Oral Communications (OC01 – OC71)

OC-01

Investigation of the Effects of Rivastigmine on Learning-Memory İmpairment and Anxiety Accompanying with Age-Varying Seizure Severity in *Wag/Rij* Rats with Genetic Absence Epilepsy in Relation to Trpv1 Channels

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AIM: Absence epilepsy and psychiatric disorders have a bidirectional relationship and also different severity at various ages. Also, recent studies have shown that Trpv1 channel expression is altered in the diseases mentioned. The present study aims to investigate whether rivastigmine (RIVA), an acetylcholinesterase inhibitor, affects age-related changes in spike-wave discharges (SWDs), learning-memory problems, anxiety, and changes in Trpv1 gene expression levels in *WAG/Rij* rats.

METHODS: In the study (OMU-HADYEK 2024/19), 5- and 13-month-old *WAG/Rij* (n=70) and only 5-month-old Wistar (n=14) male rats were used. Initially, electrophysiologic recordings were obtained from *WAG/Rij* rats after a single dose of 0.125 and 2 mg/kg injection and 24 hours after the end of the 14-day (long-term) administration of only 2 mg/kg dose to determine the effect of RIVA on SWDs. In the next step, both *WAG/Rij* and Wistar rats were subjected to y-maze and elevated-plus testing 24 hours after long-term administration. Following the behavioral tests, right-cortex and right-hippocampus of the rats were removed to used in the qPCR. Statistically, according to the results of Shapiro-Wilk test, t-test or one-way ANOVA test was applied.

RESULTS: RIVA showed similar effects in all *WAG/Rij* rats. 0.125 mg/kg was insignificant, whereas 2 mg/kg almost completely abolished SWDs ($p<0.001$) and reduced mean durations of SWDs ($p<0.05$). In the long-term; increased the number of SWDs and decreased the mean duration of SWDs ($p<0.001$), decreased short-term memory performance($p<0.05$), and decreased anxiety ($p<0.05$).The Trpv1 gene levels; decreased in all *WAG/Rij* rat groups and increased in Wistar rats ($p<0.001$).

CONCLUSIONS: RIVA shows similar effects in all age groups: anti-epileptic at acute doses and pro-epileptic in long-term. RIVA negatively affected learning-memory while decreasing anxiety in *WAG/Rij* rats. Regarding Trpv1 gene expressions, *WAG/Rij* and Wistar rats showed opposing effects. We speculate that the effect of RIVA on absence seizures and accompanying memory impairment with anxiety may be Trpv1-channel related.

Keywords: Age, Absence epilepsy, Comorbidity, Spike-wave discharges, Rivastigmine, Trpv1-channel

OC-02

The Effect of Venlafaxine on Seizure Activity in Genetically Absence Epileptic WAG/Rij Rats: The Role of Adrenergic Receptors in This Effect

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AIM: To investigate the effects of venlafaxine on spike-wave discharges (SWDs) in WAG/Rij rats, the role of adrenergic receptors in this effect, and the impact of venlafaxine on GABA-A receptor γ2 (GABAARγ2) subunit expression in brain tissues.

METHODS: Male WAG/Rij rats (n=102) aged 8-9 months were divided into 16 groups. Tripolar electrodes were implanted to rats for obtaining electrocorticogram (ECoG) recordings. The control group received sterile saline, while the venlafaxine groups received 12.5, 25, and 50 mg/kg doses of venlafaxine intraperitoneally. To investigate the role of adrenergic receptors, the non-specific alpha adrenergic receptor blocker phentolamine (10 and 30 µg) and the non-specific beta adrenergic receptor blocker propranolol (30 µg) were administered intracerebroventricularly before venlafaxine. Additionally, atomoxetine, a norepinephrine reuptake inhibitor, was used to determine the effects of increased norepinephrine. The long-term effects of venlafaxine (14 days) on absence seizures and GABAARγ2 subunit expression in the somatosensory cortex, hippocampus, and thalamus were also analyzed.

RESULTS: Single dose of 25 mg/kg venlafaxine decreased the number of SWD for 75 minutes, while 50 mg/kg venlafaxine decreased it for 90 minutes. The combination of venlafaxine (50 mg/kg) and phentolamine (10 µg) enhanced the duration of venlafaxine's effect. The effect of venlafaxine did not change when combined with propranolol. Atomoxetine increased both the number and mean duration of SWDs at the doses of 12 mg/kg and 24 mg/kg. Long-term venlafaxine administration decreased both the number and mean duration of SWDs. According to western blot and immunohistochemistry analyses, GABAARγ2 subunit expressions decreased only in the thalamus.

CONCLUSIONS: Our results suggest that the adrenergic system does not play a role in the antiepileptic effect of venlafaxine. Additionally, the antiepileptic effect observed with long-term venlafaxine administration may be due to the decreased expression of GABAARγ2 subunit in the thalamus.

Keywords: Absence epilepsy, GABA-A receptor, Phentolamine, Propranolol, Spike-wave discharge, Venlafaxine

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OC-03

Effect of Cardioselective Beta Blocker Metoprolol on Epileptiform Activity Induced by Penicillin in Rats

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AIM: Limited information is available on the effects of the cardioselective beta-blocker metoprolol, which is commonly used in the treatment of cardiac and hypertensive problems in epilepsy patients, on epileptic activity. The aim of this study is to shed light on the clinical review of metoprolol treatment in patients with epilepsy by determining whether its effects on epileptic activity are proconvulsant or anticonvulsant.

METHODS: For this purpose, fourteen male Sprague-Dawley rats were divided into two groups with 7 rats in each group. The first group (SHAM group) received a single dose of penicillin (500 IU, 2.5 µL, i.c.) and 0.9% saline (0.5 mL, i.p.). The second group (Treatment group) received a single dose of penicillin (500 IU, 2.5 µL, i.c.) and metoprolol (0.5 mL, 50 mg/kg, i.p.). Metoprolol was administered 30 minutes after the penicillin injection, as the epileptic spikes were expected to become prominent. Each rat was fixed in a stereotaxic apparatus and ECoG recordings were taken for 240 minutes with electrodes placed on the brain tissue. The evaluation of the recording data was based on the frequency and amplitudes of the epileptic spikes. The average frequency was calculated as spikes/min, and the average amplitude was calculated as µV in 10-minute periods and included in the statistics.

RESULTS: The two independent groups, SHAM and Treatment, were statistically compared based on the average spike frequency and amplitude values in 10-minute periods, and no statistically significant result was obtained.

CONCLUSIONS: In conclusion, further studies focusing on different dose ranges and cellular mechanisms in the brain are needed to fully understand the effect of metoprolol on epileptic activity.

Keywords: Epilepsy, Metoprolol, Penicillin, Rat

OC-04

The Effects of Prebiotic and Probiotic Supplements Administered with Lacosamide on Epileptic Seizures in a Post-traumatic Epilepsy Model

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AIM: Although there is currently no effective treatment for post-traumatic epilepsies, numerous studies in recent years have shown a relationship between dysbiosis and epilepsy. This study aims to investigate the contribution of prebiotic, probiotic, and synbiotic supplements to the effectiveness of lacosamide (LCM) on epileptic seizures in a rat model of post-traumatic epilepsy (PTE).

METHODS: Traumatic brain injury was induced in Sprague-Dawley rats using the weight-drop method, and EEG electrodes were implanted. Seven days later, a PTE model was induced with intraperitoneal injections of subconvulsant doses of pentylenetetrazol (PTZ, 30+15+15 mg/kg) at 30-minute intervals (SBÜ HADYEK 2023-09/03). Subconvulsant PTZ injections were repeated four times at one-week intervals, and behavioral parameters related to epileptic seizures were recorded along with EEG. Starting before the first PTZ application, 30 mg/kg LCM or LCM combined with 1 g/kg inuline, 10 x 109/kg VSL#3, or a combination of 1 g/kg inulin + 10 x 109/kg VSL#3 were administered orally via gavage for 28 days. Data were statistically analyzed using the Kruskal-Wallis test followed by the Mann-Whitney U test.

RESULTS: When comparing the group treated with LCM and probiotics to the group treated with LCM alone, it was found that probiotics led to a reduction in total seizure duration ($p<0.05$), and an increase in the subconvulsant PTZ dose required to initiate seizures and seizure onset latency ($p<0.05$).

CONCLUSIONS: It was concluded that probiotics in the form of VSL#3 administered with LCM enhanced the antiepileptic drug efficacy against epileptic seizures related to PTE facilitated by PTZ.

Keywords: Lacosamide, Post-traumatic epilepsy, Prebiotic, Probiotic

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OC-05

Investigation of Behavioral Properties of Dentate Gyrus Prodynorphin Neurons in Alzheimer's Model Transgenic Mice

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AIM: Alzheimer's Disease (AD) is marked by cognitive decline and abnormal protein accumulation. The opioid system, particularly prodynorphin (Pdyn) neurons, plays essential roles in various processes; however, its role in AD is poorly understood. This study investigates the relationship between DGPdyn neurons and AD, crucial for learning and memory.

METHODS: The experimental design included control (GFP-PBS and GFP-Aβ), chemogenetic activation (hM3D-PBS and hM3D-Aβ), chemogenetic inhibition (hM4D-PBS and hM4D-Aβ), optogenetic (GFP-PBS, ChR2-PBS, ChR2-Aβ) groups. Alzheimer's Disease (AD) was modeled by administering amyloid beta (Aβ) 1-42 intracerebroventricularly to 3-4 month-old male Pdyn-Cre mice. DGPdyn neurons were selectively activated and inhibited using chemogenetic and optogenetic techniques. Following manipulations, animals were taken into behavioral tests: Open Field (OF) for locomotor activity, Elevated Plus Maze (EPM) for anxiety-like behavior, and Novel Object Recognition (NOR) for memory. Statistical analysis was performed using Two-way ANOVA and Tukey's and Bonferroni's tests, with $p<0.05$ considered significant.

RESULTS: In the PBS group, chronic inhibition and activation of DGPdyn neurons significantly decreased center entries in the OF test ($p<0.05$). In contrast, in the Aβ group, only chemogenetic activation of DGPdyn neurons resulted in a significant reduction in center entries ($p<0.05$). Additionally, inhibition of DGPdyn neurons in the PBS group impaired novel object exploration, negatively affecting both short-long terms ($p<0.01$).

CONCLUSIONS: These findings suggest that Aβ accumulation may disrupt synaptic transmission in DGPdyn neurons, thereby impacting locomotor activity. DGPdyn neurons likely play a critical role in memory and cognitive processes, with their functions altered by the presence of amyloid beta.

Keywords: Alzheimer's Disease, Prodynorphin Neurons, Optogenetics, Chemogenetics

OC-06

Evaluation of the Effect of Asprosin on Pain and Behavioral Functions in a Mouse Model of Experimental Migraine

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AIM: Migraine is a type of headache that is localized on one side of the head and recurs periodically. The endocrine system, particularly adipose tissue, plays crucial role in pain perception and modulation. Dysregulations in the endocrine system and interactions between hormones and pain have been associated with the development of chronic pain conditions. The aim of this study is to investigate the effects of asprosin, an adipokine synthesized from adipose tissue, on pain and behavioral functions in mice with an experimental migraine model.

METHODS: In this study, male Balb/C mice weighing 25-30 grams were used. To induce migraine pain nitroglycerin (NTG) was administered intperitoneally (i.p), and sumatriptan was given to the treatment group. The mice divided into four subgroups: healty control group, NTG group (10 mg /kg), NTG+asprosin group (10 µg /kg), and NTG+sumatriptan group (300 µg /kg) (n = 10 per group). Pain response was assessed using periorbital von Frey test. Behavioral functions such as motor coordination, anxiety and depression, learnig and memory were evaluated using rota-rod, open field and novel object recognition test respectively. Statistical analysis of group differences was performed using One-Way ANOVA and post-hoc Tukey test.

RESULTS: In mice with migraine induced by NTG, decrease in periorbital mechanical threshold values compared to baseline values was obserbed. In the groups treated with sumatriptan and asprosin this effect of NTG was reversed and increase in periorbital mechanical threshold values was noted. Similarly in other behavioral test, the negative effects of migraine were mitigated by asprosin. However, the ameliorative effects of asprosin on these behavioral outcomes were not statistically singificant.

CONCLUSIONS: This study suggests that asprosin may elevate pain threshold and contribute to improvenments in locomotor activity and behavioral functions in mice with a migraine model. Further studies are needed to precisely elucidate the effects of asprosin on pain and behavioral functions.

Keywords: Asprosin, Migraine, Pain, Sumatriptan

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OC-07

Protective Potential of Boron-Based Compounds in In Vitro Nephrotoxicity Model Induced by Gentamicin in Monkey Kidney Epithelial Cell Line

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AIM: Gentamicin (GM), which is frequently used due to its wide range of activity and low cost, causes nephrotoxicity. In patients treated for more than one week, nephrotoxicity was found in 30% of cases. Several substances have been shown to protect against nephrotoxicity. Boron-containing compounds with anti-microbial, anti-oxidant, anti-cancer, and anti-arthritis effects have recently been used as therapeutic candidates in the medical and pharmaceutical sectors. The objective of this study was to examine the nephroprotective impact of boron compounds (T1B1 and T1B2) in an in vitro gentamicin-induced nephrotoxicity model.

METHODS: The Vero cell line, a monkey kidney epithelial cell used for in vitro nephrotoxicity, was divided into four groups: control, GM, GM/T1B1, and GM/T1B2. The GM group was treated with gentamicin IC50 dose only (50% inhibition of cell viability; 6000 µg/mL) for 72 hours. The GM/T1B1 and GM/T1B2 groups were treated with the gentamicin IC50 dose for 24 hours, and then T1B1 and T1B2 compounds were added to the same cell medium and incubated for 48 hours more. After incubation, cell viability and apoptic changes were determined by the MTT (3-*4,5-dimethylthiazol-2yl*-2,5-diphenyl tetrazolium bromide) test and DAPI staining, respectively. The data was examined using a one-way ANOVA test with a significance level of $p<0.05$.

RESULTS:T1B1 and T1B2 boron compounds significantly increased cell viability in Vero cells after in vitro gentamicin-induced nephrotoxicity ($p<0.05$). As a result, cell viability increased from 50% to 94% with the T1B1 compound and 86% with the T1B2 compound. Furthermore, DAPI staining microscopic imaging demonstrated that these compounds diminished apoptotic indications, including cell and nucleus shrinkage and chromatin network condensation.

CONCLUSIONS: In conclusion, this study revealed for the first time that T1B1 and T1B2 compounds may exert nephroprotective effects against gentamicin-induced nephrotoxicity. After this study, an investigation will be conducted to ascertain the nephroprotective effect of these compounds in vivo.

Keywords: Boron compounds, Nephrotoxicity, Kidney epithelial cell line, Nephro-protectant

OC-08

Effects of Apelin-13 in Diabetic Kidney Injury: Analysis of Histological and Biochemical Markers

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AIM: The mortality due to kidney damage secondary to diabetes is notably high, accounting for nearly half of all chronic kidney disease cases. This study evaluates the effects of apelin, a hormone expressed in vascular endothelial and adipose tissues, on histological changes, oxidative stress, and inflammation markers in rats with diabetes-induced kidney damage.

METHODS: Thirty-two male Wistar albino rats were divided into sham, Diabetes, Apelin, and Diabetes+Apelin groups. Diabetes was induced with a single dose of 45 mg/kg intraperitoneal streptozotocin (STZ). Apelin groups received 50 µg/kg apelin-13 intraperitoneally for seven days, while the control group received saline. Post-treatment, left kidneys were analyzed histologically with hematoxylin and eosin staining, and right kidneys were assessed for total oxidant capacity (TOC), total antioxidant capacity (TAC), interleukin 1β (IL-1β), and tumor necrosis factor (TNF-α). Serum urea and creatinine levels were also measured. Statistical analysis was performed using JAMOVI program, with $p<0.05$ considered significant.

RESULTS: Tnf-α level was significantly higher in the diabetes group compared to the sham group ($p=0.012$). While TAC level decreased significantly in those receiving only apelin compared to the sham group ($p=0.039$), it was observed that apelin intervention in diabetes significantly increased TAC level compared to the diabetes group ($p=0.014$). There was no significant difference between the groups in terms of urea, creatinine and IL-1β levels. Histological analysis revealed increased tubular dilation, epithelial shedding, brush border and nuclear loss in the diabetes and apelin groups compared to the sham group ($p<0.05$).

CONCLUSIONS: Short-term apelin treatment did not significantly mitigate diabetes-induced renal damage. Degenerative changes in the diabetes groups were also observed in the apelin-only group, particularly in glomeruli and renal tubules. These results suggest the need for further research into the long-term effects of apelin on kidney function.

Keywords: Apelin, Oxidative stress, Inflammation, Kidney injury, Diabetes

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OC-09

Investigation of the Effect of Metformin on Rat Bladder Smooth Muscle and the Mechanisms Mediating This Effect

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AIM: The effects of metformin on detrusor smooth muscle tissue are not yet fully understood. This study aims to investigate the in vitro effects of metformin on detrusor smooth muscle tissue and the possible mechanisms mediating these effects. Additionally, it seeks to contribute to the literature for its potential use in treating various diseases associated with bladder dysfunction.

METHODS: Bladder strips isolated from 12 male Wistar Albino rats were placed in an organ bath containing aerated Krebs solution and attached to a force transducer to record isometric contractions. Metformin (10^{-4} M–$3x10^{-3}$ M) was cumulatively applied in the presence of guanethidine and indomethacin to evaluate its effects on Electrical Field Stimulation (EFS)-mediated contraction responses in rat bladder detrusor strips. The effect of metformin ($3x10^{-3}$ M) on carbachol-induced contraction responses was also assessed. The effect of metformin was re-evaluated in the presence of dorsomorphin (10^{-5} M, an AMP-activated protein kinase [AMPK] inhibitor), Y-27632 (10^{-5} M, a Rho-kinase inhibitor), or N(ω)-nitro-L-arginine methyl ester (L-NAME) (10^{-4} M, a Nitric Oxide Synthase [NOS] inhibitor). Data obtained from the experiments were analyzed using the SPSS 20 statistical program with Mann-Whitney U and, where appropriate, Wilcoxon tests. Results were expressed as mean ± standard error of the mean (SEM), with $p < 0.05$ considered statistically significant.

RESULTS: Metformin did not affect EFS-mediated contraction responses. However, in the presence of dorsomorphin, an AMPK inhibitor, metformin significantly reduced contraction responses only at a concentration of $3x10^{-3}$ M ($p<0.05$). The presence of the Rho-kinase pathway inhibitor Y-27632 and the NOS inhibitor L-NAME did not alter the effect of metformin. Metformin led to a reduction in cumulative carbachol-induced contraction responses in all tissues ($p<0.05$).

CONCLUSIONS: Metformin exhibits its relaxant effects on bladder detrusor smooth muscle tissue primarily through direct smooth muscle contraction-relaxation pathways, independent of neural stimulation.

Keywords: Metformin, Detrusor, Contraction, AMPK, Rho-kinase, L-NAME.

OC-10

Phoenixin-14 Administration Acts Protective Role in Rats with Experimental Acute Kidney Injury Model

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AIM: Acute kidney injury (AKI) caused by ischemia-reperfusion (IR) injury is characterized by inflammation and oxidative stress. Phoenixin-14 (PNX-14) is a recently discovered neuropeptide. The peptide is thought to be secreted in peripheral tissues and may exert anti-inflammatory effects. This study was conducted to investigate the effects of PNX-14 in rats with ABH model.

METHODS: In the study, 40 male Wistar Albino rats (ethics committee 2024/14-2) were divided into 4 groups as control, I/R, PNX-14 (50µg/kg) and PNX-14 (100µg/kg) (n=10). While no surgical procedure was performed in the control group, both kidneys of the animals in the other groups were subjected to ischemia for 45 minutes and reperfusion for 24 hours. In the PNX-14 (50µg/kg) and PNX-14 (100µg/kg) groups, two different doses of PNX-14 (50-100µg/kg) were administered intraperitoneally before ischemia. At the end of the experiment, the animals were sacrificed and kidney tissues were removed. MDA, SOD, CAT and GSH levels were determined in the kidney tissues. In addition, histopathologic examinations in kidney tissue were determined by immunohistochemical method. Comparisons between groups were made using Mann Whitney-U test with Bonferroni correction in SPSS program.

RESULTS: PNX-14 decreased MDA level ($p<0.05$) and increased GSH, SOD and CAT enzyme activities ($p<0.05$) in the kidney tissue of ABH groups. On the other hand, histological evaluation showed that the kidney tissue in the control group had a normal histological appearance, whereas in the IR group, compared to the control group, degeneration in the tubules and glomerular structures of the kidney tissue; dilatation, hemorrhage, mononuclear cell infiltration, fluid accumulation in the tubule lumen, shedding of tubule epithelial cells, vacuolization and vascular congestion in the tubules were observed. These findings were decreased in PNX-14 (50µg/kg) and PNX-14 (100µg/kg) groups ($p<0.05$).

CONCLUSIONS: As a result of the study, PNX-14 administered intraperitoneally had protective effects against IR-induced ABH by activating antioxidant systems.

Keywords: Acute Kidney Injury, Ischemia-Reperfusion, Oxidative Stress, Phoenixin-14

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OC-11

Effects of Melatonin on Trace Element and Electrolyte Levels in Acute Kidney Injury

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AIM: Acute kidney injury is a case that occur due to many reasons such as sepsis, obstruction, nephrotoxic substances. The factor that causes apoptosis, necrosis and ferroptosis along with the nephron damage has been investigated but has not been elucidated yet. Melatonin is a powerful endogenous antioxidant and has many pleiotropic effects such as anti-inflammation. It protects from cell deaths due to iron accumulation such as ferroptosis and scavenges free radicals. Trace elements participate in enzyme structure as coenzymes. Therefore, they play an important role in antioxidant enzymatic reactions. Electrolytes affect the distribution of body fluids that change in the provision of homeostasis in septic shock. In this study we aimed to investigate the effects of melatonin on trace element and electrolyte in renal tissue in rats induced with lipopolysaccharide (LPS).
METHODS: Adult male Sprague dawley rats were divided into 4 groups; control, LPS(20 mg/kg i.p.), melatonin(10 mg/kg i.p.x3), melatonin+LPS. Rats were decapitated 6 hours after the first injection and blood samples were collected from the heart. Blood urea nitrogen (BUN) values were evaluated by auto-analyzers. Sodium, potassium, calcium, magnesium, iron, copper, zinc and selenium tissue element levels were measured by inductively coupled plasma optical emission spectroscopy technique(ICP-OES). One-way analysis of variance and Tukey tests were used for statistics.

RESULTS: It was observed that sodium, potassium, magnesium, calcium, iron, copper, zinc and selenium levels increased significantly in the LPS group compared to the others ($p<0.0001$). A significant increase in BUN levels was observed in the LPS group compared to the others ($p<0.01$).

CONCLUSIONS: We suggest that sepsis causes trace element and electrolyte accumulation caused to imbalance in oxidant/antioxidant levels in kidney tissue and melatonin may have scavenged free radicals with its antioxidant effect and increased the use of elements such as zinc and selenium.

Keywords: Sepsis, Acute kidney injury, Melatonin, Electrolytes, Trace element

OC-12

Effects of Ischemic Pre-conditioning and Boldine on Renal Ischemia Reperfusion Induced Remote Brain Injury

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AIM: One of the organs most affected by renal ischemia reperfusion (I/R) injury is brain. The aim of current study is to evaluate the effects of boldine and ischemic pre-conditioning on renal I/R induced brain damage via apoptotic, pyroptotic and inflammatory pathways.

METHODS: 5 groups (n=6) were created with rats: sham, renal I/R, pre-conditioning+renal I/R, boldine+renal I/R and boldine+pre-conditioning+renal I/R. 45 minutes of ischemia and 24 hours of reperfusion were applied. Pre-conditioning was performed with 3 sets; 2 minutes ischemia/5 minutes reperfusion. Boldine was applied intraperitoneally at dose of 20 mg/kg/day during 7 days. Total brain Bax, Bcl-2, cleaved caspase 3, Nrf2, NLRP3 and Gasdermin D levels were evaluated by Western blot. IL-2, TNF-α, IL-6 and IL-10 levels were evaluated by ELISA. Hematoxylin-eosin staining was performed and p53 and NF-κB expressions were evaluated immunohistochemically. Kruskal Wallis and post hoc Mann Whitney U test with Bonferroni correction was applied.

RESULTS: Bax/Bcl-2 ratio increased in other groups compared to sham, and decreased with boldine and pre-conditioning ($p<0.05$). Cleaved caspase 3 increased in other groups compared to sham ($p<0.05$). While Nrf2 was low, NLRP3 was high in I/R group ($p<0.05$). Gasdermin D was similar in all groups ($p>0.05$). IL-2 was found to be high in I/R group, while IL-10 was low ($p<0.05$). TNF-α and IL-6 did not statistically significant ($p>0.05$). Tubular necrosis, cytoplasmic vacuole formation and hemorrhage were reduced by boldine and pre-conditioning ($p<0.05$). Number of degenerated neurons in somatosensory cortex, which increased in I/R, was reduced by boldine ($p<0.05$). p53 and NF-κB increased with I/R and decreased with boldine and pre-conditioning ($p<0.05$).

CONCLUSIONS: The decrease in apoptotic, pyroptotic and inflammatory markers were evaluated as positive effects of boldine and pre-conditioning. It was concluded that boldine may be a potential treatment and/or prophylaxy agent.

This study was supported by Gazi University (TGA-2023-8829).

Keywords: Renal ischemia reperfusion injury, Boldine, Brain, apoptosis, Pyroptosis, Inflammation

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OC-13

Effect of Cumulative Zinc Doses on Papillary Muscle Contractions and the Zinc Finger Protein ZEB1

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AIM: In this study, we aimed to investigate the effect of cumulative $ZnCl_2$ doses on myocardial papillary muscle contractions isolated from rat hearts in vitro and the roles of ZEB1, a zinc finger protein, in this effect.

METHODS: The project protocol for the study carried out on female Wistar rats was approved by the local experimental animal ethics committee. A total of 20 female rats were randomly selected and divided into 4 equal groups. Control Group: Myocardial papillary muscle contraction recordings were taken in the animals in this group without zinc administration in Krebs solution. 1µM/L $ZnCl_2$ Group: The group in which myocardial papillary muscle contraction was recorded by administering 1µM/L $ZnCl_2$ into Krebs solution. 10 µM/L $ZnCl_2$ Group: The group in which myocardial papillary muscle contraction was recorded by administering 10 µM/L $ZnCl_2$ into Krebs solution. 100 µM/L $ZnCl_2$ Group: The group in which myocardial papillary muscle contraction was recorded by administering 100 µM/L $ZnCl_2$ into Krebs solution.

RESULTS: In the 100 µM zinc chloride group, when compared to all other groups, including the control group, there was a decrease in contraction force in both frequency-dependent parameters and pre-waiting stimuli ($p<0.05$) and an increase in contraction times ($p<0.05$). These data indicate that RyR2-mediated Ca-homeostasis is closely associated with increasing zinc doses (especially at the 100 µM zinc chloride dose). Secondly, the levels of ZEB1, a zinc finger protein, were significantly lower in the 100 µM/L $ZnCl_2$ group compared to the other groups ($p<0.05$); This suggests that high doses of zinc may be associated with increased Ca, which triggers ROS production.

CONCLUSIONS: Our data indicate that in vitro zinc administration may have a dose-dependent effect on myocardial papillary muscle contractions, with the aim of understanding zinc concentrations in the heart and uncovering new mechanisms involved in the regulation of Ca dynamics in cardiac tissue.

Keywords: Zinc, ZEB1, Papillary muscle, Oxidative stress, Excitation-contraction coupling

OC-14

Effects of GLP-1 Receptor Agonist on SIRT-1/PGC-1α Signaling Pathway in Isoprenaline-Induced Takotsubo Cardiomyopathy in Ovariectomized Female Rats

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AIM: Takotsubo syndrome (TTS) is a temporary acute heart failure condition caused by oxidative tissue damage from catecholamines released due to severe stress. It commonly occurs in postmenopausal women and those with diabetes. GLP-1 has been shown to impact glucose homeostasis and reduce cardiac ischemia-reperfusion injury. This study aims to assess the effects of liraglutide, a GLP-1 analogue, on cardiac oxidative stress, sirtuin-1 (SIRT1), PGC-1α levels, and echocardiographic outcomes in TTS.
METHODS: Female rats underwent bilateral oophorectomy to model surgical menopause and were divided into three groups: Oophorectomy (OVX), TTS, and TTS+Liraglutide, then monitored for 6 weeks. TTS was induced in the TTS and TTS+Liraglutide groups with a 150 mg/kg dose of isoprenaline. Liraglutide was administered subcutaneously at 150 µg/kg/day starting 3 days before TTS induction and continued for 5 days. Echocardiography was performed at 2, 24, and 48 hours post-isoprenaline to evaluate heart function. At 48 hours, rats were sacrificed and heart tissues collected. Cardiac SIRT1 and PGC-1α levels were measured using ELISA, while oxidative stress parameters, malondialdehyde (MDA), reduced glutathione, and nitrate levels were assessed spectrophotometrically. Statistical analysis utilized Kruskal-Wallis and Dunn tests.
RESULTS: In the echocardiographic evaluations performed at 2 and 24 hours in the TTS and TTS + Liraglutide groups, it was observed that ejection fractions (EF) decreased statistically significantly compared to the control and liraglutide groups ($P < 0.05$), and EF returned to normal after the 48th hour. In addition, while ST segment elevations were detected in the ECG in the TTS group, liraglutide application was effective in preventing ST segment elevations ($p<0.05$). MDA levels in heart tissue were found to decrease in the TTS+Liraglutide group compared to the TTS group ($p=0.049$). While SIRT1 and PGC-1α levels were lower in the TTS group compared to other groups (respectivelly $p=0.008$ and $p<0.001$), an increase in these parameters was observed with liraglutide treatment ($p=0.047$). No significant results were found in heart weight/body weight and blood glucose levels.
CONCLUSIONS: Liraglutide pretreatment was observed to be effective in reducing the impairment of myocardial functions in a rat model of TTS-like cardiomyopathy, primarily by increasing SIRT1 and PGC-1α and reducing oxidative stress.

Keywords: GLP-1, Heart failure, Sirtuin-1, PGC-1alpha, Takotsubo syndrome

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OC-15

Nesfatin-1 Alleviates Gastrointestinal, Cardiovascular and Nervous System Injury in Ovariectomized Rats: Role of Vagal Afferents

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AIM: Hormonal changes during menopause negatively affect female health. Nesfatin-1 (NES) expression varies by estrus cycle stages. This study aimed to investigate therapeutic potential of NES on menopause-induced gastrointestinal, nervous and cardiovascular system alterations and involvement of vagal afferents in NES-induced protective effects.

METHODS: Under anesthesia, female Sprague-Dawley rats underwent ovariectomy (OVX; n=12), sham-surgery (SX, n=12) or OVX+vagal afferent denervation with perivagal capsaicin (1%; OVX+VD; n=12). After recovery, rats were injected subcutaneously with NES (0.2 µg/kg/day) or saline for 25 days. Memory functions were evaluated with passive avoidance test, anxiety levels were measured using hole-board test. After sacrification, serum HDL and LDL levels were measured. Aortic contractility was examined in organ bath. Myeloperoxidase (MPO) activity, malondialdehyde (MDA), glutathione (GSH), superoxide dismutase (SOD), and catalase (CAT) levels were measured in heart, liver, and brain tissues. Microscopic damage scores were assessed with Hematoxylin-Eosin-stain. Statistical analyses were performed using one-way ANOVA.

RESULTS: Liver SOD levels were lower in OVX groups compared to SX ($p<0.05$). Cardiac CAT levels in OVX ($p<0.05$) and OVX+VD ($p<0.001$) groups were reduced compared to SX group, while NES treatment replenished CAT levels in both OVX groups ($p<0.05$). Brain SOD levels were lower in OVX ($p<0.01$) and OVX+VD ($p<0.05$) groups compared to SX. NES treatment also restored brain SOD levels. Histological evaluations of liver showed moderate inflammation in OVX and OVX+VD groups, but very mild inflammation in NES groups. OVX-induced histological cardiac damage was normalized in OVX+NES, OVX+VD, and OVX+VD+NES groups. Aortic endothelial damage by ovariectomy was rectified in NES-treated groups. Reduced aortic contraction-relaxation responses in OVX group was improved with NES treatment, except in OVX+VD+NES group.

CONCLUSIONS: At post-menopausal state, NES increased antioxidant activity in the liver, brain, and heart and preserved normal histological structures, while menopause-induced disruption in aortic function was improved by NES via vagal afferent activation.

Keywords: Menopause, Nesfatin, Vagus

OC-16

Investigation Of Oxidative Stress, İnflammatory Response and Cardioprotective Effects of Antidiabetic Liraglutide and Empagliflozin in Experimental Diabetic Rats

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AIM: This study aimed to investigate and compare effects of antidiabetic drugs liraglutide and empagliflozin on oxidative stress, inflammation markers, and cardiovascular complications in rats with induced diabetes mellitus (DM).
METHODS: 37 male Wistar Albino rats were divided into four groups: Control (n=7), DM control (n=10), DM + Liraglutide (0.6 mg/kg, subcutaneous), DM + Empagliflozin (30 mg/kg, oral gavage). Diabetes was induced using 110 mg/kg intraperitoneal nicotinamide followed by 60 mg/kg streptozotocin. Treatment was administered for 8 weeks, after which final weights and fasting blood glucose levels were measured. Blood samples were taken from the caudal vein under anesthesia, and levels of tumor necrosis factor-α (TNF-α), interleukin-1 (IL-1), malondialdehyde (MDA), superoxide dismutase (SOD), advanced glycation end products (AGEs), and insulin were determined. Heart and coronary artery tissues were also examined histopathologically.
RESULTS: Compared to healthy controls, DM control group exhibited significantly increased levels of FBG, AGE, IL-1, TNF-α, and MDA ($p<0.01$), while insulin and SOD levels were significantly reduced ($p<0.01$). Both liraglutide and empagliflozin treatments brought blood glucose levels closer to those of controls. Both drugs significantly decreased levels of TNF-α, IL-1, and AGEs ($p<0.01$) and also reduced serum MDA levels ($p=0.03$, $p<0.01$). SOD levels increased in treatment groups ($p<0.05$), only liraglutide treatment led to an increase in insulin levels ($p<0.01$). Histopathological analysis revealed that both drugs significantly improved structural changes, fibrosis, and inflammation caused by DM, with empagliflozin demonstrating a more pronounced positive effect on the myocardium compared to liraglutide.
CONCLUSIONS: Liraglutide and empagliflozin positively influence cardiovascular complications induced by DM. By alleviating oxidative stress and inflammation, they help preserve cardiac and coronary artery structures. It can be concluded that both drugs may prevent the development of cardiovascular complications in diabetic patients. This study was supported by Dicle University Scientific Research Projects Coordination with project number SBE.22.002.

Keywords: Diabetes mellitus, Cardioprotective effect, Liraglutide, Empagliflozin

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OC-17

Investigation of The Effects of Granulocytes on Hemostasis by Optical Aggregometer and Thromboelastogram

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AIM: The term "immunothrombosis" indicates that hemostasis process affects function of the immune system and that immune system components contribute to thrombosis. In many studies, it is observed that platelet-leukocyte aggregates increase in the blood, especially in inflammatory events, and even the importance of parameters such as amount and size of these aggregates in the prognosis of cardiovascular diseases is emphasized. In this study, effects of granulocytes on hemostasis were studied with aggregometry and thromboelastogram.
METHODS: Granulocytes were separated from whole blood samples. Three different conditions of granulocytes were studied: 1-immediately after separation. 2-incubation without stimulation with lipopolysaccharide for 4 hours. 3-incubation with stimulation with lipopolysaccharide for 4 hours. Granulocytes were added to platelet-rich plasma, and the effects on platelet aggregation were studied in an aggregometer and on hemostasis in a thromboelastogram. Paired t-test and Bonferroni Test was used for comparisons.
RESULTS: In the 0th hour experiments, granulocytes significantly decreased their maximum aggregation values in ADP and collagen-stimulated aggregations compared to the control group. No effect was observed on ADP and collagen-stimulated aggregations of 4th hour stimulated and unstimulated granulocytes. In thromboelastogram experiments, 0th hour and unstimulated granulocytes did not affect hemostasis parameters, while stimulated granulocytes activated hemostasis and created a hypercoagulable state.
CONCLUSIONS: It was found that granulocytes inhibit platelet aggregation immediately after separation from whole blood, and when stimulated with LPS, a hypercoagulable state was observed in the thromboelastogram. It was observed that granulocytes may have different effects on platelets depending on time and stimulation status. It was observed that granulocytes may also be effective in the coagulation process with thromboelastogram. The finding of opposite results between the aggregometer and thromboelastogram suggested that the measurement system in thromboelastogram should be considered more accurate and reliable because it simulates in-vivo conditions better and is more compatible with other hemostasis tests and clinical situations.

Keywords: Granulocyte, Platelet, Hemostasis, Aggregometer, Thromboelastogram

OC-18

Investigation of the Efficiency of Platelet-Rich Plasma (PRP) Against Central Effects of the Experimental Aluminum Toxicity

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AIM: Aluminum (Al),it affects numerous cellular processes responsible for cellular organization and cellular transmission in the central nervous system. It also inhibits long-term potentiation. It causes learning disabilities and impairs working memory.This study aimed to investigate the effectiveness of allograft platelet-rich plasma (PRP) against the behavioral and cognitive consequences of experimental Al toxicity.

METHODS: Thirtyfour male Wistar albino rats were divided into 4 groups (Control n=7, AlCl3 (n=9), AlCl3+PRP (n=9), PRP (n=7). For the experimental Al toxicity model, intraperitoneal injections (saline [0.5 mL]) or AlCl3 ([75mg/kg]) were administered on the first and eighth day of the experimental procedure. Oral gavage (saline [0.5 mL] or AlCl3 [75mg/kg]) was applied for the remaining 12 days of the experimental procedure.PRP was administered intravenously (0.15 mL) to AlCl3+PRP and PRP groups throughout the experimental procedure. In this context, locomotor activity, exploratory behavior, anxiety-like behavior and perceptual memory, as well as spatial learning and memory performances of the subject rats were evaluated with a test battery consisting of open field, light/dark field and Morris water maze tests. Evaluations were made with Kruskal-Wallis and post hoc Dunn test. (HMKÜ HADYEK,2022/06-21).

RESULTS: Although aluminum chloride (AlCl3) treatment weakened the locomotor activity and exploratory behavior measured by the total distance traveled and the number of rearing in the open field test, it was observed that this effect did not reach the level of statistical significance. It was also found that Al toxicity increased anxiety-like behavior, evaluated by the time spent in the bright field in the light/dark field test,compared to subjects treated with PRP,but the treatment effect of PRP did not reach the level of significance.Morris water maze test which is conducted in an aversive environment,it was observed that PRP application was found to be ineffective in mitigating the Al-related spatial memory impairment.

CONCLUSIONS: In conclusion, the potential benefits of PRP application in locomotor and cognitive disorders due to Al toxicity in rats has been demonstrated.It is understood that the protective effect of PRP on cognitive performance in Al toxicity is associated with and limited by anxiety-inducing factors.

Keywords: Aluminium, Toxicity, Platelet Rich Plasma, Learning, Memory

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OC-19

Investigating the Effects of Diisobutyl Phthalate Chemical on Feeding Behavior and Obesity

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AIM: Phthalates are known as a subgroup of endocrine-disrupting chemicals widely used worldwide, implicated in causing obesity. Among these, diisobutyl phthalate (DIBP), primarily used as a plasticizer, lacks clear elucidation regarding its relationship with dietary behaviors and obesity when compared to other phthalate groups. The aim of this study is to investigate the effects of DIBP on obesity and appetite metabolism.

METHODS: In this study, 32 male Sprague Dawley rats were used. The rats were divided into a control group and three different dose groups of diisobutyl phthalate (DIBP) (0.1, 0.5, and 1 g/kg/day) (n=8 per group). DIBP was dissolved in corn oil and administered orally via gavage for eight weeks. The control group received only corn oil. At the end of the experiment, the animals were euthanized, and brain and blood samples were collected. Serum levels of leptin, ghrelin, and irisin were determined using ELISA. AgRP and POMC protein levels in brain tissue were analyzed using Western blot and immunofluorescence. Differences between groups were compared using the Kruskal-Wallis test, with $p < 0.05$ considered statistically significant.

RESULTS: Statistically significant increases were observed in food intake, serum ghrelin, irisin, and AgRP protein levels in the groups treated with DIBP compared to the control group ($p<0.05$). Additionally, statistically significant decreases were noted in serum leptin and POMC protein levels in the DIBP-treated groups compared to the control group ($p< 0.05$).

CONCLUSIONS: Our study results demonstrated that the environmental pollutant DIBP influenced food intake, exerting these effects by altering the endocrine system and impacting central pathways regulating food intake.

Keywords: AgRP, DIBP, Ghrelin, Leptin, Obesity, POMC

OC-20

The Effect of Cold Exposure and Bee Venom Injection on UCP-1 Gene Expression Levels and Anxiety-Like Behaviors in Rats Fed a High-Fat Diet

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AIM: We investigated the role of increased adipose tissue activity and bee venom (BV) injection on the interaction between UCP-1, metabolic and emotional disorders, as well as its effect on the regression of emotional disorders.

METHODS: In our experiments, three-week-old male Sprague-Dawley rats were used. The rats were divided into the following groups: control, cold exposure (CE), BV 0.5 mg/kg (BV0.5), high-fat diet (HFD, %60 from fat), HFD+BV0.5, HFD+CE, and HFD+CE+BV0.5. The rats were fed a HFD for 8 weeks. During the last 21 days, they were exposed to cold at +4 °C and the last 15 days subcutaneous BV injections were administered. Anxiety and depression-like behaviors were evaluated using the open field (OF), elevated plus maze (EPM) and forced swim test (FST). At the end of the experiment, UCP-1 gene levels were measured by PCR in intra-scapular brown adipose tissue (BAT) and subcutaneous white adipose tissue (WAT) from the sacrificed rats. One Way ANOVA test was used to evaluate the data.

RESULTS: In the EPM results, HFD exhibited significantly increased activity with BV injection, spending more time in the open arms and center area, less time in the closed arms ($p<0.05$). In the FST, HFD+CE+BV0.5 showed significantly less immobility time compared to the control, CE and HFD ($p<0.05$). When comparing UCP-1 gene expression levels, the HFD+CE+BV0.5 had significantly higher BAT UCP-1 expression levels than the CE, HFD, and HFD+BV0.5 ($p<0.05$). The HFD+CE+BV0.5 also had significantly higher WAT UCP-1 expression levels than the HFD and HFD+CE ($p<0.05$).

CONCLUSIONS: Our results show that increased UCP-1 in WAT and BAT through BV injection reduces anxiety and depressive behaviors in rats. UCP-1 may mediate the link between metabolic and emotional disorders, suggesting BV's potential as a thermogenic agent.

This research was supported by Dokuz Eylul University Department of Scientific Research Projects (TDK-2021-2618).

Keywords: High-Fat Diet, Anxiety, Depression, UCP-1, Bee Venom

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OC-21

Changes in Nutrition-Related Molecules in Male and Female Rats in an Experimental Model of Autism Spectrum Disorders

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AIM: Autism Spectrum Disorders (ASD) are neurodevelopmental pathologies that affect individuals' daily lives and normal brain functions. Similar symptoms are observed between ASD and eating disorders. This study aims to investigate the changes in serum Glucose, Leptin, Orexin-A, and Nesfatin-1 levels in male and female animals in a Valproic Acid (VPA) induced model of ASD.

METHODS: The study was approved by Bursa Uludağ University's ethics committee (numbered:2024-01/08). Pups from pregnant Wistar Albino rats that received either 400mg/kg VPA (n(mother)=4, n(male pup)=8, n(female pup)=8) or Saline (S, 1ml/kg), (n(mother)=4, n(male pup)=8, n(female pup)=8) on embryonic day 12.5 intraperitoneally were included. Pups were decapitated on postnatal day-35 after 16h of fasting. Blood glucose levels were measured and serum Nesfatin-1, Orexin-A, and Leptin levels were anaylzed by ELISA kit protocols. Statistical analysis was performed with Two-Way ANOVA on Sigma-Plot, $p<0.05$ was considered significant.

RESULTS: There was a significant interaction between sex and VPA in blood glucose levels ($F(1.31)=20.145$, $p<0.001$). Compared to the S-male group, blood glucose levels significantly increased in VPA-male group ($p<0.001$), while no significant difference was found between the S-female and VPA-female groups. There was no significant interaction between sex and VPA in Leptin levels. A significant difference was found between male and female groups independent of prenatal exposure ($p=0.012$), also S and VPA groups independent of sex ($p<0.001$) in Leptin levels. There was not a significant interaction between sex and VPA in Nesfatin-1 levels. A significant difference was found between S and VPA groups independent of sex ($p=0.004$) in Nesfatin-1 levels. There was no significant difference in Orexin-A for any groups.

CONCLUSIONS: Although metabolic and nutritional disorders are frequently observed in ASD, few studies investigate the relationship between ASD and molecules which are effective in nutrition. Our results suggest changes in nutrition-related molecules in ASD which may differ by sex.

Keywords: ASD, Leptin, Nesfatin-1, Nutrition, Orexin-A, Sex

OC-22

Investigation of the Effect of Apelin on Dopamine Signalling in the Hypothalamic Paraventricular Nucleus of Mice on High Calorie Diet by Fiber Photometry

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AIM: Obesity is mainly caused by an imbalance between food intake and expenditure. Consumption of a high-fat diet is among the main causes of obesity. In addition to the paraventricular nucleus (PVN), apelin and dopamine (DA) are play role processes of food intake and obesity. The aim of this study was to investigate the effect of apelin on PVN DA'ergic activity in normal diet and high fat diet feeding conditions by fiber photometry method.

METHODS: 32 C57bl/6 male mice were divided into 4 groups: normal diet (ND), high fat diet (YYD), apelin+normal diet (A+ND), apelin+high fat diet (A+YYD) group. After injection of the dopaminergic sensor virus, fiber optic ferules were implanted into the PVN. After resting for 15 days, animals were fed with high fat diet and normal diet for 28 days according to characteristics of groups. In addition to dietary administration, 100µg/kg (ip) apelin was injected into apelin groups every other day. Feed intake, blood glucose and body weights were monitored and fiber photometry records were taken at the end of the 28th day. Fiber photometry recordings were filtered by MATLABsoftware and z-score (dF/F) and area under the curve (AUC) values calculated. Results were analysed by one-way analysis of variance.

RESULT: Body weights of ND ($p<0.01$), YYD ($p<0.001$), A+YYD ($p<0.001$) groups on day 28 were higher compared to day 0. On 28th day, body weight of A+ND group was lower than YYD and A+YYD groups ($p<0.001$). AUC values of A+ND group were higher than ND ($p<0.05$) and A+YYD ($p<0.05$) groups. AUC values in A+ND group tended to decrease compared to the ND group ($p>0.05$).

CONCLUSIONS: The results of our study show that apelin suppresses body weight gain in mice, may have a regulatory effect on PVN DA'ergic activity and may play a protective role in reduced DA'ergic tone in obesity.

Keywords: Apelin, Dopamine, Dopamine receptors, High fat diet, GRAB, PVN

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OC-23

Investigation of Hypothalamic and Hippocampal Semaphorin 3A and Receptor Gene Expression Levels in an Experimental Morphine Addiction Model

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AIM: Morphine, an opioid agonist, has a strong analgesic effect, on the other hand naloxone is widely used as a general opioid receptor antagonist. Semaphorins are neuronal guidance proteins involved in nervous system development and neurodegenerative diseases. The impact of opioid addiction on semaphorin proteins and receptors in the hypothalamus and hippocampus is unknown. This study aims to investigate if the expression levels of semaphorin 3A and its receptors in the rat hypothalamus and hippocampus change with morphine addiction.

METHODS: Adult male Wistar albino rats were used. In the study, 24 young adult male Wistar albino rats were used. Animals were divided into 4 groups as control group administered vehicle for 5 days (s.c.), morphine group administered 10mg/kg/day morphine sulfate (s.c.), naloxone group administered 3mg/kg naloxone hydrochloride (s.c.) for 5 days and morphine + naloxone group injected 3mg/kg naloxone (s.c.) on the last day after 5 days of morphine administration. Hypothalamus and hippocampus tissues were removed, and gene expression levels of semaphorin 3A, plexin, neuropilin-1 were analyzed by RT-PCR. Statistical evaluation was performed using the One-Way ANOVA test.

RESULTS: The expression level of SMF 3A receptors in the hypothalamus is significantly decreased in the MN group compared to the M group ($p<0.05$). The expressions of NRP1 and PLA1 receptors are significantly higher in the M group compared to the MN group ($p<0.05$). In the hippocampal tissue, the gene expression levels of SMF 3A and NRP1 in the M group are significantly increased compared to the MN group ($p<0.05$).

CONCLUSIONS: The higher levels of semaphorins in the brain tissues of rats with morphine addiction suggest that SMF 3A, NRP1, and PLA1 may also play a mediating role in the neuronal damage occurring in the hypothalamus and hippocampus.

Keywords: Hippocampus, Hypothalamus, mu Opioid receptor, Semaphorin 3A

OC-24

Effects of Dexamethasone-induced Insulin Resistance Model on Self-care Behaviors and Brain-derived Neurotrophic Factor

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AIM: Insulin resistance (IR) is described as an impaired response to insulin stimulation of target cells. IR causes both physical and psychological adverse effects. The present study was designed to investigate the effect of dexamethasone induced insulin resistance model on self-care behaviors and brain-derived neurotrophic factor (BDNF).

METHODS:16 adult male Wistar albino rats were divided into control and IR groups (n=8). To induce the IR model, dexamethasone was administered by intraperitoneally 1 mg/kg/day for 5 days. Open field and splash tests(Splash test procedure: spraying 10% sucrose water solution to arise emotion of contamination and observation of self care behaviors) were performed to evaluate locomotor activity and self-care-depression-like behaviors, respectively. After the subjects were sacrificed, BDNF was analyzed by ELISA in the striatum and prefrontal cortex. Homo-IR, glucose, insulin, ALT, and AST were analyzed in serum. Changes in kidney, liver, and pancreas were examined histologically. Shapiro–Wilk, Student t, and Fisher's exact test were used as statistical tests.

RESULTS: Total distance traveled, grooming frequency,and grooming time decreased in IR group compared to the control group. Serum ALT, AST, glucose, insulin, and HOMA-IR values increased in the dexamethasone-applied group ($p<0.05$). BDNF decreased in the prefrontal cortex in the insulin resistance group ($p<0.05$). Striatum BDNF level decreased slightly but was not significant ($p>0.05$). Degeneration of islets of Langerhans in the pancreas, tubular degeneration in the kidney, degeneration of hepatocytes, and mononuclear cell infiltration in the liver increased in the IR group compared to the control group ($p<0.05$).

CONCLUSIONS: Insulin resistance negatively affected locomotor activity and self-care behaviors. The prefrontal cortex was found to be a more vulnerable to insulin resistance. Our results suggest that IR deteriorates self-care behaviors and BDNF level of the prefrontal cortex, in accordance with serum biomarkers and histological parameters.

Keywords: BDNF, Insulin resistance model, Self-care behavior, Splash test

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OC-25

Effects of Apelin-13 on Oxidative Stress and Auditory Brainstem Responses in STZ-Induced Diabetic Rats

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AIM: Diabetes is one of the common endocrinological disorders worldwide and causes various complications. One of the complications caused by diabetes is hearing loss. Research on the relationship between diabetes and hearing loss has been ongoing for a long time. Apelin is typically expressed in vascular endothelium and fatty tissues, and Apelin-13 is the primary active isoform that specifically binds to the apelin receptor. Apelin receptors are also found in the auditory system. The aim of this study is to investigate the effects of apelin-13 on oxidative stress and auditory brainstem responses in STZ-induced diabetic rats.

METHODS: Thirtytwo male Wistar albino rats were divided into four groups: sham, diabetes, Apelin and Diabetes+Apelin. A single dose of 45 mg/kg ip STZ was administered to create a diabetes model. Apelin groups were given 50 µg/kg apelin-13 intraperitoneally for 7 days. The sham group was also administered ip saline for 7 days. Auditory brainstem responses (ABR) were evaluated at the end of apelin and STZ applications. Then, cochlea tissue was removed and biochemical analyzes were performed. JAMOVI program was used for statistical analysis and $p<0.05$ was considered significant.

RESULTS: Compared with diabetic groups, Apelin treatment significantly improved the total antioxidant status (TAS) of the cochlea, while reducing the total oxidant status (TOS) and oxidative stress index (OSI). According to measurements of auditory brainstem responses (ABR), Wave V latencies in diabetic groups were much longer than in control groups. Apelin treatment partially reverses this effect, especially at certain frequency and intensity levels.

CONCLUSIONS: It was determined that apelin may have a therapeutic effect against diabetes-related hearing system damage with its antioxidant effect. These findings support the potential protective role of apelin on the auditory system and are thought to be a new therapeutic approach in the treatment and prevention of diabetic auditory neuropathy.

Keywords: Diabetes, Apelin, Auditory brainstem responses, Oxidative Stress

OC-26

The Effect of Intracerebroventricular Meteorin-Like Protein Infusion on the Hypothalamic-pituitary-testicular Axis

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AIM: Reproductive behaviors are regulated by the central effectors of the brain, with the hypothalamus playing a critical role in this process. Gonadotropin-releasing hormone (GnRH) and other peptides produced in the hypothalamus regulate reproductive functions. In males, GnRH signals trigger the release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH); LH stimulates testosterone production, while FSH promotes spermatogenesis. The hypothalamic-pituitary-testicular (HPT) axis can be regulated by adipokines. Meteorin-like protein (METRNL) is a newly discovered adipokine present in components of the HPT axis, but its role in these tissues remains unclear. The aim of this study is to investigate the effects of METRNL on the HPT axis.

METHODS: In this study, 40 male Wistar rats were randomly divided into four groups (control, sham, 10 nM METRNL, 100 nM METRNL). Brain infusion kits were implanted into the rats' right lateral ventricles, and they were allowed to recover for 7 days. On the 8th day, the rats were anesthetized, and an osmotic mini-pump was connected to the brain infusion kit cannula to infuse METRNL (5 µL/hour for 14 days). At the end of the experiment, the rats were decapitated and blood samples were collected. Serum LH, FSH, and testosterone levels were measured using ELISA. Data were analyzed using the Kruskal-Wallis H test and Bonferroni-corrected Mann-Whitney U test, with $p<0.05$ considered significant.

RESULTS: Serum LH, FSH, and testosterone levels in the groups that received chronic intracerebroventricular METRNL infusion decreased dose-dependently compared to the control group ($p<0.05$). However, no significant difference was observed between the control and sham groups ($p>0.05$).

CONCLUSIONS: Central METRNL infusion in male rats may suppress reproductive functions by reducing LH, FSH, and testosterone levels.

This study was supported by TÜBİTAK (Project No: 123Z074).

Keywords: Meteorin-Like Protein, Hypothalamus, LH, FSH, Testosterone

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OC-27

Anti-Cancer Effects of Tangeretin and Delphinidin on Pancreatic Cancer Cells

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AIM: Pancreatic cancer is the 13th most common type of cancer worldwide and the 7th leading cause of cancer-related deaths. The aim of this study is to evaluate the potential anti-cancer effects of tangeretin and delphinidin on pancreatic cancer cells. The rapid progression and high fatality rate of pancreatic cancer limit the effectiveness of current treatment methods. Therefore, the development of new treatment approaches for pancreatic cancer is of critical importance. Our study aims to assess the potential anti-cancer effects of tangeretin and delphinidin on pancreatic cancer cells in an in vitro setting.

METHODS: The human pancreatic cancer cell line (PANC-1) was used in this study. Tangeretin and delphinidin were applied as treatments. In vitro experiments included MTS cell proliferation, colony formation, wound healing test, and western blot analysis. Statistical analyses were performed using SPSS v15.0.

RESULTS: In the study, significant reductions in cell proliferation and colony formation were observed at 50 and 100 µM doses of tangeretin and delphinidin ($p<0.0001$). In the wound healing test, treatment with 50 µM tangeretin and delphinidin resulted in significant reductions in cell motility. Western blot analysis showed that 50 µM and 100 µM tangeretin and 50 µM delphinidin increased Bax expression and decreased Bcl-2 expression in PANC-1 cells, leading to an increase in the Bax/Bcl-2 ratio and inducing cell death ($p<0.0001$). In combination, 10 µM tangeretin + 10 µM delphinidin and 50 µM tangeretin + 50 µM delphinidin also significantly reduced cell proliferation, colony formation, and motility while increasing the Bax/Bcl-2 ratio ($p<0.0001$).

CONCLUSIONS: The data revealed that tangeretin and delphinidin have significant effects on cell proliferation, colony formation, and apoptosis in PANC-1 cells. Combined treatment with tangeretin and delphinidin may be a useful and feasible intervention in pancreatic cancer patients pending further studies.

Keywords: Tangeretin, Delphinidinw, PANC-1, Anticancer, Proliferation, Apoptozis

OC-28

Examination of Morphological Changes, Murf1 and Atrogin1 Gene Expression Levels, and Redox Status During Hydrogen Peroxide-Induced Atrophy in Melatonin-Treated Mouse Myoblast Cell Line

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AIM: It is well known that oxidative stress plays a critical role in the development of disuse muscle atrophy. The use of antioxidants, particularly those targeting mitochondria such as melatonin, has emerged as an important therapeutic option.In this study,we aimed to investigate the effects of melatonin on the redox balance and cellular morphology in an oxidative stress-induced muscle atrophy model in C2C12 cells, as well as the expression levels of Atrogin-1 and MuRF1.

METHODS: Therapeutic doses were determined using the MTT method based on the literature. Four different C2C12 cell groups were created: Control(C),Melatonin(M, 100 µM),H2O2 (H, 50 µM), and Melatonin + H2O2(MH). To evaluate treatment outcomes, myotube morphology was assessed at three different regions (25%, 50%, and 75% of their length) using ImageJ. RNA isolation and RT-PCR were performed to examine Atrogin-1 and MuRF1 gene expression levels, with 18S rRNA as the reference gene.The redox status was evaluated by assessing total oxidant-antioxidant status in both cell lysates and culture media.

RESULTS: Statistically significant differences were found in the average myotube diameters between groups and protective effect of the M group on atrophy was confirmed ($p\leq0.00001$).Although atrogene expression levels decreased in the M group, this difference was not statistically significant. A significant increase in total antioxidant status (TAS) levels was observed in the M and MH groups compared to the C group ($p<0.05$) in the culture media. In the lysates, significant increase in TAS levels was observed in the MH group compared to the C group ($p<0.05$), while the increase in the M group was not statistically significant.

CONCLUSIONS: Our results suggest that melatonin has positive effects on muscle atrophy. Melatonin may exert these effects by influencing atrogene expression levels. The lack of statistical significance could be due to the early pronounced expression of atrogenes. Melatonin shows potential as a treatment or preventive agent for muscle atrophy by preventing myotube diameter reduction and enhancing antioxidant capacity.

Keywords: Atrogenes, Muscle Atrophy, Melatonin, Oxidative Stress

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OC-29

Evaluation of Potential Anticarcinogenic Characteristics of c-Phycocyanin and Flavonoid Combinations on MDA-MB-231 Cells

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AIM: Triple negative breast cancer (TNBC) is a heterogeneous group of tumors that are negative for estrogen, progesterone and HER2 amplification. Due to the resistance to chemotherapy and side effects seen in TNBC patients, new drug discoveries and alternative effective treatments are needed for the treatment of TNBC. C-phycocyanin; is a pigment-protein complex derived from Spirulina sp. and is a promising therapeutic agent that has been shown to have anti-inflammatory, antitumor effects. In this study, we aimed to investigate the anticancer activity of C-phycocyanin on MDA-MB-231 breast cancer cell line. Additionally, we focused on identifying a more effective and safe combination therapy that could be used to treat TNBC by preparing combinations with curcumin and quercetin, which have known synergistic effects, to increase the efficacy of C-phycocyanin.

METHODS: MDA-MB-231 and L929 healthy cell lines were treated with C-phycocyanin, curcumin, quercetin flavonoids separately and in combination. Effects of combinations on cell viability were evaluated by MTT test. Then, treated cells' morphology was determined with AO/EtBr staining, and antioxidant activity was evaluated with DCF-DA test. Effects of flavonoid combinations on cell migration and cell-cell interactions were analyzed by scratch assay method.

RESULTS: MDA-MB-231 cells were treated with five different doses of combination, 5-2.5-20 µg/ml, 10-5-40 µg/ml, 20-10-50 µg/ml, 25-15-75 µg/ml, 30-25-100 µg/ml. The effective dose was determined as 5-2.5-20 µg/ml for 48 hours. The C-phycocyanin/flavonoid combination was found to inhibit MDA-MB-231 cell viability by 90%. Based on AO/EtBr staining results, early and late apoptotic cells were determined in MDA-MB-231 cells. We also determined that C-phycocyanin/flavonoid combination inhibits cell migration by approximately 90% compared to C-phycocyanin alone and triggers oxidative stress-induced cell death ($p<0.001$).

CONCLUSIONS: The findings showed that the C-phycoyanin/ flavonoid combination created synergy between them compared to their use alone and the combined treatment was more effective on the MDA-MB-231 cell line.

Keywords: Triple-negative breast cancer, C-phycocyanin, MTT, DCF-DA, Scratch assay, AO/EtBr

OC-30

Polysaccharide Coated Silver Nanoparticle with Effectiveness in Reducing the Viability of Triple Negative Breast Cancer

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AIM: The side effects and high costs of cancer drugs have increased research on biocompatible, low-cost alternatives. Studies investigating nanoparticles' effects on cancer are growing. Chitosan is a biocompatible, biodegradable material with antibacterial and antitumoral properties. These properties are also preserved in chitosan-based nanocomposites. Using a newly developed method, N-carboxymethyl chitosan polysaccharide-based silver nanoparticles (C@AgNP) were synthesized, and their effects on triple-negative breast cancer (TNBC) cells were investigated. TNBC is a type of cancer with a poor prognosis, characterized by the deficiency of estrogen, progesterone receptors and human epidermal growth factor receptor-2. The aim of this study is to investigate the potential of newly synthesized C@AgNP to reduce the viability of TNBC cells.

METHODS: C@AgNP was synthesized using the new "White-light method" and characterized by SEM and TEM. 4T1 and MDA-MB-231 cells were seeded at 25.103 cells/well in 96-well plates. After 24 hours, C@AgNP was applied at doses of 0.00312, 0.00625, 0.0125, and 0.025 mg/mL in triplicate. The control group received culture medium. MTT lysis buffer was added at the 24th hour, and absorbances were read at 570 nm in a spectrophotometer. The control group was accepted as 100%, and %viabilities were determined. IC50 values were found using GraphPad Prism. 4T1 cells treated at IC50 for 24 hours and apoptosis rates were determined via flow cytometry using Annexin V-FITC/PI kit. One-way ANOVA was used for statistical analysis.

RESULTS: After 24 hours of application, cell viability decreased dose-dependently in both 4T1 and MDA-MB-231 cells ($P<0.05$), with IC50 values of 0.00571 ± 0.00052 mg/mL and 0.00726 ± 0.0018 mg/mL, respectively. In 4T1 cells, the reduction of viability was supported by approximately 66% apoptosis at 24 hours, consistent with the MTT results.

CONCLUSIONS: C@AgNP, synthesized using the new method at lower cost and time, effectively reduced TNBC cells viability at low doses and showing promise as a potential anticancer agent.

Keywords: Triple negative breast cancer, Chitosan-Coated Silver Nanoparticle, Nanoparticle

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OC-31

The Interplay Between Sirtuin 1 (SIRT1) and Autophagy/Mitophagy in Serum-Starved SH-SY5Y Cells

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AIM: This study aimed to evaluate the interaction between SIRT1 and autophagy/mitophagy pathways in SH-SY5Y cells under serum-starvation conditions.

METHODS: In the present study, the gene expression levels of autophagy-related markers including ULK1, and BECN1 as well as mitophagy-related markers, such as PINK1, PARKIN, and MFN2 were evaluated by qRT-PCR in SH-SY5Y cells under serum-depletion condition for 24h. In addition, these marker levels were assessed in the presence of SIRT1 siRNA in media with/without serum for 24h. Furthermore, miRNA target genes were evaluated with multiple miRNA-target prediction tools, such as TargetScan and miRWalk. Gene Ontology (GO) analysis was conducted to assess the molecular functions, biological processes, and cellular components associated with these miRNAs or their targets. Additionality, this study was approved by Kırklareli University, Scientific Research Ethics Committee with approval no: E-37844677-199-85871 on 19 May 2023.

RESULTS: The expression levels of the ULK1 and BECN1 genes significantly increased in response to serum deprivation in the cells (respectively, ***p≤ 0.001, ****p≤ 0.0001). Furthermore, the expression levels of PINK1, PARKIN, and MFN2 genes also significantly elevated under these starvation conditions (*p ≤ 0.05). SIRT1 demonstrated a positive regulatory effect on ULK1 in both serum-containing and serum-deprived media (*p≤ 0.05) while it negatively regulated PINK1 specifically in serum-containing media (**p≤ 0.01). Additionally, PARKIN gene expression tended to decrease in the presence of SIRT1 siRNA, regardless of serum conditions (p> 0.05). As a result of bioinformatics analysis, 4 miRNAs that could potentially regulate SIRT1 and ULK1 were determined.
CONCLUSIONS: As a result, prominent shreds of evidence that prove a direct link between SIRT1 and mitophagy/autophagy markers was determined in SH-SY5Y cells. Additionality, the identification of key miRNAs, hsa-miR-128-3p, hsa-miR-216a-3p, hsa-miR-181b-5p, as well as hsa-miR-181a-5p, provides an approach with novel insights, paving the way for the development of targeted therapies for neurodegenerative diseases.

Keywords: Hsa-miR-128-3p, Hsa-miR-181a-5p, Hsa-miR-181b-5p, Hsa-miR-216a-3p, Mitophagy/autophagy, SIRT1

OC-32

Ramelteon Exhibits Anticancer Effects in Different Types of Human Cancer Cells

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AIM: Cancer is a disease characterized by the uncontrolled proliferation of body cells and the involvement of apoptotic and inflammatory processes, leading to its spread throughout the body. Among proposed treatments for various cancer types, the administration of anti-inflammatory hormones or drugs plays a significant role. The hormone melatonin, known for its anti-inflammatory properties, has been extensively studied in relation to different cancer types. Ramelteon, an analogue of melatonin, is primarily used for the treatment of insomnia. Literature reviews have shown that Ramelteon suppresses the proliferation of neuroblastoma and endometrial cancer cells; however, its broader relationship with cancer has not yet been fully reported. This study aims to investigate effects of Ramelteon on cell viability and DNA damage in A2780 (ovarian), MCF-7 (breast), Caco-2 (colon), and LNCaP (prostate) cell lines.

METHODS: In this study, A2780,MCF-7,Caco-2, and LNCaP cell lines were used. Ramelteon was applied to these cell lines at concentrations of 5, 10, 25, 50, 100, and 500µM, followed by incubation for 24 hours. Changes in cell viability were assessed using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. After determining dose-dependent efficacy, 50% inhibitory concentration (IC50) values were calculated using GraphPad Prism 8. Based on the identified effective dose, cytotoxic effects were evaluated using the Comet Assay. Comparisons between the groups were made using the Kruskal-Wallis H-Test, with $p<0.05$ considered statistically significant.

RESULTS: The results showed that Ramelteon reduced cell viability in A2780 cell line at doses of 50, 100, and 500µM, MCF-7 cell line at all concentrations, Caco-2 cell line at all doses except 5µM, and LNCaP cell line at doses of 100 and 500µM($p<0.05$). Moreover, Ramelteon exhibited statistically significant cytotoxic effects on the A2780,MCF-7,Caco-2, and LNCaP cell lines($p<0.05$).

CONCLUSIONS: The results demonstrate that Ramelteon exhibits anticancer activity in these cell lines and may be a potential candidate for the development of new cancer treatment strategies.

This study was supported by the İnönü University Scientific Research Projects Unit(TSA-2024-3546).

Keywords: Ramelteon, Cancer, Melatonin

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OC-33

Effects of Intermittent Fasting on Oxidative Stress, Tissue Histology, and Behavioral Parameters in Acrylamide Exposure.

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AIM: Acrylamide is a toxic substance found in various foods, cigarettes, and industrial chemicals. Intermittent fasting has been shown to reduce oxidative stress and inflammation and aid in cell renewal and protection. This study aims to investigate the protective effects of intermittent fasting on oxidative stress parameters, tissue histology, and behavioral parameters during acrylamide exposure.

METHODS: Twentyeight adult male Wistar albino rats, weighing 200-250 grams, were divided into four groups (n=7): control (C), acrylamide (AC), intermittent fasting (IF), and acrylamide+ intermittent fasting (ACIF). For 28 days, intermittent fasting was applied every other day, and acrylamide was administered intraperitoneally at a dose of 30 mg/kg three times a week. On the final day, anxiety tests (Elevated Plus Maze, Open Field Test) and a locomotor activity test (rotarod) were performed. Oxidative stress parameters (CAT, GPX, SOD) were measured in liver, kidney, and brain tissues, and histopathological analyses were conducted.

RESULTS: In the rotarod test, the walking duration of the AC group (16.1±14.1s) was observed to be significantly lower compared to the IF group (50.7±14.9s) and the C group (47±16.9s). In liver and kidney histopathology, intermittent fasting was found to reduce the congestion and hydropic degeneration in hepatocellular and tubular epithelium caused by acrylamide. In the elevated plus maze anxiety tests, the percentage of time spent in the closed/open arm was significantly higher in the AC (68.43±41.58) group than in the IF (7.86±11.25) group. It was observed that acrylamide administration had similar effects on brain, kidney and liver tissues and decreased CAT, GPX and SOD values.

CONCLUSIONS: Intermittent fasting reduced oxidative stress and tissue damage caused by acrylamide exposure. These findings suggest that intermittent fasting may have protective effects on acrylamide exposure. This study was supported by Hacettepe University Scientific Research Projects Unit project number THD-2021-19804.

Keywords: Acrylamide, Behaviour, Histopathology, Intermittent fasting, Oxidative stress

OC-34

Regulatory T Cells in Sickle Cell Anemia: Prognostic Value and Relationship with Non-Lymphocytic Leukocytes

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AIM: Sickle cell anemia (SCA) is hereditary disease characterized by vascular occlusions and organ damage caused by sickle-shaped erythrocytes, involving inflammatory disease associated with excessive immune activation. Regulatory T cells (Tregs) play critical role in regulating immune system. Studies examining immunophenotypes of adults with SCA are limited. Our previous study, presented at hematology conference, found Treg levels were higher in acute patients presenting with painful crises. Since Tregs counts are not routinely evaluated in clinical practice, determining their possible relationship with routine complete blood count parameters may provide insight into Treg activation. This study aims to evaluate relationship between Tregs and non-lymphocytic leukocytes assessed by complete blood count.
METHODS: The study included 37 SCA patients and 31 healthy volunteers, all over 18 yearls old. Exclusion criteria included pregnancy, cancer, autoimmune diseases, acute infections, and medication use for SCA. FoxP3 was used for flow cytometric analysis of Tregs. Multiple linear regression analysis was conducted to determine parameters affecting Tregs count.
RESULTS: Moderate significant correlation was observed between Treg count and monocyte (r=0.356, p=0.003) and leukocyte counts (r=0.427, p<0.001) across all subjects. Leukocyte count significantly predicted Treg count (Treg count = 3.437 + 2.841 * leukocyte count). In patients experiencing painful crises (n=15), neutrophil and monocyte counts significantly predicted Treg count (Treg count = 21.004 + 22.361 * neutrophil - 69.864 * monocyte). In stable SCA patients (n=22), leukocyte count was significant (Treg count = -8.070 + 2.875 * leukocyte count). Significant differences in leukocyte (p=0.001) and monocyte (p=0.008) counts were observed among patient groups with low, medium and high Treg levels.
CONCLUSIONS: Tregs are promising targets for therapies aimed at modulating immune responses in SCA. Our findings suggest that Treg levels correlate with leukocyte and monocyte count variations. Despite small sample size, this study serves as preliminary investigation and is expected to guide larger-scale studies.

Keywords: Flow cytometry, Regulatory T cells, Sickle cell anaemia

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OC-35

Protective Effects of Asiatic Acid on Organophosphate Poisoning

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AIM: Chlorpyrifos (CPF), an organophosphate pesticide used in agriculture, disrupts the oxidant/antioxidant balance, causing cellular damage. Our study investigates the protective effects of asiatic acid (AA), a triterpenoid from Centella asiatica, on CPF-induced changes in oxidant/antioxidant parameters in rat liver, brain, and serum.

METHODS: A total of 30 male Sprague-Dawley rats (200-250 g) were used (n=6). AA (35, 70, or 140 mg/kg/day) was administered orally by gavage for 14 days. On the 15th day, the rats were treated with chlorpyrifos (279 mg/kg; s.c.). Twenty-four hours after chlorpyrifos administration, blood, brain, and liver tissue samples were collected from the decapitated rats. In these tissues, levels of malondialdehyde (MDA) as a marker of lipid peroxidation, advanced oxidation protein products (AOPP) as a marker of protein oxidation, and the antioxidant enzymes superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) were evaluated. Brain and liver tissue damage was examined histopathologically. Data were analyzed with One-Way ANOVA and Tukey's post-hoc test was used for intergroup comparisons.

RESULTS: CPF increased MDA and AOPP levels in the liver, brain, and serum ($p<0.05$-0.01); decreased SOD and CAT in the liver, GPX-1 in the brain, and SOD, CAT, and GPX-1 in the serum ($p<0.05$) compared to the control group. At 140 mg/kg, AA prevented the CPF-induced increase in MDA and AOPP levels in the liver, brain, and serum ($p<0.05$-0.01). Additionally, at this dose, AA prevented the CPF-induced decrease in SOD and CAT in the liver and serum, and SOD in the brain ($p<0.05$-0.01). The histopathological damage scores caused by CPF in the brain and liver ($p<0.05$) were prevented by the administration of 140 mg/kg asiatic acid ($p<0.05$).

CONCLUSIONS: It can be concluded that asiatic acid supplementation may exert a therapeutic effect by reducing CPF-induced oxidative stress and tissue damage in rat liver, brain, and serum through antioxidant mechanisms.

Keywords: Asiatic acid, Chlorpyrifos, Organophosphate, Oxidative stress, Pesticide toxicology

OC-36

Effect of Apelin-13 on Percentage Change in Body Eeight, Disease Activity Index, Colon Weight/Length Ratio and Mucus Content in the Colon Wall in an Experimental Colitis Model

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AIM: Inflammatory bowel disease (IBD), a disease characterized by recurrent inflammation in the digestive system, is a chronic global health problem that reduces the quality of life of patients. It is very important to elucidate the mechanisms involved in the development and prevention of IBD and to search for new therapeutics. Therefore, this study was planned to investigate the effects of apelin-13, whose effects in IBD are not fully known, on the colon during 2,4,6-trinitrobenzene sulfonic acid (TNBS)-induced colitis.

METHODS: Adult male Wistar rats (200-250 g) were randomly divided into four groups (n=8 in each group): 1) Control; 2) Sham; 3) TNBS; and 4) TNBS+apelin. Colitis was induced through administration of TNBS (100 mg/kg, intra-rectal) mixed with absolute ethanol in 1:1 ratio. In the TNBS+apelin group, apelin-13 (150 µg/kg/day, i.p.), was administered immediately after the TNBS administration for 3 days. Weight change, stool consistency and rectal bleeding were evaluated daily in all animals. At the end of the experiment, macroscopic damage levels and mucus content in the colon were calculated, colon weights and lengths of the subjects were determined, and the disease activity index (DAI) in the subjects was evaluated. Data are expressed as means ± standard error of the mean (S.E.M.). Comparisons between multiple groups were performed using one-way analysis of variance (ANOVA) followed by Tukey's post-hoc test.

RESULTS: Weight loss ($p<0.01$) and an increase in DAI ($p<0.05$) and colon weight/length ratio ($p<0.05$) were observed in the TNBS group. Also, TNBS application increased macroscopic injury ($p<0.001$) and decreased mucus content ($p<0.05$) in colon tissue compared with control and sham group. Apelin-13 significantly reduced the TNBS-mediated damaging effects in colon.

CONCLUSIONS: These findings suggest that apelin-13 has protective effects in TNBS-induced colitis in rats. This work was supported by Akdeniz University Scientific Research Projects Coordination Unit (Project code: TSA-2023-6412).

Keywords: Apelin-13, TNBS, Mucus, Colitis

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OC-37

Investigation of The Protective Effects of Zinc Picolinate in An Experimental Ulcerative Colitis Model

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AIM: Zinc deficiency negatively impacts gut health and can exacerbate the symptoms of inflammatory bowel diseases. It has been suggested that zinc absorption in humans can be enhanced by complexing zinc with picolinic acid. However, there is no literature on the effects of zinc picolinate on the treatment or prevention of colitis. The aim of this study is to investigate the protective effect of zinc picolinate supplementation against colitis damage in an experimentally induced ulcerative colitis model in rats.

METHODS: Sprague Dawley male rats (n=35) were randomly divided into five experimental groups: control, colitis, colitis + zinc, colitis + zinc picolinate, and colitis + sulfasalazine. To induce colitis, rats were given an anal injection of acetic acid solution (AA; 1 ml, 5% v/v) following a 24-hour fasting period under ether anesthesia. Control rats received a physiological saline (PS) injection. Treatment or PS was administered daily (10 doses) starting 10 days prior to the AA induction of colitis. Twenty-four hours after PS or AA administration, rats were anesthetized (xylazine: 10 mg/kg; ketamine: 50 mg/kg, i.p.), and intracardiac blood was collected to conclude the experiment. Colon tissues were collected for macroscopic evaluation, and were then analyzed for oxidant parameters using spectrophotometric methods and cytokine determination via ELISA.

RESULTS: The macroscopic damage score, malondialdehyde (MDA) levels, TNF-α, and IL-6 levels in the colitis group were significantly higher compared to the control group ($p<0.001$), while the antioxidant glutathione (GSH) content was decreased ($p<0.001$). Zinc administration suppressed the macroscopic damage score ($p<0.01$), whereas zinc picolinate did not produce a significant difference in the score. Both zinc and zinc picolinate reduced the elevated cytokine and MDA levels in the colitis group ($p<0.05$-0.001) and increased GSH content ($p<0.05$).

CONCLUSIONS: In the acetic acid-induced ulcerative colitis model, pre-treatment with zinc picolinate suppressed oxidative damage and inflammation in the colon tissue.

Keywords: Ulcerative colitis, Zinc picolinate, Oxidative damage, Inflammation

OC-38

Investigation of the Activity of Agomelatine on Some Female Reproductive Hormones in an Experimental Abortion Model

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AIM: Agomelatine is an antidepressant with melatonergic agonist and serotonergic receptor antagonist (5HT2C) effects. It is known to have positive effects on the female reproductive system. In this context, the main purpose of our study is to investigate the therapeutic efficacy of agomelatine in abortion, an important early pregnancy complication, in terms of biochemical parameters.

METHODS: Control, sham, abortion, melatonin (M), agomelatine (A), progesterone (P), melatonin+progesterone (MP), agomelatine+progesterone (AP) groups were formed from 80 intact female Sprague-Dawley rats of 8-10 weeks of age with regular cycles (n=10). Agomelatine (10 mg/kg/day), progesterone (3.02 ml/kg/day), melatonin (10 mg/kg/day) were administered by oral gavage. The experimental abortion model was created by administering mifepristone (50 mg/kg) on the 11th day of pregnancy. Indirect micro ELISA method was used in the study, and One-Way ANOVA and post-hoc Tukey test were used in statistical analysis ($p<0.05$).

RESULTS: Serum prolactin levels were lower in group A compared to the control group, serum β-hCG levels were lower in the other 5 groups compared to the control group, and PGF2α levels were lower in the AP group compared to the control group ($p<0.05$). It was determined that the PGF2α level was lower in the AP group compared to the abortion group and that the PGF2α level was lower in the AP group compared to the progesterone group ($p<0.05$). Serum oxytocin levels were found to be lower in the AP group compared to the control group and in the other 4 groups compared to the abortion group ($p<0.05$).

CONCLUSIONS: Agomelatine has been shown to have similar or even more positive effects than progesterone in biochemical parameters. We believe that its use in combination with progesterone, which has been the only treatment option to date, may be a possible therapeutic agent for abortion.
This study was supported by TUBITAK (Project No: 123S215).

Keywords: Abortion, Agomelatine, Pregnancy, Rat, ELISA

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OC-39

The Effect of Calorie Restriction on Hematological Parameters in the Aging Process

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AIM: Aging is a risk factor for the immune system, diabetes, obesity, atherosclerosis and coronary artery disease. Age-related changes leukocytes decrease, glucose levels increase, kidney and liver function parameters and various lipid profiles change. Calorie restriction (CR) is known to delay aging and prevent chronic diseases, including neurodegenerative disorders. This study aims to investigate CR's effects on age-related parameter changes.

METHODS: In the study, young and old (3 months, 20 months) rats were divided into randomized groups as control (n = 12) and experimental (n = 12) groups. The experimental group received a low-calorie diet comprising 14% fat, 52% protein, and 34% carbohydrates, providing about 1/3 of their daily calorie intake (~1,303 kcal/kg). In blood samples taken at the end of 10 weeks, hemogram values were measured by the impedance method, and blood glucose, HDL, LDL, cholesterol, triglyceride (TG), urea, uric acid (UA), creatine (Cre), blood urea nitrogen (BUN), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were measured by the colorimetric method. Data were analyzed using ANOVA, paired sample t-tests, and Pearson'r correlation.

RESULTS: Body weight increased with aging and decreased with CR. CR decreased WBC and mean hemoglobin count (MCH), gamma-glutamyl transferase, Cre, blood glucose in both old and young. Aging decreased leukocyte count (WBC), monocyte percentage [MO (%)] and mean hemoglobin concentration (MCHC) while increasing cholesterol, TG, BUN, Cre, UA, AST and ALT levels. CR increased neutrophil percentage, MO%, MCHC, and HDL, while reducing lymphocyte percentage, UA, and TG in aged rats.

CONCLUSIONS: Our study shows that medium-term CR is protective in healthy aging by reducing the metabolic risks caused by aging and preventing immune system, metabolic, cardiovascular risk factors and hematological disorders.

This project was supported by Gazi University Scientific Research Project Unit (Project No: TCD-2023-8842/Project ID: 8842).

Keywords: Calorie Restriction, Aging, Lipid profile, Biochemical Analysis

OC-40

Investigation of Serum Obestatin and Ghrelin Levels in Girls Diagnosed with Central Precocious Puberty

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AIM: Precocious puberty occurs before 8 in girls and 9 in boys. Central PP (CPP) is produced by early hypothalamic-pituitary-gonadal axis activation. The mechanisms that activate this axis remain unknown. Ghrelin and obestatin, which regulate energy metabolism and gonadal activity, may contribute to PP pathogenesis. This study investigated the link between blood obestatin and ghrelin levels and the obestatin/ghrelin ratio in CPP females.

METHODS: The study included 34 girls between the ages of 5-10 who were diagnosed with CPP and had not received treatment and 34 healthy girls within the same age who did not show signs of puberty as a control group. The children's age, bone age, anthropometric measurements (height, weight, BMI), puberty (Tanner) stage, and hormone levels (FSH, LH, and E2) were obtained retrospectively from file records. The CPP and control groups' blood samples were tested for obestatin and ghrelin using ELISA. Student-t tests and Mann-Whitney U tests were used to compare variables with and without normal distributions, respectively. Multiple linear regression was used to assess factors affecting ghrelin and obestatin.

RESULTS: Serum obestatin levels were higher in girls with CPP (P=0.003), while no difference was found in ghrelin levels. Ghrelin/obestatin ratio was lower in girls with CPP (P=0.005). Age (r=0,398, P=0,003) and ghrelin (r=0,323, P=0,008) levels positively affected obestatin levels, while age (r= -0,412, P=0,002) negatively affected ghrelin levels. No relationship was detected between BMI and obestatin or ghrelin levels.

CONCLUSIONS: Our study revealed that girls with CPP had higher obestatin levels, while ghrelin decreased with increased chronological age in both groups, regardless of pubertal age. Our findings also showed that age and ghrelin can modulate obestatin levels during puberty. This suggests that the balance between obestatin and ghrelin may play a role in the timing of pubertal development.

Keywords: Precocious puberty, Ghrelin, Obestatin, Tanner stage, LH, FSH

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OC-41

The Effect of Zinc Deficiency and Supplementation on Testis TEX101 and ZnT8 Expression in Maternal Zinc Deficient Rats

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AIM: There are reports showing that TEX101, a glycoprotein synthesized mainly from testicular tissue, as well as ZFAND3, a zinc-binding protein, and ZnT8, a family of zinc carrier proteins, play a role in testicular function. There are no publications investigating the possible relationship between both maternal zinc deficiency and dietary zinc status and TEX101, ZFAND3, ZnT8 and the male reproductive system. The aim of this study is to investigate the relationship between zinc, an indispensable element in the male reproductive system, and TEX101, ZFAND3 and ZnT8.

METHODS: The study, conducted on 40 male Wistar rats, was approved by the local animal ethics committee (SUDAM 22.10.2021 date and 2020-20 decision number).The first three groups in the study were obtained from mothers who were fed a zinc-deficient diet during pregnancy and until they were separated from their offspring. Group 1 was fed with a zinc deficient diet (2.8 mcg/kg zinc). Groups 2 and 4 were fed with standard rat chow. Zinc supplementation (5 mg/kg/day intraperitoneal zinc sulfate) was provided to the animals in Group 3. Group 4 was used as the control group. At the end of the treatments, TEX101, ZnT8 and ZFAND3 gene expressions were determined in testicular tissue samples taken from sacrificed animals using real-time PCR technique. ANOVA and Duncan tests were used in the statistical analysis of the study. $P<0.05$ was considered significant.

RESULTS: The lowest testicular TEX101, ZnT8 and ZFAND3 gene expressions were obtained in the zinc deficient (G1) and normal (G2) diet-fed groups ($p<0.05$). Zinc supplementation (G3) reversed testicular TEX101, ZnT8 and ZFAND3 gene expressions ($p<0.05$).

CONCLUSIONS: The current study is the first to demonstrate the existence of a critical relationship between both maternal zinc deficiency and dietary zinc status and testicular TEX101, ZnT8 and ZFAND3 gene expression, which play important roles in the male reproductive system.

Keywords: Dietary zinc status, Maternal zinc deficiency, Testis, TEX101, ZFAND3, ZnT8

OC-42

The Effects of Humanin on Sexual Dysfunction and Sperm Parameters

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AIM: Sexual dysfunction is defined as the disruption of normal physiological and psychological processes, adversely affecting quality of life. Paroxetine, one of the antidepressants used in the treatment of psychiatric disorders, is known to cause sexual dysfunctions such as decreased libido and erectile dysfunction, as well as reduced sperm concentration and motility. Although studies have explored the relationship between the mitochondrial-derived peptide humanin and the reproductive system, its effect on antidepressant-induced sexual dysfunction is unknown. This experimental study aims to investigate the effect of humanin on paroxetine-induced sexual dysfunction.

METHODS: Male Sprague-Dawley rats, approximately 3-4 months old and sexually active, were selected and divided into five groups: control, sham, humanin, paroxetine, and paroxetine+humanin (n=8). The paroxetine and paroxetine+humanin groups received paroxetine (20 mg/kg/day) via oral gavage for 8 weeks. Sexual behavior tests (SBT) were conducted in the 4th week to confirm paroxetine-induced sexual dysfunction. Subsequently, the humanin and humanin+paroxetine groups received humanin (0.25 mg/6 µL/day) subcutaneously via a mini-osmotic pump for 4 weeks. All rats underwent a 30-minute SBT. At the end of the experiment, sperm parameters were evaluated. Normality was verified using the Shapiro-Wilk test; one-way ANOVA was used for parametric data, and the Kruskal-Wallis H test was used for non-parametric data.

RESULTS: Humanin administration increased ejaculation frequency, mating ratio, and sexual activity index, which had been reduced by paroxetine ($p<0.05$); it also decreased mount frequency and ejaculation latency, which had been increased by paroxetine ($p<0.05$). Humanin increased total motility and spermatozoon density, which had been decreased by paroxetine ($p<0.05$). Sperm anomalies and total acrosomal damage, increased by paroxetine, were reduced by humanin treatment ($p<0.05$).

CONCLUSIONS: These results indicate that humanin administration has positive effects on paroxetine-induced sexual dysfunction and sperm parameters in male rats.

This study was supported by TÜBİTAK (Project No: 122S419).

Keywords: Sexual Behavior, Humanin, Paroxetine, Spermatological Parameters

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OC-43

Investigation of Effects of Repeated Hyperthermia on Skeletal Muscle and Motor Function in Mice

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AIM: Muscle functionality depend on protein and energy homeostasis, which are disrupted under hyperthermic conditions. Our study aimed to investigate the effects of repeated whole-body hyperthermia on mitochondrial dynamics in muscle and its impact on motor function and anxiety-like behavior in mice.

METHODS: Healthy Swiss albino mice were exposed to either 39°C (39E, n=16) or 41°C (41E, n=16) for 15 minutes daily over a 7-day period, while the control group (n=8) was exposed to normothermic conditions. Following exposures, half of the mice in each group were allowed a 7-day recovery period (control, n=4; 39ER and 41ER, n=8). Behavioral assessments were conducted using the open field, elevated plus maze, grip strength and rotarod tests. Mitochondrial dynamics-related gene expression in the gastrocnemius muscle was analyzed by RT-qPCR.

RESULTS: Muscle strength significantly decreased in the 39ER, 41E, and 41ER groups ($p<0.05$, $p<0.01$ and $p<0.0001$, respectively). Locomotor activity decreased in both 39E and 39ER groups ($p<0.05$, $p<0.01$, respectively). Notably, 39E and 41E groups exhibited increased closed-arm frequencies, with the 41ER group showing decreased open-arm frequency ($p<0.05$). Pgc1α expression significantly decreased in 39E and 41E groups ($p<0.05$). Levels of Lc3b, and Parkin, significantly decreased in 39E and 41E groups ($p<0.05$). Pgc1β and Parkin expressions were elevated in the 41ER group ($p<0.01$). Nrf1, Tfam, and Ucp2 expressions increased in the 39ER group ($p<0.05$).

CONCLUSIONS: Our results indicate that repeated exposure to distinct hyperthermic conditions differentially alter the muscle strength by regulating mitochondrial and autophagy-related gene expressions.

Keywords: Hyperthermia, Mitochondria, Strength

OC-44

Investigation of the Analgesic Interaction Between Melatonin and Clonidine on Rats

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AIM: The aim of the study was to evaluate the antinociceptive effects of melatonin (MEL) and clonidine (CLO) administered alone and in combination on acute thermal pain in rats.

METHODS:32 Wistar albino male rats were randomly divided into 4 groups: Control, MEL, CLO, MEL+CLO. The effect of drug applications on acute thermal nociception was evaluated by tail-flick and hot-plate tests, and the effect on locomotor activity was evaluated by the rotarod test. One Way ANOVA and Bonferroni multiple comparison test were applied for repeated measurements to evaluate the effect of the drug or drugs given to each group and its relationship with the time the measurements were taken. Between-group comparisons of each time point were made by one-way analysis of variance One Way ANOVA and post hoc multiple comparison Tukey test. $P<0.05$ was considered statistically significant.

RESULTS: Doses of 60 mg/kg melatonin and 50 µg/kg clonidine administered alone showed analgesic effects in both tail-flick and hot-plate tests ($p<0.01$). The combined application of the two drugs strengthened the effect produced by both drugs alone in all time periods after injection and prolonged the duration of effect ($p<0.001$). The findings obtained from the rotarod test we used to evaluate the locomotor function of rats showed that the doses we applied did not cause motor incoordination in the group where both agents were administered alone or in the group where they were administered in combination.

CONCLUSIONS: In light of the data obtained, it is predicted that the combination of MEL+KLO may be an alternative analgesic agent that creates a stronger antinociceptive response than the effect produced by the two drugs alone, without causing any motor disorders, and will help minimize possible side effects.

Keywords: Antinociception, Clonidine, Hot-plate, Melatonin, Rotarod, Tail-flick

OC-45

Differential Effects of Mast Cell Stabilizers on Mechanisms Responsible for Migraine in Experimental Migraine Models

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AIM: Meningeal mast cell (MMC) activation plays key role in migraine pathogenesis by inducing neurogenic inflammation via inflammatory mediators in their granules. We explored the effects of mast cell stabilizers cromolyn and quercetin on the mechanisms underlying migraine in in-vivo and ex-vivo migraine models.

METHODS: Wistar male rats (8-12 weeks-old) were divided into 6 groups(n=6/group). Following intraperitoneal administration of vehicle to control and migraine groups, 10 mg/kg cromolyn to Cr+NTG group, 25 mg/kg quercetin to Qu+NTG group, cromolyn

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and quercetin together to Cr+Qu+NTG group, and 600 µg/kg migraine-drug sumatriptan to Sum+NTG group for five days, 30 minutes later control received vehicle and the other groups received 10 mg/kg NTG for migraine induction, in-vivo. In ex-vivo experiments, vehicle was treated to control group, and capsaicin(100 nM), cromolyn (100 µM), quercetin (100 µM), sumatriptan (30 µM) or their various combinations to meningeal preparations(n=6/group). Mechanical hyperalgesia was assessed by von-Frey test, calcitonin gene-related peptide(CGRP) in trigeminal ganglia and ex-vivo samples, and brainstem c-Fos and CGRP concentrations by ELISA, and MMCs by toluidine-blue staining. Data were analyzed by one-way ANOVA.

RESULTS: Quercetin or combining quercetin+cromolyn reduced NTG-induced hyperalgesia, trigeminal ganglion CGRP and brainstem CGRP and c-fos expression, and MMC degranulation and number in vivo ($p<0.05$). Cromolyn did not affect NTG-induced hyperalgesia and c-fos expression, but reduced the other parameters. Ex-vivo, cromolyn or combining quercetin+cromolyn, but not quercetin, reduced capsaicin-induced CGRP release. Neither treatment affected basal CGRP release. Sumatriptan inhibited all the induced effects.

CONCLUSIONS: Quercetin, unlike the effects of cromolyn, reduced mechanical hyperalgesia and brainstem c-fos expression in-vivo, whereas cromolyn reduced CGRP release ex-vivo, while quercetin was ineffective, suggesting that the two mast cell stabilizers have different modes of action. The therapeutic effects of the combining quercetin and cromolyn in-vivo and ex-vivo suggest that mast cell stabilization may be an effective approach to prevent neurogenic inflammation underlying migraine.

Keywords: CGRP, Mast cell stabilizers, Meningeal mast cells, Migraine, Neurogenic inflammation

OC-46

Attenuation of Neuropathic Pain by P2X7 Receptor Antagonist Brilliant Blue G

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AIM: There is growing evidence in recent years that pro-inflammatory mediators play a key role in the development of neuropathic pain through central and peripheral sensitization mechanisms. Brilliant Blue G (BBG) is a non-competitive antagonist of the P2X7 receptor, which is exclusively activated by high extracellular ATP concentrations, causing the intense release of pro-inflammatory cytokines. This study aimed to evaluate the effectiveness of BBG following traumatic injury in a peripheral neuropathy model in rat and assess both the sensory and the affective components of neuropathic pain in the chronic process.

METHODS: Male Sprague-Dawley rats were used in the study. The neuropathic pain model was established by partial ligation of the saphenous nerve. BBG was administered intraperitoneally at a daily dose of 50 mg/kg for one week following the ligation. Animals were divided into four experimental groups: Sham, SPL, SPL + Vehicle and SPL + BBG. Mechanical pain thresholds were evaluated with the Dynamic Plantar Aesthesiometer weekly and analgesic effectiveness of BBG was evaluated with the Dynamic Hot Plate on 7th day. On the last day of the experiment, Forced Swim Test was used to assess depression-like behavior.

RESULTS: For the nerve-ligated animals, a significant decrease in mechanical pain threshold was observed compared to baseline values, from the first measurement after the ligation to the last measurement day ($p<0.05$). On the 6th day, it was found that the pain threshold of the BBG group decreased significantly less than the SPL and SPL + Vehicle groups'. Analgesic effectiveness of BBG was detected in the Dynamic Hot Plate test. In the Forced Swim Test, the immobility score of the nerve-ligated animals was significantly higher than the Sham group.

CONCLUSIONS: Treatment options for neuropathic pain are still limited. Designing pre-clinical pain models which includes both sensory and affective components may aid the development of more effective treatment modalities.

Keywords: Neuropathic Pain, P2X7 Receptor, Brilliant Blue G, Affective Component of Pain

OC-47

Differential Physiological and Inflammatory Responses to Trypophobic Stimuli

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AIM: The immune system activates an inflammatory response through pro-inflammatory proteins to defend the body against external pathogens. Previous studies have shown that stimuli evoking fear and disgust can trigger an immune response; however, specific immune proteins and physiological changes related to trypophobia remain unclear. Trypophobia is defined as a fear or disgust of irregular clusters of holes or patterns. This study aims to investigate the inflammatory and physiological responses to both skin-related and non-skin-related trypophobic images.
METHODS: Fifty healthy participants (n=50) were assessed using the Trypophobia Questionnaire (TQ). Participants were randomly divided into two groups: those exposed to skin-related and non-skin-related trypophobic images. Blood samples were collected before and after visual exposure, and IL-6 and TNF-α levels were analyzed using ELISA and RT-qPCR methods. Heart rate variability (HRV) was evaluated using photoplethysmogram (PPG) recordings, and low-frequency (LF) and high-frequency (HF) components were analyzed. LF typically reflects sympathetic nervous system activity, while HF is indicative of parasympathetic activity.
RESULTS: Significant differences were observed in IL-6 and TNF-α levels before and after exposure ($P<0.05$). There was also a significant interaction between the mRNA expression of these cytokines and participants' trypophobia scores ($P<0.05$). HR and HRV parameters, particularly LF and HF components, showed statistically significant changes during and after visual stimulation ($P<0.05$).
CONCLUSIONS: The findings suggest that trypophobic stimuli may be linked to variations in immune responses and activity levels of the sympathetic and parasympathetic nervous systems. The fear associated with trypophobia may be related to sympathetic activation, while parasympathetic activity was associated with changes in HRV.
Keywords: Trypophobia, Immune system, Inflammation, Pro-inflammatory cytokines, Heart Rate Variability (HRV)

OC-48

Investigating the Long-term Effects of UNC2025-mediated Mer Tyrosine Kinase Inhibition After Neonatal Hypoxic Ischaemia

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AIM: Neonatal hypoxic ischemia (NHI) is the major cause of perinatal morbidity and mortality resulting from insufficient supply of oxygen. Although Mer Tyrosine Kinase (MerTK) is involved in phagocytosis of apoptotic cells, our understanding of post-NHI pathophysiology remained insufficient. High MerTK expression in the chronic period following brain injury suggests that MerTK is a critical in adaptation to post-NHI conditions and degenerative processes. In this study, the long-term effects of UNC2025-mediated MerTK inhibition were investigated by employing NHI model.

METHODS:7-day-old (P7) C57BL-6 mouse pups were anaesthetized with 1% isoflurane (30% O2; N2O) and their carotid arteries were surgically ligated. Mice were kept in units containing 8% O_2 and 92% N_2 for 90 minutes and returned to cages. Mice were randomly assigned as vehicle (0.7% NaCl) or UNC2025 (65 mg/kg in 30 µL) groups before operation. Behavioral tests were conducted on P30, P42, P55 to assess the locomotor activity, anxiety, and motor coordination. Neuronal nuclei were stained for neuronal survival, biotnylated dextrane amine and Cascade Blue for axonal projection, and 5-bromo-2'-deoxyuridine for neurogenesis. MerTK's effects on gene expression were evaluated with polymerase chain reaction. Independent sample t-test was used to assess significance between groups and $p<0.05$ was considered statistically significant.

RESULTS: MerTK inhibition improved motor activity and coordination, while decreasing anxiety and depression ($p<0.05$). UNC2025 administration increased neuronal survival and axonal projection after NHI ($*p<0.05$). Neurogenesis increased in the dentate gyrus following NHI in the vehicle group. MerTK inhibition increased the expression of several genes involved in the growth, proliferation, and differentiation of nerve cells after injury.

CONCLUSIONS: In neurodegenerative conditions, MerTK inhibition was shown to have neuroprotective effects and modulate the axonal plasticity. UNC2025 administration improved the behavioral patterns after NHI. In accordance with these findings, MerTK inhibitor administration could be an alternative therapeutic approach following NHI.
Keywords: MerTK, Neonatal hypoxic-ischemia, UNC2025

OC-49

Effect of 1-Week 3',4'-Dihydroxyflavonol Administration on Motor Function and Learning in Rats: Role of AQP 4, Caspase 3 and IL-10

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AIM: Ischemia is defined as the decrease or loss of blood supply to a region of the body due to various reasons. 3', 4'-dihydroxyflavonol (DiOHF) is a synthetic flavonoid and its protective effect has been determined in different ischemia-reperfusion studies. This study aimed to determine the effect of 3',

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4'-dihydroxyflavonol on motor function and learning in rat brain ischemia-reperfusion experimentally and the role of caspase 3, AQP4 and interleukin-10.

METHODS: The study, which was conducted with 28 Wistar-albino male rats at the Experimental Medicine Application and Research Center of Selçuk University, was approved by the same ethics committee (2022-35). Experimental groups were established as 1-Control, 2-Sham, 3-Ischemia-reperfusion, 4-Ischemia-reperfusion + DiOHF (3',4'-dihydroxyflavonol) (10mg/kg). Animals were anesthetized, the carotid artery was ligated for 30 minutes and reperfused. Along with reperfusion, the animals were given DiOHF intraperitoneally at a dose of 10 mg/kg for 1 week. In hippocampus tissue samples taken from animals under anaesthesia, caspase 3 and AQP4 levels were determined by PCR and interleukin-10 levels by ELISA. The effect of ischemic injury on motor function and learning was observed behaviorally by neurological scoring and NOR (novel object recognition) test. Results were defined as mean ± standard deviation. Kruskal-Wallis analysis of variance was used for intergroup comparison and Mann-Whitney U test was applied for $p<0.05$ level. $P<0.05$ was considered statistically significant.

RESULTS: With brain ischemia reperfusion, caspase 3 and AQP4 levels in hippocampus tissue significantly increased, while interleukin-10 decreased ($P<0.001$). However, 1 week of DiOHF supplementation significantly reduced the increased caspase 3 and AQP4 levels and significantly increased interleukin-10 levels ($P<0.001$). DiOHF treatment positively affected the NOR test and neurological scoring test values.

CONCLUSIONS: Our study shows that cerebral ischemia and subsequent reperfusion in rats causes tissue damage, but DiOHF administration for 1 week has a healing effect.

Keywords: 3' 4'-dihydroxyflavonol, Apoptosis, AQP4, Brain ischemia, IL-10, NOR

OC-50

Central Neuropeptide-S Mitigates Cognitive Impairments by Regulating Hippocampal Synaptic Plasticity in Hemiparkinsonian Rats

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AIM: Neuropeptide-S (NPS) is known to ameliorate learning and memory deficits induced by experimental Parkinson's Disease (PD) models. However, the mechanisms through which NPS influences cognitive functions remain unclear. This study aims to investigate the effects of central NPS administration on learning and memory alterations associated with an experimental hemiparkinsonian model at both electrophysiological and molecular levels.

METHODS: Adult male Sprague Dawley rats (n=39) were divided into three groups: sham, 6-OHDA, and 6-OHDA+NPS. To create the hemiparkinsonian model, 6-OHDA was stereotactically injected into the right medial forebrain bundle. Central NPS (1nmol, icv) was administered into the lateral ventricle via a cannula for 7 days following the 6-OHDA surgery. Motor performance was assessed using the open field test while learning and memory were evaluated using the Morris water maze and object recognition tests. Long-term potentiation (LTP) recordings were taken to assess hippocampal synaptic plasticity. The expression levels of tyrosine hydroxylase in the substantia nigra and phosphorylated CaMKII, GluR1, and GluR2 expressions in the hippocampus were determined by immunohistochemistry. Statistical analyses were performed using ANOVA with Tukey's post-hoc test or Kruskal-Wallis test with Dunn's post-hoc test. Our study was approved by the Akdeniz University Local Ethics Committee for Animal Experiments (protocol no:1479/2022.07.006).

RESULTS: NPS administration significantly ($p<0.05$) reduced 6-OHDA-induced motor and cognitive impairments. In 6-OHDA-lesioned rats, NPS treatment significantly ($p<0.05$) increased the diminished amplitude of LTP induced at the dentate gyrus/perforant path synapses. In the hippocampus, the decreased number of pCaMKII and GluR1 immunoreactive cells due to 6-OHDA was significantly ($p<0.05$) increased with central NPS administration, except for GluR2 levels, which showed no change. Moreover, centrally administered NPS significantly ($p<0.05$) reduced nigral dopaminergic neuron loss induced by 6-OHDA.

CONCLUSIONS: These results contribute to elucidating the mechanism by which central NPS enhances cognitive function in an experimental PD model.

Keywords: Hippocampus, Neuropeptide-S, Parkinson's Disease, Synaptic Plasticity

OC-51

Potential Roles of Enriched Environmental Conditions on Motor Behavior in a Cerebellar Infarct Mice Model

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AIM: Cerebellar infarct (CI) is a rare stroke that causes severe motor deficits like ataxia and gait disturbances, leading to difficulties in daily activities and a serious decline in quality of life. This study aims to evaluate the effects of various enriched environmental conditions on motor performance in a CI mouse model and explore their potential therapeutic impacts.

METHODS: Forty male C57BL/6 mice were divided into 5 groups: physical enrichment, enriched environment, enriched environment +3 healthy mice, standard housing, and sham. The CI

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model was induced in mice via stereotaxic injection of N5-(1-iminoethyl)-L-ornithine dihydrochloride. Motor performance was assessed pre-infarct and on specific days post-infarct using the wire walk test and footprint test. The infarct area was identified by Hematoxylin & Eosin staining. Immunohistochemistry was employed to visualize Biorientation Defective 1 (BOD1), a factor associated with motor coordination, utilizing a confocal microscope. Data were analyzed by two-way ANOVA, with $p<0.05$ considered significant.

RESULTS: CI resulted in decreased motor performance and negatively impacted balance and coordination in mice; these effects were modulated by environmental factors. Statistically significant differences were observed in the overlap distance of right steps among the groups ($p<0.01$). However, no significant differences were noted in foot faults between the experimental groups.

CONCLUSIONS: This study highlights the beneficial and detrimental effects of various enriched environmental conditions on diminished motor performance following CI. Accordingly, it may offer significant insights for the development of innovative treatment and rehabilitation strategies.

Keywords: Cerebellar Infarct, Enriched Environment, Motor Performance

OC-52

Sleep Disorders with Individuals in Predictıon with Cerebral Lateralization Reasoning Ability, Evaluation of Attention

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AIM: Sleep is characterized as a temporary loss of consciousness. An adult individual needs to sleep at least 6 hours in order to perform the functions in our body. If insomnia lasts for a long time, conditions such as attention deficit, lack of concentration, and inability to flow information occur. OSAS is observed in 1-2% of middle-aged women and 2-4% of men. Studies have found that sleep disorders other than sleep apnea do not cause death. In a study, night and day shifts were compared and it was observed that assistants who were on night duty, that is, people who had insomnia problems, had a close margin of error and suffered more loss of cognitive function. The aim of this study is to examine the relationships between cognitive skills such as attention deficit, selective attention, sustained attention, reasoning ability, and reaction time in patients with OSAS and any sleep disorder (CPAP) before and after treatment.
METHODS: Our study was conducted among 41 healthy and voluntary individuals, without any age limit. Before and after using CPAP, cognitive skill tests applied in the psychotechnical laboratory were the reasoning ability test (SPMIQ), reaction time test (RTms), response speed-quality test under stress (DT- DTduration), sustained attention and problem solving (COGyes-COGno). Selective attention (SIGNAL) test was also applied. In addition, psychological surveys such as BECK depression scale, STAI1 (state anxiety), STAI2 (trait anxiety) and lateralization questionnaire were applied. Psychological surveys were administered both before and after CPAP, and comparisons were made between tests and surveys.

RESULTS: After the treatment, Dt (reaction under stress), Signal (selective attention), SPM (judgment ability) increased ($p<0.05$).

CONCLUSIONS: It has been determined that sleep disorder may have an effect on the higher functions of the brain and that there may be an increase in brain cognitive functions after its treatment.

Keywords: CPAP, Cerebral Lateralization, Handedness, OSAS, Sleep Disorder, Attention

OC-53

The Direct Effects of SARS-COV-2 Spike Protein Subunit S1 on Secondary Hemostasis and Fibrinolysis

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AIM: In patients with severe Covid-19, the clinical presentation is characterized by profound infection and inflammation, contributing to disruptions in hemostatic processes. However, the direct influence of the virus on hemostasis remains uncertain. This study aims to investigate the potential direct effects of the spike protein S1 subunit on secondary hemostasis and fibrinolysis.
METHODS: The recombinant S1 protein was prepared at concentrations of 50, 5, and 1 ng/ml in phosphate-buffered saline (PBS) and incubated at 37°C for 2 hours. The incubation involved citrated whole blood, platelet-rich plasma (PRP), and platelet-poor plasma (PPP) obtained from the same donor (n=5). Subsequently, PPP samples were isolated through the centrifugation of blood and PRP samples at 13000 rpm for 5 minutes, while PPP samples were used as it is. Measurements including prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (aPTT), fibrinogen, and D-Dimer were conducted on the obtained PRP samples.

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RESULTS: Significantly reduced aPTT values were observed in whole blood, PRP, and PPP samples, exclusively at the 50 ng/ml S1 concentration compared to the buffer control. A decrease in fibrinogen levels was observed solely in whole blood at the 50 ng/ml S1 concentration. Elevated D-Dimer levels were evident in whole blood across all doses and in PRP at the 5 ng/ml S1 concentration.

CONCLUSIONS: The combined interpretation of shortened aPTT, decreased fibrinogen, and increased D-Dimer levels underscores a direct influence of the Spike S1 protein, particularly on the intrinsic pathway. This suggests its direct involvement in the secondary hemostasis process and fibrinolysis.

This research was funded by The Scientific and Technological Research Council of TÜRKİYE (TÜBİTAK; grant number 122Z772).

Keywords: Blood coagulation, Secondary Hemostasis, Fibrinolysis, Spike S1 subunit, SARS COV-2

OC-54

Effects of Taurine Administration on Cognitive Functions, Apoptosis, miR-34a, Inflammation and Oxidative Stress Markers in Alzheimer's-Like Disease Rat Model

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AIM: Apoptotic, inflammatory, oxidative processes play important role in the pathogenesis of Alzheimer's disease. We aimed to evaluate the effects of taurine, which has antiapoptotic, antioxidant and anti-inflammatory properties, on these processes in Alzheimer's-like disease rat model induced by intracerebroventricular (icv) Amyloid Beta 1-42 (Aβ1-42) injection.
METHODS: Thirtytwo male Wistar Albino rats were divided into groups as Preliminary study (n:2), Control (n:7), Taurine(n:7), Aβ1-42 (n:8), Aβ1-42+Taurine (n:8). After icv Aβ1-42 (10µg/10µl) administration to the relevant groups, 250 mg/kg/day taurine was given to the taurine groups via oral gavage for 32 days. Morris Water Maze (MWM) test was performed to evaluate learning and memory. On day 33, rats were sacrificed and brain tissues were collected. The presence of Aβ plaques in brain tissue was evaluated by Congo red staining. Bax, bcl-2, cleaved caspase-3 proteins were analyzed by Western Blot to evaluate apoptosis and miR-34a, which is associated with apoptosis, was analyzed by qPCR. Parameters such as TNFα, IL-1β, IL-10, Total Antioxidant Status (TAS), Total Oxidant Status (TOS), Malondialdehyde, Glutathione which related to inflammatory and oxidative processes were evaluated by ELISA and colorimetric tests. Nonparametric tests were used, p<0.05 was considered statistically significant. Supported by Gazi University-BAP (Project No: TTU-2022-7774). Ethical approval: G.Ü.ET-22.013.

RESULTS: The presence of amyloid plaques with Congo Red staining and cognitive impairment in MWM test indicated the formation of an Alzheimer's-like disease model. Aβ1-42 administration increased bax, cleaved caspase-3 apoptotic proteins (p<0,05) and decreased bcl-2 antiapoptotic protein (p<0,05) which was not observed in Aβ1-42+taurine group. While plasma miR-34a decreased in Aβ1-42 injection groups (p<0,05), brain miR-34a were unchanged. IL-10 levels were higher in Aβ1-42+taurine group compared to Aβ1-42 group (p<0,05). While Aβ1-42 increased serum TOS and brain Malondialdehyde (p<0,05), this changes were not observed in Aβ1-42+taurine group.

CONCLUSIONS: Taurine may be used as a supportive agent in the treatment of neurodegenerative diseases such as Alzheimer's disease, if supported by further studies.

Keywords: Aβ1-42, Alzheimer's disease, Apoptosis, Inflammation, miR-34a, Oxidative stress

OC-55

Conjunctival IgD, LL-37, and Pentraxin Levels and Their Relationship with Visual Electrophysiological Responses in the Development of Diabetic Retinopathy

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AIM: Diabetic retinopathy (DR) involves interactions of various factors like inflammation and oxidative stress. Studies show increased serum Pentraxin-3 (PTX3) in DR, with IgD triggering PTX3 and LL-37 secretion from basophils. This study investigates conjunctival IgD, LL-37, and PTX3 levels in DR patients and evaluates their correlation with visual electrophysiological responses.
METHODS: Ninety participants: 30 healthy (C), 30 diabetic without DR (D), and 30 with DR (aged 30-69) were examined. Conjunctival samples were collected using Schirmer strips, and IgD, LL-37, PTX3 levels were measured by ELISA and immunohistochemistry. Retinal functions were assessed using 61' scaled multifocal electroretinography (mERG) and long duration ERG (ldERG). Signal intensity-s/sp in first-order kernel (1O) and N1P1-P1N2 intensities/amplitudes in second-order kernel (2O) were measured. D-wave amplitudes and intensities were measured in ldERG. Correlations with other parameters were evaluated. Normality was assessed by Shapiro-Wilk test, homogeneity by Levene test. One-way ANOVA and post-hoc Tukey test were used

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for normally distributed data; Kruskal-Wallis and post-hoc Dunn tests for non-normally distributed data. Pearson correlation was used. Ethical approval was obtained from Istanbul University-Cerrahpasa Clinical Research Ethics Committee (QDj4U8Sy).

RESULTS: No significant increase in IgD, LL-37, PTX3 in D group, but significant increases in DR group ($p<0.05$). No significant difference in mERG-1O responses between C and D, but significant decreases in DR ($p<0.05$). Significant decreases in 2O responses in both D and DR compared to C ($p<0.05$). Significant reductions in ldERG responses in D and DR compared to C ($p<0.05$). Significant correlations between 2O-mERG and ldERG responses and all conjunctival findings across all groups.

CONCLUSIONS: Findings help understand inflammatory mechanisms of DR. Increased IgD and other parameters suggest contribution to retinopathy due to disrupted blood-retina and blood-aqueous barriers. Monitoring 2O-mERG and ldERG in diabetic patients without retinopathy may provide early information for preventive measures.

Keywords: Diabetic retinopathy, IgD, LL-37, PTX3, Electroretinography

OC-56

The Role and Mechanisms of Type-1 Diabetes, Insulin and Insulin Receptor in Migraine Pathophysiology

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AIM: Clinical studies suggest that diabetes may protect against migraine, but the underlying mechanisms are unknown. We investigated the possible roles and mechanisms of type-1 diabetes, insulin and insulin receptor in migraine pathobiology in in-vivo and ex-vivo migraine models.
METHODS: Wistar male rats (8-10 weeks-old) were divided into 9 groups (n=7/group). Control, Migraine, Diabetes+Migraine, Diabetes+Insulin+Migraine, Diabetes, Diabetes+Insulin, Insulin+Migraine, BMS+Insulin+Migraine, BMS+Migraine groups were administered vehicle, insulin (9 IU, s.c.), insulin receptor antagonist BMS (12.5 mg/kg, s.c.) or BMS+insulin 7 days after vehicle or streptozotocin (60 mg/kg, i.p.) injection to induce diabetes; the next day, nitroglycerin (NTG, 10 mg/kg, i.p.) or its vehicle was administered to induce migraine. Ex-vivo meningeal, trigeminal ganglion and brainstem preparations (n=6/group) were topically administered vehicle (control), capsaicin (100 nM), insulin (10 µM), BMS(100 nM), capsaicin+insulin, BMS+insulin or capsaicin+BMS. Blood glucose was assessed by glucometer, pain threshold by von-Frey, calcitonin gene-related peptide(CGRP) levels in trigeminal ganglia and ex-vivo superfusates, and brainstem c-Fos and CGRP concentrations by ELISA, and meningeal mast cells by toluidine-blue staining. Data were analyzed by one-way ANOVA.

RESULTS: Insulin further increased NTG-induced hyperalgesia, brainstem CGRP and c-fos, trigeminal ganglion CGRP levels, and mast cell activation ($p<0.05$). BMS blocked insulin's effects ($p<0.05$) but was ineffective in the migraine model. Hyperglycemia did not alter triggered parameters in the migraine model. Insulin stimulated CGRP release in ex-vivo meningeal and trigeminal ganglion preparations and further increased capsaicin-stimulated CGRP release ($p<0.05$). BMS blocked insulin's effects ($p<0.05$) but did not alter basal CGRP release. In brainstem preparations, insulin or BMS had no effects.

CONCLUSIONS: Our findings suggest that the lower prevalence of migraine in diabetic patients is not due to hyperglycemia but to a decreased interaction between insulin and its receptor due to insulin deficiency. Modulation of the interaction between insulin and its receptor may be a good target for new therapeutic approaches. This study was supported by TUBITAK[Project-number: 222S289].

Keywords: Diabetes, İnsulin, Insulin receptor, Migraine, Neurogenic inflammation

OC-57

Impact of Metallothioneins on DNA Damage and Apoptosis in Multiple Sclerosis: A Comparative Study Using Comet Assay

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AIM: Multiple sclerosis (MS) is one of the most common neurological diseases in the young adult population worldwide. Characterized by the presence of numerous focal demyelinating areas in plaques or lesions within the central nervous system, multiple sclerosis involves inflammation and axonal loss. The aim of this study is to determine the levels of Zn and Cu in serum

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samples of patients diagnosed with multiple sclerosis, investigate the protective effects of metallothionein subtypes (MT-I, MT-II, MT-III) on neural damage, and compare DNA damage and the metallothionein-Zn/Cu balance, which are effective in the pathogenesis of multiple sclerosis.

METHODS: Seventy individuals diagnosed with MS (study group) and 30 healthy individuals (control group) were included in this study. The demographic characteristics and DNA damage levels in peripheral lymphocytes of the study and control groups were determined. Human neuroblastoma (SH-SY5Y) and mouse fibroblast (L929) cell lines were treated with ZnSO4·7H2O and CuSO4, and cell viability was assessed using the MTS assay. The gene expressions of MT-IIA, MT-III, metal transcription factor-1 (MTF-1), and metal responsive element 11 (MRE11) were analyzed by RT-PCR, while DNA damage was analyzed using the comet assay.

RESULTS: According to the comet analysis results, DNA damage was found to be higher in multiple sclerosis patients compared to healthy individuals. Following a 48-hour exposure of SH-SY5Y cells to zinc and copper salts, a significant increase in MT-IIA and MT-III gene expressions and DNA damage, dependent on MTF-1, was detected.

CONCLUSIONS: In this study, which is the first to evaluate DNA damage in multiple sclerosis patients using the comet assay, it was determined that DNA damage is pronounced and that genes encoding metallothioneins activate apoptotic cell death pathways in neuroblastoma cells. Financial Disclosure: This study was supported by the Scientific Research Projects Unit of İnönü University (Project No: TDK-2022-3012).

Keywords: Multiple sclerosis, Metallothionein, Zinc, Copper, Comet

OC-58

Effects of Circadian Rhythm Disruption on Cellular Survival and Brain Protein Profile in an Experimental Parkinson's Model

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AIM: Parkinson's disease (PD) is the second leading neurodegenerative disorder in globally, and its prevalence is steadily increasing. Circadian rhythm is a biological clock that regulates physiological processes and behaviors and is thought be involved in Parkinson's disease pathophysiology. The purpose of this study is to investigate into the effects of circadian rhythm disruption on Parkinson's disease in the brain.

METHODS: Experimental PD model was induced in 8-12 week male C57BL6/J mice by intracerebral injection of 7.5 µg 6-OHDA. The mice were randomly assigned as normal and circadian rhythm disrupted groups. Motor activity and anxiety were evaluated by rotation test and open field test on days 7, 14, 21 and 28 after PD model. Mice were sacrificed on day 28 and neuronal survival and dopaminergic cell density were analyzed by neuronal nuclei and tyrosine hydroxylase immunofluorescence staining of coronal brain slices from the striatum and substantia nigra (SN) regions. Proteomic analysis of tissue samples from the striatum and SN revealed the protein profile related to these processes. Independent samples t-test was used for statistical significance between groups and $p<0.05$ was considered statistically significant.

RESULTS: The circadian disrupted group showed increased anxiety ($p<0.05$) and decreased locomotor activity. Additionally, the circadian disturbed group had greater dopaminergic neuronal death ($p<0.001$) and reduced neuronal survival rates ($p<0.001$). Proteomic studies showed significant ($p<0.05$) changes in 115 proteins in the striatum and 427 proteins in the SN. Bioinformatic analyses uncovered that the PD and Neurodegeneration Pathways - Multiple Diseases pathways are the most effective.

CONCLUSIONS: Circadian rhythm disruption is thought to have behavioral and neuronal effects on PD. In Additionally, the identified pathways are thought to be protein biomarkers that may explain the interplay between PD and circadian rhythm.

Keywords: Circadian rhythm, Parkinson disease, Proteomics.

OC-59

The Role of Astrocytes After Ischemic Stroke

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AIM: Stroke is one of the leading causes of mortality and morbidity worldwide. In recent years, it has become clear that glial cells play an important role in the pathophysiology of stroke as well as neurons. Astrocytes are known to play an active role in this process through G protein-coupled receptors, but how different G protein-

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coupled receptors shape ischemic insult has not been elucidated. This study aims to determine the contribution of astrocytic Gq and Gi pathways to the development of ischemic brain injury pathophysiology using chemogenetic methods.

METHODS: To determine the contribution of astrocytic Gq and Gi pathways to ischemic injury, 8-12 week old GFAP-Cre (Jax: 24098) mice were divided into three groups: hM4Di, hM3Dq and GFP. The expression of hM4Di and hM3Dq receptors was induced by injecting Cre-dependent viruses into the left striatum of the animals, which allowed us to activate Gq and Gi pathways. Control animals expressed GFP in a Cre-dependent manner. Then, stroke was induced in mice by middle cerebral artery occlusion model for 30 minutes. From the onset of ischemic injury, hM4Di and hM3Dq receptors were activated until 72 hours when the injury development was complete and animals were sacrificed. Subsequently, mice were sacrificed and brains were collected. NeuN staining was performed to analyze ischemic injury and TUNEL staining was performed to identify apoptotic cells.

RESULTS: Activation of astrocytic Gq and Gi pathways exacerbated ischemic injury and reduced neuronal survival ($p<0.01$). Similarly, apoptotic cell death was increased by astrocyte-specific activation of Gq and Gi pathways ($p<0.05$).

CONCLUSIONS: Data demonstrate that activation of Gq and Gi subtypes of astrocytic G protein-coupled receptors exacerbates ischemic injury and ischemia-induced apoptotic cell death. Our results suggest that different types of G protein-coupled receptors expressed in astrocytes determine the severity of ischemic injury and may be important therapeutic targets for stroke.

Keywords: Astrocytes, Chemogenetics, G protein-coupled receptors, Ischemic stroke

OC-60

Investigation of the Effect of Systemic Irisin Administration on Locomotor Activity and Learning-Memory Function in Cerebral Ischemia Model in Rats

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AIM: Myokines produced in skeletal muscle can affect tissues/organs through autocrine, paracrine and endocrine pathways. Irisin,a myokine discovered in recent years that can cross the blood-brain barrier,can directly affect neuronal activity and synaptic plasticity.The aim of this study isto investigate the effectiveness of irisin on learning-memory in systemic administration in rats with a cerebral ischemia model.

METHODS: Thirtyeight adult male Wistar albino rats were randomly divided into 5groups (group1=control, group2=sham, group3=irisin, group4=ischemia, group5=ischemia+irisin). Bilateral occlusion of common carotid artery was applied to the ischemia groups as a model of chronic cerebral hypoperfusion. The day after the operation,100ng/kg irisin was administered intraperitoneally to the irisin groups, 3days/week for 4 weeks. Then, locomotor activity was tested with an open field (OF) test device, and learning-memory function was tested with a Morris water maze (MWM). All statistical analyzes were performed with SPSS, version22. Significance between groups was analyzed by one-way ANOVA and post-hoc Bonferroni test.

RESULTS: There was no significant difference between the groups interms of total distance moved and mean velocity in the OF device. While thetime tofind the platform decreased day by day in the control, sham and irisin groups during the 4-day learning process in MWM ($p<0.05$), no significant difference was detected in the ischemia groups. On the 5th day of the test, the time spent in the target quadrant by the ischemia group was significantly lower than the control group ($p<0.05$). However, it was observed that there was no significant difference in the ischemia+irisin group. While the frequency of entry into the target quadrant in the ischemia group was lower compared to the control and sham groups ($p<0.05$ and $p<0.01$, respectively), this significance was observed to disappear in the ischemia+irisin group. The time the irisin group spent in the opposite quadrant was shorter compared to the control, ischemia and ischemia+irisin groups ($p<0.05$).

CONCLUSIONS: This study reveals that the cerebral ischemia model negatively affects learning-memory, but systemic irisin administration may have curative effects on the impairment in learning-memory functions. In this respect, our study may form the basis of studies on the systemic use of irisin in ischemic brain diseases such as stroke and vascular dementia, where exercise is not possible.

Keywords: Cerebral ischemia, Irısın, Learning, Memory

OC-61

A New Model of Depressıon: Earthquake-induced Stress, Anxiety and Depression

Okan Tutuk

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AIM: The incidence of post-earthquake anxiety-depression and post-traumatic-stress disorder is quite-high. People exposed to earthquakes have psychological-symptoms and comorbidities that are common even 1-year after the event. It is seen that the limited number of studies examining post-earthquake depression and accompanying diseases are clinically weighted and preclinical-studies are almost non-existent.We aimed to develop a new-

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method of depression as a result of the creation of conditions that can be exposed to post-earthquake with earthquake-simulation. With this new-model, it is aimed to examine the relationship between earthquake-stress and disease in many preclinical-studies METHODS: It was performed in 2 groups as control (n=12) earthquake group (n=12). Depression by Earthquake (DD): In the automatic-shaking-cage,which we created the prototype model for earthquake-simulation, 3-major shocks (each 5 minutes) and 15-50 aftershocks (with durations ranging from approximately 30 seconds to 1-2minutes) were applied to the experimental animals at different times a day with earthquake sound. In addition, conditions that may develop after the earthquake; 6-10 hours of food/water and movement-restriction, cold-hot exposure, light-dark cycle changes were applied. Behavioral and biochemical analyzes were performed.

RESULTS: In the DD-group compared to the control-group: Decreased locomotor-activity ($p<0.0001$), in terms of anxiogenic-effect; increased time in closed/arms ($p<0.001$) dark/box ($p<0.0001$), decreased depression-related sucrose-preference ($p<0.0001$)-increased sedentary time ($p<0.0001$), slow learning ($p<0.001$) affected memory function ($p<0.0001$). 21 In the DD-group: decreased locomotor-activity ($p<0.001$), stay time in closed arms ($p<0.05$) dark box ($p<0.05$), decreased sucrose preference ($p<0.05$) increased sedentary time ($p<0.001$) indicating the continuation of depression-like behavior ($p<0.05$) increased sedentary time ($p<0.001$), slow learning in terms of learning-memory ($p<0.001$). Similarly in the biochemical-analyses, Cortisol ($p<0.0001$), ACTH ($p<0.0001$), TOS ($p<0.0001$), OSI ($p<0.0001$) indices were statistically significantly increased.

CONCLUSIONS: As a result of major earthquakes, it is seen that post-traumatic stress disorder, depression-anxiety and accompanying diseases that can affect the quality of life,including occupational performance, may occur, which is supported preclinically by our study. The behavioral-biochemical results of our DD group, which we established with earthquake-simulation, support the validity of the method in terms of further preclinical investigation of such a subject that can have such widespread effects. It is also an important result that long-term anxiety, depressive-cognitive impairment persists after earthquake-simulation. With this methodology, both post-earthquake studies and some pathological relationships can be successfully examined.

Keywords: Earthquake, Depression by earthquake, Anxiety, Stress, Behavioral tests, Methodology

OC-62

Investigation of the Effects of Nicotinamide Riboside in a Ketamine-Induced Rat Model of Schizophrenia

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AIM: Schizophrenia is a major health concern that impairs social and cognitive abilities. Brain energy metabolism and mitochondrial dysfunction are thought to be involved in the pathology of the disease. On the other hand, there are also reports that antipsychotics used in treatment have disruptive effects on mitochondrial function. This study aimed to evaluate the effects of nicotinamide riboside, a natural precursor of nicotinamide adenine dinucleotide, which is a raw material for mitochondrial function, in a rat model of schizophrenia.

METHODS: Sixty adult male Sprague-Dawley rats were included in the study. Groups were formed as follows: Control (C), Schizophrenia model-ketamine (KET), nicotinamide riboside (NR), ketamine+nicotinamide riboside (KETNR), ketamine +antipsychotic (KETAP), and ketamine+antipsychotic+nicotinamide riboside (KETAPNR). Ketamine was administered 25 mg/kg for 10 days, followed by AP (risperidone) and NR 10 mg/kg and 300 mg/kg respectively for 15 days. Following the last injection day, locomotor activity test, sucrose preference test and novel object recognition tests were performed. Statistical analyses were conducted using Kruskal-Wallis ANOVA and Games-Howell post-hoc tests.

RESULTS: The novel object recognition test revealed a significant difference between the KETAP and KETAPNR groups ($p<0.05$). A significant difference was also observed between these groups in the locomotor activity test ($p<0.05$). In the sucrose preference test, significant differences were found between the KETAPNR and C groups ($p<0.05$).

CONCLUSIONS: Our results suggest that the combined use of antipsychotics and nicotinamide riboside in a ketamine-induced schizophrenia model improves cognitive functions and reduces positive symptoms, but also negatively affects mood-related behaviors. Our findings indicate that nicotinamide riboside which is a precursor of adenine dinucleotide, is a potential candidate for improving mitochondrial dysfunctions and related symptoms in schizophrenia pathogenesis. Our study was supported by the Ege University Scientific Research Projects Coordination with project number 32205.

Keywords: Cognitive functions, Ketamine, Mitochondrial dysfunction, Schizophrenia

OC-63

Differences in the Expression of Dopamine Receptor and Dopamine Transporter mRNAs in the Brains of Nicotine-Preferring Rats

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AIM: The key brain circuit involved in the development of addiction is known as mesocorticolimbic system (MCLS). This circuit involves the mesolimbic pathway from ventral tegmental area (VTA) to the nucleus accumbens (NAc) and the mesocortical pathway from VTA to the prefrontal cortex (PFC). Dopamine is the primary neurotransmitter in MCLS. To investigate nicotine addiction, we have been breeding a nicotine-preffering rat line (N) in our laboratory. Our study aimed to investigate differences in the regulation of dopamine receptor 1 (D1R), 2 (D2R), 3 (D3R) and dopamine transporter (DAT) mRNAs in MCLS during nicotine reward in N and control (C) animals.

METHODS: Oral nicotine was administered for five weeks, 10 mg/L for the first 2 weeks and 20 mg/L for the next 3 weeks. Study groups: C receiving water (WC), C receiving nicotine (NC), N receiving water (WN), N receiving nicotine (NN). Animals were decapitated. D1R, D2R, D3R and DAT mRNA expressions were determined in PFC, NAc, VTA by RT-PCR. Data were analyzed by ANOVA, post-hoc Tukey and T-Tests.

RESULTS: N rats consumed ($p<0.001$) and preferred ($p<0.05$) more nicotine than C throughout the 5 weeks. Weeks 4 and 5, N consumed more nicotine than C ($p<0.001$) and preferred nicotine more ($p<0.001$). D1R ($p<0.02$), D2R ($p<0.01$) mRNA expression in NAc and D3R ($p<0.001$), DAT ($p<0.01$) mRNA expression in VTA decreased in nicotine-receiving animals compared to water-receiving animals. In the VTA of N rats, D3R ($p=0.008$) and DAT ($p<0.005$) mRNA decreased compared to the C. In the NAc of the NN, D1R ($p<0.05$) and D2R ($p<0.05$) mRNA was decreased compared to the WN. In the VTA of WN and NC, D3R ($p<0.05$, $p<0.005$, respectively) and DAT ($p<0.01$, $p<0.05$, respectively) mRNA decreased compared to WC.

CONCLUSIONS: D1R, D2R, D3R and DAT regulate reward process in MCLS. These findings may underlie high nicotine-preference in N animals.
(Project number: BAP TS-TUT-2023-29642– HADYEK-2024-051)

Keywords: Nicotine, Dopamine, DAT, D1R, D2R, D3R

OC-64

Investigation of the Effects of Agomelatine Administration on Apoptosis and Autophagy in Experimental Cerebral Ischemia/Reperfusion Modeled Rats

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AIM: According to World Health Organization, stroke is second leading cause of global death and is mostly characterized by blockages in cerebral vessels. This condition includes Cerebral Ischemia (CI) and Reperfusion (R) injury, leading to neuronal pathophysiological processes involving apoptotic and autophagic pathways. Current literature has limited studies on effectiveness of Agomelatine, noted for its role in melatonergic and serotonergic system activity and neurogenesis, on CI/R damage. This study aims to analyze effect of Agomelatine on proteins involved in apoptotic and autophagic pathways in CI/R damage.

METHODS: Male Sprague Dawley rats were divided into four groups (n=10): Control, CI/R and CI/R+Agomelatine (20 and 40 mg/kg). Except for control group, rats underwent Middle Cerebral Artery Occlusion (MCAO) model for 60 minutes to induce CI/R. One hour post-MCAO, hydroxyethyl cellulose was administered to CI/R group, and Agomelatine at 20 and 40 mg/kg was administered to CI/R+Agomelatine groups intraperitoneally. At end of experiment, animals were decapitated and brain tissues were collected. Western Blot analysis was used to assess levels of apoptosis (BCL-2 and BAX) and autophagy (Beclin-1, ATG5, ATG7, and p62) proteins in the infarct area of brain tissues. Statistical comparisons among groups were conducted using Kruskal-Wallis-H test in IBM-SPSS-24.0 for Windows program; $p<0.05$ considered statistically significant.

RESULTS: The analyses showed that the apoptosis protein BCL-2 was higher and BAX was lower in the CI/R+Agomelatine groups compared to the CI/R group ($p<0.05$). In addition, the autophagy protein Beclin-1, ATG5 and ATG7 levels were higher and the p62 level was lower in the agomelatine-treated groups compared to the CI/R group ($p<0.05$).

CONCLUSIONS: It was concluded that in the CI/R model agomelatine application affected levels of apoptosis and autophagy proteins in a way that would inhibit apoptosis and induce autophagy.
This study was supported by İnönü University Scientific Research Projects unit with project number TYL-2022-3072.

Keywords: Cerebral Ischemia, Reperfusion, Apoptosis, Autophagy, Agomelatine

OC-65

Rosmarinic Acid Exerts Neuroprotective Effects in an in Vitro Alzheimer's Disease Model

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AIM: Alzheimer's Disease (AD) is the most common neurodegenerative disorder, characterized by increased neurotoxicity and apoptosis. Rosmarinic acid (RA) is known to have

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anticancer, antioxidant and anti-inflammatory effects. This study aims to investigate the effects of RA on amyloid-beta (Aβ), tau protein, α-synuclein, abelson tyrosine kinase (ABL) levels and apoptosis in an in vitro AD model.

METHODS: SH-SY5Y cells were differentiated into cholinergic neurons using retinoic acid. The cells were then divided into the following groups: control, Aβ (Alzheimer's model), Aβ+RA and RA. To determine the appropriate doses of RA, Aβ, and Aβ+RA, CCK-8 assays were performed on the differentiated cells. The expression of apoptosis-related genes was analyzed using qRT-PCR, while the levels of tau, α-synuclein, abelsone tyrosine kinase (ABL) and Aβ proteins were determined by using ELISA.

RESULTS: CCK-8 analysis revealed that the 0.5, 1.5, and 5 µM doses of RA were non-toxic on the differentiated cells. Aβ IC40 dose was determined as 20 µM. After RA pretreatment, 20 µM Aβ treatment was performed and it was found that RA (1.5mM) showed neuroprotective effect. The expression levels of BAX, CASP3, CASP7, CYCS, FADD, and FAS genes in Aβ group were significantly increased compared to the control group, while a significant decrease in these gene expressions was observed in Aβ+RA group compared to the Aβ group. ELISA analyses indicated that tau, α-synuclein and Aβ protein levels were increased in Aβ group compared to control, while they were decreased in Aβ+RA group ($p<0.05$). ABL level was found to be significantly higher only in Aβ+RA group ($p<0.05$).

CONCLUSIONS: The findings of this study reveal that RA has neuroprotective and antiapoptotic effect in AD, in vitro.

Keywords: Alzheimer's Disease, Apoptosis, Abelson Tyrosine Kinase, Neuroprotection, Rosmarinic Acid, SH-SY5Y cells

OC-66

Investigation of Ccytomorphological Changes of Astrocytes in the Amygdala in Alzheimer's Disease

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AIM: Alzheimer's Disease (AD) is a progressive neurodegenerative disorder marked by the loss of neurons and synapses leading to cognitive decline. AD progression is associated with the spread of hyperphosphorylated tau proteins across the cerebral cortex and the spread of tau is used to stage AD in postmortem brains. Braak and Braak identified six stages of AD, beginning in the transentorhinal region and eventually affecting the neocortex. The amygdala was shown to have significant quantity of neurofibrillary tangles and neurotic plaques in AD. Astrocytes, crucial for neuronal support and metabolism, play a significant role in AD progression, particularly through their involvement in amyloid-beta (Aβ) clearance and their pathological changes, which may worsen cognitive and behavioral symptoms.

METHODS: In the present work we measured astrosytes area of amygdala in postmortem human brains with AD and neurotypical subjects. We carry the measurements in one pallial (Lateral) and one subpallial (Central) amygdalar nuclei. We used Nissl-stained brain sections from 4 human neurotypical, 8 AD (2 Braak I-II, 1 Braak III-IV, and 5 Braak V-VI) postmortem brains.

RESULTS: in the central and lateral nucleus, we demonstrated a statistically significant increase in astrocyte area at Braak I-II, Braak III-IV, and Braak V-VI stages compared to neurotypical subjects. In the lateral nucleus, there is no significant difference between Braak stages, suggesting that the damage in the lateral nucleus begins at the early stages of AD.

CONCLUSIONS: Our study shows that the pallial and subpallial amygdala astocytes is affected at the early, intermediate and advanced Braak AD stages. Astroglial cells play a key role in neurological diseases, influencing their pathogenesis and outcome. Astrocytes are involved in all neurodegenerative processes and show significant changes in AD. It is believed that early changes in astrocytes may influence the development of AD. Targeting astroglia could offer new treatment options for early-stage AD.

Keywords: Alzheimer's Disease, Amygdala, Astocytes

OC-67

Effect of Piriformis, Hamstring, Gastrocnemius-Soleus Muscle Statistic Stretch Exercises on Pain, Life and Sleep Quality in Women doing Instrumental Pilates

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AIM: The most common type of equipped pilates is instrumented pilates. In patients who have not been able to complete joint movement in recent years, static stretching exercises are more often preferred. The study investigated the effect of static stretch exercises on the piriformis, hamstring, and gastrocnemius-soleus muscles on pain, quality of life, and sleep in women doing instrumental pilates.

METHODS: Thirty women aged 20 to 45 who applied to do instrumental pilates at a health center in Isparta participated in the study. The study studied the effect of static stretching exercises on pain, quality of life, and sleep quality with pre-test-end test applications, using two days a week for eight weeks.

RESULTS: The participants' age, height, body weight and body mass index (BMI) were evaluated with an average age of 3 ± 5.2, an average height of 165.83 ± 3.92, a body weight of 62.46 ± 8.47 and an average BMI of 22.79 ±3.46. 63.3% of the participants were smokers, 43.3% were married, 66.7% were working in the public

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sector, and 40% came on the suggestion of their pilatese friends. Pain measurements revealed statistically significant differences between pre-test and final test data in the back, waist and lower limbs. SF-36 pre-test final test analysis revealed significant differences in physical functions, vitality, mental health, social functioning, pain, and general health variables. A significant difference was found between the pre-test and final test data of the PUKI score. According to the analysis of pre-test-final test data of PUKI components, the difference between subjective sleep quality, latency, duration, usual sleep yield and daytime dysfunction has been statistically significant.

CONCLUSIONS: The study found that static stretching exercises on piriformis, hamstring, and gastrocnemius-soleus muscles, in addition to instrumental pilates, can have a positive effect on pain, quality of life and sleep.

Keywords: Instrumental Pilates, Piriformis, Hamstring, Static Stretching, Gastrocnemius-Soleus

OC-68

Effects of Chemotherapy and Chronic Aerobic Exercise on Cognitive Functions in Glioblastoma Model Rats

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AIM: Glioblastoma (GBM) is a common, aggressive brain tumors in adults. Treatments like temozolomide (TMZ) and the tumor can reduce patients' quality of life. This study evaluates the effects of moderate aerobic exercise on oxidative stress and cognitive functions in glioblastoma-bearing rats, with and without chemotherapy.

METHODS: Male Sprague Dawley rats (n=50) were divided into five groups: sham-operated (S), glioblastoma (GBM), glioblastoma + temozolomide (GBM+T), glioblastoma+exercise (GBM+E), and glioblastoma+temozolomide+exercise (GBM+T+E). Exercise groups did moderate-intensity exercise for 8 weeks. Five weeks later, 1x106 glioma cells were injected to create the tumor model. Temozolomide (10 mg/kg) or saline was administered for five days. Spatial memory was assessed with the Y-maze test; anxiety with the hole board test; and depressive symptoms with sucrose preference and Porsolt tests. Brain tissue weight index, malondialdehyde (MDA) levels, myeloperoxidase (MPO) activity, glutathione (GSH) levels, and superoxide dismutase (SOD) activities were measured. ANOVA and Student's t-test were used.

RESULTS: Spatial memory assessed by the Y-maze test decreased in the GBM group but improvement with exercise and TMZ ($p<0.05$-0.01). In the hole board test, anxiety was lower in the GBM group but higher in the exercise groups ($p<0.05$-0.001). The sucrose preference index was higher in the TMZ and TMZ+exercise groups compared to the GBM and control groups ($p<0.05$-0.01). In the Porsolt test, immobility time increased in the GBM group and was suppressed with TMZ ($p<0.05$). The brain weight index decreased in the GBM group but increased in the exercise groups ($p<0.05$-0.001). MDA levels and MPO activity increased in the GBM group and decreased with exercise and/or TMZ ($p<0.05$-0.01). SOD activity was higher in the exercise and/or TMZ groups compared to the GBM group ($p<0.05$-0.01).

CONCLUSIONS: GBM formation increases anxiety-like behavior, decreases spatial memory, reduces brain weight index, and elevates oxidative stress. Moderate exercise improved these parameters. This study was supported by the TÜBİTAK 2209 Project.
Keywords: Glioblastoma, temozolomide, exercise, cognitive function

OC-69

Protective Effects Of Vitamin D On Pancreas Damage Induced by High-Fructose Corn Syrup Consumption

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AIM: High Fructose Corn Syrup (HFCS); It is a widely used additive for various reasons such as being very sweet, extending the shelf life of foods and being cheap. Diet rich in fructose: It causes various metabolic disorders characterized by diabetes and insulin resistance, hyperglycemia, hypertriglyceridemia and fatty liver. It is stated that vitamin D affects glucose tolerance by affecting β-cell function in HFCS-fed rats with its anti-inflammatory and antioxidant effects. It is thought that vitamin D may improve insulin secretion and insulin resistance associated with T2DM. In our study, we aimed to investigate pancreatic damage caused by chronic consumption of HFCS and protective effects of vitamin D on pancreas.

METHODS: Wistar albino male rats (6-8 week old) were divided into 3 groups; control (tap water/saline), HFCS (11% HFCS-55/saline) and HFCS+D Vit (11% HFCS-55/42 µg vitamin D). At the end of one month, rats were sacrificed and blood and pancreas tissues were collected. Biochemical, immunohistochemical and histopathological analyzes were performed.

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RESULTS: Biochemically, the MDA level in pancreas was increased in HFCS group compared to control; SOD, CAT enzyme activity and serum insulin levels were found to decrease (p=0.001, p=0.009, p=0.008 p=0.036, respectively). It was observed that MDA level decreased in Vit D group compared to HFCS group; SOD, CAT enzyme activity and serum insulin levels were found to increase (p=0.027, p=0.045, p=0.048, p=0.013, respectively). In histopathological examination, hyperemia, atrophy and degeneration of some Langerhans cells were observed in the pancreatic tissue of HFCS group rats. Significant decreases in insulin, amylin and glucagon expressions compared to control; Significant improvements were seen in these parameters in Vit D group.

CONCLUSIONS: In conclusion, vitamin D reduces lipid peroxidation and free radicals in HFCS-induced pancreatic damage; It was effective in increasing antioxidant activity. Therefore, it may affect glucose tolerance by affecting β-cell function in HFCS-fed rats.

Keywords: Vitamin D, HFCS, Pancreas, Insulin, Oxidative stress

OC-70

The Effect of Caffeine Intake on Respiratory Functions, Cardiopulmonary Exercise Test Parameters, and Post-Exercise Heart Rate Variability

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AIM: Caffeine has effects on numerous bodily systems, including the neurological system, through adenosine receptors. The aim of the study was to investigate the effects of caffeine on pulmonary function tests (PFT), cardiopulmonary exercise test (CPET), and heart rate variability (HRV) after exercise.

METHODS: The study included 16 male participants aged between 18-25, who did not have high physical activity, with the approval of the Ethics Committee for Human Research at Ankara University School of Medicine. Participants were invited twice: once for caffeine (4 mg/kg) and placebo. PFT and CPET parameters were determined 45 minutes after ingestion, and HRV analysis were performed following rapid recovery phase of HR. PFT data were recorded as percentages of the predicted values. HRV data were recorded before exercise (B), after exercise following the rapid recovery phase of HR (R1), and when HR dropped below 100 bpm (R2). The data were evaluated using SPSS-22 with significance level of $p<0.05$.

RESULTS: Caffeine increased peak expiratory flow rate (PEF), whereas placebo increased end-expiratory flow rate (MEF75) (p=0.004; 0.019). CPET demonstrated that maximal oxygen capacity, power, ventilation, and HR were higher than the placebo (p=0.002; 0.002; 0.004; 0.02). Except for three, there were substantial differences between successive HRV measurements. There were no differences in RMSSD (root mean squared differences between consecutive heartbeats) of those who received only a placebo and LF/HF (low and high frequency ratio) of individuals who received both caffeine and placebo between R2 and R1.

CONCLUSIONS: Increased PEF and decreased MEF75 in PFT suggests that more forceful contraction of expiratory muscles caused by caffeine leads to dynamic airway compression. CPET data demonstrate that caffeine improves exercise performance. The diffrence in RMSSD between R2-R1 in caffeine and placebo indicates that sympathetic activity is prevailing in caffeine consumption, and the recovery after exercise is accelerated with caffeine.

Keywords: Caffeine, Cardiopulmonary Exercise Testing, Heart Rate Variability, Pulmonary Function Tests

OC-71

Effects of Classical Massage on Some Myokines, Angiogenic and Antiangiogenic Factors in Male Individuals

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AIM: Angiogenesis, the formation of new capillaries, increases with higher angiogenic factors and decreases with higher antiangiogenic factors. Few studies have examined massage's impact on these factors, but we hypothesize that massage may influence their release through mechanotransduction. Thus, massage could benefit with conditions like cancer, stroke, paralysis, and wound healing. Our aims to investigate the effects of massage on these factors and whether applying it to different muscle areas matters.
METHODS: The study included twenty-two sedentary males aged 18-30, divided into two groups: Back Massage (SM, n=11) and Lower Extremity Massage (AEM, n=11). Venous blood samples were collected at three points: before massage (control), 2 hours after first session (acute), and 2 hours after last session (chronic). Serum levels of Vascular Endothelial Growth Factor(VEGF), Angiopoietin-1(ANG-1), Thrombospondin-1 (TSP-1), Endostatin (ES), Interleukin-6 (IL-6), and Interleukin-8 (IL-8) were measured

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using the ELISA method. Repeated Measures ANOVA was used to compare changes in both groups over time.

RESULTS: In SM, angiogenic factors VEGF and ANG-1 levels showed a nonsignificant increase, while they nonsignificantly decreased in AEM. IL-8, a myokine that promotes angiogenesis, increased significantly in both groups ($p<0.05$), with a greater increase in the SM group. Among antiangiogenic factors, TSP-1 showed no significant changes in either group, while Endostatin (ES) increased significantly (25%) in AEM compared to control in chronic ($p<0.05$). No significant changes occurred in IL-6 levels in either group, but increase was greater in SM group.

CONCLUSIONS: The back region has more red (oxidative) muscle fibers, suggesting that back massage may stimulate angiogenic factors more effectively. Therefore, back massage could be more beneficial than lower extremity massage for conditions like stroke and paralysis. Conversely, Endostatin increased only in AEM, lower extremity massage may be more effective than upper extremity massage in preventing unwanted angiogenesis (cancer). Further studies with larger sample sizes are needed to understand these changes better.

Keywords: Massage, Angiogenesis, Angiogenic Factor, Antiangiogenic Factor, Myokine

Poster Communications (PC 01 - PC97)

PC-01

Protective Effect of Aerobic Exercise Against Temozolomide-induced Hepatotoxicity in Rats with an Experimental Glioblastoma Model

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AIM: Glioblastoma (GBM) is a common and aggressive brain tumour with a median survival of 12-15 months. Temozolomide (TMZ) is the main chemotherapeutic agent used in the treatment of GBM. Liver injury has been reported in patients treated with TMZ. In this study, we aimed to investigate the protective role of moderate aerobic exercise against TMZ-induced hepatotoxicity in rats with glioblastoma.

METHODS: A total of 50 three-month-old Sprague-Dawley rats were used to form 5 groups; sham-operated (S), glioblastoma (GBM), glioblastoma+temozolamide (GBM+T), glioblastoma+ exercise (GBM+E) and glioblastoma+temozolamide+exercise (GBM+T+E). A moderate-intensity exercise protocol at 50-60% of the rats' VO2max was applied to the exercise groups for 30 min/day for a total of 8 weeks. The tumour model was established by intracerebroventricular injection of 1x106 glioma cells into the rats by the stereotaxic method. Subsequently, the chemotherapy groups were given 10 mg/kg TMZ by oral gavage. After sacrification, liver tissues were isolated and the levels of MDA, GSH and catalase, SOD and MPO in tissue; ALT and AST in serum were measured by spectrophotometer. Histopathological scoring was performed. Statistical evaluation was performed by one-way ANOVA and post hoc LSD.

RESULTS: GBM administration increased MDA levels in liver tissue. However, MDA levels decreased in the exercise groups (GBM+E and GBM+TMZ+E) ($p<0.05$). There was no significant difference in MDA levels between the GBM and GBM+T groups. The antioxidant catalase activity increased with exercise and/or TMZ administration compared to the control group ($p<0.01$). GSH levels increased in the GBM, GBM+E and GBM+TMZ+E groups compared to the control group ($p<0.05$). TMZ treatment increased plasma ALT and AST, whereas exercise decreased them ($p<0.05$). The histopathological score increased in G and GT groups and decreased in GE and GTE groups ($p<0.05$).

CONCLUSIONS: The results of the study showed that moderate aerobic exercise was beneficial in reducing the detrimental effects of temozolomide on the liver. (supported by TUBITAK-2209-A).

Keywords: Glioblastoma, Temozolomide, Exercise, Hepatotoxicity

PC-02

A Preliminary Study About Possible Effects of High Intensity Interval Training on Adipokine and Myokine Levels in Young Female Basketball Players

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AIM: Basketball challenges athletes' speed, balance, strength, and aerobic/anaerobic capacities. To improve in basketball, athletes must train frequently over long periods. High-Intensity Interval Training (HIIT) is popular for its short duration and positive impact on performance. This study aimed to investigate the effects of both acute and chronic (6 weeks) HIIT on adipokines like leptin, visfatin, obestatin and myokines like FGF-21 and BDNF in young female basketball beginners and elite players and whether these effects vary based on training status.

METHODS: With ethical approval from Pamukkale University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (16.08.2022, 12), 20 elite female basketball players (E group, training for 3 years±1 month, 14±0,8 years old) and 19