Poster Communications

PC-01

Effects of Hyperbaric Oxygen Therapy (HBOT) on Hemorheological Parameters in Patients with Chronic Wounds

Mukaddes Sinan[1], Nesrin Zeynep Ertan[1], Bengüsu Mirasoğlu[2], Özlem Yalçın[3]

[1]İstanbul Aydın University, Faculty of Medicine, Department of Physiology, İstanbul
[2]İstanbul University, İstanbul Faculty of Medicine, Department of Underwater and Hyperbaric Medicine, İstanbul
[3]Koç University, Faculty of Medicine, Department of Physiology, İstanbul, Türkiye

AIM: HBOT is effectively used in patients with chronic wounds. It has been reported that hemorheological parameters of chronic wound patients are negatively affected. These findings suggest that cardiovascular complications may occur in patients following HBOT. We investigated the effect of HBOT on hemorheological parameters in chronic wound patients.

METHODS: The study was approved by the ethics committee (number: 147/2013). 25 patients (30-56, 11F/14M) without chronic disease were included. Routine care of the wounds continued throughout the study. According to the standard treatment procedure, 100% oxygen was administered at 2.4 ATA (1 session per day, 5 sessions per week). Blood was drawn before the initial therapy and after the 20th session and the initial values were considered as control. Whole blood viscosity at 8 different shear rates (SR) and plasma viscosity were measured with a cone/plate viscometer. Erythrocyte aggregation, erythrocyte deformability and osmotic deformability indices were measured using a laser applied refractometer (LORCA). Data were statistically evaluated using the Mann-Whitney U test and presented as mean±standard deviation.

RESULTS: The mean hematocrit values were 38.42±4.67 (28-45). Compared to the initial values after 20th therapy session; plasma viscosity and all SR values of blood viscosity corrected to 45% decreased significantly ($p<0.001$ and $p<0.05$, respectively). Erythrocyte aggregation parameters using both autologous plasma and dextran70 solution, significant and positive differences were observed ($p<0.001$ and $p<0.001$, respectively). There were no significant differences in erythrocyte deformability and osmotic deformability parameters.

CONCLUSION: Our results contradict with previous studies in that they showed that the parameters we investigated were not negatively affected by the treatment. On the contrary, it has shown that it has a positive effect on clinically important parameters such as erythrocyte aggregation. We think that these contradictions may be due to differences in clinical practice and experimental conditions and/or different responses in humans and animals.

Keywords: Chronic Wound, Hyperbaric Oxygen Therapy, Blood Viscosity, Erythrocyte Deformability, Erythrocyte Aggregation, Osmotic Deformability.

PC-02

Effects of Epigallocatechin Gallate and Curcumin on Hydrogen Peroxide Toxicity to SH-SY5Y Cells

Atilla Fatih Ünver[1], Özlem Yılmaz[1], Mümin Alper Erdoğan[2]

[1]Ege University Faculty of Medicine, Department of Physiology, Izmir
[2]Katip Celebi University, Faculty of Medicine, Department of Physiology, Izmir, Türkiye

AIM: Several studies have shown that plant polyphenols have positive effects on neurodegenerative diseases. Epigallocatechin-3-gallate (EGCG) and curcumin are antioxidant polyphenols. The aim of this study is to demonstrate the effects of EGCG and curcumin pre-treatment against hydrogen peroxide (H2O2) damage in SH-SY5Y cell line.

METHODS: Various doses of H2O2 were administered to the SH-SY5Y cell line for 1 hour in the study. The LD50 dose of H2O2 was determined as 100 µM. In order to determine the protective effects of EGCG and curcumin, 0.1 µM EGCG, 1 µM EGCG, 10 nM Curcumin, 50 nM Curcumin doses and their combinations were administered as a 24-hour pretreatment. It was exposed to 100 µM H2O2 for 1 hour at the end of the application. As a result of the applications, cell viability was determined by MTS test, and colony formation abilities were determined by clonogenic test. Caspase-3 ELISA was performed to assess the type of cell death. One-way ANOVA was used for statistical analysis.

RESULTS: Our results showed that 100 µM H2O2 manifested decrease approximately half of the cell population ($p<0.0001$). Cell survival and colony formation ability were significantly increased ($p<0.0001$) and active caspase 3 levels were significantly decreased ($p<0.0001$) when 0.1 µM EGCG or 10 nM curcumin treatment was applied 24 hours before 1-hour H2O2 administration. It was observed that the combination of these doses also showed protective effects on cell proliferation and colony formation ($p<0.001$) and decreased active caspase-3 levels significantly ($p<0.001$).

CONCLUSION: Our study revealed that H2O2 decreases cell viability by increasing apoptotic cell death. Doses of 0.1 µM EGCG, 1 µM EGCG, 10 nM Curcumin, 50 nM Curcumin and their combinations reduced the neuronal damage caused by H2O2. This shows that these agents can be used as protective agents against neurodegeneration.

Keywords: EGCG, Curcumin, H202, Neuronal toxicity.

PC-03

The Effects of Darbepoetin Alfa on the Changes Induced by Ethanol in Glucose Metabolism and Lipid Profile

Emine Uygur[1], Hakkı Oktay Seymen[2], Hafize Uzun[3], Matem Tunçdemir[4], Ayşim Büge Öz[5], Elif Polat[6], Ahsen Yılmaz[7], Elif Yaman[2]

[1]Department of Physiology, Tekirdag Namık Kemal University, Tekirdag
[2]Department of Physiology, Istanbul University Cerrahpaşa, Istanbul
[3]Department of Medical Biochemistry, Atlas University, Istanbul
[4]Department of Medical Biology, Istanbul University Cerrahpaşa
[5]Department of Medical Pathology, Istanbul University Cerrahpaşa
[6]Department of Histology and Embryology, Namık Kemal University, Tekirdag
[7]Department of Medical Biochemistry, Istanbul University Cerrahpaşa, Istanbul, Türkiye

AIM: Ethanol leads to physiopathological disorders by affecting metabolic processes related to glucose metabolism and lipid profile. Darbepoetin alfa (DA) is an analogue of recombinant human erythropoietin (rHuEPO). In our study, we aimed to investigate the effects of darbepoetin alfa (DA) on the changes glucose and lipid metabolism and asprosin levels induced by ethanol in rats.

METHODS: 40 Wistar-Albino male rats were divided into four groups of control (C) (3.15 ml/kg isocaloric glucose solution, ig), ethanol (E) (3 g/kg 20% ethanol solution, ig), DA (0.25 µg/kg, ip) and E+DA. Fasting blood glucose (FBG) was measured on the first day, 15th and 30th days. On the 30th day, triglyceride, total cholesterol, HDL and insulin levels in serum and asprosin levels in plasma were measured. Liver tissues were investigated by histopathological methods.

RESULTS: FBG was significantly lower in E+DA group on the 30th day compared with C group ($p<0.05$). Serum insülin and triglyceride levels were significantly higher in E+DA group compared with C and E groups ($p<0.05$). There was no statistically difference between the groups in HOMA-IR, in the plasma asprosin levels, in the serum total cholesterol and HDL levels. Histopathologically, diffuse microvesicular fat accumulation in hepatocytes, and extensive dilatation and hyperemia in sinusoids were observed in E group compared with C group. In the E+DA group, these pathological findings were significantly reduced.

CONCLUSION: In our study, it was observed that ethanol had no effect on asprosin levels, insulin resistance and lipid profile depending on the ethanol dose and ethanol exposure time. In the E+DA group, the decrease in FBG within physiological limits is due to an increase in insulin level. In our study, there was an increase in serum triglyceride levels with the combined effect of ethanol and DA.

Keywords: Ethanol, Darbepoetin alpha, Asprosin, Glucose metabolism, Lipid profile.

PC-04

Synthesis of New Amino Acid Conjugates Containing Cinnamic Acid Derivatives and Investigation of Their Cytotoxic and Genotoxic Properties

Süleyman Sandal[1], Suat Tekin[1], Eray Çalışkan[2], Kenan Koran[3], Ahmet Orhan Görgülü[4], Ahmet Çetin[2]
[1]Department of Physiology, Faculty of Medicine, Inonu University, Malatya
[2]Department of Chemistry, Faculty of Science and Arts, Bingöl University, Bingöl
[3]Department of Chemistry, Faculty of Science, Firat University, Elazig
[4]Department of Chemistry, Faculty of Science, Marmara University, Istanbul, Turkiye

AIM: The aim of the study is to synthesize new amino acid conjugates and to investigate the effects of cytotoxicity and genotoxicity studies of these compounds on three different human cancer cells.

METHODS: The planned cinnamic acid derivatives were obtained by Claisen–Schmidt condensation, these compounds were reacted with three different amino acids using the benzotriazole method to obtain target compounds. The structures of all compounds were elucidated by FT-IR, 1H, 13C NMR spectroscopy. Cell viability of both cinnamic acid derivatives and target compounds against 3 different human cancer cell lines (human breast (MCF-7), human prostate (PC-3), and human colon (Caco-2) at 5 different doses was determined by MTT assay method. In order to understand whether all compounds that effective against cancer cells cause cell death through DNA damage, the cell death mechanism was elucidated using the comet assay method. Conformity to the normal distribution was determined by the Shapiro–Wilk test. Intergroup comparisons of quantitative variables were determined by the Kruskal–Wallis H test. When there were statistically significant differences between the groups, multiple comparisons were made with Bonferroni correction and Mann–Whitney U test. The data obtained from the comet assay were analyzed using one-way ANOVA, followed by post-hoc Tukey HSD test.

RESULTS: In general, the majority of the target compounds were effective in all cell lines, especially the leucine amino acid conjugate (Phenylbenzyl-CA-Leu-OH) bearing the Phenylbenzyl group showed activity at all doses (1, 5, 25, 50 and 100 µM) ($p < 0.05$).

CONCLUSION: The results of this study demonstrated that the tested compounds caused cell death by causing damage to the DNA of cancer cells.

This study was supported by Inonu University Scientific Research Projects Coordination Unit (Project No: TSG-2020-2183).

Keywords: Cinnamic acid, MTT assay, Comet assay, MCF-7, PC-3, Caco-2.

PC-05

Effects of Paclitaxel and/or Stattic Application on Cell Viability and Tumor Size in Triple Negative Breast Cancer

Adnan Berk Dinçsoy[1], Esra Gedikli[1], Süleyman Can Öztürk[2], Güneş Esendağlı[3], Ayşen Erdem[1]

[1]Hacettepe University Faculty of Medicine, Department of Physiology, Ankara
[2]Hacettepe University, Laboratory Animals Research and Application Centre, Ankara
[3]Hacettepe University, Department of Basic Oncology, Ankara, Türkiye

AIM: Triple negative breast cancer (TNBC) is an invasive and metastatic cancer with aggressive progress. We aimed to investigate the antiproliferative and antimetastatic effects of Paclitaxel, used alone or in combination with Stattic, a Signal Transducer and Transcription Activator-3 (STAT-3) inhibitor, in experimental TNBC models in vitro and in vivo.

METHODS: Paclitaxel and Stattic were administered individually on 4T1 mouse TNBC cell line at varying concentrations for varying durations. Having its IC80 determined as 10 µM, Stattic was applied concomitantly with Paclitaxel administered at different concentrations for varying durations. Cell viability was determined by MTT assay. In vivo model was established by inoculating 4T1 cells subcutaneously into the mammary tissue of female BALB/c mice. Mice were randomly assigned into 9 groups (n=8, each) as: 1-Control+Saline, 2-Control+vehicle(DMSO), 3-Tumor+Saline, 4-Tumor+DMSO, 5-Tumor+Stattic (20 mg/kg), 6-Tumor+Paclitaxel (1 mg/kg), 7-Tumor+Paclitaxel (10 mg/kg), 8-Tumor+ Stattic+ Paclitaxel (1 mg/kg), 9-Tumor+ Stattic+ Paclitaxel (10 mg/kg). Saline, DMSO and Stattic were administered intraperitoneally every other day and Paclitaxel every third day. On day 24, mice were euthanized, and lung and tumor tissues were weighed and kept under convenient conditions until the time of histopathological and molecular analyses. The groups were statistically compared by Kruskal-Wallis/Wilcoxon tests. (Project: TSA-2021-19017, Ethical approval: 2020/10-08).

RESULTS: Stattic reduced cell viability in vitro in a time-independent but dose-dependent manner when applied alone ($P<0.05$). Stattic+10 nM Paclitaxel application decreased cell viability significantly at 48 hours in comparison with that of higher concentrations of Paclitaxel used alone ($P<0.01$). Our in vivo findings revealed no differences between groups in terms of tumor diameter, weight and body weight. Lung weight averages were higher in all Stattic-received groups than Control+DMSO group ($P<0.05$).

CONCLUSION: Paclitaxel reduced cell viability at lower concentrations when co-administered with Stattic for a short duration. Prolonged exposure caused to increased metastasis and cell viability by inhibiting not only STAT3 but probably STAT1 as well, which has tumor suppressing activity.

Keywords: Paclitaxel, Stattic, STAT3, Triple Negative Breast Cancer.

PC-06

Cytotoxic and Genotoxic Effects of Nateglinide on A2780, LNCaP and Caco2 Cell Lines

Samet Öz[1], Furkan Yüksel[2], Güldeniz Şekerci[2], Suat Tekin[2]

[1]Osmaniye Korkut Ata University, Vocational School of Health Services, Veterinary Medicine Department, Osmaniye
[2]İnönü University, Faculty of Medicine, Physiology Department, Malatya, Türkiye

AIM: Cancer represents one of the leading causes of morbidity and mortality. Despite advances in cancer treatment, the low success rate and tumor recurrence make the discovery of new therapeutic agents important. Nateglinide is a new oral hypoglycemic agent with a carboxyl group and a peptide bond in its structure. In this study, we aimed to determine the cytotoxic and genotoxic effects of nateglinide on human ovarian cancer, human prostate cancer and human colon cancer cell lines.

METHODS: A2780, LNCaP and Caco-2 cell lines were used in the study. After the cells were incubated with 1, 10, 100 and 1000 µM concentrations of Nateglinide for 24 hours, the cytotoxicity level in the cells was determined by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay method. According to the MTT assay results, the inhibitory concentration 50 (LogIC50) of Nateglinide was calculated in the Graphpad Prism 8 program. Comet experiments were performed to determine the genotoxic properties of the concentrations showing cytotoxic effect according to the MTT assay results. Comparisons between groups were made with the Kruskal Wallis H-Test.

RESULTS: 1000 µM doses of nateglinide significantly decreased cell viability in A2780 and LNCaP cell lines, and 10, 100 and 1000 µM doses of Caco-2 cell lines ($p<0.05$). According to the Comet assay results performed in A2780, LNCaP and Caco-2 cell lines, an increase in the tail lengths (TI) and tail moments of the cells (TM); it was determined that there was a decrease in head diameters (HD) ($p<0.05$).

CONCLUSION: The results of this study show that the tested Nateglinide has anticancer activity on A2780, LNCaP and Caco-2 cells and causes cell death by damaging cell DNA.

Keywords: A2780, Caco2, Genotoxicity, LNCaP, Nateglinide, Cytotoxicity.

PC-07

Age-Related Characterization of Dental Pulp Mesenchymal Stem Cells

Egemen Kaya[1], Eda Açıkgöz[2], İlkay Aydoğdu[3], Funda Çağırır Dindaroğlu[4], Çiğdem Atalayın[5], Gülperi Öktem[6]

[1]Department of Physiology, Muğla Sıtkı Koçman University, Muğla
[2]Department of Histology and Embryology, Van Yuzuncu Yil University, Van
[3]Department of Oral and Maxillofacial Surgery, Ege University, İzmir
[4]Department of Pedodontics, İzmir Katip Çelebi University, İzmir
[5]Department of Restorative Dentistry, Ege University, İzmir
[6]Department of Histology and Embryology, Ege University, İzmir, Türkiye

AIM: Mesenchymal stem cells are cells that have the ability to self-renew and differentiate into various cells. Although dental pulp stem cells are one of the most important sources of easily available mesenchymal stem cells, they are known for their rapid proliferation and their potential to form mineralized tissue when differentiated with appropriate stimuli. Advances in stem cell biology and tissue engineering have paved the way for cell-mediated regenerative therapy options. There are studies showing that the number and functions of stem cells decrease with age. In our study, it was aimed to compare the ratios of dental pulp stem cells obtained from people aged 18-24 years, 25 years and older.

METHODS: From the obtained dental pulps, dental pulp stem cells were grown by cell culture and differentiated into adipogenic, osteogenic and chondrogenic cells. Dental pulps were compared with flow cytometry in terms of dental pulp mesenchymal stem cells. Approval for the study was obtained from the Ege University Faculty of Medicine Clinical Research Ethics Committee (18-1/26). The project was supported by Ege University BAP Coordination Unit.

RESULTS: Mesenchymal stem cell markers CD13, CD105 and hematopoietic stem cell marker CD 45 were evaluated. In the statistical analysis, no significant difference was found between the age groups.

CONCLUSION: Although more dental pulp stem cells were obtained in the 18-25 age group, no statistically significant difference was found.

Keywords: Mesenchymal Stem Cells, Dental Pulp Stem Cells, Flow Cytometry.

PC-08

Effects of Diisononil Phthalate on Different Types of Cancer Cell Lines

Elif Maide Beyoğlu[1], Semiha Özkaya[2], Suat Tekin[2], Süleyman Sandal[2]

[1]Gaziosmanpasa University, Physiology Department, Tokat
[2]Inonu University, Physiology Department, Malatya, Türkiye

AIM: Phthalates, as a class of endocrine disruptors, are widely used as plasticizers in consumer products, including building materials, medical supplies, and cosmetics. Diisononyl phthalate (DiNP) is one of most widely used primary phthalates in industry. Studies have shown that exposure to phthalates is associated with variety of disorders, most notably cancer. Compared with other phthalate groups, relationship of DiNP with cancer has not been fully elucidated. Therefore, we aimed to investigate effect of DiNP exposure cell viability in LNCaP, A2780, MCF-7 and Caco-2 cell lines.

METHODS: LNCaP, A2780, MCF-7 and Caco-2 cell lines were used in the study. Changes in cell viability were determined by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay method after cells were incubated with DiNP concentrations of 1, 10, 100 and 1000 µM for 24 hours. After determining the dose-dependent effectiveness according to the MTT assay results, the inhibitory concentration 50 (LogIC50) value was evaluated in Graphpad Prizm 8 program. The genotoxicity level was analyzed with the COMET method by determining the effective doses as a result of the data obtained. Meanwhile, a reaction test was performed between DiNP and MTT chemicals. Comparisons between groups were made using the Kruskal-Wallis H test in IBM-SPSS 24 package program.

RESULTS: After 24 hours of DiNP incubation, viability levels of LNCaP, A2780, MCF-7 and Caco-2 cell lines were significantly decreased at certain concentrations (1000 concentration) ($p<0.05$). We performed Comet analysis at significant doses of the chemical and concluded that DiNP application caused DNA damage in LNCaP, A2780, MCF-7 and Caco-2 cell lines.

CONCLUSION: The fact that DiNP tested in this study exhibited an anticarcinogenic effect on LNCaP, A2780, MCF-7 and Caco-2 cells indicates that it has positive feature in addition to its other harmful effects DiNP. In this context, further research is needed.

Keywords: A2780, Caco-2, DiNP, Cancer, LNCaP, MCF-7.

PC-09

Trimebutin Demonstrate Antitumor Effects on Different Types of Human Cancer Cells

Tuba Keskin[1], Suat Tekin[1], Çiğdem Tekin[2], Ali Beytur[3]

[1]Inonu University, Department of Physiology, Malatya
[2]Inonu University, Department of Public Health, Malatya
[3]Inonu University, Department of Urology, Malatya, Türkiye

AIM: Cancer is a major cause of death affecting millions of people and is caused by the uncontrolled growth and spread of abnormal cells. Anti-inflammatory drug intake has an important place among the pharmacological treatments recommended for cancer. Trimebutin, known for its anti-inflammatory activity, can act as an antitumor agent against low gastrointestinal tract and brain neoplasms. Trimebutin's effects on cancer are still limited. This study was conducted to determine the effects of trimebutin on cell viability of human prostate (LNCaP), ovarian (A2780), breast (MCF-7) and colon (Caco-2) cancers.

METHODS: LNCaP, A2780, Caco-2 and MCF-7 cell lines were used in the study. Trimebutin concentrations of 1, 5, 25, 50 and 100 µM were applied to these cell lines and incubated for 24 hours. Changes in cell viability were determined by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay method. Comparisons between groups were made using the Man-Witney U test with Bonferroni correction in the SPSS program. $p<0.05$ was considered significant. In addition, IC50 calculations of Trimebutin for all cells were made in the Graphpad Prizm 8 program according to the MTT assay results.

RESULTS: It was determined that there was a decrease in cell viability of LNCaP, A2780, Caco-2, MCF-7 cell lines incubated with trimebutin for 24 hours, and this decrease was statistically significant at all applied concentrations of Trimebutin ($p<0.05$).

CONCLUSION: The results of this study show that trimebutin tested has a cytotoxic effect on LNCaP, A2780, Caco-2 and MCF-7 cells.

Acknowledgements: This study was supported by Inonu University Scientific Research Projects Unit with the project number TSA-2022-2975.

Keywords: Trimebutine, Cancer, LNCaP, A2780, Caco2, MCF-7.

PC-10

In Vitro Investigation of the Effects of Desloratadine, an Antihistamine, on Different Types of Human Cancer Cell Viability

Suat Tekin[1], Semiha Nur Özkaya[1], Çiğdem Tekin[2], Ali Beytur[3]

[1]Department of Physiology, Inonu University, Malatya
[2]Department of Public Health, Inonu University, Malatya
[3]Department of Urology, Inonu University, Malatya, Türkiye

AIM: Cancer is one of the diseases with the highest prevalence and mortality worldwide and its incidence is increasing day by day. There are surgical and pharmacological treatment methods for cancer. However, more studies are needed to talk about a definitive and effective treatment. Recent studies have shown the anticancer activity of antihistamine group drugs. The in vitro study examining the effectiveness of Desloratadine, an important antihistamine, on cancer, it was emphasized that Desloratadine negatively affects the growth and development of bladder cancer cells and decreases cell viability by inducing apoptosis. In vitro and in vivo studies of desloratadine in different types of human cancer cell lines are still limited. In the light of this information, we aimed to examine the effects of Desloratadine on cell viability of prostate (LNCaP), ovarian (A2780), colon (Caco-2) and breast (MCF-7) cancer cell lines.

METHODS: In this study, 1, 5, 25, 50 and 100 µM concentrations of the original raw material form of Desloratadine were applied to LNCaP, A2780, Caco2, MCF-7 cell lines. The effect of exposure to Desloratadine on cell viability was determined by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay method. After determining the dose-dependent efficacy according to the MTT assay results, the inhibitory concentration 50 (LogIC50) value was evaluated in the Graphpad Prism 8 program. Comparisons between groups were made with Kruskal Wallis H-Test, $p<0.05$ was considered significant.

RESULTS: Desloratadine incubated with LNCaP, A2780, Caco-2 and MCF-7 cancer cells for 24 hours was found to cause significant decreases in cancer cell viability ($p<0.05$).

CONCLUSION: The results of this study show that Desloratadine has antitumor activity on LNCaP, A2780, Caco-2 and MCF-7 cells.
This study was supported by Inonu University Scientific Research Projects Unit with the project number TSA-2022-2975.

Keywords: Desloratadine, Cancer, LNCaP, A2780, Caco2, MCF-7.

PC-11

Evaluation of Lipocalin-2 and Metalloproteinase-9 Gene Expressions in Early-Stage Endometrial Cancer

Songül Ünüvar[1], Rauf Melekoğlu[2], Ezgi Bulut[3], Ayşegül Doğan[3], Neşe Başak Türkmen[1], Hande Yüce[1], Ercan Yılmaz[2], Nesibe Zeyveli Çelik[2]

[1]İnönü University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Malatya
[2]İnönü University, Faculty of Medicine, Department of Obstetrics and Gynecology, Malatya
[3]Yeditepe University, Faculty of Engineering, Department of Genetics and Bioengineering, İstanbul, Türkiye

AIM: Increased lipocalin-2 (LCN-2) expression is observed in many cancer types. The aim of this study is to investigate the molecular mechanisms of LCN-2 in endometrial cancer and to evaluate the importance of biomarkers associated with these mechanisms in the diagnosis and treatment of endometrial cancer. We aimed to evaluate the gene expression of MMP-9, and LCN-2 in endometrial cancer, as matrix metalloproteinases (MMPs) and their physiological inhibitors play an important role in tumor cell invasion, angiogenesis, and growth.

METHODS: The study was conducted with 80 women who applied to İnönü University Turgut Özal Medical Center, Department of Obstetrics and Gynecology. 40 cancer cases diagnosed with endometrial cancer and 40 women who underwent surgery for benign endometrial pathology were included in the study. This study was carried out with the approval of İnönü University Malatya Clinical Research Ethics Committee dated 10.11.2021 and numbered 2021/197. Placental MMP-9 and LCN-2 gene expressions were analyzed by real-time polymerase chain reaction (RT-PCR). NGAL and GAPDH primers were synthesized and used as GAPDH housekeeping genes. Results were given as mean±SD.

RESULTS: Placenta MMP-9 gene levels were found to be statistically significantly higher ($p<0.0001$) in the patient group (0.57±0.11) compared to the control group (0.34±0.11). Similarly, a statistically significant ($p=0.0004$) increase was observed in placental LCN-2 gene expression in the patient group (0.74±0.08) compared to the control group (0.55±0.16).

CONCLUSION: Our results show that the expressions of both MMP-9 and LCN-2 genes are increased in the endometrial patient group compared to the control group. New approaches to suppress the synthesis of these genes, which trigger cancer aggressiveness and metastasis, will yield positive results in the treatment of endometrial cancer.

Financial Disclosure: This study was supported by İnönü University Scientific Research Projects Coordination Unit (Project code: TSA-2022-2776).

Keywords: Endometrial cancer, Gene therapy, Lipocalin-2, Metalloproteinase-9, Metastasis.

PC-12

Investigation of the Effect of Salvia Aytachii Vural & Adıgüzel on Blood Glucose Levels of Streptozotocin-Induced Diabetic Rats

Aslı Şan Dağlı Gül, Okan Arıhan, Nazlı Karimi

Hacettepe University, Faculty of Medicine, Department of Physiology, Ankara, Türkiye

AIM: It is known that oxidative stress and inflammatory pathways play a role in the complications and pathophysiology of diabetes mellitus. Salvia aytachii (identified by Vural and Adıgüzel) is a perennial sage species belonging to the Lamiaceae family. This preliminary study was carried out to determine whether S. aytachii sage extract has a blood sugar lowering effect in streptozotocin-induced diabetes mellitus rats.

METHODS: 9 adult male Wistar-albino rats were used. Single dose 50 mg/kg of streptozotocin (STZ) was injected (i.p.) to induce diabetes. Blood glucose levels were measured 72 hours after the injection, and 250 mg/dL and above were considered diabetic, and rats were divided into 3 groups. Group I (STZ): STZ 50 mg/kg; Group II(SA100): STZ 50 mg/kg+100 mg/kg/day S. aytachii; Group III(SA200): STZ50 mg/kg+200 mg/kg/day S. aytachii. S. aytachii were administered by oral gavage for 8 days. OGTT (Oral Glucose Tolerance Test) test was performed on the first day of extract gavage and 24 hours before euthanasia. Statistics could not be made in the preliminary study because the number of animals was low.

RESULTS: At the 1st hour after the OGTT on the first day, the blood sugars of all 3 groups reached the highest level and then decreased. Especially at the 3rd hour, the blood glucose level of the SA100 group was lower than both the STZ group and the SA200 group. In the 8th day OGTT test, SA100 was more effective in reducing hyperglycemia compared to both groups. According to the OGTT results, the 2nd hour blood glucose of the STZ group increased by an average of 46 mg/dl compared to the 0th hour. Blood glucose level was decreased 34 mg/dl in SA100 group. SA200 group showed similarity to control.

CONCLUSION: Data suggest that S. aytachii extract at a dose of 100 mg/kg may reduce hyperglycemia in the STZ model.

Keywords: Diabetes, OGTT, Salvia aytachii, Streptozotocin.

PC-13

The Oxidant Effect of Topiramate, an Antiobesity Drug on the Liver

Sevtap Kılınç[1], Pelin Şahin[2], Zeynep Yığman[3], Ayşe Meltem Sevgili[2]

[1]Baskent University, Faculty of Medicine, Department of Physiology, Ankara
[2]Gazi University Faculty of Medicine, Department of Physiology, Ankara
[3]Gazi University Faculty of Medicine, Department of Histology and Embryology, Ankara, Türkiye

AIM: Obesity is closely related to non-alcoholic fatty liver disease (NAFLD) and oxidative stress. Topiramate (TPM), an antiepileptic agent, is also used for obesity, while it is mainly known as an antioxidant some studies suggest the opposite. However, the effects of TPM on oxidant-antioxidant parameters in neither healthy liver nor NAFLD aren't known. Therefore, this study aimed to investigate the effects of TPM on both healthy and fatty liver.

METHODS: 24 Wistar albino rats were allocated into 4 groups as control (C), TPM, diet (D) and diet+TPM (DT). A high fat diet used for 6 weeks to develop NAFLD. Thereafter, TPM given for 3 weeks (100 mg/kg/day; po). Weekly weight and blood sugar follow-ups were taken; malondialdehyde (MDA), glutathione (GSH) levels and glutathione peroxidase (GPx) activity were measured. NAFLD activity score (NAS) was calculated by evaluating steatosis, infiltration and ballooning degeneration with H&E staining.

RESULTS: While diet increased both weight and blood sugar, TPM decreased them (C-D $p=0.037$; D-DT $p=0.003$). MDA levels increased in D, TPM and DT groups (C-TPM $p<0.0001$; C-D $p=0.035$), and GSH and GPx levels decreased (C-T $p<0.0001$ for GSH; C-D $p<0.0001$ & C-T $p=0.000$ & C-D $p<0.0001$ for GPx). In histological evaluations, diet-induced steatosis and ballooning didn't decrease after TPM administration (C-D steatosis $p=0.017$; ballooning $p=0.032$). Infiltration was higher only in the DT group compared to the control ($p=0.037$). Even though TPM alone caused some histological changes, there was no statistical significance in scoring.

CONCLUSION: Even though TPM elicits weight loss, it didn't reduce visceral steatosis and showed an oxidant effect in healthy liver tissue. Although the oxidant effect wasn't higher than that of TPM or diet alone in the DT group, histological damage was more apparent. Therefore, this study suggests that the use of TPM may be problematic especially in patients with liver disease.

Keywords: Nonalcoholic Fatty Liver Disease, Topiramate, Oxidative Stress.

PC-14

Peripheral Neuropeptide-S Administration Impairs Gastric Emptying and Motility through Nitrergic Pathway

İrem Akçalı, Ebral Çubukcu, S. Mert Yüksel, Mehmet Bülbül

Department of Physiology Akdeniz University, Faculty of Medicine, Antalya, Türkiye

AIM: The expression of the neuropeptide-S (NPS) receptor (NPSR; formerly known as GPR154) has been demonstrated in gastrointestinal system (GIS) tissues suggesting that NPS/NPSR system may modulate digestive functions. This study aimed to investigate the action of peripheral exogenous NPS on (i) gastric motor functions and (ii) autonomic outflow.

METHODS: Effect of peripherally administrated NPS on gastric motility (GM) was assessed in anesthetized adult male Sprague Dawley rats through a pair of strain gage transducers sutured onto serosal surface of gastric antrum and pylorus. Spontaneous postprandial antro-pyloric contractions were recorded to assess the action of NPS (50 nmol, i.v.) or vehicle. Heart rate variability was analyzed to evaluate the effect of NPS on autonomic signalization. Additionally, effect of NPS (50 nmol, i.p.) on solid gastric emptying (GE) was measured in conscious and freely moving rats received vehicle, NPSR antagonist ML-154 (40 nmol, i.p.) or nitric oxide synthase (NOS) inhibitor L-NAME (10 mg/kg, i.p.). Data were analyzed by Mann-Whitney-U test.

RESULTS: Peripheral administration of NPS remarkably reduced the amplitudes of GM, while disturbing the coordination of antro-pyloric contractions suggesting that peripheral NPS could modulate GE rate. NPS did not affect sympathovagal balance indicates the peripheral NPC-induced gastroinhibitory action is solely local. Compared to the vehicle-injected control rats (66.91% ± 4.84, n=8), NPS significantly reduced solid GE (39.21% ±5.13, n=6, $p<0.05$). The NPC-induced delayed GE was significantly restored by preadministration of ML-154 (53.85% ± 5.10, n=8, $p<0.05$) and L-NAME (51.18% ±5.03, n=6, $p<0.05$).

CONCLUSION: The present findings indicate that peripheral NPS exerts an inhibitory action on gastric motor functions through mediation of NPSR and nitrergic pathway. Therefore, enteric NPSR appears to be a therapeutic target for treatment of GIS motility disorders.

Keywords: Neuropeptide-S, Gastric Emptying, Autonomic outflow, Gastric Motility, NPSR, Nitric Oxide.

PC-15

Dual inhibitory action of Neuropeptide-S on Gastric Smooth Muscle Contractility: The Role of Enteric Glial and Neuronal Cells

Ebral Çubukcu, İrem Akçalı, S. Mert Yüksel, Sabriye Kaya, Mehmet Bülbül

Department of Physiology Akdeniz University, Faculty of Medicine, Antalya, Türkiye

AIM: Along with its specific receptor (NPSR), the novel brain peptide neuropeptide-S (NPS) is produced in alimentary tract. The present study aimed (i) to test NPS on contractility of isolated gastric tissues and (ii) elucidate the involvement of enteric neuronal and/or glial system in the action of NPS.

METHODS: Adult male Wistar rats were anesthetized and smooth muscle strips were then harvested from gastric corpus. After mucosa layer was removed, muscle strips were mounted in organ baths and mechanical activities were recorded via isometric force transducer connected to a data acquisition system. The effect of NPS (10-9 M-10-5 M) was tested on precontracted muscle strips elicited by bethanechol (10-5 M) or electric field stimulation (EFS; 4-16 Hz, 100 V, 10ms, 15 sec). Additionally, NPC-induced responses were monitored in the presence of NPSR antagonist ML-154 (10-6 M) or nitric oxide synthase (NOS) inhibitor L-NAME (10-4 M). Finally, NPS was applied after pretreatment of fluoroacetate (FA; 5x10-5 M) to exclude the contribution of enteric glial cells. Double immunofluorescence was performed in longitudinal muscle-myenteric plexus whole-mount preparations to determine whether NPSR is produced by myenteric neuronal and/or glial cells. All protocols were approved by Animal Ethical Committee of Akdeniz University (B.30.2.AKD.0.05.07.00/99). Non-parametric Mann Whitney-U test was used to determine the significance among the treatments.

RESULTS: Application of NPS caused a remarkable attenuation both in bethanechol- and EFS-induced contractions. The NPC-induced relaxation responses were significantly attenuated by ML-154 (43.2%, $p<0.01$, n=6) and L-NAME (38.2%, $p<0.01$, n=6). Pretreatment of FA blunted the action of NPS (34.1%, $p<0.05$, n=5). Double immunofluorescence analyses revealed colocalization of NPSR and NOS in myenteric neuronal cells; whereas NPSR is in close apposition with myenteric glial cells.

CONCLUSION: The present findings suggest the inhibitory action of NPS on gastric contractility which seems to be relevant with local neuronal and glial network.

Keywords: Neuropeptide-S, Isolated organ bath, Gastric corpus, Enteric glia, Myenteric plexus.

PC-16

Effect of KML29 and URB597 on Renal Ischemia Reperfusion Injury in Rats

Murat Çakır[1], Ali Aydın[2], Suat Tekin[3]

[1]Department of Physiology, Faculty of Medicine, Yozgat Bozok University, Yozgat
[2]Department of Medical Biology, Faculty of Medicine, Yozgat Bozok University, Yozgat
[3]Department of Physiology, Faculty of Medicine, Inonu University, Malatya, Türkiye

AIM: The endocannabinoid system is a physiological system that has been defined in the last 20-30 years. Anandamide and 2-arachidonoylglycerol (2-AG) have been identified as the most important endocannabinoid substances in the body. Anandamide is degraded by the fatty acid amide hydrolase (FAAH) enzyme, while 2-AG is degraded by the monoacylglycerol lipase (MAGL) enzyme. FAAH and MAGL enzymes are widely expressed in many tissues, including the kidney. Anandamide and 2-AG levels have been shown to be associated with ischemia-reperfusion (IR) injury. Although the protective properties of different FAAH and MAGL inhibitors against IR damage have been shown in various studies, the effect of MAGL inhibitor KML29 and FAAH inhibitor URB597 on kidney IR damage has not been investigated. In this study, we investigated the protective effect of MAGL inhibitor KML29 and FAAH inhibitor URB597 against kidney IR injury.

METHODS: 60 Sprague Dawley male rats were randomly divided into 6 groups (1. control 2. IR 3. KML29 4. KML29+IR 5. URB597 6. URB597+IR). The kidneys of the rats were bilaterally administered 45 minutes of ischemia and 24 hours of reperfusion. KML29 and URB597 were administered intraperitoneally to the treatment groups at the onset of ischemia. At the end of the experiment, histopathological damage and immunohistochemically caspase-3, tumor necrosis factor alpha (TNF-α), interleukin-1 beta (IL-1β), interleukin-6 (IL-6) levels were measured in the kidney tissue.

RESULTS: Histopathological damage, caspase-3, TNF-α, IL-1β and IL-6 levels in the kidney tissue were decreased in the groups treated with KML29 and URB597 compared to the IR group ($P<0.05$).

CONCLUSION: In this study, we found the curative effect of MAGL and FAAH enzyme inhibitors KML29 and URB597 against kidney IR injury.

This work was supported by Yozgat Bozok University BAP (6602c-TF/20-353).

Keywords: Ischemia reperfusion injury, Kidney, KML29, URB597.

PC-17

A Novel Adipokine, Asprosin May Play a Key Function in Metabolism

Gülendam Özbeg[1], Zeynep Dila Öz[1], Mehmet Rıdvan Özdede[1], Aslışah Özgen[1], Samet Ramazan Koçoğlu[1], Abdullah Yaşar[3], Emine Kaçar[1], İhsan Serhatlıoğlu[2], Bayram Yılmaz[4], Haluk Keleştimur[1]

[1]Department of Physiology, Faculty of Medicine, Fırat University, Elazig
[2]Department of Biophysics, Faculty of Medicine, Firat University, Elazig
[3]Vocational School of Health Services, Firat University, Elazig
[4]Department of Physiology, School of Medicine, Yeditepe University, İstanbul, Türkiye

AIM: Impaired energy metabolism leads to many diseases, such as obesity, also may reduce the quality of life. Adipose tissue, one of the essential energy sources, is an effective organ in regulating energy metabolism. However, the function of asprosin, an adipokine secreted from white adipose tissue, in energy metabolism is still unknown. Therefore, our study was carried out to determine the effects of asprosin administration on some hormones related to energy metabolism in female rats.

METHODS: For experimental studies, 24 Sprague-Dawley female rats weighing 35 ± 2 g, 21 days old, were used and randomly divided into two groups as control and asprosin groups (n=12). Asprosin (500 ng/kg) was administered intraperitoneally to the animals in the asprosin group between 13.00-15.00 every day starting from the 21st day after birth. Similarly, physiological saline (1 ml/kg) was given to the control group. ELISA method was used to analyse ghrelin, GH (growth hormone), corticosterone, leptin and insulin hormones in serum from blood samples taken after decapitation at the end of the experiment. An autoanalyser was used for triglyceride. The experiment protocol was approved by Firat University Ethical Committee. The student's t-test was used for the analysis of the obtained data.

RESULTS: Asprosin administration significantly increased blood ghrelin, GH, corticosterone and glucose levels compared to the control group ($p<0.05$). However, no significant difference was observed in leptin, insulin and triglyceride levels.

CONCLUSION: The effects of long-term asprosin administration on appetite and energy metabolism in healthy female rats from the prepubertal phase were evaluated, and asprosin treatment significantly increased blood ghrelin, GH, corticosterone, and glucose levels in rats. Thus, asprosin may exert its effect on glucose metabolism by affecting some other hormones related to energy metabolism.

Acknowledgement: This study was supported by TUBITAK (project#220S744).

Keywords: Asprosin, Metabolic Hormones, Glucagon, Corticosterone, Ghrelin, Growth Hormone.

PC-19

The Effect of Cold on Angiogenesis in Cardiac Muscle of Hibernator Hamster and Non-hibernator Rats

Durmuş Deveci

Niğde Ömer Halisdemir University, Medical School, Department of Physiology, Niğde, Türkiye

AIM: The fact that angiogenesis formation in the cardiac muscle of a hibernator and a non-hibernator group of mammals exposed to cold under the same conditions has not been studied in detail has led us to this study.

METHODS: Male Wistar rats (~270 g, n=6) and hibernator hamsters (~166 g) were divided into two groups. The control group was kept at room temperature (~21oC, n=6) and the cold exposed group (4oC) was kept in an environment with free access to food and water for 7 weeks. At the end of the experiment, the animals were sacrificed by overdose anesthesia and immediately afterwards their hearts were removed, weighed, and frozen in cold nitrogen gas. Sections taken with a cryostat were stained with alkaline phosphatase to count capillaries (CD, mm-2).

RESULTS: While the body weights did not change, it was observed that the ventricular weights increased significantly in both species. When looking at the ventricle as a whole, capillary density didn't change in rats, while capillarity significantly increased in the cold hamsters. When hamsters were compared with the control group, it was observed that the mean number of capillaries in both the whole ventricle muscle (2176±48 –2774±74, $P<0.001$, ANOVA) and in the epicardium, endocardium and papillary muscles increased significantly in those exposed to cold.

CONCLUSION: These results show; CD did not change in rats exposed to cold, while CD increased when both the entire ventricle (~27%) muscle of hamsters and the regions where it was studied in detail. Hypertrophy of the heart of hamsters and possibly prolonged exposure to cold resulted in vascular development as a preliminary to increase their oxygen carrying capacity before hibernation. In conclusion, the increase in heart rate, cold-induced other parameters and the increase in metabolic end-products, and ultimately the increase in angiogenic factors, may have stimulated angiogenesis.

Keywords: Angiogenesis, Heart, Hiernator, Nonhibernator, Cold Exposure.

PC-19

Asprosin Increases Sexual Instinct in Male Rats

Fatih Tan[1], Zeynep Dila Öz[2], Mehmet Rıdvan Özdede[2], Gökhan Zorlu[3], Gaye Göksu Avcu[2], Abdullah Yaşar[4], Emine Kaçar[2], İhsan Serhatlıoğlu[3], Bayram Yılmaz[5], Haluk Keleştimur[2]

[1]Vocational School of Health Services, Osmaniye Korkut Ata University, Osmaniye,
[2]Department of Physiology, Faculty of Medicine, Firat University, Elazig
[3]Department of Biophysics, Faculty of Medicine, Firat University, Elazig
[4]Vocational School of Health Services, Firat University, Elazig
[5]Department of Physiology, Faculty of Medicine, Yeditepe University, Istanbul, Türkiye

AIM: Asprosin is a novel discovered glucogenic adipokine synthesized from white adipose tissue during fasting. Also, asprosin has been shown to improve the sense of smell. In previous studies, it was revealed that the increase in oxytocin in the systemic circulation during ejaculation helps sperm release by stimulating contractions in the reproductive system, and therefore oxytocin has endocrine and paracrine roles on the reproductive system. Our aim was to reveal the effect of asprosin on sexual dysfunction in male rats for the first time with the non-contact erection (NCE) test.

METHODS: Control, sham, paroxetine, asprosin and paroxetine&asprosin groups (n=12) were randomly generated from 60 male Sprague-Dawley rats. The rats in the sham, asprosin and paroxetine&asprosin groups were implanted with a brain infusion kit and received a 28-day infusion (saline, asprosin 500 ng/kg). After NCE test, blood oxytocin levels were determined by ELISA method. One Way ANOVA test was used for the evaluation of the data.

RESULTS: As a result of the NCE test, there was no significant difference between the mean NCE numbers of the control, sham and paroxetine groups. However, when comparing the asprosin and the paroxetine&asprosin groups, the mean NCE numbers of the control ($p<0.05$), sham ($p<0.01$) and paroxetine ($p<0.01$) groups increment were observed. As the oxytocin values were examined, there was no significant difference between the control, sham and paroxetine groups. However, there was a significant increase in the asprosin and the paroxetine&asprosin groups compared to the control, sham and paroxetine groups ($p<0.01$).

CONCLUSION: Asprosin increased the number of NCEs by increasing the olfactory sensitivity, oxytocin level, and thus the sexual instinct in the sexual dysfunction model. We think that asprosin is a physiological mediator of penile erection and ejaculation by increasing oxytocin secretion in male reproduction.

Acknowledgement: This study was supported by TUBITAK (project no: 220S744).

Keywords: Asprosin, Scent, Oxytocin, Non-contact Erection Test.

PC-20

Asprosin May Play Important Roles in Spermatogenesis

Mehmet Rıdvan Özdede[1], Zeynep Dila Öz[1], Nalan Kaya Tektemur[3], İbrahim Halil Güngör[4], Aslıhan Çakır[4], Gaffari Türk[1], Abdullah Yaşar[5], Emine Kaçar[1], İhsan Serhatlıoğlu[2], Bayram Yılmaz[6], Haluk Keleştimur[1]

Departments of Physiology[1] and Biophysics[2], Faculty of Medicine, Firat University, Elazig
[3]Department of Histology and Embryology, Faculty of Medicine, Firat University, Elazig
[4]Department of Reproduction and Artificial Insemination, Faculty of Veterinary Medicine, Firat University, Elazig
[5]Vocational School of Health Services, Firat University, Elazig
[6]Department of Physiology, Faculty of Medicine, Yeditepe University, İstanbul, Türkiye

AIM: Asprosin, a fasting-related glucogenic hormone, is synthesized and secreted by white adipose tissue. It is known that asprosin can improve olfactory performance in rodents via OLFR-734. Moreover, odours play a vital role in sperm chemotaxis. Therefore, we aimed to investigate the effects of the asprosin hormone on male rat sperm.

METHODS: 21 days old, 24 Sprague-Dawley male rats (35g ± 2g) were randomly divided into two groups, control and asprosin (n=12). For ten weeks, the animals in the control group were given % 0,9 NaCl solution (1 ml/kg). The animals in the asprosin group were given asprosin (500 ng/kg) every day intraperitoneally. The right cauda epididymis of each animal was thoroughly dissected with the help of a scalpel in 1 ml of Tris buffer solution at 38°C, thus allowing the sperm to pass into this solution. Sperm motility, sperm concentration and proportions of morphologically abnormal sperm were determined from the obtained Tris buffer-sperm mixture. Testicular tissues fixed in Bouin's solution were washed with ethanol and then embedded in paraffin blocks. Sections of 5 µm thickness were taken from the paraffin blocks. Hematoxylin-Eosin and Masson's trichrome staining were applied to the preparations. Student t-test and Mann-Whitney U test were used for statistical analysis.

RESULTS: Chronic asprosin administration increased spermatozoon density ($p<0.001$). Asprosin did not affect the number of sperm tail anomalies and sperm motility. However, it decreased the number of sperm head anomalies ($p<0.01$). In the asprosin group, separations in the basement membranes of the seminiferous tubules were detected ($p<0.05$). Also, there was a decrease in seminiferous tubule diameters, and oedema (in the interstitial area) was detected ($p<0.05$).

CONCLUSION: Asprosin may affect sperm concentration directly and decrease head anomalies. As a result, asprosin may become a new treatment for oligozoospermia.
Acknowledgement: This study was supported by TUBITAK (project# 220S744).

Keywords: Asprosin, Sperm concentration, Morphology of sperm, Oligozoospermia.

PC-21

Protective Effect of L-carnitine on Liver, Kidney and Intestine Toxicity of Cadmium in Prepubertal Female Rats

Gözde Öğütçü[1], Ülfet Farisoğlu[2], Gamze Kocamaz[1], Emine Koç[2], Aysel Kükner[1]

[1]Near East University, Faculty of Medicine, Department of Histology and Embryology, Lefkoşa, Turkish Republic of Northern Cyprus
[2]Near East University, Faculty of Medicine, Department of Physiology, Lefkoşa, Turkish Republic of Northern Cyprus

AIM: Cadmium is a toxic element with a half-life of more than 10 years that accumulates in tissues, especially in kidney and liver. Nickel-cadmium mixture taken into body with batteries, accumulators, cigarettes, water and food. Aim of this study was to investigate the effect of L-carnitine against cadmium-induced changes in liver, kidney and small intestine tissues in prepubertal female rats.

METHODS: 21-day-old female Wistar Albino rats were used in study. Control, CdCl2 (2mg/kg CdCl2 intraperitoneally), L-carnitine (LC) (300 mg/kg orally) and CdCl2+L-carnitine groups were formed. Sections were stained with H&E and Masson Trichrome. Histological scoring was performed in liver. Results were statistically evaluated with one-way analysis of variance using Graphpad Prism (Version9) program.

RESULTS: Necrosis, increase in connective tissue around the portal area, bile duct proliferation, sinusoidal congestion, increase in inflammatory cells were observed in the liver of the Cd group. Congestion in intertubular capillaries in kidneys, dilatation in tubules and also irregularity in villi structures in small intestines were detected. Structural changes in organs were found to be alleviated in cadmium group treated with L-carnitine. In inflammatory cell scoring of the liver, Cd with control(p:0.009), Cd with LC(p:0.004), in fibrosis scoring, Cd with control(p:0.002), Cd+LC with control(p:0.03), Cd with LC (p:0.006), also in necrosis scoring between control and Cd(p:0.001), LC and Cd(p:0.001), and between control and Cd(p:0.001), LC and Cd(p:0.02) groups in bile duct proliferation statistically significant increase was observed.

CONCLUSION: In conclusion medium-dose cadmium has toxic effects in liver, kidneys and small intestines of prepubertal female rats in subacute period, these effects are alleviated with L-carnitine. It is necessary to examine the effects of cadmium with advanced laboratory techniques to support the results.

Keywords: Cadmiyum, Intestine, Kidney, L-carnitine, Liver.

PC-22

The Effects of Irisin Hormone on Seminal Vesicle Fluid in Male Rats Administered Paroxetine

Özgür Bulmuş[1], Funda Gülcü Bulmuş[2], İhsan Serhatlıoğlu[3], Sinan Canpolat[4]

[1]Balikesir University, Faculty of Medicine, Department of Physiology, Balikesir
[2] Balikesir University, Faculty of Health Sciences, Departmant of Nutrition and Dietetics, Balikesir
[3]Firat University, Faculty of Medicine, Department of Biophysics, Elazig
[4]Firat University, Faculty of Medicine, Department of Physiology, Elazig, Turkiye

AIM: It is known that antidepressants cause some negative effects in the reproductive system and especially in sperm parameters. It is stated that exercise is an effective factor on the transition to puberty, reproductive system and sexual dysfunction. Fructose, ions and molecules in the seminal vesicle fluid excreted the nutrition and mobility of the sperm. The aim of this study was to investigate the possible effect of irisin hormone on certain components of seminal vesicle fluid in male rats treated with paroxetine (antidepressant).

METHODS: In the study, 32 adult male Spraque Dawley rats were used. Rats were randomly divided into 4 groups as Control (C), irisin (I), paroxetine (P), and paroxetine+irisin (PI) (n=8). Paroxetine was given to the P and PI groups by oral gavage at a dose of 20mg/kg for 8 weeks. In the 4th week of the applications, irisin (100ng/kg/day) was administered to the I and PI groups by an osmotic pump as a subcutaneous infusion. At the end of the experiment, seminal vesicle fluids of sacrified rats were taken and analyzed (Advia 2400 analyzer and HPLC).

RESULTS: Calcium, magnesium and fructose levels were significantly decreased in the paroxetine group when compared to both the control group and irisin group, respectively ($p<0.05$). However, it was determined that fructose levels increased in paroxetine+irisin group compared to paroxetine group ($p<0.05$). In the irisin group, potassium and phosphorus levels were increased significantly compared to the control group ($p<0.05$).

CONCLUSION: The positive effect of irisin on fructose and some ion levels that decreased with paroxetine application suggests that this hormone may contribute to sperm vitality and motility. The increase of potassium and phosphorus levels caused by irisin hormone compared with the control group suggests that irisin has important effects on the reproductive system.

This work was supported by TUBITAK, Project No: 118S519.

Keywords: Paroxetin, Irisin, Seminal vesicle, Rat.

PC-23

Rotenone administration to the hypothalamus decreases the firing frequency of AgRP neurons without altering food intake in transgenic mice

Cihan Suleyman Erdogan, Yavuz Yavuz, Huseyin Bugra Ozgun, Volkan Adem Bilgin, Sami Agus, Bayram Yilmaz

Yeditepe University, Faculty of Medicine, Department of Physiology, Istanbul

AIM: Agouti-related peptide (AgRP)-expressing neurons in the arcuate nucleus (ARC) of the hypothalamus are a major orexigenic population driving the food intake. Rotenone, which is a broad-spectrum pesticide and insecticide occurring in stems and seeds of several plants, is widely used in the mitochondrial energy dynamics research as it blocks and disrupts mitochondrial complex I and oxidative phosphorylation. In this study, we aimed to investigate the effect of intracranial rotenone administration to the ARC on food intake and electrophysiology of AgRP neurons.

METHODS: Male AgRP-IRES-Cre knock-in mice were infected with AAV-CAG-Flex-GFP virus tagging the AgRP neurons intracranially together with the injection of dimethyl sulfoxide (vehicle) or rotenone into hypothalamic ARC (posterior: -1.35 mm, lateral: ± 0.35 mm and vertical: 5.85 mm). Fifteen days after infection of the targeted neurons, animals were housed as single in caged and food intake was monitored for 25 days. At the end of experimental period, animals were sacrificed, and electrophysiological recordings were obtained ex vivo from the brain slices. Statistical analyses were conducted by using t-test.

RESULTS: Food intake of the animals after rotenone administration was not altered significantly, while the firing frequency of AgRP neurons were significantly reduced by intracranial rotenone administration ($p<0.05$).

CONCLUSION: Our results suggest that mitochondrial activity may be a regulatory factor for the hypothalamic AgRP neuronal activity in the regulation of energy metabolism.

Keywords: AgRP neurons, Electrophysiology, Food intake, Hypothalamus, Neuronal firing frequency, Rotenone.

PC-24

The Effect of Carotid Artery Cannulation and Femoral Artery Cannulation With The Cardiac Vagal Denervation On The Ischemia And Reperfusion Induced Arrhythmia

Şevval Özdemir, Ömer Bozdoğan
Department of Biology, Bolu Abant Izzet Baysal University, Bolu, Türkiye

AIM: Myocardial infarction in humans is one of the leading causes of sudden death. Experimental myocardial infarction has been produced by the occlusion of the left main coronary artery or other branches in animals. The carotid artery is cannulated to measure blood pressure in this model. Our hypothesis in this study is that the reflex sympathetic stimulation occurring in carotid artery cannulation may decrease arrhythmia. This study is aimed to investigate the effect of femoral artery cannulation, considered, to have low-baroreceptor stimulation and the effects of unilateral-vagal denervation on ischemia/reperfusion arrhythmias.

METHODS: In this study 58, 6-7 months-old male Sprague-Dawley rats were used; Four groups were produced. In the first group right carotid artery was cannulated and the right femoral artery was in the second. The left main coronary artery is ligated with the silk thread and reperfusion by loosening ligature to produce myocardial ischemia. In the others, vagal denervation is produced by cutting the N-Vagus. In sham operations, the nerve is just separated from the carotid artery. Blood pressure, heart rate, arrhythmia types, and durations were determined during ischemia/reperfusion. Statistical analyses were done by using one-way ANOVA with LCD posthoc test, one-tailed t-test, and Chi-squared test.

RESULTS: During ischemia/reperfusion, blood pressure and heart rate were lower in the femoral artery group than in the carotid artery group ($p<0,05$). The arrhythmia score was higher in the femoral group than in the carotid group ($p<0,01$). Unilateral-vagal denervation increased arrhythmias in the carotid group ($p<0.01$), but was ineffective in the femoral artery group.

CONCLUSION: The reflex sympathetic stimulation induced following carotid artery cannulation decreases the arrhythmia observed during ischemia and reperfusion. In the model of experimental myocardial infarction, femoral artery cannulation is more favorable to decrease the effect of baroreceptor stimulation on the ischemia-reperfusion-induced arrhythmias.

This study was supported by the Scientific and Technological Research Council of Turkey (TUBİTAK) as an ARDEB-1002 project. (Project number; 121S401).

Keywords: Myocardial Ischemia, Reperfusion, Arrhythmia, Vagal Denervation, Baroreceptor

PC-25

Role of Erythrocytes from Pulmonary Arterial Hypertension Patients in ATP-mediated Vascular Relaxation Responses

Ahmet Yıldırım[1], Leyla Abueid[1], Nur Özen[1], Ece Kılavuz[1], İbrahim Başarıcı[2], Filiz Basralı[1], Pınar Ülker[1]

[1]Department of Physiology, Medical Faculty, Akdeniz University, Antalya
[2]Department of Cardiology, Medical Faculty, AkdenizUniversity, Antalya, Türkiye

AIM: Pulmonary arterial hypertension (PAH) is characterized by increased pulmonary artery resistance. Although pathogenesis of PAH has not been fully elucidated, decreased NO bioavailability have shown to contribute the mechanism. Considering erythrocytes contain eNOS enzyme, the aim of this study was to examine ATP-mediated vascular relaxation responses in the presence of erythrocyte suspension obtained from healthy and

PAH individuals and to reveal whether the erythrocyte eNOS enzyme has an effect on these responses.

METHODS: 8-10 weeks Wistar albino rats were used in our study (n=20). The study was approved by Akdeniz University Animal Experiments Local Ethics Committee. Blood samples were taken from healthy individuals and PAH patients who applied to Akdeniz University Hospital Cardiology Clinic. Thoracic aorta segments obtained from healthy rats were placed in an organ bath, and vascular responses recorded in response to ATP (10-8-10-4 M) after precontraction in the presence of suspension containing erythrocytes from healthy individuals (n=8) and PAH patients (n=8). Experimental protocols were repeated in the presence of non-selective eNOS inhibitor and eNOS substrate L-arginine. 'Repeated Measure 2-way ANOVA' test followed by Tukey post-hoc analysis was used. Statistical significance was $p<0.05$.

RESULTS: In the presence of erythrocytes obtained from healthy individuals, ATP mediated vasodilation responses were found to be significantly higher compared to Krebs solution ($p<0.001$). This increase in the vasodilation response was abolished in the presence of erythrocytes obtained from PAH patients ($p<0.001$). While L-arginine increased the vasodilation response, L-NAME abolished vasodilation responses in all groups.

CONCLUSION: Erythrocytes have incresead ATP-mediated relaxation responses in the aorta, and NO, derived from erythrocyte eNOS, may play an important role in this response. Due to decreased eNOS activity in PAH erythrocytes, increased vasodilation responses were abolished under PAH conditions. Therefore, reduction in erythrocyte-mediated NO may play a role in the pathogenesis of PAH, with increased vascular resistance. Acknowledgements: This study was supported by a grant from TUBITAK #122S799.

Keywords: ATP, eNOS, Erythrocyte, Pulmonary Arterial Hypertension, Vasodilation.

PC-26

The Effect of Isatin on Cardiac Hemodynamic Function in Physically Active Rats

Selma Arzu Vardar[1], Muhammed Ali Aydın[1], Orkide Palabıyık[2], Ecem Büşra Değer[1], Esra Akbaş Tosunoğlu[1], Nihayet Fırat[1], Necdet Süt[3]

[1]Medical School, Department of Physiology, Trakya University, Edirne
[2]Department of Medical Services and Techniques, Trakya University Health Services Vocational College, Edirne
[3]Department of Biostatistics, Medical Faculty, Trakya University Edirne, Türkiye

AIM: Isatin (1H-indole-2,3-dione) has been proposed as an effective factor for muscle function and shows dose dependent different effects. This study aimed to determine the effects of low and high doses of isatin administration on cardiac hemodynamic changes, in an experimental model of voluntary physical activity.

METHODS: After ethical-approval, female rats were housed in cages with running-wheels. Control rats were kept in cages without a running-wheel during 28 days. In the last fourteen days of exercise, 20 mg/kg/day i.p isatin were given to the control-isatin-low-dose (CI-L) and physically active-isatin-low-dose (PAI-L) groups; 100 mg/kg/day i.p isatin were given to the control-isatin-high-dose (CI-H) and physically active-isatin-high-dose (PAI-H) groups; physiological saline was given to the control-vehicle (C-V) and PA-V groups. Daily physical-activity was recorded during isatin administration period. The hearts were extirpated and perfused ex vivo with a Krebs-Henseleit solution for 15 minutes. Left developed ventricular pressure, maximum and minimum rate changes of left ventricular pressure, and heart rate were recorded. Cyclic guanosine monophosphate (cGMP) levels were measured in the perfusate in groups.

RESULTS: In this study, no significant difference was shown in daily physical activity in the physically active groups in comparison to control group. Left ventricular developed pressure in the FAI-D group (69.75±17.49) were significantly lower than in both the KI-D (123.97±18.90) and FA-V (117.76±8.68) groups but similar to the FAI-Y (108.99±21.38) group ($p=0.017$ and $p=0.018$, $p=0.386$, respectively). Minimum rate changes of left ventricular pressure in the FAI-D group was found lower than CV, CI-L and CI-H groups ($p=0.036$, $p=0.016$ and $p=0.037$, respectively). Heart rate values were similar in groups. The cGMP level was higher in the PAI-H group than in the CI-H group ($p=0.001$).

CONCLUSION: The administration of isatin does not alter physical activity levels. However, isatin may have deleterious effect on ventricular contractility and relaxation function in female rats.

Keywords: Isatin, Heart, Isolated Heart.

PC-27

Identification of Protein Interacting Partners of Na^+/K^+-ATPase Pump α1 Subunit by Proteomic and Bioinformatic Analysis in In-Vitro Hypoxic Cardiomyocytes

Emel Baloğlu[1], Gizem Gençay[2], Beyza Gürler[3], Emel Timuçin[4], Zeynep Durer[5], Evren Kılınç[5]

[1]Acibadem Mehmet Ali Aydinlar University, School of Medicine, Department of Medical Pharmacology, Istanbul
[2]Acibadem Mehmet Ali Aydinlar University, Graduate School of Natural and Applied Sciences, Department of Molecular and Translational Biomedicine, Istanbul
[3]Acibadem Mehmet Ali Aydinlar University, Institute of Health Sciences, Department of Medical Biotechnology, Istanbul
[4]Acibadem Mehmet Ali Aydinlar University, School of Medicine, Department of Biostatistics and Medical Informatics, Istanbul
[5]Acibadem Mehmet Ali Aydinlar University, School of Medicine, Department of Biophysics, Istanbul, Türkiye

AIM: Regular activity of Na^+/K^+-ATPase pump is essential for the function of the heart. Pump activity and subunits' expression decreases in ischemic heart diseases. However molecular mechanisms are not well known. This study aims to identify protein interacting partners of α1 NKA in in-vitro ischemic heart disease model by proteomic and bioinformatic analysis.

METHODS: H9c2 cardiomyocytes were used for the experiments. Cells were kept in 1% O_2+ 5% CO_2 for 24 hours as in-vitro ischemic heart model; normoxic cells were maintained in ~19% O_2 +5% CO_2. Immunoprecipitation experiments were performed by using same amounts of protein from total cell lysates; mixed with specific antibody against α1 NKA and Protein A Agarose beads. Each elution fraction was analyzed by mass spectrometer three times, peptides identified at least in two replicates were included for the analysis. Proteome Discoverer 2.4 module was used for analysis of specific protein differences. Bioinformatic analysis was performed with Cytoscape software based on abundance ratio and coverage; functional enrichment analysis was performed with STRING DB. False discovery rate (FDR) was <0.05.

RESULTS: In normoxic and hypoxic cells α1 NKA non-specifically interacted with cell structure-cytoskeleton, muscle contraction-relaxation and focal adhesion associated proteins. Specifically, in hypoxic cells NKA β1, β3 interactions decreased compared to normoxic cells; proteins involved in glycolysis, cell metabolism such as GAPDH, LDH, PKM increased. Additionally, interactions with Hsp1,5, PDI, Hsp90aa1, Hsp47 related with endoplasmic reticulum (ER) homeostasis and ubiquitin-proteasome pathway increased.

CONCLUSION: This study identified new protein interacting partners of α1 NKA in cardiomyocytes that has not been previously reported. Specific interacting partners of α1 NKA in hypoxic cells emphasize that ER stress and ubiquitin-proteasome pathway may control cellular trafficking. Comprehensive analysis of α1 NKA interaction network is important for revealing molecular mechanisms in cardiovascular disease-hypoxia axis.
This study is supported by TÜBİTAK project no: 119S688.

Keywords: Cardiac ischemia, Hypoxia, Na^+/K^+-ATPase, Proteomic, Structural Bioinformatics.

PC-28

The Role of the Vascular Endothelial Layer in the Effect of Fospropofol on Vascular Tonus

Meriç Demeli[1], Mehmet Emin İnce[2], Bilge Pehlivanoğlu[1], Nadide Örs Yıldırım[2], Alperen Kutay Yıldırım[3], Suat Doğancı[4], Vedat Yıldırım[2]

[1]Hacettepe University Faculty of Medicine, Department of Physiology, Ankara
[2]University of Health Sciences, Gulhane Training and Research Hospital, Department of Anesthesiology and Reanimation, Ankara
[3]Gazi University Faculty of Medicine, Department of Cardiovascular Surgery, Ankara
[4]University of Health Sciences, Gulhane Training and Research Hospital, Department of Cardiovascular Surgery, Ankara, Türkiye

AIM: The tonus of vascular smooth muscles are among the factors controlling blood pressure via vascular resistance. As stabilisation and/or control of blood presure of the patients is crucial for tissue perfusion under general anaesthesia and sedation, the effect of the applied pharmacological agents on vascular smooth muscles is critical. In addition, endothelial damage and mal/dysfunction is frequent in patients with cardiovascular dieseases. On this background we aimed to investigate the effect of fospropofol, a water soluble prodrug of propofol employed for induction of anesthesia and sedation.

METHODS: After the consent is obtained from the patients who will udergo coronary artery bypass graft (CABG) surgery, arterial rings (3mm) (n=15) were prepared from the discarded parts of the left internal mammary artery (LIMA) harvested for vascular greft. Full thickness endothelium-intact and mechanically destroyed endothelium-denuded rings were mounted in baths filled with Krebs' solution, gassed with 5% CO2 and 95% O2 at 37□C. After equilibration for 60 min, maximum contraction response to KCl (120mM) for 10 minutes was recorded followed by cumulative dose-response curves with 10-7-10-5 M fospropofol were obtained. The contraction response is presented as the percentage of KCl-induced contraction.

RESULTS: Both the endothelium-intact and endothelium-denuded rings were contracted when stimulated with KCl. Fospropofol decreased vascular tonus cumulatively at increasing doses in endothelium-intact rings, but not in endothelium-denuded rings. Vascular tone was different between the two groups at the higher doses (10-6 and 10-5 M) (p<0,05).

CONCLUSION: Fospropofol, acts via endothelial transformation into the active substance propofol, can be preferred because of its lower risk of hypotension, especially in patients who are hypertensive, smoker, have valvular disease, and have a high risk of endothelial damage.

Keywords: Vascular tonus, Smooth muscle, Endothelium, Fospropofol.

PC-29

The role of opioid peptides in pulmonary edema

Şevin Güney, Hatice Betül Moğulkoç

Department of Physiology, Gazi University, Faculty of Medicine, Ankara

AIM: Pulmonary edema (PE) is common in overdose of opioid derivatives. The mechanism of PO caused by opioids needs to be clarified. Disruption of alveolar sodium transport impairs fluid clearance (AFC), causing fluid accumulation in the alveolar space and PE. We tested whether opioids cause PE by disrupting AFC through epithelial sodium channels (ENaC).

METHODS: First we tested whether opioids could affect the AFC depending on the dose. An instillate containing 5% BSA and three different doses of morphine (0.1; 1; 10 µM) were instilled into the rats' lungs and bronchoalveolar lavage (BAL) samples were collected an hour later. AFC was calculated from the increase in the protein concentration in the BAL. Then the detection of opioid receptors involved with inhibition of AFC and whether their effect was on ENaC were tested. Antagonists specific to µ, κ and δ opioid receptors (10 µM) and/or amiloride (1mM), an ENaC inhibitor, were added to the instillate containing 10 µM morphine used in

previous experiments. One-way ANOVA followed by Tukey test used for statistical analyses. P< 0.05 was accepted as significant.

RESULTS: AFC was significantly decreased in Amiloride and 10 µM Morphine groups compared to the control, 0.1 and 1 µM morphine groups ($p<0.05$). AFC was also decreased in all antagonist groups compared to the control and morphine groups ($p<0.05$). Decrement of AFC in the δ opioid receptor antagonist group was even more than amiloride group ($p<0.05$). However, this decrease was not significant in the µ and κ opioid antagonist groups.

CONCLUSION: Opioids may cause edema by reducing AFC depending on the dose. However, this effect probably occurs via another pathway independent of sodium transport. On the other hand, µ and κ opioid antagonists disrupt AFC via ENaC and δ opioid receptors via another mechanism and contribute to the formation of edema.

Keywords: Opioid Peptides, Pulmonary Edema, Epithelial Na Channels.

PC-30

Muscle Damage and Oxidative Stress Responses Following a Single Bout of Downhill Running in Different Menstrual Cycle Phases

Bircan Dokumacı, Hayriye Çakır Atabek
Eskişehir Technical University, Faculty of Sports Science, Department of Coaching Education Eskişehir, Türkiye

AIM: This study aimed to investigate the muscle damage and oxidative stress (OS) responses after eccentric (downhill-running-DR) exercise in the follicular (FP) and luteal phases (LP).

METHODS: Thirteen women (age: 20±2.0 years; menstrual cycle: 27.9±2.4 days; VO2max:40.6±4.7 mL.kg-1.min-1) participated. The main exclusion criteria were using any hormone preparation or antioxidant supplement. Participants were tested in random order at different phases of the menstrual cycle (FF: 6-13 days and LF: 17-24 days) confirmed by hormone analysis. The tests were applied with an interval of 1-week. The 3-day-food consumption was analyzed. Active knee joint range of motion (AROM), active muscle soreness perception, and VO2max were determined on the 1st_day. 48h after the VO2max test, DR with –10% slope was performed at a speed coincide with 75% of their VO2max for 30min. Indirect muscle damage measurements and blood samples were obtained at rest (PRE) and immediately (POST), POST24h, POST48h, POST72h, and POST96h after the DR.

RESULTS: The estrogen (E2) and progesterone hormones were significantly higher in LP than FP; estrogen: 148.8±69.7 vs. 45.6±17.9 pmol. L-1, progesterone: 6.6±5.3 vs. 0.22±0.2 nmol.L-1, respectively ($p\leq0.001$). There was no significant difference between phases in terms of vitamins A, C and E ($p>0.05$). No significant time-dependent changes within and between phases were observed in AROM ($p>0.05$). Muscle soreness didn't change in LP but significantly increased in FP ($p<0.01$). The oxidized protein carbonyl (PCO) values significantly increased following DR independently of the phases ($p<0.05$), reached the highest values at the POST96h (from 0.337±0.04 to 0.429±0.16 in FP; from 0.301±0.06 to 0.349±0.11 nmol/mg protein in LP). Moderate positive correlation was determined between %ΔE2 and %ΔPCO only in FP at the PRE-POST48h time interval ($r=0.564$; $p=0.045$).

CONCLUSION: The eccentric exercise protocol applied didn't cause serious muscle damage, but significantly increased the PCO concentration. The findings showed that the estrogen hormone doesn't prevent oxidative damage, but reduces the increase in oxidative stress.

Keywords: Muscle damage, Oxidative stress, Estrogen, Menstrual cycle, Eccentric Exercise.

PC-31

Investigation of Circadian Electrical Activity of Hypothalamic Arcuate Nucleus POMC Neurons in POMC-Cre Transgenic Mice

Hüseyin Buğra Özgün, Yavuz Yavuz, Özge Başer, Cihan Süleyman Erdoğan, Habibe Gören, Bayram Yılmaz

Yeditepe University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

AIM: Several hypothalamic neural circuits and peripheral hormones/factors play role in the regulation of energy homeostasis. Food intake is temporarily regulated by the brain during circadian cycle (~24 hour). Pro-opiomelancortin (POMC) neurons sense physiological energy state and regulate feeding, but the regulation of these neurons by the circadian rhythm is not fully elucidated. In our study, we aimed to investigate the daily electrical activity changes of these neurons using the electrophysiology patch clamp technique.

METHODS: Ten POMC-Cre transgenic mice were used in the study. Adeno-associated virus containing green fluorescent protein virus was intracranially injected into the arcuate nucleus of the hypothalamus to tag the arcuate POMC neurons and determine their electrical activity characteristics. After the injections, the mice were divided into two groups as fasted and fed. The mice fed with standard mouse chow and 16-hour fasted mice were decapitated at three different times of the day (10:00, 15:00, 18:00). Patch clamp technique was used to determine the electrophysiological changes in the POMC neuron activity. In addition, immunofluorescence staining was performed on brain sections obtained from mice using c-fos and POMC antibodies. Data were analysed using One-way ANOVA or Student's t-test, and $p<0.05$ was considered statistically significant.

RESULTS: When the electrical activity recordings taken from the brain slices at three different time points are compared, it is seen that the electrical activity of POMC neurons reaches the highest value at 15.00 hours and then decreases gradually ($p<0.05$). In addition, the activity of electrically altered POMC neurons was demonstrated by immunofluorescence as changes in c-fos activity.

CONCLUSION: In this study, daily electrical activity changes of POMC neurons were investigated ex-vivo for the first time with the patch clamp technique. These findings demonstrate that electrical activity of the POMC neurons required in the regulation of food intake change in a circadian-manner.

Keywords: Pro-opiomelancortin (POMC), Food intake, Circadian Cycle, Electrophysiology, Immunofluorescence.

PC-32

Cerebellum and Oxidative Stress in Natural and Accelerated Aging Model

Hatice Kavak[1], Aslı Nur Bahar[1], Arzu Keskin Aktan[2], Kazime Gonca Akbulut[1]

[1]Department of Physiology, Gazi University, Ankara
2Department of Physiology, Afyonkarahisar Health Sciences University, Afyonkarahisar, Türkiye

AIM: Intracerebroventricular administration of galactose causes motor coordination deficiency by decreasing glutathione (GSH) level in the cerebellum. It has been shown that aging increases oxidative stress and Sirtuin 2 (Sirt2) expression in rat cerebellum tissue and Sirt2 inhibition has a protective effect in aging. In our study, we aimed to investigate the effect of AGK-2 administration, a specific Sirt2 inhibitor, on oxidative stress in an accelerated aging model with natural and D-galactose (D-GAL) administration.

METHODS: In the study, 7 groups were formed using 48 male rats of Wistar (W) and Sprague-Dawley (SD) species;1) Young-Control (3 months, n=6), 2) Young-AGK-2 (3 months, n=6), 3) Old-Control (22 months, n=6), 4) Old-AGK- 2 (22 months, n=6), 5) D-GAL (3 months, n=9), 6) Solvent+D-GAL (3 months, n=8), 7) Solvent+D-GAL+AGK- 2 (3 months, n=7). Control groups were given 4% DMSO+PBS, and experimental groups were given AGK-2 (10 µM/bw) subcutaneously (SC). For the accelerated aging model, D-galactose (150 mg/kg/day, SC) was administered for 10 weeks. Malondialdehyde (MDA) and GSH levels in cerebellum tissue were measured by spectrophotometric method. In the statistical analysis, one-way ANOVA (post-hoc LSD) was used to determine the differences between groups. The statistical significance level was set at $p<0.05$.

RESULTS: The D-GAL administration increased the cerebellum MDA level significantly compared to the young control group ($p<0.001$). In the D-GAL group, AGK-2 administration decreased the MDA levels and increased the GSH levels ($p=0.003$; $p=0.006$). D-GAL administration increased MDA levels more and decreased GSH levels significantly compared to aged rats ($p=0.006$; $p<0.001$). AGK-2 administration in natural aging was found to be more effective in increasing GSH levels compared to the accelerated aging model ($p<0.001$).

CONCLUSION: Both models compared increased oxidant stress in the cerebellum. AGK-2 application was found to be more effective than D-GAL on oxidant stress in natural aging.

Keywords: AGK-2, Accelerated aging, Cerebellum, D-galactose, Natural aging, Oxidative Stress.

PC-33

MOTS-c Levels in Acute Ischemic Stroke, Alzheimer's and Parkinson's Disease

Murat Çakır[1], Hikmet Saçmacı[2], Seda Sabah Özcan[3]

[1]Department of Physiology, Faculty of Medicine, Yozgat Bozok University, Yozgat
[2]Department of Neurology, Faculty of Medicine, Yozgat Bozok University, Yozgat
[3]Department of Medical Biology, Faculty of Medicine, University of Manisa Celal Bayar, Manisa, Türkiye

AIM: Mitochondial dysfunction is associated with the development of neurological diseases and neurodegeneration. Mitochondria produce various peptides that play a role in cellular functions and communication. MOTS-c (mitochondrial open reading frame of the 12S rRNA-c) is one of these peptides. In this study, we investigated whether plasma MOTS-c levels change in Alzheimer's-Parkinson's Disease (AD, PD) and acute ischemic stroke (AIS).

METHODS: Participants were divided into 4 groups as AD (n=32), PD (n=32), AIS (n=32) and control (n=30). Plasma MOTS-c levels of the participants were determined by the Enzyme-Linked ImmunoSorbent Assay (ELISA) method using commercial kits.

RESULTS: Plasma MOTS-c level was decreased in AIS and AD groups compared to control ($p<0.05$).

CONCLUSIONS: These results suggested that MOTS-c levels may have a role in the pathophysiology of AIS and AD. Further studies are required to understand the relationship of this peptide with AIS and AD. This work was supported by Yozgat Bozok University BAP (6602c-TF/19-345).

Keywords: MOTS-c, Acute ischemic stroke, Alzheimer's Disease, Parkinson's Disease.

PC-34

Right and Left-Hand Reaction Times to Regular and Irregular Auditory Stimuli in the Sympathetic Phase of Ultradian Rhythm in Right-handed Young People

Işınsu Karaoğlu[1], Lamia Pınar[2], Mehmet Düzlü[3], Erhan Kızıltan4

[1]Department of Physiology, Gazi University, Ankara
[2]Department of Physiology, Okan University, Ankara
[3]Department of Ear Nose and Throat, Gazi University, Ankara
[4]Department of Biophysics, Baskent University, Ankara, Türkiye

AIM: Ultradian rhythm can change the sympathetic and parasympathetic system activation by affecting cerebral lateralization. In this study, the reaction times (RTs) to regular and irregular auditory stimuli were tested and compared with resting period findings, by shifting of ultradian rhythm to sympathetic activation period.

METHODS: This study which received the necessary ethical permission was carried out with the voluntary participation of right

handed 23 female and 7 male students. After measuring participants' blood pressure, heart rate and nasal dominance in the resting period, right and left-hand RTs against auditory stimuli were measured. Sympathetic activation was provided by 5 minutes running of the participants on a treadmill after doubled the heart rate of the resting period. The sympathetic activation phase was confirmed by related tests and RT measurements were repeated. The data were analyzed using the paired t-test for time-dependent comparisons, as they have a normal distribution.

RESULTS: Right and left-hand RTs were shortened after sympathetic activation, compared to resting period in both stimulus types (P<0,05). In regular stimuli, although the right-hand RT is faster than the left, the difference is not significant neither in resting period nor in sympathetic activation. In irregular stimuli, the left-hand RT was faster than the right, both in the resting and sympathetic activation period (p<0,01).

CONCLUSION: In regular stimuli, the right hand may have an advantage over the left in the motor component of the reflex due to the learned automatic motor movement speed. However, in irregular stimuli, it was thought that the speed of the sensory component of the reflex, due to known speed of the right hemisphere in the process of processing non-verbal sounds increases with the involvement of attention also and the left hand shortens the RT to irregular stimuli in both resting and sympathetic processes.

Keywords: Ultradian Rhythm, Cerebral Lateralization, Nasal Cycle, Auditory Reaction Time, Sympathetic Activation, Acute Intense Exercise.

PC-35

Comparison the Respiratory Function between Trained and Untrained 11-14 Aged Children

Hayriye Çakır Atabek

Eskişehir Technical University, Faculty of Sports Science, Department of Coaching Education Eskişehir, Turkiye

AIM: This study aimed to compare various respiratory parameters between trained and untrained 11-14-aged girls and boys.

METHODS: A total of 253 students divided into 4 groups (trained boys: n=63; untrained boys: n=61; trained girls: n=65; untrained girls: n=64) participated. Subjects with any disease that could limit respiratory test performance were excluded. The study was approved by local Ethics committee and required permissions were obtained from National Education Directorate. All participants and their families were informed about the possible risks and benefits of the study and written consents were obtained. Forced vital capacity (FVC), forced expiratory volume in one second (FEV1), peak expiratory flow (PEF), forced mid-expiratory flow rate (FEF25-75) and maximum voluntary ventilation (MVV) measurements were taken to determine the respiratory function using the Spirolab III device. During the spirometer measurements, the noses of the participants were closed with a latch, and the results were recorded by reading from the digital display of the spirometer. Spirometry measurements were taken when the participants were sitting. Statistical analysis was performed with One-way ANOVA, significance was accepted as p<0.05.

RESULTS: A statistically significant differences were determined for all respiration parameters (FVC, FEV1, PEF, FEF25-75% and MVV), except FEV1/FVC, between groups (p=0.005; p=0.004; p=0.021; p=0.016; p=0.004; respectively). Following the pairwise comparison (post hoc test: Tukey), the findings showed that the main difference was between trained and untrained girls. All examined variables were recorded significantly higher in thetrained-girls group. Such a difference was not found between the trained and untrained-boys groups.

CONCLUSION: Many studies have showed the positive effects of exercise programs on respiratory functions in individuals who have not yet completed their development. Although it's thought that growth may have an effect on respiratory parameters, research findings show that training has a positive effect on respiratory functions in girls who are disadvantaged in the society.

Keywords: Respiratory, Age group, Training, Sexes.

PC-36

Exam Anxiety Evaluation by Heart Rate Variability in University Students

Hasan Kazdağlı[1], Hasan Fehmi Özel[2], Süleyman Öztürk[3], Deniz Ceylan Tufan Özalp[4], Burak Erdeniz[3], Mustafa Özbek[5], Makbule İlgi Şemin[6]

[1]İzmir University of Economics, Vocational School of Health Sciences, İzmir
[2]Manisa Celal Bayar University, Vocational School of Health Sciences, Manisa
[3]İzmir University of Economics, Faculty of Arts and Sciences, Dept. of Psychology, İzmir
[4]Koç University, Faculty of Medicine, İstanbul
[5]Manisa Celal Bayar University, Faculty of Medicine, Manisa
[6]İzmir University of Economics, Faculty of Medicine, İzmir, Türkiye

AIM: The majority of the previous research used questionnaire data to examine academic stress, however physiological reactions, such as changes in heart rate variability (HRV) is still relatively unexplored. Aim of this study is to evaluate the effects of exam stress on HRV parameters.

METHODS: 31 healthy volunteers (mean age: 21±0.38) from medicine, nursing and physical therapy and rehabilitation departments participated to the study. Participants underwent 24-hour HRV recordings one day prior to and during written exams and another 24-hour recording during an exam-free day. Westside test anxiety scale, State Trait Anxiety Inventory 1-2, and Test Attitude Inventory were applied and anxiety scores were calculated. During the experiment, participants were assigned to two groups based on their anxiety scores: (i) participants with test anxiety (PTA+)(n=14) and (ii) participants without test anxiety (PTA-)(n=17). HRV parameters were compared between two

groups using the independent sample t-test and p<0,05 was considered statistically significant.

RESULTS: During the exam day, heart rate (HR), standard deviation of normal beats (SDNN), stress index, low-frequency and short-term detrended fluctuation analysis were significantly higher, root mean square of successive differences between regular heartbeats was significantly lower in PTA+ group (p<0,01) whereas total HRV did not differ between groups (p>0,05). However, during the exam free day only stress index was statistically higher in PTA+ group (p<0,05). In addition, participants in the PTA- group slept more and studied less before the exam compared to PTA+ group (p<0,05).

CONCLUSION: Being examined by others is a highly stressful event for the students. Our results showed that stress can alter heart rate variability parameters. Based on that finding we suggest that HRV may be a useful tool for evaluating the effects of stress and further investigation is required.
Keywords: Heart Rate Variability, Test Anxiety, Stress Detection.

PC-37

The Relationship between Handgrip Strength and Fatigability with Cognitive Function in Individuals Over 65 Age

Nazemin Gürsoy Karaman, Emine Koç
Near East University, Medical School, Department of Physiology, Lefkoşa, Turkish Republic of Northern Cyprus

AIM: The aim of the study is to investigate the relationship of handgrip strength and fatigability with cognitive functions in elderly individuals. The main hypothesis was determined as "There is a relationship between handgrip strength and fatigability with cognitive function in elderly individuals".

METHODS: The research was approved by Ethics Committee of Dr. Burhan Nalbantoğlu State Hospital (LBNDH) (06.01.2021-no. YTK.1.01). The sample consists of 89 individuals who applied to the LBNDH Physical Therapy and Rehabilitation Service between the ages 65-85 years. They also agreed to sign the informed consent form. Handgrip strength and fatigability was measured by BIOPAC USA Student Lab's and the cognitive functions were evaluated with Standardized Mini Mental Test (SMMT). Relationships between variables were examined by Pearson correlation and standard multiple regression analysis. The differences in cognitive functions were tested by Mann-Whitney and Kruskal Wallis tests.

RESULTS: As a result of the study, a moderate correlation was found between cognitive functions and grip strength (r= +0.31, p= 0.004). No statistically significant relationship was found between the fatigability index and cognitive functions. Cognitive functions were statistically significant according to gender (p=0.001), education (p=0.005) and employment status (p=0.000). Whole regression model was significant (F=12.236, p=0.001) and a unit change in the grip strength would cause an increase of 0.59 points in the SMMT score. In terms of education variable, the SMMT score of secondary, high school and university graduates was 2.28, 2.94 and 3.45 on average compare to primary school graduates. It can be said that 37% of the variance in the SMMT score is explained by the grip strength and education variable (R2=0.368).

CONCLUSION: Our results suggest that the decline in cognitive functions due to aging should be considered together with motor functions such as muscle strength and many individual variables.
Keywords: Handgrip Strength, Fatigability, Cognitive Function, Older Age.

PC-38

Effect of Transcranial Direct Current Stimulation on Pain and Physical Functions in Individuals with Lumbar Spinal Stenosis: A Double-Blind Randomized Sham-controlled Study

Enes Efe İş[1], Serkan Aksu[2], Sacit Karamürsel[3], Ayşegül Ketenci[4], Dilşad Sindel[4]

[1]Physical Medicine and Rehabilitation Clinic, Sisli Hamidiye Etfal SUAM, University of Health Sciences, Istanbul
[2]Department of Physiology, Muğla Sıtkı Koçman University Faculty of Medicine, Muğla, Türkiye; Department of Physiology, İstanbul University İstanbul Faculty of Medicine, İstanbul
[3]Department of Physiology, Koç University Faculty of Medicine, İstanbul
[4]Department of Physical Medicine and Rehabilitation, İstanbul University İstanbul Faculty of Medicine, İstanbul, Türkiye

AIM: Lumbar spinal stenosis (LSS) is one of the most common reasons for spinal surgery in geriatric individuals. Transcranial Direct Current Stimulation (tDCS) is a neurophysiological treatment that was indicated to be efficacious in chronic pain syndromes. In this study, we aim to assess the efficacy of tDCS on pain and physical functions in individuals with LSS for the first time.

METHODS: In this double-blind study, 30 individuals with LSS (15 active, 15 sham) were administered 10 sessions of active/sham tDCS over the primary motor cortex consecutively on weekdays of 2 weeks. The pain was evaluated with the Visual Analogue Scale (VAS) and walking distance and duration were assessed with Self-Paced Walking Test before the first session, immediately after the last session and 3-months after the last session. Mann-Whitney U and Fisher's tests were utilized to assess baseline group differences and Friedman tests were utilized to assess treatment effect.

RESULTS: No baseline group differences were observed. Mean resting VAS (p<0,001), maximum resting VAS (p=0.001), mean VAS during walking (p<0.001) and maximum VAS during walking (p<0.001) were lower while symptomless walking duration after tDCS (p=0.004) and at 3-month follow-up (p=0.001), symptomless walking distance after tDCS (p=0.002), at 1-month follow-up (p<0.001) and at 3-month follow-up (p=0.006) were higher in the active tDCS group. No significant differences were found in other assessed variables.

CONCLUSION: Similar to other chronic pain syndromes, the present results highlight tDCS as a promising approach in LSS. Efficacy was considered to be achieved via both increased enkephaline release in descending pain modulatory pathway and increased emotional and cognitive control over pain. New studies evaluating treatment mechanisms using neuroimaging techniques are warranted.

Keywords: Lumbar Spinal Stenosis, Neurophysiology, Pain, Transcranial Direct Current Stimulation.

PC-39

Object Capturing with Photogrammetric Method and Use of Augmented Reality in Education of Heart Cycle and Heart Sounds

Aslı Şan Dağlı Gül

Hacettepe University Faculty of Medicine, Department of Physiology, Ankara, Türkiye

AIM: Augmented reality have become widespread for medical education in recent years. Augmented reality provides the opportunity to add sound, 3D images and animations on the existing reality. The aim of this study is to create our own physiology educational material by preparing an application supported by augmented reality for better learning of the heart cycle and sounds.

METHODS: The "object capture" process was applied with Agisoft Metashape program to get 3D model of heart. For this, a sheep's heart was taken because of similarity to human heart. Totally 90 photographs were taken from 3 different axes by rotating 360 degrees on black background. The same process was repeated by taking frontal section to obtain the internal structure. After the photographs were converted into 3D models with the photogrammetric software program, they were brought into proportions suitable for human anatomy. Electrical activity, systole, diastole and blood filling were animated with Blender 3D animation program. Animation was converted to android application via Vuforia with Unity game engine. The program was activated by pointing the camera of the mobile device to the symbol placed in front of sternum of a real person. The heart animations were displayed inside the thorax. In addition to monitoring the movements simultaneously with heart sounds and Wigger diagram, theoretical information has been added to the application.

CONCLUSION: Distance education necessitated the inclusion of computer-assisted applications in education all over the world. In this sense, it is important that we can produce our own physiology education content in our country. This application, in which the heart cycle and heart sounds are presented with augmented reality, was made for this purpose. Further studies are planned in which students will be included after the addition of more detailed topics.

Keywords: Augmented Reality, Cardiac Cycling, Heart sounds, Object Capture, Simulation.

PC-40

Physiology Course Success Levels and Student Satisfaction in Face-to-Face and Distance Education Periods

Oktay Kuru
Muğla Sıtkı Koçman University, Faculty of Health Sciences, Department of Physical Therapy and Rehabilitation, Muğla, Türkiye

AIM: Face-to-face theoretical and applied education process is partly different than distant education. The aim of this study is to determine and compare the success level and satisfaction levels of the students who are engaged in Physiology course in face-to-face education and distance education period.

METHODS: The questionnaire data were collected from students in the Faculty of Health Sciences by the end of the term and after the permission of the ethics committee. The survey application was performed in classrooms and online as it was possible during the two periods with students in Physiology courses. All data was processed in digitized form.

RESULTS: 156 usual education period students and 133 distance education students completed the survey. Chi-square and unpaired t-tests were used for the given statistical analysis. Gender distribution ratios in both periods were found similar. There was a significant difference in terms of explaining the course objectives and using current tools/equipment ($p<0.05$), and those in the distance education period were found to be significantly higher in terms of the compatibility of the exam questions with the course content ($p<0.05$). The use of carefully prepared visual aids was found to be statistically higher in the distance education period ($p<0.05$). In terms of providing a suitable environment for asking questions freely, the rates in the distance education period were significantly higher ($p<0.01$). There was a significant difference between the two periods in terms of mean achievement (face-to-face: 70.26±9.71 and distance education: 73.17±9.19 SD).

CONCLUSION: Our results show that both education types can be applied successfully. Despite a difference in certain stages in the distant education process the learners' ability to obtain information and the level of success were not adversely affected. The supervised exam practice in the distance education period provides a testing environment under equal conditions.

Keywords: Face-to-face education, Distance education, Course Satisfaction Level.

PC-41

Determination of Nutritional Status and Protein-Energy Wasting in Patients with Diabetic Nephropathy

Elif Al Karakaş[1], Fatma Esra Güneş[2], Berna Karakoyun[3]

[1]Marmara University, Faculty of Health Sciences, Department of Nutrition and Dietetics, Istanbul
[2]Medeniyet University, Faculty of Health Sciences, Department of Nutrition and Dietetics, Istanbul
3University of Health Sciences, Hamidiye Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

AIM: The aim of this study is to evaluate the nutritional status of patients with stage 3 and 4 diabetic nephropathy (DN) and to explain the effect of DN stages on the prognosis of protein-energy wasting (PEW).

METHODS: Data from demographic characteristics, nutritional habits, anthropometric measurements, biochemical findings and food consumption records of 49 patients (25 DN stage 3; 24 DN stage 4) who were followed at Marmara University(M.U.) Pendik Training and Research Hospital, Department of Nephrology were collected. To evaluate the nutritional status of patients, Subjective

Global Assessment (SGA) screening tool and to determine the PEW, the criteria of the International Society of Renal Nutrition and Metabolism (ISRNM) were used. Statistical analysis was performed using SPSS 22.0 program. This study was approved by the M.U. Faculty of Medicine Clinical Research Ethics Committee (09.2018.800).

RESULTS: 56% of stage 3DN group and 66.7% of stage 4DN group have been diagnosed with diabetes for more than 15 years. Anthropometric measurements (total body weight, muscle weight) were different between the groups ($p<0.05$). The creatinine and microalbuminuria levels of the stage 3DN group were lower than the stage 4DN group; eGFR values were higher ($p<0.05$). Energy (kcal/day), carbohydrate (g/day) and fat (g/day) intakes did not differ between the groups, while protein (g/kg) intakes were different ($p<0.05$). In both groups, most of the patients had the SGA-A score (well-nourished). The PEW incidence was lower in the stage 3DN group ($p<0.05$). According to SGA data, the PEW incidence was found to be higher in patients with moderately-malnourished nutritional status (SGA-B score) ($p<0.05$).

CONCLUSION: In patients with stage 3 and 4DN, daily energy, protein and fat intakes are lower than recommended, but carbohydrate intakes are high. According to the ISRNM criteria, PEW is observed at a higher rate as the disease stage progresses.According to the SGA results, moderately-malnourished patients have a higher rate of PEW.
Keywords: Protein-Energy Wasting, Diabetic Nephropathy, Subjective Global Assessment, Diabetic Kidney Disease.

PC-42

Evaluation of Sarcopenia Parameters in Patients with Multiple Sclerosis

Günnur Koçer[1], Sevda Lafcı Fahrioğlu[2], Nazemin Gürsoy Karaman[1], Musa Muhtaroğlu[3]

[1]Near East University, Faculty of Medicine, Department of Physiology, Lefkoşa, Turkish Republic of Northern Cyprus
[2]Cyprus International University, Faculty of Medicine, Department of Anatomy, Lefkoşa, Turkish Republic of Northern Cyprus
[3]Near East University, Faculty of Medicine, Department of Anatomy, Lefkoşa, Turkish Republic of Northern Cyprus

AIM: Multiple Sclerosis (MS) is a central nervous system disease that causes muscle weakness, balance disorder and gait disturbance. Sarcopenia is a muscle disease with a decrease in muscle mass, muscle strength and function. The aim of our study is to reveal the sarcopenia parameters in MS patients living in the Turkish Republic of Northern Cyprus (TRNC) and how these parameters change with the “Expanded Disability Status Scale” (EDSS) score.

METHODS: 26 people participating in our study, who applied to the Physical Therapy Rehabilitation Department of Dr. Burhan Nalbantoğlu Hospital, were divided into 2 groups patients with MS (13) and without MS (13) matched for age and sex. The EDSS scores of patients with MS were between 1 and 5. Fatigue times, muscle strength, timed up and go (TUG) test and anthropometric measurements of all participants were recorded. Independent samples t test and Mann Whitney U test were used for statistical analysis. Statistical significance level was accepted as $p \leq 0.05$.

RESULTS: The TUG test results were significantly higher in the MS group (MS group 8,097 ± 3,029 sec, non-MS group= 5,565 ± 0,5994 sec, $p=0.002$), while the dominant (right hand) hand grip strength was also lower in the MS group compared with the non-MS group (MS group 17,64 ± 6,619 kg, non-MS group= 24,74 ± 6,983 kg, $p=0.0136$). Fatigue time recorded in the right ($p=0.009$) and left hands ($p=0.0185$) was significantly shorter in the MS group compared to the non-MS group. There was a statistically significant negative correlation between EDSS scores and right-hand fatigue time ($p=0.0265$).

CONCLUSION: The results of our study showed that sarcopenia criteria were getting worse in MS patients. We believe that MS patients can assist to retain their quality of life by exercising regularly and altering their diets before they get sarcopenic.
Keywords: MS, Sarcopenia, EDSS.

PC-43

The Effect of the Acetylcholinesterase Inhibitor Rivastigmine on the Pentylenetetrazole-Induced Kindling Model of Experimental Epilepsy

Elif Türkdönmez, Büşra Okuyucu, Burcu Hatipoğlu, Emre Soner Tiryaki, Gökhan Arslan, Erdal Ağar, Mustafa Ayyıldız

Department of Physiology, Faculty of Medicine, University of Ondokuz Mayis, Samsun, Türkiye

AIM: Epilepsy is one of the most prevalent neurological diseases and has no known currently cure. The effects of acetylcholine mechanisms on epilepsy are contradictory in the literature and the effects of acetylcholinesterase inhibitor rivastigmine (RIVA) on epilepsy are unknown. The aim of this study is to investigate the effect of RIVA on the pentylenetetrazole (PTZ)-induced kindling model of experimental epilepsy.

METHODS: After the approval of the Animal Experiments Local Ethics Committee (OMU HADYEK 2022/35); firstly, Wistar albino rats weighing 245-265g were divided into four main groups: Sterile Physiological Saline (SPS)+PTZ (n=32) as a control group; 0.5mg/kg RIVA+PTZ (n=8); 1mg/kg RIVA+PTZ (n=8), and 2mg/kg RIVA+PTZ (n=8) to investigate the RIVA's effect on kindling: SPS; 0.5; 1, and 2mg/kg RIVA was administrated intraperitoneally 15 minutes before PTZ (35mg/kg) once every other day for 21 total injections. After the kindling procedure was completed, kindled animals in the control group were divided into four sub-groups considering the effects of these doses in the kindling process: SPS; 0.25; 0.5, and 1mg/kg RIVA, and these were delivered intraperitoneally 15 minutes before the acute PTZ (35mg/kg) application. The first myoclonic jerk latency and seizure scores (according to the Fischer & Kittner seizure scale) were observed and statistically analyzed with one-way ANOVA.

RESULTS: While the number of injections required for the kindling of the SPS+PTZ group was 14,12±1,02, the number of injections for

the 0.5mg/kg RIVA+PTZ group was 18,63±0,98 ($p<0.05$). 1 and 2mg/kg RIVA+PTZ groups were insignificant compared to the SPS+PTZ group. The first myoclonic jerk latency increased ($p<0.05$) and the seizure score decreased ($p<0.05$) only in the 0.5mg/kg RIVA+PTZ group compared to the SPS+PTZ group.

CONCLUSION: According to the data obtained, it was concluded that 0.5mg/kg dose of RIVA delayed the development of PTZ-induced kindling and showed anticonvulsant effect in kindled rats.

Keywords: Acetylcholinesterase, Epilepsy, Pentylenetetrazoel, Rivastigmine.

PC-44

Comparison of the Effects of Levetiracetam and Valproic Acid on Spike-Wave Discharges in WAG/Rij Rats with Genetic Absence Epilepsy

Elif Türkdönmez, Büşra Okuyucu, Burcu Hatipoğlu, Emre Soner Tiryaki, Mustafa Ayyıldız, Gökhan Arslan, Erdal Ağar

Department of Physiology, Faculty of Medicine, University of Ondokuz Mayıs, Samsun, Türkiye

AIM: Valproic acid (VPA) is the most commonly used drug in the treatment of absence epilepsy. However, VPA has serious side effects. In this study, we aimed to compare the effects of the second-generation antiepileptic drug levetiracetam (LEV) and VPA on absence seizures.

METHODS: All animal experimental procedures were approved by the OMU Animal Experiments Local Ethics Committee. 7-8 months old male WAG/Rij rats (n=21) were divided into three groups as control (sterile physiological saline; saline), LEV (100 mg/kg), and VPA (200 mg/kg). Tripolar electrodes were placed in all rats for electrocorticogram (ECoG) recording. One week after surgery, ECoG recordings of the rats were obtained for 3 hours before and after the first injection, and 24 hours after the 7th and 14th injections of the saline, LEV or VPA. One-way ANOVA and post-hoc Bonferroni test were used for comparisons between groups.

RESULTS: When the pre-injection periods were compared, there was no significant difference among groups. When the post-injection periods were compared, acutely administration of LEV and VPA significantly decreased the number of spike-wave discharges (SWDs) and the mean duration of SWDs compared to the control group ($p<0.001$). When the LEV and VPA records taken after acute, 7 days and 14 days injections were compared, there was no significant difference between the two groups in terms of the number of SWDs and the mean duration of SWDs ($p>0,05$).

CONCLUSIONS: While VPA is preferred as the first choice in the treatment of absence epilepsy, the use of LEV is more limited. Studies have shown that VPA has a higher hepatotoxic and hematologic side effects than LEV. From this point of view, we suggest that LEV may be the first choice in the treatment of absence epilepsy.

Keywords: Absence epilepsy, Electrocorticogram, Levetiracetam, Spike-wave Discharge, Valproic Acid.

PC-45

The Effects of Orexin Receptor Agonist Orexin-A in Wag/Rij Rats With Genetic Absence Epilepsy

Fatma Banu Ayçık, Büşra Okuyucu, Mustafa Ayyıldız, Erdal Ağar

Department of Physiology, Medical School, University of Ondokuz Mayıs, Samsun, Türkiye

AIM: Orexin, a neuropeptide, regulates sleep-wake cycle, energy homeostasis, analgesia, learning, and memory. Orexins cause depolarization in neurons and increase in firing frequencies of neurons. In the present study, we aimed to investigate the effect of Orexin-A, an orexin receptor agonist, on absence epilepsy models of WAG/Rij rats.

METHODS: The rats were anesthetized with ketamine (90 mg/kg) and xylazine (10 mg/kg), and electrodes were placed after the coordinates were determined according to the bregma points of animals placed on the stereotaxic device. Records were taken from the operated animals after a 7-day recovery period. After 3 hours of baseline recording, 4, 8, and 16 µg doses of Orexin-A were injected intracerebroventricular (i.s.v.) and recorded for another 3 hours.

RESULTS: The number of spike-wave discharges (SWDs) ± SEM 140th minute value after DMSO was 66.6 ± 4.7 clusters/20 min. Orexin-A (4 µg, 1.33 µl) post-injection SWDs 140th minute value was 27.9 ± 8.7 and when compared with control group, it was observed that it decreased statistically from the 100th minute to the end of the recording ($p<0.05$). Orexin-A (8 µg, 2.66 µl) post-injection SWD's 140th-minute value was 17.9 ± 8.9 and post-injection from the 20th minute it was found to decrease the number of SWDs according to control group. Orexin-A (16 µg, 5.33 µl) post-injection SWDs 140th minute value 19.6 ± 6.0, and it was observed that the number of SWDs was statistically reduced compared to control group from the 20th minute after the injection.

CONCLUSION: Although the effect of 4 µg of Orexin-A has weak, all doses of Orexin-A showed anticonvulsant effects. Since there was no statistical difference in effect between 8 µg and 16 µg, the lower dose of 8 µg was accepted as the effective dose. The results of the study of Celli et al. support our study.

Keywords: Epilepsy, Orexin-A, {WAG/Rij} rat.

PC-46

The Effect of Magnesium Sulphate on Spike Wave Discharges in Genetic Absence Epileptic WAG/Rij Rats

Burcu Hatipoğlu, Büşra Okuyucu, Elif Türkdönmez, Emre Soner Tiryaki, Gökhan Arslan, Erdal Ağar, Mustafa Ayyıldız

Department of Physiology, Faculty of Medicine, Ondokuz Mayıs University, Samsun, Türkiye

AIM: The aim of this study was to investigate the effect of acute administration of MgSO4 on spike-wave discharges (SWDs) in genetic absence epileptic rats.

METHODS: Male WAG/Rij rats (8-9 months old, 288±19 g, n=36) were randomly divided into six groups. Tripolar electrodes were placed on the skulls of all animals by stereotaxic device for electrocorticogram (ECoG) recording. After a seven-day recovery period, animals were attached to the data acquisition unit for electrophysiological recordings. After 1-hour of ECoG recording, the control group was given sterile physiological saline (the solvent of MgSO4). MgSO4 was administered intraperitoneally to other rats at the doses of 100, 200, 400, 600, and 800 mg/kg, and 2-hours of ECoG were obtained. The total number of SWDs for each group was compared statistically with the GraphPad Instant (v3.06) software in 15-minute periods. One-way ANOVA and after post-hoc Bonferroni tests were used for statistical analysis.

RESULTS: When the 1-hour period before the injections was evaluated, there was no significant difference among the groups. 800 mg/kg MgSO4 administered animals died. When 100 and 200 mg/kg MgSO4 administered, there was no significant difference in the total number of SWDs compared to the control group during 2 hours after injection. Administration of 400 mg/kg MgSO4 increased the total number of SWDs at the 30th and 45th minutes ($p<0.01$; $p<0.05$, respectively). When 600 mg/kg MgSO4 was administered, SWDs activity completely disappeared in the first 15 minutes ($p<0.001$), while an increase was detected in the total number of SWDs at 45, 60 and 75 minutes ($p<0.01$; $p<0.01$; $p<0.05$, respectively).

CONCLUSION: Studies have reported that MgSO4 activates GABA-A receptors, and also GABA-A receptor activation causes an increase in absence seizures. The present study suggests that MgSO4 increases absence seizures probably via GABA-A receptor activation.

Keywords: Absence epilepsy, Spike-wave discharge, Electrocorticogram, Magnesium Sulphate.

PC-47

N-Acetylcysteine Enhances the Antihyperalgesic Effect of Levetiracetam in the Posttraumatic Epilepsy Model

Recep Başaran[1], Mustafa Efendioğlu[2], Metehan Akça[3], Duygu Ceman[1], Cumaali Demirtaş[4], Yunus Emre Sürmeneli[4], Mehmet Yıldırım[4]
[1]University of Health Sciences, Sancaktepe Training and Research Hospital, Department of Neurosurgery, Istanbul
[4]University of Health Sciences, Haydarpaşa Numune Training and Research, Department of Neurosurgery, Istanbul
[3]Tokat Gaziosmanpasa University, Medical School, Department of Physiology, Tokat
[4]University of Health Sciences, Hamidiye Medical School, Department of Physiology, Istanbul, Türkiye

AIM: Pain is an important clinical and social problem that affects the quality of life and has a cost to society in terms of economy and workforce. Traumatic brain injury (TBI) is one of the most common causes of chronic pain. In the present study, it was aimed to investigate the effects of the interaction of levetiracetam (LEV) and gabapentin (GBP) with n-acetylcysteine (NAC) on mechanical and thermal pain threshold in a model of subconvulsant pentylenetetrazole (PTZ) induced posttraumatic epilepsy (PTE).

METHODS: In the study, after 57 male Sprague-Dawley rats were divided into 7 groups, mild- TBI was performed to the animals except the control group (SBU HADYEK 2018-03/06). PTE model was created by applying subconvulsant dose of PTZ (30+15+15 mg/kg) intraperitoneally (i.p.) after mild-traumatic brain injury (TBI). Experimental groups with PTE were injected with 50 mg/kg/i.p. LEV, 100 mg/kg/i.p. GBP or the combination of these antiepileptic drugs with 100 mg/kg/i.p. NAC for 14 days. After drug administrations were completed, PTZ was given again in a subconvulsant dose and open field test for locomotor activity, dynamic and thermal plantar tests for pain threshold were applied respectively. Mann-Whitney U test was used after Kruskal-Wallis for statistical analysis.

RESULTS: According to the pain test findings, while the thermal pain threshold decreased significantly in the PTE group ($p<0.05$), it increased in the PTE+LEV, PTE+GBP and PTE+LEV+NAC groups ($p<0.05$, $p<0.001$ and $p<0.01$, respectively) was detected. While NAC alone was not effective on thermal pain threshold, it was determined that when applied together with LEV, it increased the thermal pain threshold more in the PTE+LEV+NAC group compared to LEV alone ($p<0.01$).

CONCLUSION: It was concluded that LEV and GBP exhibited antihyperalgesic effect in PTE model facilitated with PTZ, and NAC, which was used as an adjuvant, further strengthened the antihyperalgesic effect of LEV.

Keywords: Levetiracetam, N-acetylcysteine, Post-traumatic Epilepsy.

PC-48

Effects of Interaction of Clonazepam with Second-Line Antiepileptic Drugs Related to Treatment of Status Epilepticus on Motor and Cognitive Behaviors

Cumaali Demirtaş[1], Uğur Aykın[1], Metehan Akça[2], Yunus Emre Sürmeneli[1], Hava Yıldırım[3], Mehmet Yıldırım[1]

[1]University of Health Sciences, Hamidiye Medical School, Department of Physiology, Istanbul
[2]Tokat Gaziosmanpasa University, Medical School, Department of Physiology, Tokat
[3]University of Health Sciences, Hamidiye Medical School, Department of Medical Biology, Istanbul, Türkiye

AIM: In the presented study, it was aimed to examine the effect of the interaction of clonazepam (CLZ), which is in the first step of the status epilepticus treatment algorithm, with the second-line antiepileptic drugs levetiracetam (LEV), lacosamide (LCM), valproic acid (VPA) and fosphenytoin (fPHT) on the motor and cognitive behaviors. In this way, it is aimed to the investigation of neuronal damage related to the status and polytherapy through motor and cognitive function tests in a possible polytherapy option.

METHODS: After the male Sprague-Dawley rats were divided into 6 groups (n=8), the experimental status epilepticus model induced by lithium/pilocarpine (5mEq/320mg/kg) was performed in 5 groups (SBU-HADYEK-2020-03/15). 30 minutes after the onset of seizures, groups with status epilepticus were given 1 mg/kg CLZ, 1+200 mg/kg CLZ+LEV, 1+50 mg/kg CLZ+LCM, 1+300 mg/kg CLZ+VPA or 1+100 mg/kg CLZ+fPHT. Physiological saline was applied to the control group. Between 15-18th days after the status and drug combination, open field tests for locomotor activity, rotarod for forced motor activity, radial arm maze for spatial memory, and passive avoidance tests for fear memory were performed, respectively. Mann-Whitney U test was used for statistical analysis of behavioral data.

RESULTS: While LCM and VPA applied together with CLZ did not have a negative effect on learning and memory performance, performance loss related to spatial memory was detected in the CLZ+fPHT group($p<0.05$). When compared with the control group, there was a decrease in forced motor functions in CLZ+VPA and CLZ+fPHT applied groups ($p<0.01$). In addition, an increase in anxiety levels was detected in the CLZ+LCM and CLZ+VPA groups compared with the control group ($p<0.05$).

CONCLUSION: It was observed that the combination of CLZ+LCM, one of the polytherapy options used to control experimental status epilepticus, did not adversely affect either motor functions or cognitive performance.
This study was supported by SBU-BAP. Project no: 2020/092.

Keywords: Antiepileptic, Klonazepam, Learning and Memory, Motor Behaviour, Status Epilepticus.

PC-49

The Effects of GLP1 Analogue, Liraglutide on Mitochondrial Dynamics and Inflammation in the Rat Model of Lithium-Pilocarpine-Induced Temporal Lobe Epilepsy

Fatma Merve Antmen[1], Zeynep Fedaioglu[2], Dilan Acar[1], Sevcan Demircan[3], Lala Rzyave[3], Farah Kardouh[3], Bengisu Karakose[3], Ece Ada[3], Ilayda Esma Yavuz[3], Simge Senay[4], Devrim Oz Arslan[5], Guldal Suyen[1]

Acibadem Mehmet Ali Aydinlar University, Medical School, Departments of Physiology[1], Molecular Biology & Genetics[2], Istanbul
[3]School of Medicine, Acibadem Mehmet Ali Aydinlar University, Istanbul
[4]Department of Medical Biotechnology, Acibadem Mehmet Ali Aydinlar University, Istanbul
[5]Department of Biophysics, Acibadem Mehmet Ali Aydinlar University, Istanbul, Türkiye

AIM: Mitochondrial stress and inflammation have been proposed to have central role in the pathophysiology of temporal lobe epilepsy (TLE). Anti-diabetic drugs, such as Glucagon-like peptide-1 receptor agonists (GLP-1RAs), have been shown to possess neuroprotective effects in several neurodegenerative diseases. The objective of the present study is to evaluate the possible effects of liraglutide, a GLP-1RA under phase-2 clinical studies, in rat model of TLE.

METHODS: Healthy control and epileptic Sprague Dawley adult (3 months old), male rats (200 – 300 g) treated with saline and liraglutide were used. TLE was formed by inducting status epilepticus (SE) with low-dose-repetitive-lithium chloride (3 mEq/kg)–pilocarpine hydrocholoride (20 mg/kg) intraperitoneal injections. Treatments were applied 3 hours after the SE to target the early stage of epileptogenesis. Intraperitoneal injections of liraglutide (300 µg/kg/day) or 0.9% saline (1 mg/kg/day) was continued for 3 days. Blood specimen and hippocampus tissues were collected. The changes in mitochondrial dysfunction (mitochondrial membrane potential, mitochondrial mass, and mitochondrial Sox levels) were evaluated in peripheral mononuclear blood cells. Inflammation markers (NRLP3, Caspase-1, IL-1β); antioxidant pathways (Nrf-2, phospho-Nrf-2) protein levels and mitochondrial dynamics were evaluated by western blot analysis on hippocampal tissues. Protocols have been approved by ACU-HADYEK (Approval number: HDK-2021-28). Statistical analysis was performed with GraphPad Prism 9. The mean value differences between the two groups were analyzed with student's t-test.

RESULTS: Liraglutide altered mitochondrial dynamics and antioxidant capacity in healthy control and TLE model of rats. Mitochondrial dynamics-related proteins showed that Pink1 and Mfn2 levels increased upon liraglutide treatment in the hippocampus of epileptic rats ($p<0.05$). Furthermore, inflammation markers such as NLRP3, IL-1β, and Caspase-1 decreased in liraglutide-treated epileptic rats ($p<0.001$; $p<0.05$; $p<0.0001$, respectively) whereas antioxidant phopsho-Nrf2 levels increased ($p<0.001$).

CONCLUSIONS: Our results suggest that liraglutide may provide potential beneficial effects for TLE through mitochondrial dynamics and anti-inflammatory pathways.

Keywords: Liraglutide, Epilepsy, Rat, Inflammation.

PC-50

TRPV1 Agonist Capsaicin Reduces Neurodegeneration in Alzheimer's Disease Model Induced with Okadaic Acid

Murat Çakır[1], Furkan Yüksel[2], Mahmud Mustafa Özkut[3], Suat Tekin[2], Emin Kaymak[4]

[1]Department of Physiology, Faculty of Medicine, Yozgat Bozok University, Yozgat
[2]Department of Physiology, Faculty of Medicine, Inonu University, Malatya
[3]Department of Histology and Embryology, Faculty of Medicine, Afyonkarahisar Health Sciences University, Afyonkarahisar
[4]Department of Histology and Embryology, Faculty of Medicine, Yozgat Bozok University, Yozgat, Türkiye

AIM: In recent years, it has been shown that Transient Receptor Potential Vanilloid 1 (TRPV1) channels, which are widely distributed in the central nervous system, play a role in many physiological and pathological processes in the nervous system. In this study, we investigated the effects of TRPV1 agonist capsaicin (CAP) and antagonist capsazepine (CPZ) in Alzheimer's Disease model induced with okadaic acid (OKA).

METHODS: 60 Sprague Dawley male rats were randomly divided into 6 groups. 1. Control group: no application was made. 2. Sham group: 5 µl of artificial cerebrospinal fluid (aCSF) was injected as bilateral ICV. 3. OKA group: 200 ng OKA dissolved in 5 µl aCSF was injected as bilateral ICV. 4. OKA+CAP group: Unlike the OKA group, 1mg/kg CAP injection was performed intraperitoneally for 13 days. 5. OKA+CPZ group: Unlike the OKA group, 1mg/kg CPZ injection was performed intraperitoneally for 13 days. 6. OKA+CAP+CPZ group: Unlike the OKA group, 1mg/kg CAP and CPZ injections were performed intraperitoneally for 13 days. Immunohistochemically, caspase-3, phosphorylated tau (ser396), amyloid beta, phosphorylated glycogen synthase kinase-3 beta-ser-9 (GSK3β-ser9), tumor necrosis factor alpha (TNF-α), interleukin-1 beta (IL-1β) levels were examined from the cortex and hippocampus regions of the brain. At the same time, histopathological examination was performed from the cortex and hippocampus regions.

RESULTS: CAP application decreased the increased caspase-3, phosphorylated tau (ser396), amyloid beta, TNF-α, IL-1β levels in the cortex and hippocampus caused by ICV OKA application, while it increased the decreased GSK3β-ser9 levels ($P<0.05$). At the same time, CAP application reduced histopathological damage in the cortex and hippocampus ($P<0.05$).

CONCLUSIONS: In this study, we found that the administration of TRPV1 agonist CAP reduced neurodegeneration and neuroinflammation in the Alzheimer's Disease model induced by OKA.

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Keywords: Alzheimer's Disease, Okadaic Acid, Transient Receptor Potential Vanilloid 1, Capsaicin, Capsazepine.

PC-51

Effect of Forced Nicotine on Oxytocin and Vasopressine Levels in Striatum and Hippocampus in Nicotine Preferring Rat Lines

Zümra Kul[1], Servet Kızıldağ[2], Fulya Tuzcu[1], Lütfiye Kanıt[1], Burcu Balkan[1], Ayşegül Keser[1]

[1]Ege University Medical School, Department of Physiology, İzmir
[2]Dokuz Eylül University Medical School, Department of Physiology, İzmir, Türkiye

AIM: This study aimed to determine the differences in hippocampal and striatal oxytocin and arginine-vasopressin (AVP) levels in Nicotine-preferring (NP) (male/female) and control (male/female) animals during chronic oral nicotine exposure.

METHODS: NP line is developed by selective breeding at Ege University Center for Research on Laboratory Animals. This study is a continuation project of previous project (TDK-2020-21454). Same animals were used in both projects; there were 4 groups (n=10/group): Control Male (CM), Control Female (CF), NP Male (NPM), NP Female (NPF). All groups received forced nicotine administration in drinking water for 4 weeks. In the previous project, we analyzed differences in empathy-like behavior of NP and control groups during baseline and chronic nicotine exposure. In this project, animals were decapitated following behavioral testing; striatum and hippocampus were dissected and stored at -80°C. Oxytocin and AVP levels in samples were measured by ELISA. One-way ANOVA and post-hoc Tukey tests were performed using SPSS for statistical analysis.

RESULTS: There were significant differences between the groups ($p<0.001$). Hippocampal oxytocin levels were higher in NPM compared to CM ($p=0.002$), in NPF compared to CF ($p=0.05$), in NPM compared to NPF ($p=0.05$), and in NPM compared to CF ($p<0.001$). Striatal oxytocin levels in NP were lower than controls ($p=0.05$). Striatal oxytocin levels in NPF were lower than CM ($p=0.02$). Hippocampal AVP levels in NP were higher than controls ($p=0.005$). Hippocampal AVP levels in NPM were higher than CF ($p=0.02$). Striatal AVP levels were not different between groups.

CONCLUSION: Alterations in brain oxytocin and AVP levels of NP animals may underlie the changes observed in empathy-like and social behavior of these animals. These differences may contribute to the susceptibility of NP rats to nicotine addiction.

Supported by Ege University, Scientific Research Projects Commission (TYL-2020-22397).

Keywords: Addiction, Hippocampus, Nicotine, Oxytocin, Striatum, Vasopressin.

PC-52

Interaction of Nitrergic and Cholinergic Systems on Anxiety and Depression-Like Behaviors in Diabetic Rats with Streptozotocin

Mehmet Öz[1], Durmuş Ali Aslanlar[2], Kısmet Esra Nurullahoğlu Atalık[2]

[1]Aksaray University, Faculty of Medicine, Department of Physiology, Aksaray
[2]Necmettin Erbakan University, Meram Faculty of Medicine, Department of Medical Pharmacology, Konya, Türkiye

AIM: This study was planned to evaluate the effects of donapezil alone or through nitric oxide on anxiety- and depression-like behaviors in streptozotocin-induced diabetic rats.

METHODS: A total of 30 Wistar-rats were used in 5 groups in the study. Experimental diabetes was induced using streptozotocin (60 mg/kg). 30-days after induction, one group left as diabetic-control, while the other three-groups received 4 mg/kg donepezil for 20-days. One of the groups receiving Donapezil received 20 mg/kg L-NAME for 20-days, and the other 40 mg/kg i.p., L-arginine for 20-days. The open-field test (OF) was used to evaluate anxiety-like behaviors and forced-swimming test (FST) was used to evaluate depression-like behaviors. Obtained data were analyzed with one-way ANOVA and Tukey test. $p<0.05$ was considered significant.

RESULTS: The immobility times of all diabetic rats in the FST were found to be significantly higher than the control-group ($p<0.05$). While L-Arginine increased the immobility time ($p<0.05$), the effect of L-NAME was not statistically significant ($p>0.05$). In the OF, the time spent in the center and exploratory behavior of all diabetic rats were found to be lower than the control-group ($p<0.05$). However, there was no difference between the rats in the L-NAME and L-Arginine groups and the rats in the donepezil group ($p>0.05$). There was no significant difference between the groups in the number of line crossings in which locomotor activity was evaluated ($p>0.05$).

CONCLUSION: Rats induced diabetes by streptozotocin had increased levels of anxiety as assessed by OF and depression as assessed by FST. In our study, while donepezil did not have an effect on these parameters, an increase in depression-like behaviors was detected in the group receiving concomitant L-arginine. These findings may suggest that cholinergic and nitrergic systems may interact on depression-like behaviors in diabetic rats.

Keywords: Diabetes, Depression, Anxiety, Acetylcholinesterase, Nitric Oxide.

PC-53

The Relationship between Parkinson's Disease and TRP Channels; Possible Therapeutic Effects of Carvacrol

Tülay Koca[1], Yasemin Aydın[2], Tansel Korkmaz[2], Emel Ulupınar[3], Faruk Saydam[4]

[1]Afyonkarahisar Health Science University, Medical Faculty, Department of Physiology, Afyonkarahisar
[2]Eskişehir Osmangazi University, Medical Faculty, Department of Physiology, Eskişehir
[3]Eskişehir Osmangazi University, Medical Faculty, Department of Anatomy, Eskişehir
[4]Recep Tayyip Erdoğan University, Medical Faculty, Department of Medical Biology Rize

AIM: Parkinson's disease (PD) is a neurodegenerative disease characterized by degeneration of dopaminergic neurons. Carvacrol (CA) modulates Transient Receptor Potential (TRP) cation channels. In our study, the effects of CA on TRPC1 in dopaminergic neurons and TRPA1 in astrocytes and the role of these channels in PD were investigated in the model of Parkinson's induced by 6-hydroxydopamine (6-OHDA).

METHODS: Experiments were performed in 4 groups of male Sprague-Dawley rats. Groups; 1) Sham (Placebo Surgery), 2) 6-OHDA, 3) 6-OHDA+Vehicle (DMSO=Dimethyl sulfoxide), 4) 6-OHDA + CA (10 mg/kg). TRPC1 and TRPA1 immunoreactivity in brain tissue sections of 8 animals of each group was determined by immunohistochemical staining method. The SNpc and striatal areas of the brains of the other 8 animals in the groups were used for molecular studies.

RESULTS: the immunohistochemical analysis; there was a decrease in the number of TRPC1(+) dopaminergic neurons due to the Parkinson. This decrease in cell number was also observed in the DMSO and CA groups. However, dopaminergic neurons in the preparations of the CA group had a healthier appearance due to the neuroprotective effect of CA, and their cell integrity was preserved compared to the cells in the DMSO group. CA had no significant effect on gene expression and protein levels of dopaminergic neuron TRPC1 channels. While the number of TRPA1(+) cells in astrocytes decreased in the CA treatment group compared to the control group, gene expression levels increased significantly. As in TRPC1(+) dopaminergic cells, it was observed that cellular integrity was preserved by CA in treatment group astrocytes.

CONCLUSION: CA showed neuroprotective effect in the presented Parkinson animal model, TRPC1 is inhibited by CA in dopaminergic cells İn addition, CA activates TRPA1 channels, because of increased channel expression in astrocytes may be useful in neuron survival by triggering the neuromodulatory effects.

Keywords: Parkinson's Disease, TRP Channels, Carvacrol, Neuroprotection.

PC-54

The Effect of Ginkgo Biloba on Hyperalgesia Induced by REM Sleep Deprivation

Elif Ezgi Gürel[1], Levent Öztürk[2], Gülnur Öztürk[3], Ecem Büşra Değer[2], Esra Akbaş Tosunoğlu[2]

[1]Trakya University Keşan Hakkı Yörük College of Health, Department of Emergency Aid and Disaster Management Edirne
[2]Trakya University, Faculty of Medicine, Department of Physiology, Edirne
[3]Trakya University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Edirne, Türkiye

AIM: Ginkgo-biloba extract contains ginkgo-flavone glycosides and has free-radical scavengers and platelet activating factor antagonist activity. Recent studies have also shown effects in modulation of pain. In this study, the antinociceptive effect of Ginkgo-Biloba was investigated in a model of REM sleep deprivation-induced hyperalgesia.

METHODS: After ethical approval, 40 female Wistar-Albino rats, 8-12 weeks old, were divided into five groups of eight animals each (PLS, placebo; GB30, Ginkgo-Biloba 30mg/kg; GB100, Ginkgo-Biloba 100mg/kg; GB300, Ginkgo-Biloba 300mg/kg and FLP40, flurbiprofen 40mg/kg). Flurbiprofen was added as a positive control. All groups were included in the 72-hour REM sleep-deprivation protocol with the modified multiple-pot technique and pain assessment was performed with hot-plate and tail-flick tests at the beginning, end and after drug administration of the sleep-deprivation period. Mean values for pain assessment were produced from triple-measurements and expressed in seconds. Drugs and placebo were administered by single-dose gastric-gavage after measurements after sleep-deprivation. In order to compare pre and post sleep-deprivation pain measurements between groups, the change from the first test to the post-test was calculated for each condition. Kolmogorov-Smirnov was used to determine the normal distribution of the groups, and one-way ANOVA and Post-hoc Tukey were used to determine the difference between groups in pain measurements.

RESULTS: Sleep-deprivation caused hyperalgesia in all groups. (Hot-plate time decreased at the stated rates: PLS=60.8%, GB30=65.8%, GB100=65.9%, GB300=67.5%, FLP40=70.8% ($p<0.05$); Decreases in tail-flick test: PLS=67.2%, GB30=67.7%, GB100=58%, GB300=71.4%, FLP40=64.6% ($p<0.05$). Ginkgo-biloba showed analgesic effect at all doses (Hot-plate: GB30=30%, GB100=28%, Tail-flick: GB30=24%, GB100=26.9%) ($p<0.05$). Especially at a dose of 300mg/kg, its effect was closest to flurbiprofen in the tail-flick test. (Hot-plate: GB300=43.5%, FLP40=94.8%, tail-flick GB300=43.7%, FLP40=48.5%) ($p<0.05$).

CONCLUSION: Ginkgo Biloba reduces the decrease in pain threshold due to sleep-deprivation and has an antinociceptive effect. We think that Ginkgo-Biloba has the potential to be added to the treatment in painful-symptoms associated with sleep-disorders.

Keywords: REM sleep deprivation, Hyperalgesia, Ginkgo Biloba.

PC-55

Effect of Ethyl Pyruvate on Sleep Deprivation-Induced Cognitive Dysfunction in Young Female Rats

Nazan Elma[1], Salih Erdem[2], İnci Turan[1], Hale Sayan Özaçmak[1]

[1]Zonguldak Bülent Ecevit University Faculty of Medicine, Department of Physiology, Zonguldak
[2]Zonguldak Bulent Ecevit University Health Science Instute, Department of Physiology, Zonguldak, Türkiye

AIM: REM sleep deprivation (SD) affects various physiological processes such as learning and memory. The effect of ethyl pyruvate on cognitive functions has been studied in a limited number of studies and has not been investigated on sleep deprivation before.Therefore, the aim of our study was to investigate the effects of ethyl pyruvate treatment on learning and memory in female rats undergoing REMSD for 72 hours.

METHODS: 25 female Wistar albino rats aged 6months were divided into four different groups(7 sleep deprived rats, the others 6 rats).Control,wide platform(WP),SD,SD groups treated with ethyl pyruvate.WP group rats were placed in a tank with a large platform(13cm diameter) as environmental control of sleep deprivation.The rats in the WP group, which could sleep without falling into the water, remained in the tank for 72 hours.REMSD was created using the multi-platform(6.5cm diameter) method for 72 hours.Ethyl pyruvate treatment(50 mg/kg) was administered as a single daily dose(i.p) for 5 days.The Morris water maze(MWM) test was used to evaluate the effects of ethyl pyruvate on learning and memory.At the end of the experiment, the hippocampus and brain tissues of the rats were taken.

RESULTS: The results showed that the effects of SD on memory assessed by the MWM test were prolonged in the daily time to find the platform and shortened in the time spent in the platform area on the last day ($p<0.05$).It also proved that SD increased MDA and nitrate levels in brain tissue and AchE activity in hippocampus tissue ($p<0.05$).When the ethyl pyruvate treatment group was compared with the SD group, nitrate levels were found to be decreased ($p<0.05$). Finally, it was found that there was no difference between the groups in terms of GSH and glycogen levels.

CONCLUSION: Our results show that ethyl pyruvate administered after 72 hours of REMSD has no effect on learning and memory in young female rats.

Keywords: Ethyl Pyruvate, Learning and Memory, REM Sleep Deprivation.

PC-56

The Effect of Morphine Dependence and Morphine Withdrawal on Neuritin and Some Markers of Neurogenesis in the Rat Hippocampus

Yasin Ali Çimen[1], İbrahim Yildiz[2], Canan Eroğlu Gunes[3], Alpaslan Ozkurkçuler[2], Ercan Kurar[4], Selim Kutlu[4]

[1]Bezmialem University, Faculty of Medicine, Department of Physiology, Istanbul
[2]Necmettin Erbakan University, Meram Faculty of Medicine, Department of Physiology, Konya
[3]Necmettin Erbakan University, Meram Faculty of Medicine, Department of Medical Biology, Konya
[4]Necmettin Erbakan University Neuroscience Research and Application Center (NENRC), Konya, Türkiye

AIM: Neuritin, which was first identified in the rat hippocampal dentate gyrus, is known as the candidate plasticity gene 15. The effects of neuritin on neurite development, dendritic branching, synaptic activity and neuronal survival in the nervous system in some neurodegenerative diseases and psychopathologies have been determined. However, there is no research finding on how neuritin expression is affected in processes related to opioid addiction. In this study, we aimed to determine the neurogenesis status and neuritin gene expression level in the hippocampus in morphine-dependent and naloxone administered rats.

METHODS: Morphine addiction was constituted by subcutaneously administering morphine to adult male rats for 7 days in the study. In the morphine withdrawal group, in addition to morphine administration, naloxone was injected 1.5 hours after the last injection. Hippocampus tissues were removed from all animals. Neuritin and neurogenesis biomarkers such as doublecortin, brain-derived neurotrophic factor, NeuN and MASH1 gene expression levels were evaluated by using quantitative RT-PCR. One-way ANOVA was used for statistical evaluation.

RESULTS: The expression level of hippocampal neuritin in the morphine addiction group was significantly lower compared to control ($p<0.05$). Neuritin expression in naloxone group significantly increased compared to the addiction group ($p<0.001$). Brain derived neurotrophic factor, doublecortin and NeuN expression levels were significantly higher in the morphine withdrawal group compared to the addiction group ($p<0.05$, $p<0.001$ and $p<0.05$, respectively). There was no significant difference in MASH1 expression level.

CONCLUSION: The results of this study show that administration of naloxone significantly increases the return of hippocampal neurogenesis biomarkers in morphine-dependent rats. The fact that morphine addiction lowers the level of neuritin in the hippocampus and that morphine withdrawal significantly increases its expression suggests that neuritin may play a mediating role in the opioidergic modulation of neurogenesis and neuroplasticity in the hippocampal dentate gyrus.

Keywords: Hippocampus, Morphine addiction, Neuritin, Neurogenesis, Rat.

PC-57

On the Role of Cell Death Mechanisms in the Pathophysiology of Neuropathic Pain: An in-silico Study

Arif Kamil Salihoğlu

Department of Physiology, Karadeniz Technical University, Faculty of Medicine, Trabzon, Türkiye

AIM: Neuropathic pain is caused by damage or injury to nerves that transfer information between the peripheral structures and spinal cord-brain. It is common and receives high research interest. However, the cellular mechanism of neuropathic pain has not been clarified yet. In addition to clinical studies, recent evidence indicates expectations from in silico analysis. Cell death and autophagy are recently discovered mechanisms involved. This study aimed to detect possible pathophysiological factors for neuropathic pain, by using bioinformatics tools, in the neuropathic pain rat model by Chung-method spinal nerve ligation.

METHODS: GSE38038 dataset obtained from the Gene Expression Omnibus database was re-analyzed in the R program. In the dataset, total RNA samples in dorsal root ganglia tissues from the neuropathic group (n=4) and control group (n=4) were recruited. Mann-Whitney U test and Benjamini-Hochberg correction analysis were performed in the data analysis, and adjusted p values <0.05 were accepted as significant.

RESULTS: Gene expression levels indicated that autophagy-related proteins (ATG4B, ATG7,12*), sequestosome-1 (SQSTM1), lysosomal membrane glycoprotein-2 (LAMP2*) [responsible for autophagy]; caspases (CASP1,3-8*, CASP9), B-cell leukemia-2 (BCL2), Bcl2-associated X protein (BAX*), tumor protein p53 (TP53*), somatic cytochrome C (CYCS), neuroblastoma ras oncongene (NRAS*) [for apoptosis]; tumor necrosis factor related genes (TNF, TNFRSF1A-B,11B,12A*, TNFSF13*), interleukins (IL1B,6*), toll-like receptor 4 (TLR4*) [for necrosis] and androgen receptor (AR), granzyme-B (GZMB*), cortactin (CTTN*) [for entosis] genes were up-* and down- regulated ($p<0.05$) in neuropathic group, compared with control group.

CONCLUSION: Results from this in silico preliminary study indicate imbalances in the expression levels (up- and down-regulation) of genes known to be involved in many cell death processes, implicating the involvement of impaired autophagic, apoptotic, necrotic, and entotic signaling in the pathophysiological mechanisms of neuropathic pain.

Keywords: Neuropathic pain, Autophagy, Apoptosis, Necrosis, Entosis, In silico analysis.

PC-58

Effects of Meteorin-Like Protein on Pain in an Experimental Diabetes Model

Furkan Yüksel[1], Suat Tekin[1], Mete Özcan[2], Süleyman Sandal[1]

[1]Inonu Unuversity, Faculty of Medicine, Physiology Department, Malatya
[2]Fırat University, Faculty of Medicine, Department of Biophysics, Elazıg, Türkiye

AIM: Diabetes is a chronic disease that develops as a result of insufficiency or ineffectiveness of insulin secretion from the pancreas or disorders in the insulin molecule and progresses with neuropathic pain. Meteorin-like protein (METRNL), known to have neuroprotective effects, is thought to improve insulin resistance and be therapeutic for metabolic syndrome and type 2 diabetes. In addition, the role of METRNL in mitochondrial biogenesis shows that it may be effective on neuropathic pain, but its effectiveness is not fully known. Therefore, in our planned study, we aimed to investigate the effect of METRNL on pain threshold in an experimental diabetes model.

METHODS: In the study (ethics committee 02.04.2020, 2020/5-6-9742) in which 35 Balb-C mice were used, the animals were randomly divided into 5 groups (n=7). Diabetes model was created by administering a single dose of streptozotocin (200mg/kg) to all groups by intraperitoneal (ip) injection. Pain threshold values were recorded with hot-plate and tail-flick tests of animals before and after diabetes was established. Animals in the control group were treated with ip solvent, while the other groups were administered 0.1,1,4 and 10mg/kg METRNL, respectively. Tests were repeated after drug administration. In statistical evaluation, one-way analysis of variance with IBM SPSS-24 package program and post-hoc Dunnett's test following this analysis were used to reveal time-dependent differences between groups. $P<0.05$ was considered significant.

RESULTS: It was observed that the duration of stay in the hot-plate and tail-flick tests of the animals in the METRNL applied groups increased (hot-plate average 7 sec delay, tail-flick average 3 sec delay) and thus their pain thresholds increased compared to the control group. This increase was found to be significant at all doses of METRNL in the hot-plate test, and at 1,4 and 10mg/kg doses in the tail-flick test ($p<0.05$).

CONCLUSION: The results of this study show that tested METRNL may have analgesic activity on diabetic neuropathic pain.
Acknowledgment: This study was supported by the Scientific Research Projects Unit of Inonu University with the project numbered TSG-2020-2088.

Keywords: Pain, Diabetes, METRNL, Neuropathy.

PC-59

Investigation of the Effects of Meteorin-Like Protein in a Model of Neuropathy Induced by Sciatic Nerve Injury

Suat Tekin[1], Furkan Yüksel[1], Mete Özcan[2], Süleyman Sandal[1]

[1]Inonu Unuversity, Faculty of Medicine, Physiology Department, Malatya
[2]Fırat University, Faculty of Medicine, Department of Biophysics, Elazıg, Türkiye

AIM: Neuropathic pain,which mechanisms such as mitochondrial dysfunction, oxidative stress,apoptosis and calcium signaling play a role in its pathogenesis,is a clinical finding that may develop due to nervous system lesions or disorders.It is stated that meteorin-like protein(METRNL) improves intracellular calcium signaling,lipid-induced inflammation and insulin resistance.We aimed to investigate the efficacy of METRNL,which also plays a role in mitochondrial biogenesis,but whose effectiveness is not fully known,on neuropathic pain and motor behavior induced by sciatic nerve damage.

METHODS: In the study conducted with 35 Balb-C mice, with the approval of İnönü University Animal Experiments Local Ethics Committee (02.04.2020, 2020/5-6, 9742), the animals were control, METRNL (0.1 mg/kg, 1 mg/kg, 4 mg/kg and 10 mg/kg) were randomly divided into 5 groups (n=7). Damage was created by clamping the right leg sciatic nerves of animals in all groups. Before and after the sciatic nerve injury, the pain threshold values of the animals with hot-plate and tail-flick tests, and motor activities with the rotarod test were recorded. Animals in the control group were administered intraperitoneally (ip) solvent (isotonic sodium chloride), while the other groups were administered ip 0.1 mg/kg, 1 mg/kg, 4 mg/kg, 10 mg/kg METRNL, respectively. Tests were repeated after drug administration. In statistical evaluation,one-way analysis of variance with IBM SPSS-24 package program followed by post-hoc Dunnett's test,and Tukey HSD test for intergroup comparisons, $p<0.05$ value was considered significant.

RESULTS: It was observed that the application of METRNL in animals with sciatic nerve damage increased the residence time in hot-plate, tail-flick and rotarod tests and increased pain thresholds and motor activities compared to the control group. This increase was found to be significant at all doses of METRNL ($p<0.05$).

CONCLUSION: The results of this study show that the tested METRNL has positive efficacy in both analgesic and motor activity on the model of sciatic nerve injury-induced neuropathy.

Acknowledgment: This study was supported by the Scientific Research Projects Unit of Inonu University with the project numbered TSG-2020-2088.

Keywords: METRNL, Neuropathy, Rotarod, Sciatic Nerve Injury.

PC-60

Investigation of the Antıconvulsane Effects of Venlafaxine in Experimental Penicillin Generated Epilepsy Model

Selim Göksu[1], Ayhan Çetinkaya[2]

[1]Department of Interdisciplinary Neuroscience, Bolu Abant İzzet Baysal University, Bolu
[2]Department of Physiology, Bolu Abant İzzet Baysal University, Bolu, Türkiye

AIM: In this study, it was aimed to evaluate the antiepileptic activity of venlafaxine with electrophysiological and biochemical analysis methods. This study is the first to investigate the antiepileptic effects of venlafaxine in a penicillin-induced acute-epilepsy model according to the literature. The antiepileptic effects of venlafaxine were investigated, as it has less side effects and better tolerance than other antidepressants, increasing the rate of use.

METHODS: This study was approved by the BAİBU Animal Experiments Local Ethics Committee (Decision no: 2020/56). 35 Wistar Albino rats were divided into 5 groups. Rats were placed in stereotaxy device for electrocorticography (ECoG) measurement of the electrical activity of the brain. After five minutes of basal activity measurement, epilepsy was induced to rats with penicillin (500IU, 2.5µl, icv). After 30 minutes of recording, the control group was injected with saline, the positive control group was injected with 5mg/kg diazepam, and the experimental groups were injected with 50mg/kg, 100mg/kg, 150mg/kg venlafaxine (0.1ml, i.p.). ECoG recorded for ninety minutes and blood samples were collected by cardiac puncture method. Afterwards, experiment was terminated. The spike wave numbers and the amplitudes in records were compared in 5-minute segments. Also, the Total Antioxidant-Oxidant Level (TAS-TOS) and thiol-disulfite levels were determined by ELISA and electrolytes by ion-selective electron methods both in the serum, formed by centrifugation of blood samples.

RESULTS: Statistically, it was determined that 100mg/kg and 150mg/kg venlafaxine administration decreased spike wave numbers compared to diazepam and controls and kept the amplitudes similar to the diazepam group. Besides, it was observed that 100mg/kg and 150mg/kg venlafaxine administration increased TAS, calcium and magnesium levels compared to the control group.

CONCLUSION: In conclusion, venlafaxine showed antiepileptic property by decreasing spike wave numbers and antioxidant property by increasing TAS values. Venlafaxine may be an alternative and promising option in the treatment of epilepsy.

Keywords: Epilepsy, Venlafaxine, Electrocorticography (ECoG), Rat, Penicillin.