide variety of edible plants. It has been reported to exhibit antioxidant, antimicrobial, anti-inflammatory effects. Crohn's disease is a chronic inflammatory disease involving any part of gut. Aim of the study is to investigate anti-inflammatory effects of CA on trinitro-benzene-sulfonic acid (TNBS) induced colitis model.

METHODS: Following 24-h of starvation, Spraque Dawley rats (female=male, 200-300gr) were divided into 5 groups. Rats were given 1ml TNBS (30 mg/ml dissolved in 40% ethanol) or 1ml saline intrarectally. Groups were treated with either p-coumaric acid (250-500-1000 mg/kg suspended in 1ml tween-80) or tween-80 (Colitis and control groups) by oral gavage for 5 days and were euthanized. Colon samples were collected for macroscopic evaluation, tissue wet weight index (WI), myeloperoxidase (MPO) activity as the indicator of neutrophil infiltration, malondialdehyde (MDA) which is the end-product of lipid peroxidation and endogen anti-oxidant glutathione (GSH) levels. Values were compared by ANOVA and Tukey-Kramer test.

RESULTS: The macroscopic score and WI of colitis group (6.86±0.63 and 0.66±0.33); respectively) is significantly higher compared with the control group (0.43±0.43 and 0.27±0.20; respectively) ($p<0.001$ for both MS and WI) and 500 mg/kg CA treatment (3.86±0.72) reduced both parameters significantly ($p<0.05$ for both MS and WI). Both 500 mg/kg (10.22±2.08 nmol/g) and 1000 mg/kg (12.31±2.68 nmol/g) CA treatment attenuated increased MDA levels (21.91±2.47 nmol/g-colitis group) ($p<0.01$ and $p<0.05$; respectively) and MPO activity (142.4±19.17 U/g, $p<0.05$ and 111.5±31.89 U/g, $p<0.05$; respectively) in rats with colitis (211.6±19.6 U/g). The GSH depletion in colitis group (0.84±0.09 µmol/g) is prevented by only 500 mg/kg CA treatment (1.35±0.12 $p<0.05$ µmol/g).

CONCLUSION: The results of the study indicated that CA ameliorates the inflammation induced by TNBS. As most effective dose 500 mg/kg, CA ameliorates colitis by protecting endogen anti-oxidant content and preventing neutrophil infiltration.

Keywords: Colitis, coumaric acid, inflammation, TNBS, inflammatory bowel diseases

OC59

The Role of Asprosin in the Physiopathology of Renal Ischemia/Reperfusion Injury in Rats

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AIM: Secreted by white adipose tissue, Asprosin,is a novel protein hormone that is involved in glucose metabolism. We aimed to investigate the relationship between asprosin and glomerular and tubular functions in ischemia-reperfusion (I/R) injury and its role in the pathophysiology of I/R kidney injury.

METHODS: Ethics committee approval was received. Male Spraque Dawley rats weighing 300-350 grams were divided into three groups (n = 7). Under anesthesia; Except for the rats in the control group, the blood flow in the renal vessels of rats in the IR48 and IR168 groups was clamped and 60 min ischemia was performed. IR48 group rats were reperfused for 48 hours and IR168 group rats for 168 hours. After 24 hours urine collection of rats in all groups; Blood and both kidneys were taken under anesthesia and euthanasia was performed. Mann-Whitney U test was used for statistical comparisons, $p<0.05$ was considered significant.

RESULTS: Serum urea, creatinine, Mg^{2+} levels and fractional Na^+, K^+, Ca^{2+}, Mg^{2+} and phosphate excretion were increased in IR48 group compared with control group; creatine clearance decreased and urine asprosin level increased ($p<0.05$). Serum urea, creatinine and Ca^{2+} levels increased in IR168 group; serum asprosin levels and creatine clearance decreased ($p<0.05$). Fractional Na^+, K^+, Ca^{2+} and Mg^{2+} excretion and urine asprosin levels were increased. When IR48 and IR168 groups were compared; decrease in serum asprosin, urea, creatinine, Na^+, Mg^{2+} and phosphate levels; increased creatine clearance and fractional Mg^{2+} excretion; fractional Na^+, K^+ and phosphate excretion were decreased ($p<0.05$).

CONCLUSION: In the period of severe damage (IR48), impaired functions improved towards the late reperfusion period (IR168). Urine asprosin levels correlated with glomerular and tubular functions. Further research is needed to determine the role and effect of asprosin in renal ischemia reperfusion injury.

This project was funded by TÜBİTAK (1919B011800680).

Keywords: Asprosin, acute kidney Injury, ischemia/ reperfusion, glomerular function, tubular function

OC60

Administration of Acute Agomelatine Reduces Increased Oxidative Stress Due to Experimental Renal Ischemia / Reperfusion Damage in Rats

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AIM: Sepsis, shock, hypotension, some renal surgeries, renal stone-related surgical procedures, renal transplantation and partial nephrectomy may cause renal ischemia. As these conditions endanger the supply of continuous oxygen needed by the tissue and organ, the process of tissue damage begins. Clinical and experimental studies reported that ischemia/reperfusion injury occurs through Reactive Oxygen Species (ROS). Agomelatine, a melatonin (MT1/MT2) receptor agonist and serotonin antagonist, has been reported to have antioxidant effects. The aim of this study was to investigate the effects of agomelatine on oxidative damage due to ischemia.

METHODS: Forty male Sprague Dawley rats were used in the study. The rats were divided into 4 groups as control, sham, 20 and 40 mg/kg agomelatine group (n = 10). The control group did not receive any treatment, while the sham group exposed to 1hour ischemia and 24 hours reperfusion in both kidneys. In agomelatine groups, agomelatine 20 and 40 mg/kg concentrations were given orally 1 hour before the surgical procedures applied to the sham group. The rats were decapitated after 24 hours and renal tissues were collected. MDA and GSH levels and SOD, CAT, GPx enzyme activity were measured in the collected kidney tissues.

RESULTS: Renal ischemia/reperfusion caused an increase in MDA level ($p < 0.05$), and decreased SOD, CAT, GPx enzyme activity and GSH levels ($p < 0.05$). However, it was determined that 20 and 40 mg/kg oral agomelatine decreased MDA levels in rats in the ischemia/reperfusion groups ($p < 0.05$), and increased SOD, CAT, GPx activity and GSH levels ($p < 0.05$).

CONCLUSION: These results show that agomelatine has protective effect against ischemia / reperfusion induced kidney damage with its antioxidant and free radical scavenging effect. This study was supported by Inonu University BAP (Project no: TYL-2019-1762).

Keywords: Agomelatine, ischemia, reperfusion, Reactive oxygen species, antioxidant

OC61

The Protective Effects of Carvedilol on Diabetic Nephropathy in A Streptozotocin-Induced Diabetic Rat Model

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AIM: Diabetic nephropathy (DN) is a common, severe complication of diabetes, developing in 20–40% of diabetic patients. Hyperglycemia, hypertension, dyslipidemia, oxidative stress and inflammation have been proposed to account for the development of nephropathy in diabetic subjects. Carvedilol, an antihypertensive drug, exhibits additional effects on ameliorating oxidative stress and inflammation, making it an attractive candidate for diabetic nephropathy. Moreover, diabetes and hypertension frequently coexist and patients are at high risk for DN. Thus, the aim of the present study was to evaluate the protective and therapeutic effect of carvedilol on streptozotocin (STZ)-induced DN in rats.

METHODS: Twenty-one adult male rats were included in the study. This study was approved by the Institutional Animal Care and Ethical Committee of Ege University. Fourteen rats were administered a single dose of 60mg/kg intraperitoneal (i.p.) streptozotocin (STZ) to induce diabetes. Seven rats served as control group (Group 1). Diabetic rats were randomly divided into two groups: Group 2 (n=7) and Group 3 (n=7) were treated with 4 ml tap water/day and Carvedilol 25 mg/kg/day (in 4 ml water) by oral gavage for 4 weeks, respectively. Then, the animals were euthanized, blood and urine samples were collected, and nephrectomy were performed for histopathological examination. Statistical analyses were performed using non-parametric (Mann-Whitney U) and Student's t-test.

RESULTS: In diabetic Group 2, all biochemical and histopathological parameters were increased significantly compared with control group (Group 1) ($p<0.0001$). Administration of Carvedilol (Group 3) caused a significant decrease in glomerular area, severity of sclerosis, fibronectin immunoexpression, VEGF, TGF-beta, BUN, creatinine, proteinuria levels ($p<0.05$). Blood glucose levels were significantly increased in Group 2, but there was no significant difference between Group 2 and 3.

CONCLUSION: Results of the present study demonstrate the anti-inflammatory, anti-oxidant and beneficial effects of Carvedilol on the functional properties of the kidney in STZ-induced diabetic nephropathy model in rats.

Keywords: Carvedilol, diabetic nephropathy, inflammation, oxidative stress, streptozotocin

OC62

The Effects of Agomelatine, Fluoxetine and Sertraline on Overactive Bladder

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AIM: We aim to determine the possible effects of selective serotonin reuptake inhibitor group of antidepressants; agomelatine, fluoxetine and sertraline's contraction responses in rat bladder tissues and to compare the effects of three popular antidepressant agents in overactive bladder syndrome.

METHODS: Adult (300-350 g) male Wistar Albino rats were used. Animals were undergone cervical dislocation under ether anesthesia. Bladder was rapidly separated and taken into Krebs solution. After removal of tissue and blood debris, strips of 3-4 millimeters were cut from bladder, placed into isolated organ bath with 37°C, continuously gassed (95% O2 and 5% CO2) in Krebs solution and tension was adjusted to 1 g. Tissues were washed for 1 hour with 15 minutes periods. Isometric contractions were induced with 10^{-5} M Ach and agomelatine (10^{-9} M and 10^{-4} M), fluoxetine (10^{-8} M and 10^{-3} M), sertraline (10^{-8} M and 10^{-3} M), were added separately. Contractions were recorded as frequency and amplitude parameters.

RESULTS: Inhibition observed with agomelatine at 10^{-8} M and 10^{-7} M. Statistically significant inhibitions were noticed at 10^{-4} M and 10^{-3} M doses ($p<0.001$). Although significant inhibitions were observed in fluoxetine from 10^{-7} M, statistically significant responses were recorded at 10^{-5} M, 10^{-3} M ($p<0.001$). Sertraline responses were similar, statistically significant results were obtained at 10^{-4} M and 10^{-3} M doses ($p<0.001$).

CONCLUSION: Different doses of agomelatine, fluoxetine and sertraline showed markedly inhibitory effect on bladder smooth muscle. Selective serotonin reuptake inhibitor antidepressants slowed down the re-uptake of neurotransmitter molecules (specifically serotonin) by presynaptic neurons. Since serotonin reuptake was inhibited, serotonin molecules remained in synaptic range longer and had a greater chance of activating postsynaptic neurons.

Keywords: Overactive bladder, bladder, agomelatine, fluoxetine, sertraline