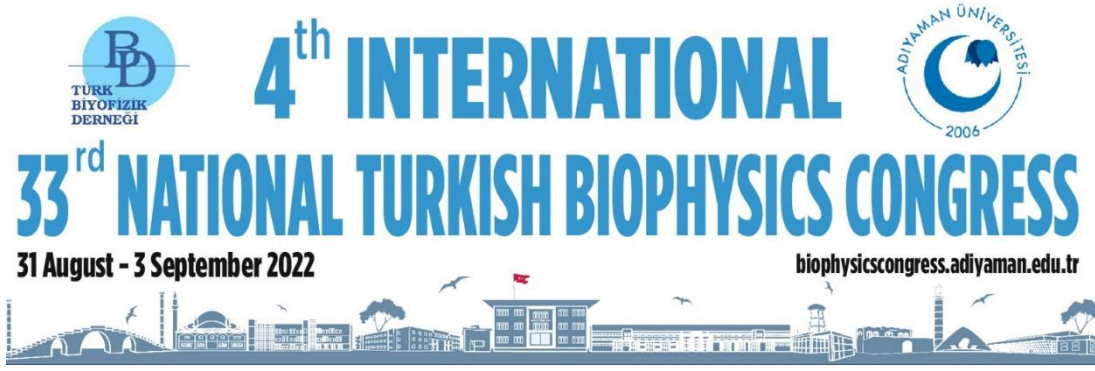
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Abstract Book

Edited by

Celal GUVEN and Salih Tunc KAYA

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ABSTRACT BOOK OF 4TH INTERNATIONAL 33RD NATIONAL BIOPHYSICS CONGRESS

AUGUST 31- SEPTEMBER 3, 2022

ADIYAMAN-TÜRKİYE

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Dear Colleagues,

It was a great honor and pleasure to host the 4th International and 33rd National Turkish Biophysics Congress held on 31 August-3 September 2022 in Türkiye, which was organized by Faculty of Medicine, Adıyaman University and was also financially supported by TÜBİTAK Scientist Support Programs Presidency (BİDEB) within the scope of "2223-B Domestic Scientific Event Organization Support".

The congress bought together leading scientists in the domain of interest from around the world. Around 12 invited speakers from 10 different countries presented panel and conference. We would like to thank all participants for their attendance and contribution to the symposium. This book contains abstracts of the presentations (panel, conference, oral and poster).

The congress was an opportunity to establish new scientific and professional bridges with other geographical realities. In addition, it was also Culture Bridge for our attendance as we had many cultural activities.

Many thanks to the scientific and organizing committee, and the others worked voluntarily.

Yours sincerely,

Celal GUVEN

Chair of the Congress

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PROGRAM

HOUR	SESSIONS (DAY1)	WEDNESDAY (August 31, 2022)
09:00-12:30		**REGISTRATION (Medicine Faculty)**
12:30-13:30	**LUNCH**	**(University Dinner Hall)**
13:30-14:05	**ADYU Rectorate Conference Hall**	**WELCOME AND PROTOCOL SPEECH**
14:10-14:40	**ADYU Rectorate Conference Hall**	**MUSIC AND FOLK DANCE SHOW**
14:40-14:55	**ADYU Rectorate Conference Hall**	**COFFEE BREAK**
14:55-15:40	**ADYU Rectorate Hall Conference** **Prof. Cemil SERT** **Prof. Beki KAN**	**Keynote Speaker** **Prof. Elena POHL** **Title:** Dual transport function of mitochondrial uncoupling proteins
15:40-16:25		**Conference** **Prof. Naranjan S. DHALLA** **Title:** Mechanisms for the Loss of Adrenergic support in Heart Failure.
16:45-19:00	**City Tour**	**Travel (Perre Roman Antique City, Mor Petrus Mor Pavlus Syriac Church)**
19:30	**Dinner**	**Welcome Reception and Dinner (ADYU Tourism Practice Hotel)**

HOUR	SESSIONS (DAY2)	THURSDAY (September 1st, 2022)
09:00-09:45 09:45-10:30	**Ibni Sina Conference Room** **Conference** **Prof. Bayram YILMAZ** **Prof. Mete OZCAN**	**Prof. Morad MARTIN** Title: Cardiac Calcium signaling and Arrhythmia: CPVT1, Cardiac Ryanodine Receptors, and Human Stem Cells derived Cardiomyocytes
		Assist Prof. Akifumi KISHI **Title:** Towards understanding and controlling human sleep Dynamics

10:30-10:45	***Coffee Break***	
10:45- 11:35	**Ibni SINA Conference Room** **Oral presentations** **Prof. M. Tunaya KALKAN** **Assoc. Prof. Devrim OZ ARSLAN**	**Ozlem Bozkurt Girit**; Hatice Fulya Yılmaz; Gizem Dönmez Yalçın; Mehmet Dinçer Bilgin **Title:** Low-intensity low-frequency pulsed ultrasound and withaferin A ameliorates nerve damage in diabetic neuropathy
		Fatma Ozlem; Gokcer Eskikurt; Aslı Ceren Macunluoglu; Asiye Nurten; Ayfer Dayı **Title:** Evaluation of The Effect of Caffeine Consumption on Cognitive Functions by Electroencephalography in University Students
		Hesam Saghaei Bagheri; Ozlem Oztopuz; Fulya Yontem; Reza Rahbarghazi; **Emel Sokullu** **Title:** Melatonin coupled with low-level laser irradiation potentially exerted oncostatic effects on rat glioma cells via Apoptosis Pathway
	Prof. Aziz SANCAR Conference room **Oral presentations** **Prof. Oya ORUN** **Assoc. Prof. Zeynep Aslıhan DURER**	**Salih Varol**; Yasin Karamazi; Muhammed Ali Gencaslan; Osman Cagri Ilhan; Burak Tan; Betül Yalcin; Süleyman Dasdag; Korkut Yegin; Arzu Hanim Yay; Fazile Cantürk Tan **Title:** Enzymatic and Histopathological Changes in Rat Liver Exposed to Pre-and Postnatal Radiofrequency Electromagnetic Field: A Generation Study
		Gunnur Guler; Eda Acıkgoz, Mustafa Cakir **Title:** Investigation of metabolic signatures of polyploid giant cancer cells in colon cancer with infrared spectroscopy
		Sercin Ozlem-Caliskan; Rahsan Ilikci-Sagkan; Hatice Karakas; Sevgi Sever; Cansu Yildirim; Mısra Balikci; Hatice Ertabaklar **Title:** Photodynamic inactivation of Leishmania tropica promastigotes by malachite green: An in vitro study
		Serkan Sahin

	Exploring the Color Change in the Partially Coherent Light Beams Passing Through Human Eye Lens
Prof. Hulusi BEHCET **Conference room** **Oral presentations** **Prof. Alev Meltem ERCAN** **Asst. Prof. Guven AKCAY**	**Cosar Uzun**; Nurten Erdal; Ozlem Izci Ay; Umit Karakas; Didem Derici Yildirim; Huseyin Durukan; Mahmut Berat Akdag; Mehmet Emin Erdal **Title:** Examining the Genetic Effects of Radiofrequency Electromagnetic Radiation (Mobile Phone Frequency; 1800, 2100 MHz) On Amniocyte
	Yasin Karamazi; Mustafa Emre; Salih Cetiner **Title:** The Effect of 5G (6 GHz) Radiofrequency Electromagnetic Field on Vitality and Apoptosis in Rat Blood Cell
	Burak Tan and Nurcan Dursun **Title:** Investigation of Subsequent Long-Term Potentiation in Primed Hippocampal Dentate Gyrus by Low-Frequency Stimulations Varying Among 0.5-5 Hz
	Fazile Canturk Tan; Burak Tan; Betul Yalcin; Suleyman Dasdag; Korkut Yegin; Arzu Hanim Yay **Title:** Changes in the Histopathology and in the Proteins Related to the MAPK/ERK Pathway in the Brains of Rats Exposed to Pre-and Postnatal Radiofrequency Radiation
Conference room A **Oral presentations** **Prof. Isıl ALBENIZ** **Asst. Prof. Evren KILINC**	**Gizem Samgane**; Sinem Tuncer; Rafig Gurbanov **Title:** Investigation of the Synergistic Effects of Treatment with Chlorhexidine and Azithromycin on Escherichia coli by Infrared Spectroscopy
	Hatice Fulya Yilmaz and Özlem Bozkurt Girit **Title:** Therapeutic Potential of Agmatine on Methotrexate-Induced Peripheral Neuropathy
	Osman Cagri Ilhan; Muhammed Ali Gencaslan; Salih Varol; Sumeyye Arikan; Dicle Aslan; Fazile Canturk Tan

		Title: Evaluation of The Effect on Telomere Length of Occupational Radiation Exposure of Health Professionals
		Mehmet Esref Alkis; Mehmet Zulkuf Akdag; Sevgi Irtegun Kandemir **Title:** Effects of 50 Hz magnetic fields on chemotherapy and electrochemotherapy treatments
	Conference room B **Oral presentations** **Prof. Ayse DEMIRKAZIK** **Assos. Prof. Aykut PELIT**	**Denizhan Karis**; Gulfidan Cakmak; Alev Meltem Ercan; Fatma Ates **Title:** The Relationship of Serum Zinc and Copper with Nitric Oxide and Asymmetric Dimethylarginine in Smokers
		Muhammet Bektas; Bircan Dinc; Tahsin Ertas; Recep Ustunsoy **Title:** Effect of Solvent on Molecular Interactions: NAD-Diphtheria Toxin Case
		Aysegul Gemici and Osman Sinen **Title:** The Effect of Anesthesia/Stereotaxic Surgery on Cognitive Function in Male Rats
		Sevgi Gunes; Cagatay Han Turkseven; Belgin Buyukakilli **Title:** Effects of Thymus Vulgaris Oil on Sodium Hypochlorite Toxicity in Rats
11:40-12-30	**Ibni Sina Conference Room Conference** **PANEL** **Prof. Belma TURAN**	**Prof. Belma Turan** **Title:** The effects of insulin resistance on membrane ion transport mechanisms in mammalian cardiac cells
		Associate Prof. Yusuf Olgar **Title:** Insulinotropic therapy in aging: GLP agonism and cardiovascular effects
		Associate Prof. Erkan Tuncay **Title:** The Role of Lysine Acetylation on KATP Channel Function in Cardiomyocytes
		Assistant Aysegul Durak **Title:** The role of stim1-orai1-mediated Ca^{2+} entry in heart contraction in the model of insulin resistance
		Associate Prof. Deniz Billur **Title:** The Relationship Between Connexin-43 and Prolonged QT-interval in surface recorded ECGs of the insulin-resistant Mammalian Heart

12:30-13:00	**Lunch (University Dinner Hall)**	
13:00-13:30	**Poster Presentations**	
13:30-14:15 **14:15-15:00**	**Ibni Sina Conference Room Conference** **Prof. M. Zulkuf AKDAG** **Assoc. Prof. Fatma ATES**	**Prof. Hua-Qian YANG** Hua-Qian Yang, Marta Pe´rez-Herna´ndez, Jose Sanchez-Alonso, Andriy Shevchuk, Julia Gorelik, Eli Rothenberg, Mario Delmar, William Coetzee **Title:** Ankyrin-G mediates targeting of both Na^+ and K_{ATP} channels to the cardiac intercalated disk
		Prof. Ferit PEHLIVAN **Title:** Specialisation and Integration in Science and its Reflections to Education
15:00-15:45	**Coffee Break and Poster Presentations (20-40)**	
15:45- 16:35	**Ibni SINA Conference Room Oral presentations** **Prof.Yekbun ADIGUZEL** **Assoc. Prof. Erkan TUNCAY**	**Fulya Dal Yontem**; Sefer Baday; Seyma Bulut; Behnaz Ghaderkalankesh; Ebru Haciosmanoglu; Gulden Budak; Muhammet Bektas; Handan Akcakaya **Title:** Development of Novel Mitochondrial Fission Inhibitors Targeting Drp1-GTPase Interaction
		Simge Senay; Deniz Agirbasli; **Devrim Oz-Arslan** **Title:** The impact of high-density lipoprotein on the polarization and mitochondrial function of monocytes and macrophages
		Asli Aykac; Dilek Ozbeyli; Kerem Teralı; Duygu Hanoglu; Kemal Husnu Can Baser; Goksel Sener **Title:** Evaluation of the Cognitive and Cholinergic Effect of R. Damascena in a Rat Amnesia Model
		Ferdi Dogan; Miktat Aktas; Mehmet Ismail Gursoy **Title:** Classification of Skin Diseases with Different Deep Learning Models and Comparison of the Performances of the Models
		Esra Karakoc; Cagla Celik; Guven Akcay

Prof. Aziz SANCAR **Conference room** **Oral presentations** **Prof. Murat PEHLIVAN** **Prof. Isıl OCAL**	**Title:** Investigation of Neuroprotective and Therapeutic Effects of Transcranial Direct Current Stimulation in Experimental Traumatic Brain Injury Model
	Huseyin Emre Ozturk and **Guven Akcay** **Title:** Investigation of Therapeutic Effects of tDCS on Hippocampal Glutamate and Calcium Excitotoxicity in an Experimental Traumatic Brain Injury Model
	Harun Basoglu **Title:** Identification of a New In-Vitro Model of Epilepsy Due to Trk-B Receptor Activation in Brain Slices
	Yusuf Muslum Ergul and Güven Akçay **Title:** Therapeutic Effects of Transcranial Direct Current Stimulation on the Glutamatergic Pathway in an Experimental Model of Cerebral
Prof. Hulusi BEHCET **Conference room** **Oral presentations** **Prof. Belgin BUYUKAKILLI** **Assos. Prof. Mehmet SARAC**	**Ceylan Verda Bitirim**; Yusuf Olgar; Kardelen Genc; Dunya Aydos; Ebru Kocakaya; Okan Ekim; K.Can Akcalı **Title:** Effects of Exosomal Modulation on Cardiac Regeneration and Cardioprotection in Cardiomyocytes and Cardiac Stem Cells
	Handan Kayhan; **Elif Taspinar Simsek**; Sanem Gökcen; Elcin Ozgur Buyukatalay **Title:** Hyperthermic effects on healthy fibroblast and leukemia cells
	Hesam Saghaei Bagher; Emel Sokullu; **Ozlem Oztopuz** **Title:** The combination of cyclophosphamide treatment and low-level laser irradiation (LLLI) attenuates cell growth ın RG2 cell line
	Emel Sokullu **Title:** Micro/Nano Platforms for Optogenetic Technologies and Photobiomodulation
Conference room A **Oral presentations** **Prof. Nazmi YARAS**	**Ibrahim Bozgeyik** **Title:** Curcumin selectively activates the expression of HIF1A-AS1 but not HIF1A in triple-negative breast cancer cell
	Pinar Bayram and Muhammed Yayla **Title:** The effect of jaceosidin on insulin resistance in human hepg2 cells

	Assoc.Prof. Bilge OZERMAN EDIS	**Ferah Bulut**; Munevver Gizem Hekim; Batuhan Bilgin; Muhammed Mirac Kelestemur; Muhammed Adam; Aslisah Ozgen; Mete Ozcan **Title:** Humanin Inhibits Diabetes-Induced Apoptosis and Inflammation in Hippocampus and Prefrontal Cortex in Mice
		Muhammed Adam; Ferah Bulut; Batuhan Bilgin; Muhammed Mirac Kelestemur; Münevver Gizem Hekim; Semih Dalkilic; Mete Ozcan **Title:** Asprosin Modulates miRNA-181a Expression in Dorsal Root Ganglions of Diabetic Mice
	Conference room B **Oral presentations** **Assoc. Prof. Ismail ABIDIN** **Assoc. Prof. Ozlem BOZKURT**	**Gökhan Zorlu**; Özge Zorlu; Aslısah Ozgen; Gulendam Ozbeg; Aysun Ucer; İbrahim Halil Gungor; Aslihan Cakir; Gaffari Turk; Ihsan Serhatlioglu **Title:** Consumption of High Fructose Corn Syrup Delays Puberty in Male Rats
		Seval Musuroglu Keloglan; Leyla Sahin; Sayad Kocahan **Title:** Effect of Caffeine on Hippocampal SNAP25 and GFAP in a Social Isolation Stress
		Nimet Temur; **Yusuf Muslum Ergul**; Cagla Celik; Ismail Ocsoy; Guven Akcay **Title:** Early Diabetes Estimation with Machine Learning
		Sanem Arikan **Title:** Associations of IL-6 Polymorphisms and Haplotypes with Obesity in a Turkish population
16:35-17:20	**Ibni Sina Conference Room** **CONFERENCE** **Prof. Ferit PEHLIVAN** **Assoc. Prof. Fazile CANTURK TAN**	**Prof. Zehra Sayers** Zehra SAYERS, Goksin LIU and Canan ATILGAN **Title:** Use of synchrotron radiation for structural studies of metal binding proteins
17:25	**Travel**	**Sightseeing and Dinner (Samsat)**

HOURS	SESSIONS (DAY3)	FRIDAY (September 2nd, 2022)
09:00-09:45	Ibni Sina Conference Room Conference Prof. M. Can AKYOLCU Assoc. Prof. Asli AYKAC	**Prof. Erol Eroglu** **Title:** In Silico an Investigation of Allostery in Proteins: Applications to MPro and Carbonic Anhydrase II
09:45-10:30		**Prof. Erdinc Sezgin** **Title:** Measuring biophysical properties of cells in health and disease
10:30-10:45	*Coffee Break*	
10:45-11:40	Ibni SINA Conference Room Oral presentations Assoc.Prof. Devrim SARIBAL Assoc.Prof. Ayhan UNLU	Celal Guven; **Salih Tunc Kaya**; Eylem Taskin Guven **Title:** The Protective Effect of Melatonin on Doxorubicin-Induced Damage in Cardiomyocytes Via HMGB1/TLR4/MAPK Pathways
		Hande Kasap Can; Devrim Oz-Arslan; Beki Kan; **Zeynep Aslıhan Durer** **Title:** An Investigation into the effect of the Different Vinculin Isoforms in the Morphology of H9C2 Cells
		Ekrem Yasar; Erol Eroglu; Nazmi Yaras **Title:** An Investigation Effect of AngII and Ang (1-7) Binding on The Dynamics of AT2 Receptor by Micro-Second MD Simulation
		Gulsun Memi; Elif Merve Betul Yanılmaz; Ebru Annac; Mehmet Salih Kaya **Title:** Effects of thymoquinone on kidney and bladder in cyclophosphamide-induced oxidative damage
	Prof. Aziz SANCAR Conference room Oral presentations Prof. Erol EROGLU	**Fatma Ates**; Ramazan Sabirli; Duygu Tarhan; Aylin Koseler; Alev Meltem Ercan **Title:** Evaluation of Trace Element Alterations Caused by Coronary Artery Disease

	Assoc. Prof. Bilge GUVENC	**Evren Kılınc**; Zeynep Aslihan Durer; Merve Oztug; Emel Baloglu **Title:** Proteomic investigation of acute and chronic hypoxia reoxygenation responsive hemostatic proteins and pathways in H9C2 cardiomyocytes
		Elif Merve Betul Yanilmaz; Gulsun Memi; Mehmet Salih Kaya; Ebru Annac **Title:** The Protective Effects of Thymoquinone on Cyclophosphamide-Induced Cardiotoxicity
		Ceren Celik; Fulya Kucukcankurt; Ayca Dogan; Rafig Gurbanov; Esra Basar Gursoy; Bedile Irem Tiftikcioglu; Feride Severcan **Title:** The role of pyridostigmine (mestinon®) treatment in myasthenia gravis disease: an infrared spectroscopic study by using human serum
	Prof. Hulusi BEHCET **Conference room** **Oral presentations** **Prof. Muhammet BEKTAS** **Asst. Prof. Fulya DAL YONTEM**	Selcuk Sen and **Ebru Hacıosmanoglu** **Title:** Comparing the Effects of Telmisartan, Perindopril, and Nebivolol on Neuroprotection in LPS-induced Neuron Like Cells
		Hakan Er **Title:** Effects of Acetyl-L-Carnitine Administration on EEG in Rats Exposed to Chronic Ethanol
		Hatice Keser; Ozlem Bozkurt Girit; Selcen Aydın Abidin; Mehmet Dincer Bilgin; Ahmet Alver; Ismail Abidin **Title:** Behavioral and Neurochemical Effects of High Cholesterol Diet on Brain Derived Neurotrophic Factor (Bdnf) Heterozygous Mice
		Kamil Savas **Title:** The effect of end plate distribution on motor unit potential duration and consecutive motor unit potential instability

	Conference room A **Oral presentations** **Assoc. Prof. Metin BUDAK** **Assoc. Prof. Erdal BINBOGA**	**Mehmet Saraç**; Unal Bakal; Tugay Tartar; Tuncay Kuloglu; Süleyman Aydin; Ibrahim Akdeniz; Meltem Yardim; Mustafa Yilmaz; Mustafa Aydin; Ahmet Kazez **Title:** A new biomarker for the diagnosis of experimental uniateral ureteropelvic junction obstruction: renalase
		Melike Nur Yangin; Esra Basar Gursoy; Bedile Irem Tiftikcioglu; Feride Severcan **Title:** Evaluation the effect of prednisolone (deltacortril®) on myasthenia gravis by infrared spectroscopy
		Muhittin Önderci; Mehmet Bulbul; İlyas Sahin **Title:** Investigation of Proline Rich Acidic Protein 1 (Prap1) Levels in Preterm Delivery
	Conference room B **Oral presentations** **Prof. Nihal HAMAMCI** **Assoc. Prof. Mehmet Esref ALKIS**	**Selma Solgun Dag**; Davut Ozbag; Egemen Kizilay **Title:** Investigation of Thorax Deformities in Different Clinical Types of Patients with Cerebral Palsy
		Gulru Esen; Rabia Ruya Gurler; Erman Altunisik; Mehmet Sirik **Title:** Retrospective Evaluation of Brainstem Volume in Migraine Patients
		Serhat Yaslikaya **Title:** Determination of the effect of vitamin D on the sense of smell
	Conference room C **Oral presentations** **Prof. Mehmet Kaya OZER** **Assoc. Prof. Ihsan SERHATLIOĞLU**	**Suleyman Uçuncuoglu** **Title:** DNA Tension may increase CRISPR-Cas9 and sgRNA dissociation/association rate
		Yasin Gokce **Title:** The Efficacy of Some Pharmacological Agents with Suppressive Properties Against SOCE

		Nazlı Ezer Ozer; Bahar Ozturk Kurt; Ayca Dogan; Semra zdemir **Title:** Effects of high carbohydrate and high fat diets on skeletal muscle lipid and trace element contents
11:40-12:30	**Ibni Sina Conference Room** **PANEL** **Prof. Bahar GUNTEKIN**	**Prof. Bahar Guntekin** **Title:** Event-related EEG Brain Oscillations Methods and Applications
		Prof. Bahar Guntekin **Title:** Event-related EEG oscillations in healthy individuals and dementia groups and non-invasive neuromodulation of oscillations
		Phd student Tuba Akturk **Title:** The use of transcranial alternating current stimulation to modulate EEG-brain oscillations with measurable effect on cognition
		PhD. Ebru Yildirim **Title:** Investigation of Cognitive Functions in Different Types of Dementia by the Event-related EEG Brain Oscillations
12:30-13:30	**Lunch**	**(University Dinner Hall)**
13:30-13:45 **13:45-14:30**	**Ibni Sina Conference Room Conference** **Prof. Ismail GUNAY** **Prof. Eylem TASKIN GUVEN**	**Prof. Bayram Yilmaz** Yavuz Yavuz, Ozge Baser, H. Bugra Ozgun, Deniz Oyku Ozen, Sami Agus, Zehra Yagmur Erol, Bayram Yilmaz **Title:** Hypothalamic Circuits Controlling Energy Metabolism: Use of Electrophysiology, Fluorescent Microscopy and Opto/Chemogenetic Methods with Transgenic Mice Models
		Prof. Zoltan Papp **Title:** Cardiac myofilament protein alterations during health and disease
14:30-14:15	**Coffee Break**	
14:45-15:30	**Ibni Sina Conference Room Conference**	**Prof. Suresh Tyagi** Suresh C. Tyagi, M.Phil., Ph.D., D.Sc. (Hon), FAHA, FAPS, FIACS

15:30-16:15	**Prof. Erdinc SEZGIN** **Asist. Prof. Omer Can DEMIRTAS**	**Title:** Dysbiotic 1-Carbon Metabolism in Growth Retardation
		Prof. Murat Pehlivan **Title:** Biophysical Overview of the Occurrence of Diseases and Application of Bioresonance as a Complementary Treatment Option
16:15-16:30	**Coffee Break**	
16:30-16-50	**Ibni Sina Conference Room Showing Respect to the Master** **Assoc. Prof. Celal GUVEN** **Asst. Prof. Ebru HACIOSMANOGLU**	**Prof. Ferit Pehlivan** **Title:** Commemoration of "Prof. Hamza ESEN"
		Prof. Isıl Albeniz **Title:** Commemoration of "Prof. Demir TIRYAKI"
16:50-17:30	**Closing & Awards Ceremony**	
19:00	**Dinner**	**Gala Dinner (Adıyaman Perre Practice Hotel)**

Notice. We will depart at 3:00 am to watch the sunrise on Mount Nemrut and the ruins of the ancient kingdom of Commagene. Please register at the registration desk.

	Saturday, (September 3rd, 2022)
03:00	Departure from Hotel
05-45-06:40	Nemrut Mountain
07:40-08:40	Breakfast (Gerger Falcon Hill)
09:10-09:40	Arsameia Sacred Area
09:55-10:20	Cendere Bridge
10:35-11:20	Tumulus and Mounds
13:00-15:00	Lunch (Çat Dam Social Facilities Çelikhan)

ORAL PRESENTATIONS

1. Elena Pohl
Dual transport function of mitochondrial uncoupling proteins

2. Naranjan S. Dhalla
Mechanisms for the Loss of Adrenergic support in Heart Failure

3. Morad Martin
Cardiac Calcium signaling and Arrhythmia: CPVT1, Cardiac Ryanodine Receptors, and Human Stem Cells derived Cardiomyocytes

4. Akifumi Kishi
Towards understanding and controlling human sleep Dynamic

5. Ozlem Bozkurt Girit, Hatice Fulya Yilmaz, Gizem Donmez Yalcın and Mehmet Dincer Bilgin
Low-intensity low-frequency pulsed ultrasound and withaferin A ameliorates nerve damage in diabetic neuropathy

6. Fatma Ozlem, Gokcer Eskikurt, Aslı Ceren Macunluoglu, Asiye Nurten and Ayfer Dayi
Evaluation of the effect of caffeine consumption on cognitive functions by electroencephalography in university students

7. Hesam Saghaei Bagheri, Ozlem Oztopuz, Fulya Yontem, Reza Rahbarghazi and **Emel Sokullu**
Melatonin coupled with low-level laser irradiation potentially exerted oncostatic effects on rat glioma cells via apoptosis pathway

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11. Serkan Sahin
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56. Ekrem Yasar, Erol Eroglu and Nazmi Yaras
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Keynote Speakers

DUAL TRANSPORT FUNCTION OF MITOCHONDRIAL UNCOUPLING PROTEINS

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Abstract

The mitochondrial carrier superfamily (SLC25) comprises at least 53 proteins and is the largest family of solute transporters in humans. Members of this family transport various solutes across the mitochondrial membrane, including carboxylic acids, fatty acids, amino acids, inorganic ions, and nucleotides.

Although these membrane proteins are critical to many cellular processes, their precise structures, biological functions, and transport mechanisms remain elusive. I focus on two subfamilies: adenine nucleotide translocases (ANT) and uncoupling proteins (UCP). I present our new concept for UCP expression in mammalian tissues, explaining their involvement in mitochondrial metabolism and their dual function as proton and C4 metabolite transporters. Finally, I discuss the existing hypotheses on UCP and ANT-mediated proton transport and present our model for ANT-mediated fatty acid (FA) anion translocation as part of the FA cycling mechanism.

Keywords: Mitochondrial carrier superfamily, Adenine nucleotide translocase, Long chain fatty acids, C4 metabolites, Obesity

MECHANISMS FOR THE LOSS OF ADRENERGIC SUPPORT IN HEART FAILURE

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Abstract

Although there occurs a loss of adrenergic support for maintaining cardiac function in heart failure, the mechanisms for this defect are not fully understood. We have investigated alterations in the inotropic responses to isoproterenol in myocardial infarction induced heart failure in rats at different stages upon occluding the coronary artery. Furthermore, changes in different components of adrenergic signal transduction pathway including β1-adrenergic receptors (β1-AR), G-proteins and adenylyl cyclase were examined in the failing left ventricle. Depressions in the inotropic responses to isoproterenol were associated with reductions in the β1-AR density at early, moderate, and severe stages of heart failure. The activation of adenylyl cyclase and the increase in cardiac cyclic AMP content by isoproterenol were also decreased in the failing hearts. Gi-protein content, mRNA levels for Gi-protein as well as pertussis toxin (PT) catalyzed ADP-ribosylation and PT-induced activation of adenylyl cyclase were increased in heart failure. On the other hand, cholera toxin (CT) induced ADP- ribosylation and CT-induced activation of adenylyl cyclase were reduced in heart failure. The mRNA level for Gs-protein were increased in heart failure whereas Gs-protein content was depressed in failing hearts at severe stages only. It was also observed that alterations in β1-AR mediated signal transduction pathway in heart failure were attenuated by treatment of heart failure animals with blockers of the renin-angiotensin system. These observations indicate that the depressed activation of adenylyl cyclase by isoproterenol may not only be due to decreased β1-AR density but also due to increased Gi-protein content as well as decreased bioactivity of Gs-proteins in the failing hearts. In addition, various pathogenic factors such as oxidative stress, Ca2+-handling abnormalities and metabolic defects appears to explain changes in the β1-AR signal transduction as well as loss of adrenergic support in heart failure.

Keywords: Heart failure, Myocardial infarction, β-adrenoceptors, Adenylyl cyclase, G-proteins

Invited Speeches

CARDIAC CA^{2+} SIGNALING AND CPVT1-ASSOCIATED RYR2 POINT MUTATIONS: EVIDENCE FOR EPIGENETIC REMODELING

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Abstract

Aim: Contraction of the Mammalian heart is initiated by entry of calcium through calcium channel that triggers release of calcium from ryanodine receptors (RyR2). Over 150-point mutations in RyR2 are associated with CPVT1 arrhythmia. Studies on CPVT1 have used either transgenic mice or recombinant mutant RyR2 expressed in HEK cells. Although much has been gained by these two approaches on the structure/function of RyR2, the mice heart is farfetched from human heart in size and ion-channel composition, and HEK cells fail to express all the calcium signaling pathways of human heart, obviating remodeling.

Material and Methods: CRISPR/Cas9 gene editing technique in human induced pluripotent stem cells (hiPSC) was used to mutate RyR2 Ca^{2+}-binding residues associated with CPVT1, where I_{Ca}- and caffeine-triggered SR Ca^{2+} releases were measured in voltage-clamped and TIRF-imaged cardiomyocytes.

Results: 1) Ca^{2+}-signaling aberrancies in CPVT1-associated (RyR2-Q3925E) and CPVT1-unassociated (RyR2-E3848A) mutants were similar. 2) I_{Ca} densities of mutant-cells were enhanced, but their Ica- and caffeine-triggered cytosolic Ca^{2+}-rise or SR Ca^{2+} release were suppressed. 3) Arrhythmic Fura-2 Ca^{2+}-transients persisted in mutant cells but were not accompanied by ER-GCaMP6 SR-release signals. 4) Caffeine failed to trigger Ca^{2+} release in voltage-clamped mutant cells, but in intact cardiomyocytes ~20% to ~70% of cells responded to 5 & 20mM caffeine, respectively. 5) 20mM caffeine triggered responses were, however, delayed, slow, and 2-APB-, or ruthenium red-sensitive.

Conclusion: 1) Mutations of RyR2 Ca^{2+} binding residues, irrespective of CPVT1 association, have suppressed I_{Ca}- and caffeine-triggered Ca^{2+} releases, suggesting interaction between RyR2 Ca^{2+} and caffeine binding-sites. 2) Ca^{2+} influx and Ca^{2+} release from extra-SR pools of remodeled mutant cardiomyocytes underlie the spontaneous arrhythmic Ca-transients.

Keywords: Catecholaminergic polymorphic ventricular tachycardia (CPVT1), Epigenetic, EC-coupling remodeling, SR Calcium release, Cardiac Ryanodine Receptor, CPVT1 Mutations in RYR2 Calcium binding residues, L-type Calcium Current

CARDIAC MYOFILAMENT PROTEIN ALTERATIONS DURING HEALTH AND DISEASE

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Abstract

Myocardial systolic and diastolic performances are impaired in heart failure (HF) with reduced ejection fraction (HFrEF) and HF with preserved ejection fraction (HFpEF). Cardiomyocyte contractile function depends on the interplay between intracellular Ca^{2+} concentration changes and the Ca^{2+} responsiveness of myofilament proteins. Recent evidence points to a central role of inherited/acquired sarcomeric protein alterations not only in cardiomyocyte dysfunction but also in the remodeling process of the myocardium (e.g., in hypertrophic cardiomyopathy, and in dilated cardiomyopathy). Changes in the expression of genes encoding cardiomyocyte proteins (e.g., during postnatal development or during the development of HF), oxidative post-translational protein alterations (e.g., sulfhydryl group oxidation, carbonylation, fragmentation, etc. during ischemia/reperfusion injury), and/or changes in intracellular signaling processes (leading to distinct patterns of myofilament protein phosphorylation) are all considered to contribute to the impaired sarcomere function. Characterization of the molecular aspects of cardiac contractile performance (i.e., determination of Ca^{2+} dependent force production, its Ca^{2+} sensitivity, and the Ca^{2+} independent passive force) typically requires in vitro investigations of simplified biological systems, e.g., physiologic measurements in single isolated cardiomyocytes or biochemical assays on myofilament proteins. Elucidation of the mechanical consequences of sarcomeric protein alterations can bring us closer to the development of therapeutic solutions to preserve healthy morphological and functional state of the heart muscle. Recently, small molecules are increasingly considered for the modulation of cardiac performance via sarcomeric protein targeting (e.g., Ca^{2+} sensitizers, direct myosin activators, and direct myosin inhibitors) and thereby to prevent the progression of myocardial remodeling and HF. In short, substantial progress has been made in exploring the cellular and subcellular background of healthy/diseased cardiac function in recent decades. The accumulation of knowledge holds promise for the accurate molecular interpretation in a high number of conditions associated with abnormal cardiac contractile function.

Keywords: Heart failure, Cardiomyocyte function, Sarcomere dynamics, Post-translational protein alterations, Therapy

HYPOTHALAMIC CIRCUITS CONTROLLING ENERGY METABOLISM: USE OF ELECTROPHYSIOLOGY, FLUORESCENT MICROSCOPY AND OPTO/CHEMOGENETIC METHODS WITH TRANSGENIC MICE MODELS

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Abstract

Obesity has become a major public health problem worldwide. The fundamental cause of obesity is the energy imbalance between calorie intake and expenditure. However, genetics, individual, social, and environmental factors also play role in the etiology of this complex metabolic disorder. The hypothalamic arcuate nucleus (ARC) Agouti-Related Peptide (AgRP) and Proopiomelanocortin (POMC) neurons play important roles in hunger and satiety feelings, respectively. Our recent findings have shown the importance of Tyrosine hydroxylase (TH) neurons in the hypothalamic feeding pathways. These three circuits process and maintain energy balance. Signaling between the brain and peripheral factors is usually impaired in obesity and metabolic syndrome. Recent discovery of opto/chemogenetic techniques have allowed neuroscientists to better elucidate the hypothalamic circuits controlling energy metabolism by selective excitation or inhibition of specific neuron groups. Use of viral vectors and transgenic mice technology are very useful tools in examining AgRP, POMC and TH projections and circuitry in the brain. In this presentation, utilization of electrophysiology (including patch-clamp technique), opto/chemogenetic and fluorescent microscopy methods in neuroendocrine research will be reviewed.

Acknowledgement: This study was supported by TÜBİTAK (Project # 118S245).

Keywords: Hypothalamus, Obesity, Feeding, AgRP, POMC, Optogenetic, Chemogenetic

DYSBIOTIC 1-CARBON METABOLISM IN GROWTH RETARDATION

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Abstract

Epigenetic DNA methylation (i.e., 1-carbon metabolism) generates homocysteine, unequivocally. That is why during pregnancy folic acid is administered, to control detrimental effects of elevated levels of homocysteine (i.e., hyperhomocysteinemia) in gene imprinting and off-printing (i.e., epigenetic memory). Children born with HHcy have very several muscular skeletal deformities, including growth retardation. Here we focus that gut dysbiotic microbiome instigates 1-carbon metabolism and HHcy that causes growth retardation and create skeletal muscle deformities. We test here whether high methionine diet (HMD, substrate for homocysteine, an amino acid rich in red meat) can cause skeletal muscle and growth retardation and treatment with probiotic mitigates skeletal muscle growth retardation. To test this hypothesis, we employed wild type (WT) and cystathionine beta synthase (CBS) heterozygote KO mice with and without HMD and with and without probiotics (PB, Lacto bacillus) in drinking water for 16 weeks. Skeletal muscle matrix metalloproteinase (MMP) activity (a hallmark of remodeling) was measured by zymography. The muscle function was measured by electric stimulation. The results suggest that the compared to WT, CBS mice has reduced growth. The MMP-2 activity was robust in CBS and HMD mice and was attenuated by PB treatment. The electrical stimulation magnitude was decreased in CBS and CBS treated with HMD, interestingly; the PB treatment mitigated the skeletal muscle growth retardation and atrophy. The results suggest that individuals with moderate homocysteinemia, on red meat diet, are more prone to get skeletal muscle injury and dysfunction.

Keywords: Epigenetics, DNMT, TET, Gene writer, Gene eraser, Homocysteine

TOWARDS UNDERSTANDING AND CONTROLLING HUMAN SLEEP DYNAMICS

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Abstract

Sleep is a fundamental life phenomenon that occupies about one-third of our lives. Considering that sleep contributes significantly to mental and physical health, elucidating the mechanism of sleep is of great biological and clinical importance. I have been engaged in research on the analysis and evaluation of the dynamics of sleep stage transitions in humans (including healthy subjects and patients). In this presentation, I would like to discuss the analysis, assessment, and control of human sleep dynamics, including the development of novel techniques that contribute to the acquisition of good quality of sleep.

Keywords: Sleep deprivations, Sleep dynamics, Sleep quality

MEASURING BIOPHYSICAL PROPERTIES OF CELLS IN HEALTH AND DISEASE

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Abstract

Remodelling of our cells as response to environmental changes is essential for their survival and function. Ability of immune cells to pass through tight epithelial cell layers from circulating blood during infection, ability of tumour cells to travel through the body during metastasis, migration potential of the cells after epithelial-to-mesenchymal transition could be examples where cells undergo extensive remodelling. Although numerous studies aimed at finding protein markers during such cellular processes, there is a major gap in our understanding of how collective biophysical properties of the cells (such as stiffness, membrane fluidity, viscosity etc) alter during these crucial biological processes. Similarly, our understanding of how biophysical properties of cells change in diseases is also limited. To gain a thorough mechanistic perception of cellular processes and diseases, it is essential to fill this gap and have a clear and quantitative picture of biophysical remodelling of the cells.

We and others have made extensive effort to unravel the biophysical aspects of cells in a quantitative manner. To achieve this, we developed advanced imaging approaches that could reveal the molecular details with very high spatiotemporal resolution. These technologies allowed us to see how biophysical properties of cells play crucial roles for signalling from molecular to cellular level. Although these technologies were extremely useful to study biophysical aspects of cellular life at the molecular level, their low sampling (one cell at a time) has been a major obstacle to apply them to medical problems that require measuring thousands of cells. This can be overcome with high throughput methodologies that can robustly report on the ensemble biophysical properties of cells which require reliable reporters and instruments. Thus, while developing advanced instrumentation, we also develop reliable probes to quantify different biophysical properties of cells. Here, I will discuss our approach from probe development to high throughput biophysical analysis.

Keywords: Plasma membrane, Microscopy, Cellular biophysics, Cellular signalling

ANKYRIN-G MEDIATES TARGETING OF BOTH NA^+ AND K_{ATP} CHANNELS TO THE CARDIAC INTERCALATED DISK

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Abstract

It is a common theme in cardiac electrophysiology that ion channels in the same subdomain have the potential to interact with each other, as well as with other channels and transporters. Voltage-gated Na^+ channels are responsible for the initiation and propagation of action potentials in cardiac myocytes with pore-forming subunit of Nav1.5. The sarcolemmal ATP-sensitive K^+ (K_{ATP}) channel with the pore-forming subunit of Kir6.2 is one of the most abundant channels expressed in cardiac myocytes and it promotes action potential shortening adaptation with elevated heart rates. We investigated targeting mechanisms of Na^+ and K_{ATP} channels to the intercalated disk of cardiac myocytes. Patch clamp and surface biotinylation data show reciprocal downregulation of each other's surface density. Mutagenesis of the Kir6.2 ankyrin binding site disrupts this functional coupling. To allow sequential measurements of Na^+ and K_{ATP} currents in the same membrane patch, we have developed a novel duplex patch clamp technique show that Na+ and K_{ATP} currents functionally co-localize at the intercalated disk, but not at the lateral membrane of cardiomyocytes, which was confirmed by angle scanning ion conductance microscopy (SICM) recordings at higher resolution. Quantitative super resolution imaging with stochastic optical reconstruction microscopy (STORM) shows that Na^+ and K_{ATP} channels are localized close to each other and to Ankyrin-G, but not to Ankyrin-B, at the intercalated disk. Peptides corresponding to Nav1.5 and Kir6.2 ankyrin binding sites dysregulate targeting of both Na^+ and K_{ATP} channels to the intercalated disk, but not to lateral membranes. Finally, a clinically relevant gene variant that disrupts K_{ATP} channel trafficking also regulates Na^+ channel surface expression. In conclusion, we provide evidence that Na+ channels and K_{ATP} channels are morphologically clustered (particularly at the intercalated disk) and that they interact functionally, most likely due to the fact that they are targeted to a common subcellular location by Ankyrin-G. These studies provide a new paradigm when considering pharmacological and genetic aspects of arrhythmogenesis.

Keywords: Ion channel, Nav1.5, K_{ATP}, Ankyrin, Intercalated disk

USE OF SYNCHROTRON RADIATION FOR STRUCTURAL STUDIES OF METAL BINDING PROTEINS

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Abstract

Understanding complex biological mechanisms, such as metal homeostasis, require cross-disciplinary tools to acquire static and dynamic data on the molecular structure. For example, cryo-electron microscopy and/or macromolecular crystallography can be used together with X-ray spectroscopy to obtain static atomic structure of a protein. This information can be complemented with data obtained by techniques like X-ray solution scattering to follow molecular conformations in solution which are needed for explaining protein-protein or protein-ligand interactions. In the last decades a wide range of complementary structural analysis tools have been developed in synchrotron radiation (SR) facilities for such studies.

In this talk I will introduce properties of SR, which make it suitable for structural studies of biological molecules and present our results on two proteins involved in metal homeostasis; a Cd-binding metallothionein isolated from durum wheat (dMT) and the periplasmic ferric binding protein from H. influenzae (FbpA). We used small angle X-ray solution scattering, X-ray absorption spectroscopy and other structural tools to gain a better understanding of the solution structures of dMT and FbpA with and without metals and compared our results with those from macromolecular crystallography. Effects of environmental conditions such as pH and ionic strength on the structures were also studied. Our results show that these proteins display heterogeneous conformational states in solution, and that subtle changes in environmental conditions regulate their metal binding and release mechanisms.

Key words: Synchrotron X-rays, Metallothionein, Ferric binding protein

Conferences

SPECIALIZATION AND INTEGRATION IN SCIENCE AND ITS REFLECTIONS TO EDUCATION

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Abstract

It is possible to divide the history of science into three periods in regard the tendencies of specialization or integration in sciences.

1- The period of polymath scientists (Nearly 1600-1900). Scientists in this period usually were trained in medicine and were competent in every field of science. Galileo, Sanctorius, William Harvey, Galvani, Thomas Young, Julius Mayer, Hermann Helmholtz are both physician ard physicist. They used knowledge gained in one field to explain events in another, they were also biophysicists, in accordance with our definition today.

2- The period of specialization in science (1900-1950). Increase in scientific knowledge exceeding a critical level, the discovery of atoms and subatomic particles, and the theory of relativity caused physicists to move away from the biological world and biology lagged behind. In this period, reductionist approaches were dominant. According to this approach, if you determine the properties of the smallest parts, you can extract the properties of the whole.

3- Holistic or Integrative approaches (1950-…). In the middle of the last century, it was understood that the divisions in science were not correct, bridges between sciences began to be built. Among the most important of these initiatives are Shrodinger's "What is life", Wiener's "Cybernetics", Shannon's "Mathematical Theory of Communication" and Bertalanffy's "General System Theory". The walls between the branches of science begin to break down, collaboration between different disciplines, and consultation of different specialties in practice begin to come to the fore. In the holistic approach, reductionism is avoided, it is realized that the system gains new features that its elements do not have.

In the second half of the last century, biophysics has also emerged as the branch that best represents holism among the biomedical sciences, fusing again two seemingly distant fields such as physics and biology.

Keywords: Specialization, Integration, Interdisciplines

BIOPHYSICAL OVERVIEW OF THE OCCURRENCE OF DISEASES AND APPLICATION OF BIORESONANCE AS A COMPLEMENTARY TREATMENT OPTION

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Abstract

Despite many studies, there is no satisfactory success in the treatment of many diseases today. In most cases, only symptom-suppressing treatments are applied, but the side effects also cause new undesirable situations on the patient. For this reason, different perspectives and different treatment methods are needed for the concepts of disease and health.

A human being can be thought of as a biological machine consisting of software and hardware. Organ systems, which are the biological equipment of this machine, have to work in harmony with each other with certain regulation algorithms. At the heart of this software are the programs to maintain the existence as long as possible and to continue the generation. Molecular stability, maximum function with minimum energy and maximum durability with minimum material are the other basic rules of this process.

In order to maintain its existence, the human biological machine can make modifications in its software and hardware as a result of what it has lived or learned. From a biophysical point of view, organism creates a “new normal" after this adaptation process. Then, it is possible to argue that there is no disease. Disease is the new normal of the body's regulation mechanisms trying to adapt to the new conditions.

Bioresonance is a kind of complementary treatment method which applies very low intensity energy to body by various ways such as electric current, magnetic field, or light at specific frequencies assuming that every organ or tissue has a resonance frequency. Bioresonance therapy seems to restore the systems of the body to their former normal, most stable state.

In the speech, the hardware and software elements of the human as a biological machine will be explained, bioresonance devices will be mentioned and examples of how this method affects as a complementary treatment option will be discussed.

Keywords: Disease, Health, Treatment, Bioresonance, New Normal

IN SILICO AN INVESTIGATION OF ALLOSTERY IN PROTEINS: APPLICATIONS TO MPRO AND CARBONIC ANHYDRASE II

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Abstract

Molecular dynamics (MD) simulation is a powerful and popular method to study allostery in proteins, the phenomenon in which a stimulus at one site on a protein influences the properties of another site on the protein. By calculating the motions of constituent atoms of a protein, MD simulations can enable us to discover the allosteric binding sites and the determination of the mechanistic basis for allostery. Identifying atomic-level mechanisms of allostery is critical for the understanding of many biophysical phenomena in functions of some proteins and structure-based drug design.

Here, we present the results of the investigations of allosteric inhibition mechanisms of two enzymes namely MPro and Carbonic Anhydrase II (CA II) using molecular dynamics simulations. 200 ns all-atom MD simulations were performed for both ligands bonded and apo states. To reveal the allosteric inhibition mechanism of MPro and CA II, some computational analysis approaches such as hydrogen bonding, dynamics cross-correlation, communication propensity, dynamic residue network, and transfer entropy were applied to the trajectory files obtained from MD simulations.

Results indicated that the binding of ligand DHE to the MPro through the hydrogen bonding interactions with GLU278 and THR28 residues. These interactions seem to be able to quantitatively modify the χ1 angle of CYS145 of the catalytic dyad. The modification of the χ1 angle results in a diminishing of the catalytic activity because the modified angle causes an enlargement of the distance between the sulfur (SG) atom of CYS145 and nitrogen (NE2) atom of HIS41. In the case of CA II, the binding of ligand 3G1(benzoic acid) to the CA II causes changes in the χ1 angles of some active site residues such as GLN92, GLN103, ASP110, and THR198. It seems that these changes affect the water network in the active site and result in a diminishing of the catalytic activity.

Keywords: Allostery, Enzyme inhibition, MPro, Carbonic Anhydrase II

PANELS

EVENT-RELATED EEG BRAIN OSCILLATIONS METHODS AND APPLICATIONS

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Abstract

Electroencephalography (EEG) was first recorded in the human brain in 1929 by Hans Berger (Berger 1929). EEG has been a fundamental methodology in the last 30 years to understand brain dynamics and cognitive processes. There are different ways to investigate brain dynamics with EEG. These methods can be listed as follows: (1) Spontaneous EEG studies (2) Event-related Potentials (3) Event-related Oscillations.

The method and theory of event-related oscillations were first developed by Erol Başar and his colleagues at the Institute of Biophysics at Hacettepe University. In the last decade, this methodology and theory have proven their validity and invaded the literature, the new methods have also been described. In this methodology, event-related potentials (ERPs) are recorded during a sensory, cognitive, or emotional paradigm, and ERPs are analyzed in the time and frequency domain.

Delta (0.5-3.5 Hz), theta (4-7 Hz), alpha (8-13 Hz), beta (15-28 Hz), and gamma (28-48 Hz) responses and their dynamics were analyzed in healthy subjects and in different patient groups who had a cognitive impairment. Our group's studies and other studies in the literature showed that during increased cognitive load, delta and theta responses increase, especially over frontal-central areas. However, the patients with cognitive decline had reduced delta and theta responses. There were also abnormal responses in higher frequencies (alpha, beta, and gamma). In this symposium talk, event-related power spectrum analysis, phase-locking analysis, and event-related coherence analysis will be described by giving examples of EEG data from healthy controls and different groups of patients with cognitive impairment.

Keywords: EEG, Brain Oscillations, Event-related oscillations

EVENT-RELATED EEG OSCILLATIONS IN HEALTHY INDIVIDUALS AND DEMENTIA GROUPS AND NON-INVASIVE NEUROMODULATION OF OSCILLATIONS

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Abstract

The electroencephalogram (EEG) is a neurophysiological imaging method often used to understand the functioning of the human brain besides its clinical usage. The brain's oscillatory signals recorded by EEG in a spontaneous state or during a cognitive task can be investigated with various signal analysis methods. The event-related EEG-brain oscillations method shows us how the oscillatory brain responses reflect the working mechanism of the brain during cognitive functions. By investigating (and comparing) event-related EEG-brain oscillations recorded during a cognitive task in normal and cognitively impaired groups, abnormal event-related oscillations can be identified by certain pathologies. In addition, research on the causality of the cognition-brain oscillations relationship can be performed by rhythmic non-invasive neuromodulation methods through brain oscillations that have been linked to a specific cognitive function. Within the scope of this symposium, how brain oscillations can be related to human cognitive processes will be discussed through the findings of both pathology and rhythmic non-invasive neuromodulation research.

Keywords: Brain oscillations, EEG, Neuromodulation, Dementia, Event-related oscillations

THE USE OF TRANSCRANIAL ALTERNATING CURRENT STIMULATION TO MODULATE EEG-BRAIN OSCILLATIONS WITH MEASURABLE EFFECT ON COGNITION

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Abstract

Previous correlational studies have demonstrated that the theta-gamma coupling appears to be an ideal postulation for the neural mechanism of memory functions. In this concept, the larger one cycle of the theta indicates the higher memory capacity by accommodating the more cycle of the gamma. In this study, one of the transcranial electrical stimulation methods, which conducts alternating current through placed electrodes, was used to investigate the oscillatory mechanism of cognitive functions: transcranial alternating current stimulation. It seems quite reasonable to use alternating current stimulation, which allows rhythmic stimulation at a certain frequency, to specifically intervene in the oscillatory activity of the brain. Here, we used individualized theta transcranial alternating current stimulation to "slow down" individual theta frequency (ITF) and assess after effects on memory task performance and/or theta brain oscillations. For this purpose, the 46 healthy young-adult participants were randomly assigned to three groups: sham, stimulation at ITF, and stimulation at ITF-1 Hz. The stimulation was applied to the left frontoparietal area at the frequency calculated over the ITF. During pre- and post-EEG recordings, visual and auditory memory tasks were applied. Results of this study showed that visual memory scores increased in the ITF-1 group after the stimulation. And the possible oscillatory mechanisms that may underlie this behavioral performance enhancement have been studied to help understand the relationship between brain oscillations and cognitive functions with the correlation analyses. It has been observed that the underlying oscillatory mechanism of the modulated behavioral performance is related to the modulated connectivity between the stimulated brain regions. Results of this study suggest that, in healthy individuals, transcranial alternating current stimulation at individual theta frequencies calculated from the individuals' own EEG data can positively affect their behavioral performance beyond the stimulation period. These results are indeed very promising for clinical use in relevant pathologies.

Keywords: EEG, Transcranial alternating current stimulation, Neuromodulation, Brain oscillations, cognition

INVESTIGATION OF COGNITIVE FUNCTIONS IN DIFFERENT TYPES OF DEMENTIA BY THE EVENT-RELATED EEG BRAIN OSCILLATIONS

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Abstract

Dementia is characterized by a decline in cognitive functions. EEG event-related oscillations methodology is used in the evaluation of cognitive functions. Previous studies investigated cognitive functions in patients with dementia by using EEG event-related oscillations methodology. However, these studies compared event-related EEG responses of only a type of dementia and healthy subjects. To our knowledge, there is no study comparing the event-related oscillations of Alzheimer's disease dementia, Parkinson's disease dementia, and Lewy body dementia. Based on this, we aimed to compare the event-related oscillations of patients with Alzheimer's disease dementia, Parkinson's disease dementia, and Lewy body dementia during cognitive functions and investigate possible differences among event-related responses in three different types of dementia. EEGs of 20 patients with Alzheimer's disease dementia, 20 patients with Parkinson's disease dementia, 17 patients with Lewy body dementia, and 20 healthy elderly controls were recorded during visual and auditory oddball paradigms. Event-related power spectrum and phase-locking analysis were performed in the delta, theta, alpha, and beta frequency bands. Delta and theta responses decreased in patients with Alzheimer's disease dementia, Parkinson's disease dementia, and Lewy body dementia compared to healthy controls ($p<0.05$). The decrease in delta and theta responses was more pronounced in patients with Parkinson's disease dementia and Lewy body dementia ($p<0.05$). Alpha and beta responses decreased in patients with Parkinson's disease dementia and Lewy body dementia compared to healthy controls ($p<0.05$). In conclusion, delta, theta, alpha, and beta responses decrease as a result of cognitive decline in patients with dementia. The event-related delta and theta responses are more reduced correlated to the increase in the severity of cognitive impairment. Accordingly, it can be concluded that cognitive impairment is more severe in patients with Parkinson's disease dementia and Lewy body dementia than in Alzheimer's disease dementia.

Keywords: Dementia, EEG, Event-related oscillations

THE EFFECTS OF INSULIN RESISTANCE ON MEMBRANE ION TRANSPORT MECHANISMS IN MAMMALIAN CARDIAC CELLS

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Abstract

The MetS prevalence is increasing rapidly in Türkiye too, and this is currently accepted as a serious health problem. In addition, the average lifetime is significantly prolonged among humans worldwide and the prevalence of systemic insulin resistance parallel to several organ dysfunctions (as about 50% among aged populations) is remarkable as clinical. Cardiovascular diseases are the first cause of mortality among elderly populations (about 40%). Therefore, understanding the underlying mechanisms of insulin resistance-associated pathological conditions are very important for healthy elderly lives. Some experimental and clinical studies pointed out the impact of organ-dependent insulin resistance including heart and vascular system besides systemic insulin resistance on the development of elderly heart insufficiency and/or dysfunction. In insulin resistance-induced experimental animals, there were significantly prolonged QT-intervals in surface ECGs, and the voltage-dependent K^+-channel currents were depressed significantly in freshly isolated left ventricular cardiomyocytes, while there were significantly prolonged action potential duration and increased the voltage-dependent Na^+-channel currents. Furthermore, the Na^+/K^+-pump currents and the Na^+/Ca^{2+}-exchanger currents as well as intracellular levels of Ca^{2+} and Na^+ were increased significantly. Parallel to these changes, there were marked increases in the production of reactive oxygen species and decreases in ATP levels together with depolarization in mitochondrial membrane potential in the isolated cells. Moreover, all these changes could be able to reverse with insulin application. Overall, these experimental data provide strong evidence of the role of cellular insulin resistance in the development of cardiovascular diseases behind systemic insulin resistance.

This work was supported by grants (No. SGAB-216S979) from The Scientific and Technological Research Council of Türkiye.

Keywords: Heart, ECG, Oxidative stress, Metabolism

INSULINOTROPIC THERAPY IN AGING: GLP AGONISM AND CARDIOVASCULAR EFFECTS

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Abstract

Aim: Since incretin action plays a crucial role in glucose metabolism, promoting that agents may have a substantial role in hyperglycemic aging subjects. Recently, sodium-glucose transporter-2 inhibitors and Glucagon-like peptide-1 (GLP-1) agonists are widely used for regulating type 2 diabetes in favor of reducing blood glucose and increasing insulin secretion and appetite suppressant properties. As GLP-1 activation exerts biphasic action (early and late) we aimed to elucidate the early effect of GLP-1 agonists on aging-related cardiac dysfunction in aged mice.

Material and Methods: 6 months old (Adult) and 24 months old (Aged) BALB/c mice were used. We performed in-vivo electrocardiography and cellular-based in vitro electrophysiology experiments.

Results: Electrocardiography measurements from the body surface indicates irregular atypical fibrillations and significant prolongation of the QT intervals were observed shortly after the administration of the acute GLP agonist (0.3 mg/kg liraglutide). Unlikely to adult group, GLP agonism (Liraglutide 1 µM) prolonged the action potential, reduce the K-currents, and increased the Ca^{+2} spark frequency in aged cardiomyocytes. Interestingly, Na-channels become resurgent after GLP activation implying a higher propensity for arrhythmias. Biochemical analysis showed Casein Kinase 2 (CK2) but not Protein Kinase C hyperphosphorylated following early action of GLP agonists in whole-cell aging homogenates. Finally, CK2 inhibition with Silmitasertib (5 µM) completely reversed the GLP-associated downstream signaling.

Conclusion: Incretin effects exhibit downhill processes by dysregulates Na-Ca handling and increasing the propensity for arrhythmia in an aging heart. CK2 inhibition significantly reversed GLP1 agonism pointing to a good translational target for the treatment of cardiovascular diseases.

Keywords: Aging, GLP-1 Agonism, Na-Ca handling

THE ROLE OF LYSINE ACETYLATION ON K_{ATP} CHANNEL FUNCTION IN CARDIOMYOCYTES

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Abstract

Aim: Sirtuins are NAD+ dependent deacetylases and their activities are determined by the NAD+ content. Sirtuins are thought to play an important role in the treatment of type II diabetes, obesity, cancer, aging, and various neurodegenerative diseases. Studies have shown that the electrical and mechanical activities of the heart are significantly reduced as a result of metabolic stress, and these changes are associated with post-translational modifications such as phosphorylation, glycosylation, and acetylation of contractile proteins. In our study, we investigated the role of lysine (K)-Acetylation and sirtuins on K_{ATP} channel function.

Material and Methods: In order to understand the role of K-Acetylation, we incubated the Kir6.2/SUR2A stable transfected HEK293 cells with NAM (20mM; 24h) or Sirtuin1 (Ex527;10µM, 24h) and Sirtuin2 inhibitors (AGK2;5 µM, 24h). We increased the cytosolic NAD+ level by preincubation with the NAD+ precursor nicotinamide mononucleotide (NMN; 2 mM, 24h). Protein K-acetylations, K_{ATP} channel currents, and trafficking were measured using western-blot, inside-out patch-clamp, and biotinylation methods, respectively.

Results: We observed that the K-acetylation of KATP channels was decreased, and total and single-channel K_{ATP} current and surface density were increased with NMN incubation. Inhibiting sirtuins activities with EX5720 and AGK2 abolished the ability of NMN to increase KATP channel surface and current density. EX5720 and AGK2 incubation of the HEK293 cells together with NMN restored the K_{ATP} channel current by increasing the probability of K_{ATP} channel surface expression. To determine the pathophysiological relevance, we performed cellular ischemia assays using isolated rat ventricular myocytes. The results showed that K-Acetylation increased cell death rate due to the decrease in K_{ATP} channel functions, and NMN was reversed by activating sirtuins.

Conclusion: In summary, sirtuin-dependent K-deacetylation positively regulates KATP channels and has a cardioprotective role that depends on K_{ATP} channels (This project was supported by TUBITAK SBAG 117S386).

Keywords: Heart, K_{ATP}, Sirtuin, Lysine-Acetylation

THE ROLE OF STIM1-ORAI1-MEDIATED CA^{2+} ENTRY IN HEART CONTRACTION IN THE MODEL OF INSULIN RESISTANCE

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Abstract

Aim: Metabolic syndrome (MetS) is a serious health problem that is rapidly increasing in all societies today. The main mechanism responsible for intracellular Ca^{2+} intake in cardiomyocytes is L-type Ca^{2+}-channels. However, it has been reported that it contributes to Ca^{2+}-influx, which is activated by the decrease of Ca^{2+} in stores, especially in hypertrophic hearts, and plays a key role in cardiomyocytes. Its role in altered intracellular Ca^{2+} hemostasis in MetS is still unclear. Therefore, we aimed to examine the possible role of SOCE and its components (STIM1 and Orai1) in MetS-induced cardiac hypertrophy.

Material and Methods: 3-month-old Wistar albino rat (n=20) was used in this study. Animals were randomly divided into two groups as control and MetS. For the MetS experimental model, animals were given water with 33% sucrose instead of water for 24 weeks. Animals with metabolic syndrome were included in the experiment, and various electrophysiological analyzes were performed on papillary muscle function and isolated cardiomyocytes. In addition, STIM1 and Orai1 protein and mRNA expressions were analyzed.

Results: We observed a deterioration in contractility in MetS animals and demonstrated the contribution of SOCE by applying a SOCE inhibitor (BTP2). Calcium spark frequency was increased while its amplitude was decreasing in MetS hearts, which was reversed after SOCE inhibition. The amplitude of transient calcium changes in the MetS group was decreased, and it decreased further BTP2 application. Both protein and mRNA levels of STIM1 and Orai1 were increased significantly in MetS hearts.

Conclusion: Although the role of SOCE in hypertrophic and neonatal hearts has been widely demonstrated, we could not encounter any study that concluded whether SOCE chronically regulates the levels of intracellular calcium. In our study, it has been shown that the SOCE mechanism is activated and may contribute to the changes in the calcium mechanism in MetS.

Keywords: SOCE, Cardiac, Calcium, Metabolic syndrome

THE RELATIONSHIP BETWEEN CONNEXIN-43 AND PROLONGED QT-INTERVAL IN SURFACE RECORDED ECGS OF THE INSULIN-RESISTANT MAMMALIAN HEART

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Abstract

Aim: Connexins are the main transmembrane proteins in gap-junction type junctional complexes, and form channels called connexons in the cell membrane. Connexin-43 (Cx43) is the main protein in the myocardium and its localization, relative amount, distribution, and its level of phosphorylation can affect the conduction properties of cardiomyocytes. Studies on metabolic syndrome (Mets; developed insulin resistance) and the elderly heart have also drawn attention to the relationship between insulin resistance and the development of cardiovascular diseases in both conditions. In light of our previous studies, where we have shown that a significant percentage of aged rats have insulin resistance and long QT-intervals similar to those of rats with high-carbohydrate diet-induced MetS, we hypothesized that "in these conditions, there may be structural and functional changes in the connexin protein and may be effective in prolonged QT-intervals".
Material and Methods: Under this hypothesis, comparative histological and biochemical analyzes were performed on left ventricle from 24-month-old male-rats with insulin resistance,8-month-old male-rats with MetS, and 8-month-old male-normal-rats.
Results: Long QT and low heart rate were prominent findings in both experimental groups. In the biochemical analysis, it has been shown that not only did the protein levels of Cx43 and phosphorylated-Cx43 levels decrease in the intercalated discs, but also there was marked internalization of these proteins into the cytoplasm (immunohistochemical findings) and lateralization to the cell long side.
Conclusion: Consequently, in the present study, it has been shown that a decrease in Cx43 protein level, phosphorylation, and abnormal changes observed in their localization may be associated with changes in electrical activity in the heart and decreased heart rate.

Keywords: Connexin 43, MetS, Prolonged QT-interval

Abstracts for Oral Presentations

EVALUATION OF THE COGNITIVE AND CHOLINERGIC EFFECT OF R. DAMASCENA IN A RAT AMNESIA MODEL

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Abstract

Aim: In addition to evaluating the effect of R. damascene-essential-oil (RDEO) on learning and memory functions in scopolamine (SC)-induced amnesia model, we aimed to evaluate acetylcholine (ACh)-activity, M1 mAChR and the changes in Brain-derived neurotrophic factor (BDNF) expression level using molecular/biochemical methods in rat brain tissues.

Material and Methods: We used GC/MS to determine the components of RDEO. We applied Morris water maze (MWM) and new object recognition (NOR) tests to our control (0.9%NaCl), amnesia (SC; 1 mg/kg/i.p) and treatments [RDEO; 100 µl/kg/p.o. or galantamine (GL) 1.5 mg/kg/i.p) groups. We evaluated the ACh-activity in the brain tissues after behavioural experiments by ELISA and determined the changes in M1 and BDNF expression levels by the western-blotting. Moreover, using computational tools, we modelled human M1 in an active conformation and docked the major components of RDEO (specifically ()-citronellol, geraniol, and nerol) onto this receptor.

Results: It was determined that GL and RDEO treatments given to the amnesia group increased discriminating index (p<0.05–0.01). MWM test results, it was seen that the increase in the time spent in the target quadrant detected on the 5th day in the RDEO group almost approached the values of control (p<0.05). The expressions of M1 and BDNF significantly decreased with the administration of SC compared to the control in tissues. M1 and BDNF levels in GL and RDEO groups significantly increased compared to SC-group (p<0.05-0.01). In silico studies revealed that the principal components of RDEO could be accommodated favourably inside the allosteric binding pocket of active-state human M1 and anchored here primarily via hydrogen-bonding and alkyl–π interactions.

Conclusion: This study will be effective in understanding the effect of RDEO treatment on impaired cognitive functions and explaining the molecular roles of cholinergic system parameters.

Keywords: Amnesia, Scopolamine, R. damascene, M1 mAChR, BDNF

THE EFFECT OF ANESTHESIA/STEREOTAXIC SURGERY ON COGNITIVE FUNCTION IN MALE RATS

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Abstract

Aim: Postoperative cognitive dysfunction (POCD) is a common complication after major surgery and anesthesia exposure and is associated with advanced aging. However, the effects of anesthesia/stereotaxic surgery (A/SS) on cognitive function are not fully known in rats. The aim of this study is to investigate the effects of A/SS on cognitive function in male rats.

Materials and methods: For the A/SS group, male Sprague Dawley rats (6-month-old) were anesthetized with ketamine/xylazine (90/10 mg/kg, ip). The rats were then placed on a stereotaxic frame and a burr hole (1.0 mm diameter) was drilled above the lateral ventricle site. One week after surgery, the anxiety-like behavior and locomotor activity were examined by open-field test. Y-Maze was used to assess spatial memory and learning. Moreover, to determine hippocampal synaptic plasticity we evaluated hippocampal long-term potentiation (LTP) at perforant pathway-dentate gyrus synapses.

Results: No statistically significant differences were found between groups for anxiety and motor activity. The A/SS group rats explored a significantly ($p<0.05$) more novel arm of the Y maze as compared to the no-treatment group. Compared to the no-treatment group, LTP induced by high-frequency stimulation in the dentate gyrus region of rats was attenuated in the A/SS group on postoperative day 7.

Conclusion: These results indicated that A/SS induced cognitive decline and functional synaptic plasticity dysfunction. The results of the present study may be useful for future studies that examine cognitive functions containing stereotaxic surgery.

Keywords: Stereotaxic surgery, Anesthesia, Postoperative cognitive dysfunction

INVESTIGATION OF SUBSEQUENT LONG-TERM POTENTIATION IN PRIMED HIPPOCAMPAL DENTATE GYRUS BY LOW-FREQUENCY STIMULATIONS VARYING AMONG 0.5-5 HZ

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Abstract

Aim: Metaplasticity (MP) is the ability to modulate the subsequent plasticity due to a previous history of synaptic activity. According to MP, afferent activity regulates the transition point from long-term depression (LTD) to long-term potentiation (LTP) of active synapses. Although experimental results from hippocampus and visual cortex have supported MP, it remains unclear whether previous activity of synapses regulates the output of neuron populations in vivo, as expected from MP. The aim of the study is to investigate the effects of priming stimulation at different frequencies (0.5, 1, 2 and 5Hz) on the magnitude of LTP at synaptic and somatic levels in dentate gyrus (DG) of hippocampus.

Material and Methods: A total of forty rats were enrolled and randomly divided into five groups (n=8/group) to investigate LTP (n=8) and MP (n=32). Primed or unprimed synapses in DG was induced by delivering of tetanic stimulation to the perforant pathway (PP) in anesthetized rats. The field excitatory-postsynaptic potential (fEPSP) slope and population spike (PS) amplitude were evaluated to measure the magnitude of subsequent LTP.

Results: Under control conditions, four trains of (high-frequency stimulation) HFS, without low-frequency stimulation (LFS), enhanced the fEPSP slope and PS amplitude after the last HFS. 1Hz and 5Hz, but not 0.5Hz and 2Hz, stimulation of the PP led to an early LTD of fEPSP. The LTP of fEPSP was completely inhibited by previously delivering 0.5 Hz and 2 Hz LFS, but instead converted to LTD by 1 Hz LFS. However, none of frequencies used was able to inhibit the LTP of PS.

Conclusion: These results suggested that the priming of PP by LFS may inhibit the induction of subsequent LTP of fEPSP depending on previous activity frequency, however, no effect on plasticity of neuronal output. This study was financially supported by Erciyes University Research Found (grant number: TSA-2022-11465).

Keywords: Hippocampus, Synaptic plasticity, Metaplasticity, Priming stimulation, Subsequent LTP

THE ROLE OF PYRIDOSTIGMINE (MESTINON®) TREATMENT IN MYASTHENIA GRAVIS DISEASE: AN INFRARED SPECTROSCOPIC STUDY BY USING HUMAN SERUM

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Abstract

Aim: Myasthenia gravis (MG) is a chronic and antibody-mediated autoimmune rare disease characterized by weakness and fatigue of skeletal muscles. Mestinon (pyridostigmine bromide), is the most commonly used symptomatic drug in MG treatment. Infrared spectroscopy is a technique that enables the monitoring of amount, content, and structural changes in biomolecules. This molecular-level study aimed to determine the role of Mestinon therapy for MG pathogenesis compared with those of MG patients not receiving Mestinon therapy via infrared spectroscopic investigation of human sera.

Material and Methods: Three experimental groups were formed for the study; A control group of age- and sex-matched healthy individuals, a Patient group using Mestinon: M (+), and a Patient group not using Mestinon: M (-). During the study, informed consent was obtained from each participant, and human blood samples were collected from which serum samples were obtained. The spectra of serum samples were acquired using the ATR mode of Fourier transform infrared spectrometer.

Results: Integrated area values of specific spectral bands belonging to lipids, proteins, nucleic acids, and their ratios were calculated. The results revealed that Lipid/Protein, Aliphatic chain length, Glucose/Protein amounts decreased in (M-)patients with respect to the control group but increased towards the values of the healthy control group in (M+) patients. In addition, Protein concentration, Nucleic acid/Protein amount, and DNA concentration increased in (M-) patients with respect to the healthy control group, while decreased in (M+) patients towards to those of the healthy group.

Conclusion: These results clearly indicate that Mestinon has a recovery effect against MG-induced alterations in serum biomolecules.

Keywords: Myasthenia gravis, Rare disease, Infrared spectroscopy, Spectral characterization

EFFECTS OF EXOSOMAL MODULATION ON CARDIAC REGENERATION AND CARDIOPROTECTION IN CARDIOMYOCYTES AND CARDIAC STEM CELLS

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Abstract

Aim: The limitation in exosome therapy is the lack of understanding of the regenerative properties of injected exosomes and how these properties can be activated. We aim to investigate the cardioprotective effects of estrogen hormone, which is known to have a positive effect on cardiac protection, and ticagrelor, an antioxidant-acting purinergic receptor P2Y12 inhibitor, on exosomes secreted from cardiac stem cells (CPC).

Material and Methods: In this study, we used both in vitro and in vivo models. For hyperglycemia experiments, to mimic DM in cardiomyocytes, we used high glucose incubated H9c2-cells (HG). HG cells were treated with exosomes derived from ticagrelor-pretreated H9c2-cells. CPCs were isolated from male mouse heart. The functional effects of exosomes released from estrogen pretreated- CPCs and ticagrelor pretreated-cardiomyocytes were investigated by cell migration and angiogenesis assays. To examine the effect of estrogen treatment in transplanted CPCs we used mouse models. Dil-labeled estrogen pretreated male-CPCs were intramyocardially injected into female mouse heart which has heart failure.

Results: Effect of both factors on angiogenesis and endothelial cell migration of exosomes was significantly higher compared to non-incubated exosomes. Exosomes from ticagrelor pretreated H9C2 suppress apoptotic, ER-stress and autophagy-related genes in DM and significantly reduce ROS production altering oxidative stress-associated miRNA expressions. Exosomal miRNAs, known to act as positive modulators in neo-angiogenesis and cell migration released from CPCs increased significantly upon estrogen treatment. Transplanted cells were observed to persist in the myocardium for longer compared to control cells. According to our electrophysiological and morphometric analyzes, damage recovery is significantly increased after estrogen pretreated transplanted stem cells compared to control.

Conclusion: Considering the paracrine hypothesis, we suggest that pre-treatment of stem cells and cardiomyocytes with exogenous factors may regulate mechanisms effective in cardiac regeneration and protection causing changes in the exosomal miRNA profile.

Keywords: Exosome, Ticagrelor, Estrogen, miRNA, Heart

EXAMINING THE GENETIC EFFECTS OF RADIOFREQUENCY ELECTROMAGNETIC RADIATION (MOBILE PHONE FREQUENCY; 1800, 2100 MHZ) ON AMNIOCYTE

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Abstract

Aim: In terms of electromagnetic pollution and human health, radiofrequency electromagnetic fields (RF-EMF) emitted by mobile phones and other quickly evolving electronic devices are a significant global issue. It's crucial to look at the effects both positive and negative of RF-EMF on human cells to comprehend the molecular changes they bring about. The aim of this study was to thoroughly investigate the genetic effects of commonly used RF frequencies of 1800MHz and 2100MHz on amniocyte cells.

Material and Methods: Amniocyte cells were divided into 4 groups as Control (C), Sham (SH), RF-1 (1800MHz-0,89W/kg) and RF-2 (2100MHz-2,73W/kg). The effects of RF-EMFs were determined by examining the changes in the expression level of Wnt/β-catenin pathway and neurogenesis related genes in the cells of the groups by Real-Time-PCR.

Results: When the groups were compared in terms of neurogenesis related genes, it was observed that the expression levels of HES1, Neurod1, Neurod2 and Neurog2 of the RF-2 group increased statistically significantly compared to the C, SH and RF-1 groups ($p<0.001$). When genes with important functions in different steps of the Wnt signaling pathway are compared, the gene expression levels of APC1, APC2, β-Catenin, DKK1, DKK3, SFRP2, SFRP4 and SFRP5 of the RF-2 group it was observed that they increased statistically significantly compared to the C, SH and RF-1 groups ($p<0.001$). The genes crucial for the Wnt/-catenin signaling pathway and neurogenesis were demonstrated to have a high correlation, according to correlation analyses ($r>0.6$).

Conclusion: It can be said that exposure to 2100 MHz radiofrequency affects the genes that are active during the developmental period. The findings confirm that RF-EMFs can influence maternal and fetal biological tissue cells and related genes during pregnancy. Additionally, it may be claimed that RF-EMF can alter several cellular metabolisms, including neurogenesis, by influencing the associated proteins of the Wnt/β-catenin pathway.

Keywords: Radiofrequency electromagnetic field, Amniotic fluid cells, Wnt pathway, Neurogenesis, Gene expression

THE RELATIONSHIP OF SERUM ZINC AND COPPER WITH NITRIC OXIDE AND ASYMMETRIC DIMETHYLARGININE IN SMOKERS

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Abstract

Aim: Smoking induces inflammation and oxidative stress via radical production from chemicals resulting in cardiocerebrovascular and respiratory diseases, cancer, and stroke. Copper (Cu) and zinc (Zn) play important role in oxidative balance related with nitric oxide (NO) and asymmetric dimethylarginine (ADMA). Zn is crucial in cellular growth, membrane stability and possesses a fundamental antioxidant role in endothelial cells aligning the circulatory system. Cu is accepted to have pro-oxidative effects. Oxidant capacity in circulatory and respiratory systems diminishes bioavailability of NO deteriorating tissue perfusion. ADMA-an inflammatory competitive inhibitor of NO synthase-increases in oxidative stress. The present study was aimed to evaluate alterations of serum Zn and Cu, and plasma NO and ADMA levels as endothelial damage markers in smokers without clinical diagnosis of chronic obstructive pulmonary disease (COPD).

Material and Methods: The individuals attended to Outpatient Respiratory Clinic in Haseki Hospital were categorized in three groups; ex-smokers who quitted smoking (ES-n:40), current-smokers(S-n:40) and healthy non-smokers (HC-n:40). Serum element levels were measured using Inductively Coupled Plasma Atomic Emission Spectroscopy in Cerrahpasa Medical Faculty. Plasma NO and ADMA levels were analyzed by commercial enzymatic kits and ELISA assay, respectively.

Results: Serum levels of NO in S were significantly lower than ES and HC ($p<0.05$); moreover, ES had lower plasma NO levels than HC ($p<0.001$).

Conclusion: The present study pointed out the hazardous effect of smoking via endothelial dysfunction based on decreased plasma NO level. Higher serum Zn levels of current-smokers and ex-smokers even with no statistical significance might present the protective effect of Zn against inflammation due to oxidative stress. Monitorization of serum Zn, Cu, NO and ADMA should be considered as beneficial biomarkers of tissue oxygenation and defense mechanism before COPD clinic onset in smokers.

Keywords: Smoking, Zinc, Copper, Nitric oxide, Asymmetric dimethylarginine

THE IMPACT OF HIGH-DENSITY LIPOPROTEIN ON THE POLARIZATION AND MITOCHONDRIAL FUNCTION OF MONOCYTES AND MACROPHAGES

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Abstract

Aim: Atherosclerosis and other metabolic disorders are linked to dysfunctional mitochondria. Increased mitochondrial reactive oxygen species (ROS) production disrupts endothelial nitric oxide synthase (eNOS), resulting in endothelial cell dysfunction. This causes the pro-inflammatory response, leading to the induction of leukocyte adhesion molecules and chemotactic factors in monocytes, and then the development of atherosclerosis. It is known that High-Density Lipoprotein (HDL) is cardiovascular protective and reduces the risk of atherosclerosis. The development and aggravation of atherosclerosis depend on monocytes and their progeny, macrophages. It remains elusive how the antioxidant effect of HDL affects monocytes/macrophages and their differentiation. This study aims to examine the effects of HDL on mitochondrial function and the differentiation of a monocytic cell line (U937 cells).

Material and Methods: U937 cells were differentiated to macrophages in the presence of PMA and then treated with HDL. Mitochondrial functions of differentiated cells were investigated by flow cytometry and confocal microscopy imaging. In addition, oxygen consumption rate (OCR) was measured by Agilent Seahorse XFP Cell Mito Stress Kit. Macrophage polarization was determined by flow cytometry using M1 and M2 phenotype markers.

Results: Mitochondrial mass, mitochondrial membrane potential levels, and mitochondrial respiration decreased upon HDL treatment. Furthermore, HDL led to increase in the M2 polarization of macrophages.

Conclusion: These findings suggest that HDL may actively affect the polarization of monocytes and macrophages as well as mitochondrial functions. This study was supported by ABAPKO (2020/03/10)

Keywords: HDL, Mitochondria, Monocytes, Macrophages, Atherosclerosis

COMPARING THE EFFECTS OF TELMISARTAN, PERINDOPRIL, AND NEBIVOLOL ON NEUROPROTECTION IN LPS-INDUCED NEURON LIKE CELLS

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Abstract

Aim: The effect of antihypertensive drugs, especially drugs modulating the renin-angiotensin-aldosterone-system (RAAS), on neurodegenerative diseases still needs to be investigated. The aim of this study was to compare the effects of three different classes of antihypertensive drugs (telmisartan, perindopril, and nebivolol) on neuroprotection and acetylcholine levels against lipopolysaccharide (LPS)-induced injury in differentiated SH-SY5Y cell line.

Material and Methods: Cells were treated with retinoic acid for differentiation to neuronal phenotype. 20 µg/ml LPS was implemented to cells for 1 hour. Then, cells were treated with 1, 5, and 10 µg/ml concentrations of telmisartan, perindopril, and nebivolol separately for 24 hours, except for the control and LPS alone groups. The cell viability was evaluated with 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. Acetylcholine levels were analyzed using ELISA in the culture medium. TNF-α, IL-1β, and NFKβ expressions were evaluated via western blot analysis.

Results: Telmisartan has demonstrated the highest cell viability against LPS induced injury whereas the protective effect of perindopril was moderate. Nebivolol did not show a neuroprotective effect. The protective effect of 10 µg/ml telmisartan, was superior to 10 µg/ml perindopril ($p=0.006$); 5 µg/ml perindopril ($p=0.001$); 1 µg/ml perindopril ($p=0,001$); 1, 5, and 10 µg/ml nebivolol ($p<0.001$). Among all the study drugs, only the administration of telmisartan has provided a statistically significant increase in acetylcholine levels against LPS induced injury. Additionally, administration of telmisartan provided a concentration-dependent reduction in TNF-α, IL-1β, and NFKβ expression against LPS-induced neuroinflammation.

Conclusion: These findings suggest that telmisartan has a superior neuroprotective effect against LPS induced injury compared with both perindopril and nebivolol.

Keywords: Telmisartan, Perindopril, Nebivolol; Neuroprotection, Acetylcholine

AN INVESTIGATION EFFECT OF ANGII AND ANG (1-7) BINDING ON THE DYNAMICS OF AT2 RECEPTOR BY MICRO-SECOND MD SIMULATIONS

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Abstract

Aim: Angiotensin receptor type 2(AT2R) is an important drug target, which play a role in pathological conditions from cardiovascular disorders to cancer. Our aim is to provide new information about the activation mechanism of AT2R in response to AngiotensinII (AngII) and Angiotensin (1-7) (Ang (1-7)) binding and to determine the structural and energetic changes upon ligands binding.

Material and Methods: AngII and Ang (1-7) was docked to the inactive (GPCRdbID: agtr2_human) and active (PDBcode:6JOD) structures of the AT2R. MDockPep docking-server was used and the one pose with the lowest binding-energy-score was selected. All ligand-receptor systems were built in a membrane containing cocktail lipids (POPC: POPE: CHL, 2:2:1; TIP3P water and 0.15M KCl) using the CHARMM-GUI server. The temperature was maintained at 310K and a Parrinello-Rahman barostat (1atm) was used. After minimization and equilibration for 10ns, microsecond MD simulations were run using the CHARMM36m force field with the GROMACS (2020.5). Along with the trajectory analyses, Poisson-Boltzmann surface area, principal component analysis and residue interaction network analysis carried out.

Results: The binding of AngII to AT2R compared to Ang (1-7) was stronger considering the binding energy results, despite both ligands remained bound to the receptor throughout the simulation period. In particular, the distance increment between the TM3 and TM6 as a result of AngII binding was more than Ang (1-7). Furthermore, analysis results and the changes of key motifs such as CWxP, DRY, Na+-pocket, NPxxY and PIF between active and inactive structures gave us clues about the activation mechanism of AT2R.

Conclusion: Free energy analysis and macro-switches (TM3-TM6 distance) properties reveal that AngII and Ang (1-7) can be connected to AT2R(Met128) and enable during simulation time. However, AT2R receptor activation by Ang (1-7) may take longer time than AngII activation.

Keywords: AT2R, Ang II, Ang (1-7), GPCR, Molecular dynamics simulation

THE PROTECTIVE EFFECTS OF THYMOQUINONE ON CYCLOPHOSPHAMIDE-INDUCED CARDIOTOXICITY

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Abstract

Aim: Cyclophosphamide (CP), an agent used in antineoplastic chemotherapy, has a toxic effect on many tissues. In this study, the protective effect of thymoquinone (TQ), the dominant component of black cumin essential oil was investigated against cardiotoxicity caused by cyclophosphamide in long-term use.

Material and Methods: A total of 32 8-week-old male Sprague Dawley rats were randomly divided into 4 groups (n=8). The control group was gavaged with 1 ml of saline daily for 28 days. Thymoquinone group was given 10mg/kg/day thymoquinone dissolved in 1 ml of hot water via gavage for 28 days. In the cyclophosphamide group, 50 mg/kg cyclophosphamide ip injection was given once a week. In the Thymoquinone + Cyclophosphamide group, 10mg/kg/day thymoquinone was given by gavage and 50mg/kg cyclophosphamide ip once a week. After 28 days of applications, animals were sacrificed by cardiac exsanguination method under ketamine anesthesia. MDA and GSH levels were measured in the heart tissue and histopathological examinations were performed.

Results: Cyclophosphamide caused significant increases in MDA levels in heart tissues. Thymoquinone administration alone caused significant increases in GSH levels. A decrease in MDA levels and an increase in GSH levels were observed in the thymoquinone and cyclophosphamide administered group, but this was not statistically significant level. In histological preparations stained with Hematoxylin-Eosin (H&E), Masson triple staining and Toluidine blue staining method, it was determined that the morphological structures of the muscle fibers degenerated significantly in the heart tissues in the cyclophosphamide group compared to the other groups, and the connective tissue edema between the muscle fibers increased significantly.

Conclusion: It was concluded that the application of thymoquinone has a cardioprotective potential against cyclophosphamide-induced cardiotoxicity by reducing oxidative damage.

Keywords: Cyclophosphamide, Cardiotoxicity, Thymoquinone, Antioxidant

HYPERTHERMIC EFFECTS ON HEALTHY FIBROBLAST AND LEUKEMIA CELLS

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Abstract

Aim: It is mentioned in several reports that hyperthermic treatments may have a good impact on cancer healing. That's why successful applications of hyperthermia are increasing as a side treatment of cancer. This study, it was aimed to investigate the response of leukemia cells (MEC-1) and healthy cells (Human Fibroblast cells-hFB) to hyperthermia.

Material and Methods: After the Human Healthy Fibroblast (hFB) and leukemia (MEC-1) cells were cultured under appropriate conditions, they were exposed to 42°C and 43°C for different periods and then incubated for 24 hours. Then, cell proliferation (Cell Proliferation Kit, BI) tests with XTT, apoptosis and necrosis (eBioscience-Annexin V-FITC Apoptosis Detection Kit) and cell cycle analysis (Abcam Cell Cycle Assay Kit) tests were performed by flow cytometry. Student's t-test was used to evaluate the statistical results.

Results: After exposure of hFB cells at 42°C for 0, 5, 15, and 20 minutes, the total death rate was 6%, 25%, 27%, and 32%, respectively; Total death was detected in 5%, 20%, 27% and 78% of MEC-1 cells. At 43°C, after exposures of 0, 15, 30, and 45 minutes, total death was detected in hFB cells at the rates of 4%, 55%, 56%, 75%, respectively; Total death rates of MEC-1 cells were 7%, 28%, 34% and 58%.

Conclusion: The effectiveness of hyperthermia varies depending on temperature and exposure time. Our results reveal that heating at 42˚C and 43°C induced cell apoptosis and necrosis, and inhibited cell proliferation. However, our data showed that exposure to hyperthermia at 42°C drives cells towards apoptosis, but at higher temperatures, cells prefer to undergo necrosis rather than apoptosis in healthy and cancer cells.

Keywords: Hyperthermia, Apoptosis, MEC-1, hFB

MELATONIN COUPLED WITH LOW-LEVEL LASER İRRADIATION POTENTIALLY EXERTED ONCOSTATIC EFFECTS ON RAT GLIOMA CELLS VIA APOPTOSIS PATHWAY

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Abstract

Aim: Low-Level Laser Irradiation (LLLI) is a cornerstone in treating cancer cells in vitro. Melatonin (MLT) is a pineal hormone that boards numerous cancer types. Nevertheless, MLT antitumor pathways and mechanisms of action are still not fully vivid. This study investigated melatonin coupled with LLLI antitumor cellular and molecular mechanisms to inhibit cell proliferation via the apoptosis pathway of RG2 cancer cell lines.

Material and Methods: RG2 Cells were classified into cells without any MLT and LLLI treatment as a control group and cells treated with melatonin (MLT) concentrations (0.5–2 mM) and LLLI energy intensity at 30, 60, 120, 240 J/cm2 for 24, 48, and 72h. effective and optime concentration of MLT was 2 mM, and the energy density of LLLI was 240 J/Cm2. The potential cytotoxicity effect of melatonin, LLLI alone, and combined on RG2 cells was determined by a convenient MTT assay. A flow cytometric assay evaluated the apoptosis and inflammatory response of RG2 cells in vitro. Apoptosis pathway markers were found using RT-qPCR analysis. Biomarkers of Antioxidants and oxidative stress were executed using a colorimetric assay. Mitochondrial membrane potential ($\Delta\Psi m$), aquaporins (AQPs), Potassium Voltage-Gated Channel Subfamily Q Member (KCNQ), and cytokine factors (IL-1β, IL-18, IL-6, IL-10, TNF-α, TLR4, and EDN1) expression activity were monitored after a single 2mM MLT and 240 J/cm2 48h as well as MLT+LLLI combined treatments. Furthermore, for evaluated the mitochondrial network dynamics, we used confocal imaging with Mitotracker Red staining, and lastly, the data were analyzed by ImageJ software.

Results: Melatonin yield a remarkable steady decrease in the viability of RG2 cells at a concentration range between 0.1-2 mM and LLLI energy dose 240 J/Cm2. MLT, LLLI, and MLT coupled with LLLI treatment groups decreased survival rates by 39.71%, 67.14%, and 86.38%, respectively, and induced apoptosis.

Conclusion: These results illuminate the oncostatic effectiveness of melatonin coupled with LLLI treatment on glioma.

Keywords: Photobiomodulation, Laser, RG2, Melatonin

MICRO/NANO PLATFORMS FOR OPTOGENETIC TECHNOLOGIES AND PHOTOBIOMODULATION

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Abstract

Optogenetic tools comprise a variety of different light-sensitive proteins from single-cell organisms that can be expressed in mammalian neurons and effectively control their excitability by allowing to either depolarize or hyperpolarize, and respectively generate or inhibit action potentials in selective populations of neurons, so it may be considered for developing potential treatment strategy for different neurodegenerative diseases. One of the great challenges in this effort is to develop implantable systems that are capable of processing the activity of large ensembles of cortical neurons. In vitro platforms are essential tools for optimize dose/energy parameters of laser based advanced photobiomodulation techniques. Micro nano technologies have great potential to generate coculture platforms for optogenetic experiments. The aim of this study was to create an easy-to use device to fabricate precisely designed 3D hydrogel scaffolds for co-culturing, tri-culturing and multi-culturing practices. In this study, gelatin methacryloyl (GelMA) was synthesized and textured three-dimensional hydrogel scaffolds were fabricated via photopolymerization using compartmental fabrication device. This device allowed fabricating computer aided designed (CAD) geometries precisely and encapsulating different cells in different hydrogel posts while building a whole geometry. The hydrogel texture characterization was performed using colored hydrogel solutions and it is observed that the device keeps the distinct posts in contact precisely. A neural tissue model was created using neural, epithelial, and endothelial cells as a proof of concept. Cell distribution was evaluated using cell trackers. The viability and the proliferation assays were also performed, and the viability was above 80% while a positive proliferation has been observing. Overall findings showed that this device offers a practical way to fabricate and align precisely designed three-dimensional hydrogel scaffolds for optogenetic experiments.

Keywords: Nanotechnology, Photobiomodulation, Optogenetics, Hydrogel platforms

CURCUMIN SELECTIVELY ACTIVATES THE EXPRESSION OF HIF1A-AS1 BUT NOT HIF1A IN TRIPLE-NEGATIVE BREAST CANCER CELLS

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Abstract

Aim: Long non-coding RNAs (lncRNAs) are RNA transcripts without protein-coding potential. A growing body of evidence suggests that lncRNAs play important regulatory roles in the development and progression of human diseases, including cancer. Curcumin (diferuloylmethane) is the main natural polyphenol found in the rhizome of Curcuma longa (turmeric). Previous studies suggest that this polyphenol has several promising therapeutic properties, particularly antitumor activity via multiple mechanisms, including induction of epigenetic changes. Accordingly, present study was aimed to decipher the role of hypoxia inducible factor 1 alpha (HIF1A) and its antisense RNA HIF1A-AS1 in curcumin-mediated inhibition of cell proliferation.

Materials and Methods: HTB-26 (MDA-MB-231) triple negative breast adenocarcinoma cells were cultivated using Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10 % fetal calf serum and maintained in humidified carbon dioxide incubator at 37 °C. For MTT cell viability assay, cells were treated with varying concentrations of curcumin (200 µM, 100 µM, 50 µM, 25 µM, 12.5 µM, 6.25 µM). Following determinations of the IC50 values, 1×10^6 cells were treated with the active dose of curcumin and incubated 24 hours. Then, RNA isolated from cells and gene expression changes were analyzed by RT-qPCR method.

Results and Conclusions: Results of the present study indicated that curcumin inhibited cell proliferation of MDA-MB-231 breast cancer cells in a dose-dependent manner and half-maximal inhibitory concentration (IC50) was determined to be 45.49 µM. Notably, HIF1A-AS1 (40-fold) is selectively activated while HIF1A not significantly altered in triple negative breast cancer cells treated with the active dose of curcumin. Consequently, results obtained in the present study indicates that HIF1A-AS1 but not HIF1A is involved in the curcumin mediated inhibition of cell proliferation, suggesting that selective activation of HIF1A-AS1 might be associated with the chemoresistance to curcumin in triple negative breast cancer.

Keywords: Breast cancer, Curcumin, HIF1A, HIF1A-AS1, TNBC

THE EFFECT OF END PLATE DISTRIBUTION ON MOTOR UNIT POTENTIAL DURATION AND CONSECUTIVE MOTOR UNIT POTENTIAL INSTABILITY

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Abstract

Aim: The analysis of motor unit potential (MUP) recorded during voluntary muscle contraction provides important information to help in the diagnosis and characterization of neuromuscular pathology. MUP parameters such as duration, jitter, and jiggle may show evidence of denervation with subsequent re-innervation in motor neuron diseases such as amyotrophic lateral sclerosis. During re-innervation, new neuromuscular junctions alter the end plate distribution. Also, instability of new neuromuscular junctions affects the consecutive MUP wave shape and changes the jiggle value which represents the consecutive MUP shape variability. The aim of this study is to investigate the effect of motor unit end plate distribution on the MUP instability and duration.

Materials and Methods: 500 MUP trains were simulated for normal and pathologic muscle parameters by using the volume conduction method. MUP simulations were also conducted according to clinical concentric needle electrode parameters and 30 consecutive MUPs in every MUP train were simulated for every end plate distribution value. For a normal MUP simulation, end plates are located near the center of muscle fibers and distributed within the muscles in a narrow band (2-10mm). Band distribution was changed according to the percentage of re-innervation with a standard deviation (1-5SD). Also, consecutive MUP variability was quantified using the jiggle calculation method for every MUP train.

Results: Jiggle values do not have statistical changes for normal and pathologic motor units when the end plate distribution changed from 1SD to 5SD. However, the duration of MUP was increased statistically with increasing end plate distribution SD of pathologic motor units.

Conclusion: Consecutive MUP simulation using real muscle parameters is necessary to understand the factors affecting the function of MU during neuromuscular pathology. To conclude, the wider motor fiber end plate distribution increases the MUP duration but does not change consecutive MUP instability.

Keywords: Consecutive motor unit potentials, Motor and plate distribution, Motor unit Potential duration

THE COMBINATION OF CYCLOPHOSPHAMIDE TREATMENT AND LOW-LEVEL LASER IRRADIATION (LLLI) ATTENUATES CELL GROWTH IN RG2 CELL LINE

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Abstract

Aim: There is great interest in combining Low-Level Laser Irradiation (LLLI) with Cyclophosphamide (CP) chemotherapy drugs aiming at maximizing their efficacy on rat glioma 2 (RG2) cells toxicity in vitro. Hence, the present study aimed to investigate the effect of CP coupled with LLLI treatment on RG2 cell fate via the apoptosis pathway. This study aimed to investigate the anti-tumor and inhibitory tumor growth potential of CP and LLLI alone, their combined treatment, and their effects on inducing the apoptosis pathways through the immune response to KCN, AQP, and Gaba pathways to treat RG2 malignant gliomas in vitro.

Material and Methods: Three main groups were formed to study the effects of CP, LLLI treatment, and CP coupled with LLLI treatment on RG2 cell growth inhibition. In the first group, cells were treated with different concentrations of CP (0.1, 0.5, 1, 2 mM) for 24, 48, and 72 hours. RG2 cells in the second group were treated with different laser doses (495 nm) (30, 60, 120, and 240 J/cm2) for 24, 48, and 72 hours. All treatment groups were compared with the non-treated (control) group. RG2 cell viability was determined by MTT assay. In continue, Aquaporins (AQPs) channel activity, inflammation-mediated factor response in vitro, and apoptosis-related gene expression level in axis were evaluated by flow cytometric method. Hence ROS level analyses in treatment groups were evaluated by the colorimetric method.

Results and Conclusion: CP is an alkylating mediator used to treat a variety of cancers. CP treatment on RG2 cancer cells activates innate and adaptive immunity leading to significant regression of gliomas. The present results demonstrate that the CP coupled with LLLI effectively induced the apoptosis pathway and reduced the migration through the multiple signaling pathways, which contain AQPs channel activity, inflammatory cytokine activity, and changes in ROS level expression.

Keywords: Photobiomodulation, Glioma, Aquaporin, Apoptosis, Inflammation, Cyclophosphamide

INVESTIGATION OF NEUROPROTECTIVE AND THERAPEUTIC EFFECTS OF TRANSCRANIAL DIRECT CURRENT STIMULATION IN EXPERIMENTAL TRAUMATIC BR

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Abstract

Aim: The aim of this study was to investigate neuroprotective and therapeutic effects of transcranial direct current stimulation on learning and memory, which is impaired as a result of glutamate and calcium excitotoxicity after traumatic brain injury (TBI).
Material and Methods: 40 male Wistar rats, each of which weighs 290-310 g, were divided into four groups as Sham, TBI, TBI+tDCS and tDCS+TBI+tDCS groups, with 10 rats in each group. TBI was created with moderate trauma model by dropping an iron weighing 200 g, 1.5 cm in diameter, 9.5 cm long, from a height of approximately 1 m, on head of subject under anesthesia. 2 hours after tDCS application trauma injury, 1mA anodal tDCS application will be applied for 30 minutes on the 1st and 2nd days. On the other hand, in tDCS+TBI+tDCS group, 1mA anodal tDCS stimulation will be performed 5 days before and 2 hours after trauma injury, for 30 minutes on the 1st and 2nd days. Novel object recognition was used to evaluate learning and memory, and open field test was performed to evaluate locomotor activity. Glutamate, Ca^{2+} and N-Methyl-D-Aspartate (NMDA) levels in hippocampus tissues were evaluated.
Results: There was an increase in learning and memory results in treatment groups compared to TBI group, and a significant decrease in TBI group according to Sham($p<0.05$). Glutamate, Ca2+ and NMDAR levels were significantly higher in TBI group compared to Sham group($p<0.001$), while they were significantly lower in TBI+tDCS and tDCS+TBI+tDCS groups compared to TBI group($p<0.05$). In particular, the change was more in tDCS+TBI+tDCS group.
Conclusion: In our study, it was concluded that post-TBI tDCS application improves learning and memory disorders and has a neuroprotective effect on learning and memory by regulating glutamate and Ca^{2+} levels, which play a role in hippocampal glutamatergic cell death as a result of excitoxicity.

Keywords: Glutamate, Traumatic brain injury, Learning and memory, Tdcs

PROTEOMIC INVESTIGATION OF ACUTE AND CHRONIC HYPOXIA REOXYGENATION RESPONSIVE HEMOSTATIC PROTEINS AND PATHWAYS IN H9C2 CARDIOMYOCYTES

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Abstract

Aim: Ischemic heart disease continues to rank highly among cardiovascular diseases in the world. Myocardial reperfusion (R) is provided with an effective and rapid treatment however, it can lead to fatal results as well as ischemia (I). The goal of this study was to use proteomic analysis to assess the proteins and pathways that changed in H9C2 cardiomyocyte cells exposed to (I) and (R) for durations that represented acute and chronic conditions.

Material and Methods: H9C2 cardiomyocyte cells, a useful model for simulating in vivo (I)/(R) damage, were used to create five experimental groups: normoxia (the control), acute hypoxia (3 hours), acute hypoxia (3 hours) + reoxygenation (3 hours), chronic hypoxia (21 hours), chronic hypoxia (21 hours) + reoxygenation (3 hours). Analyses were performed in Thermo Scientific Q Exactive ™ HF mass spectrometer coupled with Thermo Scientific ™ UltiMate ™ 3000 RSLC Nano Ultra performance liquid chromatography. Proteins were quantified using the label-free quantification (LFQ) algorithm in Proteome Discoverer 2.4.

Results: Proteomic analysis resulted in identification of 2563 protein groups. The entire protein list was screened for proteins involved in complement and coagulation cascades, platelet activation, degranulation as well as fibrin clot dissolution and formation which eventually result in the listing of 83 proteins. Proteins that differentially expressed in the various groups were identified ($p<0.05$ among mean values for groups). Following acute hypoxia stimulation, tissue factor, factor V, plasminogen activator inhibitor 1, and antithrombin III were all overexpressed. Tissue factor and antithrombin III were also overexpressed in chronic hypoxia. Complement C3 was only found to be overexpressed in chronic hypoxia.

Conclusion: We showed that proteins essential for hemostasis may also affect cardiac health in response to acute and chronic hypoxia based on the levels of their expression. The potential biological outcomes of these changes will be extensively discussed.

Keywords: Proteomics, H_9C_2 cells, Hypoxia, Reoxygenation, Hemostasis

THE PROTECTIVE EFFECT OF MELATONIN ON DOXORUBICIN-INDUCED DAMAGE IN CARDIOMYOCYTES VIA HMGB1/TLR4/MAPK PATHWAYS

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Abstract

Aim: Doxorubicin is an anticancer drug commonly used in the treatment of various types of cancer. However, Doxorubicin has undesired side effects on many tissues such as the heart, pancreas, liver, kidney, and testis. Therefore, the aim of the present study is to investigate the possible protective effect of melatonin on doxorubicin-induced damage in cardiomyocytes via High Mobility Group Box 1 (HMGB1)/Toll-Like Receptor 4 (TLR4)/mitogen-activated protein kinase (MAPK) pathways.

Material and Methods: Five groups were created: Control (C), Box-A-HMGB1 inhibitor (B), Doxorubicin (D), Doxorubicin+Melatonin (DM), and Doxorubicin+Melatonin+Box-A (DMB) by using H9c2 cell lines. Total antioxidant activity (TAS), total oxidant activity (TOS), oxidative stress index (OSI), apoptotic cell death, mitochondrial membrane potential (MMP), and proteins expression of HMGB1, TLR2, TLR4, Glucose-regulated protein 94 (GRP94), extracellular signal-regulated protein kinase (ERK1/2), c-Jun N-terminal kinases (JNK), Adenosine monophosphate-activated kinase (AMPK), apoptosis-inducing factor (AIF), P38, Cytochrome-c, L-type Ca^{2+} channel were measured.

Results: TOS and OSI increased in the D group; however, melatonin improved them in the DM group. In addition, apoptotic cell death surged in D and B groups while it decreased in DM and DMB groups. The F-actin structure was found to be destructed in D and B groups whereas melatonin improved it in DM and DMB groups. Similarly, MMP decreased in D and B groups; however, melatonin improved it in DM and DMB groups. The protein expression of HMGB1, TLR2, TLR4, GRP94, ERK1/2, P38, JNK, AMPK, AIF, and Cytochrome-c protein expressions were found to decrease in the D group. On the other hand, melatonin increased the protein expression of HMGB1 and ERK1/2 while it did not change JNK and AMPK protein expressions.

Conclusion: HMGB1/TLRs/MAPK plays a role in doxorubicin-induced damage in cardiomyocytes and melatonin may exert its protective effect through these signaling pathways.

Keywords: Doxorubicin, Melatonin, F-actin, Oxidative stress, HMGB1

EVALUATION OF TRACE ELEMENT ALTERATIONS CAUSED BY CORONARY ARTERY DISEASE

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Abstract

Aim: Coronary artery disease (CAD), which is the most common cardiovascular system disease, is one of the leading causes of death all over the world and also in Türkiye. Lipid membrane peroxidation and protein degradation increase, and antioxidant metabolites decrease due to the increased oxidative stress in cardiovascular diseases, it has been determined that trace elements function as essential components of some antioxidant enzymes. In our study, the effect of coronary artery disease on serum trace element levels were investigated.

Material and Methods: The study involved 86 subjects who attended to the Department of Cardiology in Pamukkale Hospital and were pre-diagnosed as having CAD. Individuals were divided in two groups; CAD group (n:59) and healthy control (HC)(n:27). Serum iron (Fe), copper (Cu), magnesium (Mg), manganese (Mn), selenium (Se) and zinc (Zn) levels of study groups were analyzed by using ICP-OES. Moreover, biochemical parameters were also determined in study groups. Statistical analysis was evaluated using SPSS 20.0. Mann Whitney U and Independent-T tests were performed to control whether data presented normal distribution.

Results: Serum Fe levels were significantly statistically higher in CAD group than HC group ($p<0.001$). CAD group had higher serum Cu and Zn, and lower serum Se, Mn and Mg levels compared to HC group with no significancy.

Conclusion: Fe element plays an active role in free radical formation and lipid peroxidation mechanisms. A statistically significant increase in serum total cholesterol values in CAD group also supported the higher serum levels of Fe. The present study pointed out that alterations of serum trace elements primarily serum iron levels by means of both increment or decrement might have close relationship with mechanisms of CAD and its complications. Thus, analyses of serum trace elements in CAD patients may be important biomarkers by means of diagnosis, treatment, and follow-up intervals.

Keywords: Coronary artery disease, Trace elements, Serum lipid profile

CHANGES IN THE HISTOPATHOLOGY AND IN THE PROTEINS RELATED TO THE MAPK/ERK PATHWAY IN THE BRAINS OF RATS EXPOSED TO PRE-AND POSTNATAL RADIOFREQUENCY RADIATION

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Abstract

Aim: The development of new technologies and industry increases variety of electromagnetic field (EMF) sources. Researchers are increasingly interested in effects of EMF on brain health. We investigated the effects of brain development in the fetus, histopathological changes in female rats and the hippocampal level of MAPK proteins in male rats after exposed to pre-and postnatal 2450-MHz continuous wave (CW) radiofrequency radiation (RFR) over four generations.

Material and Methods: Four groups; sham, irradiated female, irradiated male, irradiated male and female, with each consisting of four rats (one male and three females) were created. Rats in the exposure groups were whole-body exposed to 2450-MHz CW-RFR for 12h/day during the experiment. Irradiation started one month before fertilization in experimental group. On the 18th day of the gestational period, one pregnant rat from each group was decapitated under general anesthesia and the fetuses were taken. The remaining two pregnant rats completed the normal gestation period. When the offspring were two months old, four rats, one male and three female, were allocated for the second-generation study. Next generation animals were also experienced the same processes as the first-generation rats. This study was evaluated development of brain in fetuses and histopathological changes in brain of female rats using hematoxylin eosin staining, and the hippocampal level of MAPK proteins in brain of male rats by Western Blotting.

Results: We observed hemorrhagic areas, irregular cellular localization and vascular structures in the brain of fetal and adult female rat of exposed groups in all generations. pERK,pTau,pJNK and pP38 were increased in the brain of adult male rat of exposed groups in all generations ($p<0.005$).

Conclusion: Pre-and postnatal 2450 MHz CW-RFR exposure may cause changes in the function of the MAPK pathway affecting cognitive processes and may cause damage to both the fetus and adult brain tissue.

Keywords: 2450 MHz RF, MAPK, ERK1/2, Pre and postnatal exposure, Continuous wave, Brain

HUMANIN INHIBITS DIABETES-INDUCED APOPTOSIS AND INFLAMMATION IN HIPPOCAMPUS AND PREFRONTAL CORTEX IN MICE

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Abstract

Aim: Diabetes is associated with hormonal imbalances and increased cell death in many memory-related brain regions and different tissues, such as the hippocampus and prefrontal cortex. The mitochondrial derived peptide humanin is known to prevent apoptosis and protect against oxidative stress in diabetes. However, its effect on complications in the brain regions caused by diabetes is not yet fully known. This study aims to evaluate the effect of chronic humanin administration to cognitive impairment and memory problems caused by diabetes mellitus.

Material and Methods: Forty adult mice were randomly selected for this study. Mice were divided into four groups (10 mice for each group): Control group (saline), humanin group (4 mg/kg), streptozotocin (STZ) group (diabetic control) and STZ+Humanin group. Mice were administered humanin daily for 15 days. The prefrontal cortex and hippocampus were taken by micropunch and subjected to the necessary enzymatic processes. Caspase 3, caspase 9, IL-1β, IL-6 and IL-10 were measured from tissue homogenate obtained by ELISA method.

Results: Diabetes induced apoptosis and inflammation in the hypothalamus and prefrontal cortex. Humanin inhibited caspase 3 and 9 levels in the hypothalamus and prefrontal cortex of diabetic mice. Also, humanin decreased IL-1 and IL-6 levels, while it increased IL-10 level in the hypothalamus and prefrontal cortex of diabetic mice.

Conclusion: In line with our results, we conclude that humanin is a therapeutic agent with protective effects against apoptosis and oxidative stress in cognition and memory problems caused by STZ. There is a need for further studies on this subject in order to understand the mechanisms of action of humanin.

Keywords: Humanin, Diabetes, Apoptosis, Inflammation

CLASSIFICATION OF SKIN DISEASES WITH DIFFERENT DEEP LEARNING MODELS AND COMPARISON OF THE PERFORMANCES OF THE MODELS

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Abstract

Aim: Classification of skin diseases is important for early diagnosis and treatment. The process of determining the disease by the specialist physician also delays the treatment process to be applied to the patient. Computer-aided diagnosis systems play an important role in early diagnosis and initiation of treatment by minimizing such processes. High performance results are obtained with Deep Learning based approaches in diagnostic processes on the images. In this study, high-performance classification of skin lesions was performed by using Deep Learning models.

Material and Methods: Dataset used for study includes 887 images obtained with dermatoscope from International Skin Imaging Collaboration (ISIC), dataset were expanded to 3548 images by using data augmentation techniques. In this dataset, there are images of Actinic Keratosis, Dermatofibroma, Pigmented Benign Keratosis, Seborrheic Keratosis, Vascular Lesion skin diseases. These 5 skin diseases have been classified by Deep Learning models using the supervised learning method. SequeezeNet, AlexNet, GoogleNet, Vgg-19, ResNet101, DenseNet201, ResNet-50, ResNet-18, Vgg-16 models were used. 80% of the dataset is used for training and 20% for testing. Pre-trained Deep Learning models were used. Each model was trained three times and tested after each training. Average of these three results were used for calculating final results.

Results: To evaluate classification success of models, F1-score, precision, sensitivity and accuracy metrics obtained from confusion matrix were used. According to the results of the metrics, the highest performance has been achieved by Vgg16 and ResNet18 models. According to the F1-score, the most successful model is Vgg16 with 97.41%, while the highest accuracy rate obtained by ResNet18 with 98.06%.

Conclusion: While it can take a long time to make such a diagnosis by the specialist physician, such diagnosis made by artificial intelligence-based Deep Learning models are obtained in a few seconds. High success rate shows that such systems can be used for diagnosis and treatment processes.

Keywords: Skin diseases, Artificial intelligence, Deep learning, Skin classification

DEVELOPMENT OF NOVEL MITOCHONDRIAL FISSION INHIBITORS TARGETING DRP1-GTPASE INTERACTION

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Abstract

Aim: Mitochondria is a highly dynamic organelle responding to cellular stress through mitochondrial mass alterations, fusion and fission and location changes in cell. Mitochondrial fusion can be explained by mitochondria's forming an elongated mitochondrial network and vice versa small fragmented mitochondria are formed by mitochondrial fission. Mitochondrial functions and mitochondrial dynamics play an important role in terms of understanding the biological processes like apoptosis and aging along with molecular basis of many complex diseases such as diabetes, neurodegenerative diseases like Parkinson's and Alzheimer's and ultimately cancer. Recent studies revealed that cancer cells alter mitochondrial dynamics (increase mitochondrial fission protein, Drp1) to gain resistance against apoptosis and regulate bioenergetics and biosynthetic requirements to support proliferation, migration and therapeutic resistance acting on tumor origination and transformation characteristics. Therefore, development of new inhibitors targeting mitochondrial fission becomes an important subject to deliver novel treatment options for diseases with mitochondrial dynamic alterations.

Material and Methods: This study mainly comprises of two parts. In first part mitochondrial fission inhibitor design is performed by computational methods. In the design calculations, it is aimed to inhibit the interaction between Drp1-GTPase. Candidate molecules for bioactivity tests are determined by virtual screening of 3.6 million molecules with docking calculations and MD simulations. At second part effects of synthesized inhibitor molecules on Drp1-GTPase interaction and mitochondrial fission/fusion rate was studied by confocal microscopy.

Results: We found 3 successful small molecules that inhibited mitochondrial fission by targeting Drp1-GTPase interaction at human pancreatic beta cells (11B4), human neuroblastoma cells (SHSY-5Y) and adenocarcinomic human alveolar basal epithelial cells (A549).

Conclusion: Developing a new inhibitor for Drp1-GTPase interaction has a great importance for many diseases such as cancer, diabetes, cardiovascular and neurodegenerative diseases and for understanding the mechanism of mitochondrial dynamic processes.

Keywords: Mitochondrial dynamics, Small molecule inhibitor, Mitochondrial fission

INVESTIGATION OF THE SYNERGISTIC EFFECTS OF TREATMENT WITH CHLORHEXIDINE AND AZITHROMYCIN ON ESCHERICHIA COLI BY INFRARED SPECTROSCOPY

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Abstract

Aim: Although the combinatorial effects of various antibiotics have been extensively reported, the synergistic effects of antiseptics with antibiotics have received less attention. This study aims to investigate the biomolecular alterations in Escherichia coli treated.

Material and Methods: The effect of CHX and AZM on the growth of E. coli (ATCC 8739) was achieved by OD600 measurements and agar spot-plating assay. The Attenuated Total Reflectance-Fourier Transform Infrared Spectroscopy (ATR-FTIR) technique was used to determine the biomolecular alterations. In qualitative and quantitative spectral analyzes, vector normalization was applied by taking the second derivatives with OPUS 5.5 (Bruker) software. GraphPad Prism 6.01 (GraphPad, CA, USA) was used for the preparation of the graphs and statistical analysis. t-test was applied to compare the means of two treatment groups or to the comparison of the treatment group with the untreated control. Differences at $p \leq 0.05$ were considered significant.

Results: CHX and AZM treatments were shown to have a synergistic growth inhibitory effect on E. coli. When the second order derivative absorbance spectrum was examined, statistically significant ($p \leq 0.05$) structural and quantitative changes in the regions of cell-wall components and lipid (3100-2800 cm-1 and 1800-1700 cm-1, respectively), protein secondary structures (1700-1500 cm-1), and nucleic acids and carbohydrate (1300-900 cm-1) were determined in the cells treated with both CHX and AZM.

Conclusion: The concomitant treatment of CHX and AZM enhances the anti-bacterial effects. The synergistic action of the CHX and AZM on the various biomolecules was also evident. Thus, it can be concluded that the combination of CHX with conventional antibiotics can be a promising strategy to combat antibiotic resistance.

Keywords: Chlorhexidine, Azithromycin, Anti-microbial effect, Synergy, ATR-FTIR Spectroscopy

INVESTIGATION OF THE SYNERGISTIC EFFECTS OF TREATMENT WITH CHLORHEXIDINE AND AZITHROMYCIN ON ESCHERICHIA COLI BY INFRARED SPECTROSCOPY

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Abstract

Aim: The consumption of High Fructose Corn Syrup (HFCS) has increased in children and adolescents and is partially responsible for the high incidence of metabolic diseases. But the effects of fructose-rich diet in prepuberty on male rat of puberty onset are still poorly evidenced. The aim of this study was to investigate the effects of HFCS consumption on pubertal maturation.

Material and Methods: The male rats to be used in the study were selected when they were 21 days old. The rats were divided into control and HFCS-55 (15% diluted, 55% fructose) groups (n=10 each group). Food and water intakes and body weights were measured daily. From the 30th day of the rats in the HFCS and control groups, preputial separation was performed every day to determine the onset of puberty. In serum samples after decapitation, reproductive hormone levels (Testosterone, Estrogen, LH, FSH) were measured by ELISA method. In addition, testicular weights and sperm parameters were analyzed.

Results: The body weight did not show any significant difference in the HFCS group compared to the control group. However, there were a significant increase in liquid consumption and a significant decrease in food consumption compared to the control group. When pubertal transition data in the HFCS group were compared with the control group, it was seen that HFCS application delayed the transition to puberty. While there was a decrease in serum testosterone levels in the HFCS group, there was a significant increase in serum estradiol, LH and FSH levels. It was observed that testicular weights and sperm count decreased significantly. It was observed that HFCS consumption negatively affected sperm parameters.

Conclusion: As a result, it was determined that HFCS consumption in peripubertal rats led to changes in the reproductive system, which delayed the transition to puberty through primary hypogonadism

Keywords: Puberty, HFCS, Hypogonadism

RETROSPECTIVE EVALUATION OF BRAINSTEM VOLUME IN MIGRAINE PATIENTS

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Abstract

Aim: Migraine is a complex, multifactorial neurovascular disease of the brain, characterized by recurrent, unilateral hemi-cranial pain that occurs in the form of attacks as well as impaired information processing in the brain. Some functional and morphometric changes can be seen in the brain. There is conflicting information regarding structural changes in the literature. The aim of our study is to contribute to the literature by performing volumetric analysis of brain stem volume in migraine with and without aura.

Material and Methods: In our study, brain Magnetic Resonance (MR) of 108 individuals (F:80, M:28) with a mean age of 34.78±10.83 between the ages of 18-65 who were diagnosed with migraine according to the International Classification of Headache Disorders (ICHD)-3 beta criteria. Images were reviewed retrospectively. Then, migraine with aura (28), migraine without aura (49), and control groups (31) were formed, and brain stem volume was measured with volBrain (online brain MRI volumetry system).

Results: The mean brain stem volume was found to be 17.21±2.79 cm3 in the migraine with aura group, 17.33±2.48 cm3 in the migraine without aura group, and 19.27±2.76 cm3 in the control group. There was no statistically significant difference between migraine with and without aura groups ($p>0.05$). A statistically significant difference was observed between the control group and both migraine with and without aura groups ($p<0.05$).

Conclusion: The pathophysiology of migraine is still one of the controversial issues. However, it is known that functional and morphometric changes are seen in important neural structures such as cortical, subcortical and brain stem, especially during migraine attacks. As a matter of fact, in our study, the brainstem volume of the migraine group with and without aura was found to be lower than the control group.

Keywords: Migraine, MRI, Brain stem volume, Volbrain

EFFECTS OF THYMOQUINONE ON KIDNEY AND BLADDER IN CYCLOPHOSPHAMIDE-INDUCED OXIDATIVE DAMAGE

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Abstract

Aim: Cyclophosphamide is a cytotoxic agent used as an immunosuppressant in various diseases. In this study, we aimed to investigate the possible protective role of thymoquinone with proven antioxidant effect on kidney and bladder in oxidative damage due to long-term use of cyclophosphamide.

Material and Methods: Male Sprague Dawley rats (8 weeks old, n=32) were randomized into control, thymoquinone (10mg/kg, p.o, 28 days), cyclophosphamide (50mg/kg, 1 day a week for a total of 4 doses) and cyclophosphamide+thymoquinone groups. At the end of the experimental procedure, kidney and bladder tissues were removed under ketamine+xylacine anesthesia by cardiac exsanguination. Muscle strips were taken from the bladder tissue and contraction-relaxation responses were measured in the isolated organ bath. For oxidative damage, the malodialdehyde (MDA) and glutathione (GSH) levels were measured in the renal tissue. Also, myeloperoxidase (MPO) activity, which is an indicator of leukocyte migration into the tissue, was measured in renal tissue. Damage degrees of renal and bladder tissues were evaluated by light microscopy. Results were analyzed by ANOVA.

Results: Thymoquinone treatment significantly decreased the MPO activity and MDA levels which is increased by cyclophosphamide ($p<0.05$). GSH levels increased with thymoquinone and decreased GSH levels with cyclophosphamide($p<0.05$). But GSH increased significantly when co-administered with thymoquinone and cyclophosphamide($p<0.01$). We also observed that the administration of cyclophosphamide caused deterioration in bladder contraction and relaxation responses and thymoquinone had a positive effect. Histological evaluations revealed that cyclophosphamide caused damage to renal and bladder tissue. It was observed that both kidney and bladder tissues were preserved when thymoquinone was administered together with cyclophosphamide.

Conclusion: In this study, we demonstrated the protective role of thymoquinone in the oxidative damage and the deterioration of bladder functions caused by cyclophosphamide with and without aura was found to be lower than the control group.

Keywords: Cyclophosphamide, Kidney, Timokinon, Bladder, Oxidative damage

INVESTIGATION OF METABOLIC SIGNATURES OF POLYPLOID GIANT CANCER CELLS IN COLON CANCER WITH INFRARED SPECTROSCOPY

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Abstract

Aim: Phenotypic profiles, including morphological features, gene expression changes, metabolic activities, and metastatic potentials of different cells within tumor mass, are associated with "tumor heterogeneity" and reflect evolutionary dynamics. Polyploid giant cancer cells (PGCCs) with high genome content and increased cell size exhibit treatment-resistance, tumor recurrence and metastatic properties, thus posing a major obstacle to the development of effective treatment strategies. In the current study, our aim was to investigate the metabolic changes in PGCCs by using infrared (IR) spectroscopy (optical-vibrational spectroscopic technique).

Material and Methods: To induce hypoxia-induced polyploidy, human HT-29 (colon cancer) cells were incubated by cobalt chloride. Alterations in cell morphology were monitored using inverted microscope while cellular DNA content and cell cycle profiles were performed with flow cytometry. The glycogen and lipid contents in cells were determined by PAS and Oir Red staining, respectively. After the cell groups were re-suspended in isotonic solution, they were measured with IRTracer-100 Fourier transform-infrared spectrometer (Shimadzu) combined with attenuated total reflection (ATR) unit and DLATGS detector. Advanced spectral analysis combined with multivariate statistical analysis was performed with 'Kinetics' software (kindly provided by Prof. E. Goormaghtigh, ULB, Belgium) operating under MATLAB.

Results: Morphological images and flow cytometry analysis show that PGCCs exhibited enlarged cell sizes with high DNA content. Based on the IR data, significant alterations are observed in the spectral regions of proteins, lipids, nucleic acids and glycogen in PGCCs, indicating structural/compositional alterations. PAS and Oil Red staining images reveal increments in the glycogen and lipid droplet contents in PGCCs compared to control, suggesting a high metabolic activity.

Conclusion: IR spectroscopic analysis combined with biological assays provided determination of characteristic features of polyploidy in colon cancer cells. This study shows the potential use of IR spectroscopy as a powerful tool to gain new insights into the understanding of polyploidy features.

Keywords: Polyploidy, Polyploid giant cancer cells, Colon cancer, Infrared spectroscopy, Multivariate statistical analysis

INVESTIGATION OF THERAPEUTIC EFFECTS OF TDCS ON HIPPOCAMPAL GLUTAMATE AND CALCIUM EXCITOTOXICITY IN AN EXPERIMENTAL TRAUMATIC BR

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Abstract

Aim: The aim is to investigate the effects of tDCS application on learning and memory changes after TBI. In addition, the effects of tDCS on hippocampal glutamate level, NMDAR1 and calcium, which play an important role in learning, were also investigated.

Material and Methods: 30 male Wistar rats, each of which weighs 290-310 g, were divided into three groups as Control, TBI and TBI+tDCS groups. TBI was created with a moderate trauma model by dropping a weighing 200 g, from a height of approximately 1 m, on the head of the subject under anesthesia. 2 hours after tDCS application trauma injury, 1 mA anodal tDCS application will be applied for 30 minutes on the 1st and 2nd days. Novel object recognition was used to evaluate learning and memory, and open field test was performed to evaluate locomotor activity. Glutamate, Ca^{2+} and NMDA levels in hippocampus tissues were evaluated by ELISA method. Statistical analyzes were performed by One-Way ANOVA test.

Results: While a significant decrease was observed in the learning and memory behavior experiments results of the TBI group compared to the control group, there was a significant increase in the results of the tDCS+TBI group compared to the TBI group ($p<0.05$). Similar to the behavioral experiment results, Glutamate, Ca^{2+} and NMDAR1 levels were found to be significantly higher in the TBI group than the control group ($p<0.05$), and significantly lower in the TBI+tDCS group than in the TBI group ($p<0.05$).

Conclusion: Our results indicate that tDCS administration after TBI improves learning and memory disorders by regulating glutamate and Ca^{2+} levels, which play a role in hippocampal glutamatergic cell death as a result of Ca^{2+} and glutamate excitoxicity and may have a neuroprotective effect on learning and memory.

Keywords: Glutamate, Traumatic brain injury, Learning and memory, tDCS

EXPLORING THE COLOR CHANGE IN THE PARTIALLY COHERENT LIGHT BEAMS PASSING THROUGH HUMAN EYE LENS

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Abstract

We demonstrate color shifts in the partially coherent light beams during the course of interaction with the crystalline human eye lens. The result we obtain may have an impact in bio-optics and in the cognitive science since there is a profound change in the color of random light beams during its propagation in the human eye. After the initial study of the crystalline human eye lens' response to stochastic light, it is now possible to analyze the interaction of any type of light with the human eye lens. The eye is the only optical element of the human body and the biconvex lens together with the cornea constitutes the main optical elements of the eye. And the light which enters the eye is broadband and has a range of coherence values, from incoherent light to fully coherent light, but mostly it is the partially coherent light where an example is the sunlight after atmospheric propagation or after scattering. Therefore, based on the diffraction theory of optics together with the ray tracing methods we will detect the wavelength shift in the partially coherent light passing through human eye lens. In detail, A directional un-polarized random light of cross-sectional radius ~0.3 mm will be sent numerically to the lens surface which resides in the minimum possible pupil radius of ~0.5 mm. Consequently, owing to the fact that the eye is mostly exposed to partially coherent light, we examine a partially coherent beam in the lens to be able to see the correlation effects of natural light on the polarization and on the interaction of light with the eye lens.

Keywords: Human eye, Human eye lens, Partially coherent light, Polarization

EFFECTS OF ACETYL-L-CARNITINE ADMINISTRATION ON EEG IN RATS EXPOSED TO CHRONIC ETHANOL

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Abstract

Aim: Ethanol consumed in various beverages is considered by the World Health Organization as one of the substances that cause both physiological and psychological addiction. One of the organs negatively affected by chronic alcohol consumption is the brain, and this effect can be seen most easily on EEG signals. Acetyl-L-carnitine (ALC) is an endogenous antioxidant agent which contains carnitine and acetyl moieties and is thought to have neuroprotective effects. Therefore, in this study, it was aimed to investigate the effects of ALC administration on EEG in rats exposed to chronic ethanol.

Material and Methods: 3 months old 48 male Wistar rats were divided equally into 4 groups namely sham (Sh), chronic ethanol (CE), ALC administered (ALC), and chronic ethanol+ALC (CE+ALC). Distilled water to the Sh group, 5g/kg ethanol (25% v/v) to the CE group, 50 mg/kg ALC to the ALC group, and the same doses of ethanol+ALC to the CE+ALC group were given by gavage for 4 weeks. After this period, spontaneous EEG recordings were taken from the frontal and temporal regions of the rat brain under urethane anesthesia (1.2 g/kg), and EEG power spectra in different frequency bands were analyzed.

Results: According to the EEG power spectrum analysis results, theta and alpha powers in the frontal region and theta, alpha, and beta powers in the temporal region were decreased in the CE and ALC groups compared to the control group. On the other hand, there was no significant difference in EEG power between the CE and CE+ALC groups.

Conclusion: As a result, in this study, it was observed that chronic alcoholism caused a decrease in EEG power in the frontal and temporal regions of the rat brain, while ALC could not ameliorate this decrease in the dose and duration applied here.

Keywords: Chronic alcoholism, Rat, Acetyl-L-Carnitine, EEG

IDENTIFICATION OF A NEW IN-VITRO MODEL OF EPILEPSY DUE TO TRK-B RECEPTOR ACTIVATION IN BRAIN SLICES

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Abstract

Aim: Epilepsy is a disease, characterized by recurrent seizures as a result of synchronized activity of a group of neurons. The cellular mechanisms that cause epilepsy are still not fully understood. Reliable experimental models are needed to elucidate the pathogenesis of epilepsy and to discover new drugs for treatment. In fresh brain slices, where synaptic connections are preserved and neuronal circuits functions like in vivo, epilepsy-like activities are induced in the experimental settings. Existing in vitro models have shortcomings such as mimicking some epilepsy pathologies and acting on a single pharmacological target. They also fall short of modeling drug-resistant types of epilepsy. In this study, it was investigated whether a newly developed Trk-B receptor agonist 7,8 Dihydroxyflavone(DHF) and 4-AP, would be a model of epilepsy with their synergistic effect by applying them at low doses that would not cause epilepsy alone.

Material and Methods: 30-35 days old C57BL-6 mice were used in the experiments. Brain slices (400 micrometers) containing hippocampus and neocortex were taken and rested in artificial cerebrospinal fluid (ACSF) for at least 1 hour, and then the experimental procedure was performed. Extracellular local field potentials were recorded from the CA1 region of hippocampus and entorhinal cortex with the glass micropipette electrodes.

Results: In the study, when either 40 microM 4-AP or 20 microM 7,8-DHF was applied, an epilepsy-like event did not occur in the CA1 and entorhinal cortex regions. However, when they were applied together synchronized discharges, which could be defined as epilepsy-like activities, occurred in both regions.

Conclusion: A new epilepsy model described in which 7-8-DHF and 4-AP were used together with the results of the preliminary study. Both neurotransmitter release and neuronal excitability levels are affected to form epileptic synchronizations. Therefore, we think our model has the potential to be a useful in vitro model.

Keywords: Epilepsy, Brain slice, 7,8-DHF, 4-AP

THERAPEUTIC POTENTIAL OF AGMATINE ON METHOTREXATE-INDUCED PERIPHERAL NEUROPATHY

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Abstract

Aim: Chemotherapeutic agents, such as methotrexate (MTX), can damage peripheral nerves leading to chemotherapy-induced peripheral neuropathy. This study aims to investigate the therapeutic efficacy of agmatine (AgM), an endogenous neuromodulator, on MTX-induced peripheral neuropathy in the sciatic nerve.

Material and Methods: 40 Wistar albino male rats were randomly divided into four experimental groups as control, MTX, AgM and MTX-AgM. MTX was administered at a weekly dose of 37.5 mg/kg/week (intraperitoneal) for 3 weeks. Then, AgM was injected at a 40 mg/kg dose (intraperitoneal) twice a day for 7 days. Nociceptive pain perception and behavioral alterations were determined via hot plate, tail-flick, water maze, rotarod and open field tests. Assessment of the sciatic nerve conduction and histopathological evaluations were performed.

Results: MTX administration resulted in the increase in escape latency ($p<0.05$) and the time spent in the quadrant ($p<0.01$) in the water maze test and led to the decrease in nociceptive pain perception ($p<0.001$) and the decrease in the line crossing frequency ($p<0.001$) in the open field test in comparison to the control. Nerve conduction velocity was also reduced in MTX group compared to that of control ($p<0.001$). In addition, MTX injection led to a decrease in the axon diameter ($p<0.001$), myelin thickness ($p<0.001$) and perineurium thickness ($p<0.001$) and resulted in a higher glial fibrillary acidic protein (GFAP) immunoreactivity in sciatic nerves in comparison to those of control group. AgM administration improved the MTX-induced alterations in behavioral performance, nociceptive pain perception ($p<0.05$), nerve conduction, GFAP immunoreactivity and sciatic nerve histology in comparison to the MTX group.

Conclusion: The results revealed the therapeutic potential of AgM in restoring the alterations produced by MTX-induced peripheral neuropathy. However, dose regulation and/or combined treatment may increase the effectiveness of the treatment. This study was supported by ADU-BAP through the grant number TPF-21004.

Keywords: Methotrexate, Agmatine, Sciatic Nerve, Peripheral Neuropathy, Glial fibrillary acidic protein

BEHAVIORAL AND NEUROCHEMICAL EFFECTS OF HIGH CHOLESTEROL DIET ON BRAIN DERIVED NEUROTROPHIC FACTOR (BDNF) HETEROZYGOUS MICE

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Abstract

Aim: Cholesterol is a lipid vital for many cellular functions and synthesized de-novo. However, a high cholesterol diet has been suggested to trigger neurodegeneration by increasing neuroinflammation and oxidative stress. In addition, individual genotypic differences may be important in determining the effect of diet on these changes in the brain. The aim of the study is to investigate the possible protective effects of BDNF against high cholesterol diet-induced damages by behavioral and biochemical methods.

Material and Methods: 20-25 g male thirty C57BL/6 mice were divided into four groups as n=9 control diet fed wild type (CD-Wt), n=8 control diet fed BDNF heterozygous (CD-Ht), n=7 high cholesterol diet fed wild type (HCD-Wt) and n=6 high cholesterol diet fed BDNF heterozygous (HCD-Ht). After the ad libitum diet protocol applied for 16 weeks, cylinder test and hang wire test were performed to test cortical sensory-motor functions. In addition, tumor necrosis factor-alpha, interleukin-6 levels together with the oxidative stress parameters of MDA, SOD and CAT were measured from the cortical homogenates. Statistical comparisons of the data were analyzed with the two-way ANOVA test and Dunnett post hoc test was used to compare other groups with the control wild type group.

Results: HCD-Ht group performed poorly in the behavioral tests. In cylinder test the number of contacts were changed significantly between CD-Wt and CD-Ht groups (p<0,05). In hang wire test CD-Wt was found significantly higher than HCD-Ht group (p<0,05). High cholesterol diet significantly affected oxidative stress among CD-Wt and HCD-Wt groups (p<0,001). Two-way ANOVA revealed a significant diet effect on IL-6 (p<0.005). No significant difference in IL-6 levels and TNF- α levels in groups compared to control group.

Conclusion: Endogenous BDNF levels is a factor that determines the levels of inflammation and subsequent loss of function in the brain caused by high cholesterol diet.

Keywords: BDNF, High cholesterol diet, Neuroinflammation, Oxidative stress, Sensory-motor functions

EFFECTS OF 50 HZ MAGNETIC FIELDS ON CHEMOTHERAPY AND ELECTROCHEMOTHERAPY TREATMENTS

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Abstract

Aim: Due to the rapid increase in cancer cases and cancer-related death rates, the development of effective treatment techniques has become an indispensable need. Despite some negative effects on healthy tissues and cells, chemotherapy (CT) is frequently chosen for the treatment of cancer patients. Electrochemotherapy (ECT), on the other hand, is a treatment technique in which cancer cells are made permeable to anticancer drugs and the dose of drugs required for cancer treatment is minimized. Exposure to extremely low frequency (50 Hz) magnetic fields can cause various changes at the cellular level. In this study, it was aimed to investigate the effect of short-term extremely low-frequency magnetic fields (ELF-MFs) on CT and ECT treatments in Caco-2 colon cancer cell line.

Material and Methods: Caco-2 cancer cells were treated with 5-fluorouracil alone (CT, 50 µM), ECT alone (pulse strength:1125 V/cm, pulse duration:100µs, frequency:1 Hz), CT+ELF-MF (4mT, 10 min) and ECT+ELF-MF (4mT, 10 min) treatment modalities. The effectiveness of the treatments was evaluated using the MTT test.

Results: Our study's results demonstrated that, in Caco-2 colon cancer cells, ECT was significantly effective than CT treatment alone ($p<0.05$). When the CT group compared to the CT+ELF-MF group and the ECT group compared to the ECT+ELF-MF group, less Caco-2 cancer cell death occurred in the plus ELF-MF treated groups ($p<0.05$).

Conclusions: The results demonstrate that CT and ECT therapy efficacy in Caco-2 colon cancer cells is severely decreased by exposure to ELF-MF at 4 mT flux density.

Keywords: Magnetic field, Caco-2 cancer cells, 5-FU, Chemotherapy, Electrochemotherapy

A NEW BIOMARKER FOR THE DIAGNOSIS OF EXPERIMENTAL UNILATERAL URETEROPELVIC JUNCTION OBSTRUCTION: RENALASE

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Abstract

Aim: It was aimed to investigate serum and urine renalase levels in the diagnosis of experimental unilateral ureteropelvic junction obstruction (UPJO) in rats.

Material and Methods: In this study, 3-month-old Sprague-Dawley young-adult male rats (n: 30) were used. Rats were divided into five groups, six in each group: Group 1, control group; Group 2, Sham group; Group 3, right nephrectomy group; Group 4, unilateral UPJO group; and Group 5, the group with right nephrectomy and unilateral UPJO. On the 15th day of experimental unilateral UPJO, renal tissues were obtained along with serum and urine samples. The changes in renalase, dopamine, epinephrine, metanephrine, normetanephrine, urea and creatinine levels in serum and urine samples were analyzed. In addition, renalase levels were examined immunohistochemically in the renal tissue.

Results: In Group 1 and Group 2, no significant changes were observed in both serum and urine renalase, dopamine, epinephrine, metanephrine, normetanephrine, urea and creatinine levels on the 15th day of unilateral UPJO.A decrease in serum renalase level was detected in Groups 3, 4 and 5 compared to Group 1. At day 15, urinary renalase, dopamine, epinephrine, metanephrine, and normetanephrine levels were increased in Group 5 compared to Groups 1 and 2.

Conclusions: Renalase may be a simple, effective, and noninvasive descriptive new biomarker in the diagnosis of UPJO. However, there is a need for extensive new clinical studies to be used in routine practice in UPJO cases.

Keywords: Ureteropelvic junction obstruction, Renal damage, Biomarker, Renalase, Catecholamines

EVALUATION THE EFFECT OF PREDNISOLONE (DELTACORTRIL®) ON MYASTHENIA GRAVIS BY INFRARED SPECTROSCOPY

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Abstract

Aim: The neuromuscular junction deteriorates as a result of Myasthenia Gravis (MG). Myasthenia Gravis, which is a rare and autoimmune disease, has a prevalence of 15-20/100,000 people. Skeletal and extraocular muscle involvement is prevalent in the disease's history. Furthermore, myasthenic crises can occur in 10% of patients. Myasthenic crisis is a life-threatening complication caused by the involvement of the respiratory muscles. Prednisolone (Deltacortril®) is an immunosuppressive drug used in the treatment of MG. It suppresses the immune system in MG. Therefore, it is often used in the treatment of MG. The aim of this study is to investigate the effect of deltacortril® on MG at the molecular level by utilizing the ATR-FTIR spectroscopy technique.

Material and Methods: In this study, three groups were used. Age and gender-matched control group, the MG patient group who did not receive immunosuppressive treatment, and the treatment group using deltacortril®. Subjects' informed consent was obtained by the requirements of the study ethics boards. Blood samples were collected from all three groups. Afterward, blood serum samples were obtained. Spectra of serum samples were collected by ATR-FTIR spectroscopy.

Results: In the spectral analyzes, aliphatic chain length, protein structural changes, protein concentration, lipid/protein, DNA concentration, and saturated lipid content band area ratios were investigated. The results revealed that protein structural changes, protein concentration, DNA concentration, and saturated lipid content were significantly increased, while aliphatic chain length and lipid/protein ratio were significantly decreased in MG patients. However, for patients treated with deltacortril®, the results were found to be similar to the control group.

Conclusions: This study investigates the impact of deltacortril® on MG at the molecular level. The results clearly show the recovery effect of deltacortril® on MG patients. Acknowledgment: This work is supported by the TUBİTAK-1003 project (Grant no: 218S986, 218S987, and 218S988).

Keywords: Myasthenia gravis, Neuromuscular disorder, ATR-FTIR Spectroscopy, Rare disease

ASPROSIN MODULATES MIRNA-181A EXPRESSION IN DORSAL ROOT GANGLIONS OF DIABETIC MICE

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Abstract

Aim: Recent studies demonstrate there is strong link between adipokines and neuropathic pain. The level of asprosin, a novel adipokine, has been found to be changed in conditions such as diabetes, obesity. Diabetes-induced gene expression changes within the dorsal root ganglia (DRG) neurons contribute to neuropathic pain. MicroRNAs (miRNA) are non-coding functional RNAs that negatively regulate multiple gene expressions. miRNA-181a is known to suppress apoptosis, autophagy, and chronic inflammatory conditions such as diabetes. However, it is not known whether asprosin changes miRNA-181a levels in DRG of healthy and diabetic animals. This study was aimed to investigate the effects of asprosin on miRNA-181a levels in DRG of diabetic mice.

Material and Methods: In this study, adult Balb/C male mice weighing 25-30 g were used. They were randomly divided into four groups: control, asprosin, streptozotosin (STZ) induced diabetic control and STZ+asprosin (n=7 for each group). Asprosin was injected intraperitoneally four times at 3-day intervals to all mice in the asprosin and STZ+asprosin groups. After decapitation, the lumbar-4 and -5 DRGs of mice were taken, and the miRNA-181a levels were analyzed by the real-time polymerase chain reaction method at the end of the experiment.

Results: miRNA-181a levels in the DRG significantly decreased in diabetic mice compared to the control group. However, asprosin administration to diabetic animals significantly increased miRNA-181a level ($p < 0.05$).

Conclusions: These results clearly demonstrate, for the first time, that asprosin increased miRNA-181a levels in DRG of diabetic mice. Considering that miRNA-181a plays a role in the mechanism of apoptosis, autophagy, and inflammation, we suggest that asprosin may have a neuroprotective effect in diabetes.

Keywords: miRNA-181a, Asprosin, Dorsal root ganglion, Neuropathic pain

INVESTIGATION OF PROLINE RICH ACIDIC PROTEIN 1 (PRAP1) LEVELS IN PRETERM DELIVERY

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Abstract

Aim: Preterm birth is defined delivery between gestational weeks of 20 and 36. It is a significant cause of perinatal mortality and complications. Several factors play role in development of preterm birth. A specific blood marker would be a milestone for prevention; however, such a molecule has not been described. In this study, maternal serum PRAP1 protein assumed to function as a molecule for implantation of embryo was measured and its relation to preterm delivery was assessed.

Material and Methods: This study was conducted at Adıyaman University Medical School Department of Obstetrics and Gynecology between September 2020 and May 2021. 25 pregnants with preterm labor between the gestation weeks of 24 weeks + 0 days – 36 weeks + 6 days were classified as preterm delivery group and 25 with term labor and without any obstetrical complaints were classified as control group. Serum PRAP1 levels were measured using a commercial ELISA kit. Groups were compared in term of gestational weeks, age, body mass index, obstetric status (gravida, parity, abortus).

Results: Mean serum PRAP1 levels were found 20.06 ng/ml in control group and 15.76 ng/ml in preterm group (p=0.273). Body mass index, age, gravidity, parity, abortus difference between two groups were not statistically significant.

Conclusions: Serum PRAP1 levels were found lower in preterm group. However, this difference statistically was not significant (p=0.273). Increasing sample size might result in larger difference in the result. Based on the results lower levels of serum PRAP1 might be a factor causing preterm delivery.

Keywords: Preterm delivery, PRAP-1, Pregnancy, Delivery

EFFECTS OF HIGH CARBOHYDRATE AND HIGH FAT DIETS ON SKELETAL MUSCLE LIPID AND TRACE ELEMENT CONTENTS

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Abstract

Aim: In this study, it was aimed to investigate the effects of high-fat and high-carbohydrate diets on the structure and amount of lipids, and changes in trace element levels in inbred female C57BL/6J mouse skeletal muscle tissue.

Material and Methods: In this study, mice were fed for six months and divided into three groups as control (CD), high-fat diet (HFD), and high-carbohydrate diet (HCD). Biomolecular changes induced by high-calorie diets in skeletal muscle tissues of female C57BL/6J mice were investigated by Attenuated Total Reflectance-Fourier Transform Infrared (ATR-FTIR) spectroscopy, and changes in trace element levels were analyzed by Inductive Coupled Plasma-Optical Emission Spectroscopy (ICP-OES).

Results: Both in the HFD and HCD groups, the amounts of saturated lipids, triglycerides, lipid/protein ratio and lipid peroxidation increased. These results lead to fat storage in the skeletal muscle tissues of mice. In addition, the significant reduction of essential trace elements was seen in skeletal muscle tissues of mice fed a high-carbohydrate diet.

Conclusions: High-calorie diets cause global changes that may affect skeletal muscle functions at the molecular level. In the HCD group, the significant reduction of essential trace elements in skeletal muscle tissues of mice fed with high-carbohydrate diet can be a potential biomarker to distinguish these two diets from each other. According to our results, a high-carbohydrate diet caused more damage to skeletal muscle tissue than a high-fat diet. This study was funded with TUBITAK-3501-SBAG-118S484 project.

Keywords: High fat diet, High carbohydrate diet, Skeletal muscle, ATR-FTIR, ICP-OES

EVALUATION OF THE EFFECT ON TELOMERE LENGTH OF OCCUPATIONAL RADIATION EXPOSURE OF HEALTH PROFESSIONALS

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Abstract

Aim: Medical professionals and especially in the fields of interventional radiology, cardiology, nuclear medicine and radiation oncology, and all other medical professionals are constituting the largest group of occupational exposures to ionizing radiation (IR).IR is one of the most important physical hazards that can lead to the development of radiation-related cancer and other non-communicable diseases of medical radiation workers. Telomeres are nucleoprotein complexes comprised of tandem arrays of repetitive DNA sequence that serve to protect chromosomal termini from inappropriate degradation, as well as to prevent these natural DNA ends from being recognized as broken DNA and triggering of inappropriate DNA damage responses. However, the effects of IR exposure on telomeres per se are much less well understood. Our aim is to investigate the effect of occupational IR exposure of medical radiation workers on telomere length.

Material and Methods: The control group was healthy volunteers (n=8),experimental group was interventional radiology (x-ray, CT, fluoroscopy, n=26),cardiology (angiography n=9), nuclear medicine (n=11) and radiation oncology (n=11).2 ml of whole blood from all consenting groups was taken into tubes with EDTA, and telomere length was evaluated from serum samples using a Absolute Human Telomere Length Quantification qPCR Assay Kit (ScienceCell).Demographic information was obtained from all groups regarding age, gender, occupational years (about 11 years), smoking and alcohol consumption, and whether they had any chronic diseases. Age range and professional years were tried to be equal as much as possible between the groups.

Results: Telomere length of the control group was 22.08 and ionizing radiation groups were 7.29 ($p<0.005$). Telomere length shorting may be associated with genomic instability, cancer, or senescence in a variety of settings.

Conclusions: The results showed the critical importance of telomere length in the radiation response. Ionizing radiation exposure in medical staff may be associated with increased telomere length shortening.

Keywords: Occupational exposure, Ionizing radiation, Cancer, Telomere length, Medical staff

LOW-INTENSITY LOW-FREQUENCY PULSED ULTRASOUND AND WITHAFERİN A AMELIORATES NERVE DAMAGE IN DIABETIC NEUROPATHY

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Abstract

Aim: Diabetic neuropathy initiates the progressive degeneration of neurons, generally in lower extremities. This study was conducted to assess the therapeutic efficiencies of low-intensity low-frequency pulsed ultrasound and withaferin A (a leptin sensitizer) on diabetic neuropathy.

Material and Methods: Adult male Wistar rats were randomly divided into five groups (n=10) as control, diabetic, withaferin A (1.25 mg/kg) and 1 MHz 0.5 W/cm2 and 1.5 W/cm2 pulsed ultrasound treated diabetic groups. Diabetes was induced by 50 mg/kg streptozotocin injection, and the rats having high blood glucose levels (>300 mg/dl) were maintained untreated for 4 weeks for diabetic neuropathy formation, which was confirmed by increased nociceptive latencies. Then, ultrasound and withaferin A treatments were applied daily for 14 days. Ultrasound was applied onto the dorsolateral part of each leg for 3 minutes. Alterations in nociceptive pain perception and nerve conduction were assessed. Histopathological changes were evaluated by Masson's trichrome and luxol fast blue staining of the sciatic nerve sections together with immunohistochemical determination of glial fibrillary acidic protein (GFAP), Iba-1, S100β and myelin protein zero reactivities.

Results: Diabetes resulted in increased nociceptive latencies, decreased sciatic nerve conduction velocities, and increased duration of compound muscle action potentials, which were restored upon treatments especially in withaferin A and 1.5 W/cm2 ultrasound treated groups. Moreover, diabetes led to demyelination and degeneration in sciatic nerves with a significant decrease (p<0.001) in myelin thickness, axon and myelinated axon diameters. Besides, higher immunoreactivity of GFAP, Iba-1, S100β and myelin protein zero were observed in diabetic nerve sections. These histopathological alterations were recovered upon treatments, especially in the 1.5 W/cm2 ultrasound treated group.

Conclusions: The findings revealed that withaferin A and 1 MHz 1.5 W/cm2 pulsed ultrasound treatments exhibit a therapeutic potential in restoring diabetes-induced alterations and warrants further investigations. This study was supported by TÜBİTAK (grant number 219S443).

Keywords: Diabetic peripheral neuropathy, Ultrasound, Withaferin A, Sciatic nerve, Myelination, Nerve conduction

THE EFFECT OF JACEOSIDIN ON INSULIN RESISTANCE IN HUMAN HEPG2 CELLS

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Abstract

Aim: Insulin resistance (IR) is a pathological condition, in which the normal level of insulin in the circulation cannot give the required response due to the decrease in the sensitivity of target organs and tissues to insulin at the receptor level. Jaceosidin is a pharmacologically active flavone with apoptotic, antioxidant, anticancer, anti-inflammatory and immunosuppressive activities. Liver is affected by insulin resistance. After insulin resistance, glucose metabolism and glycogen synthesis are impaired in the liver. Therefore, in our study, unlike the literature, we aimed to show the effects of jaceosidin on glucose metabolism and glycogen synthesis in the insulin resistance model created in the human hepatocellular carcinoma cell line (HepG2).
Material and Methods: MTT analysis was performed in HepG2 cells to determine non-toxic doses of jaceosidin. In order to induce IR, HepG2 cells were exposed to high-dose glucose (30mM) and high-dose insulin (500nM) for 48 hours. In this process, varying doses of jaceosidin (40, 30, 20 and 10µM) were applied. In order to determine the glucose consumption rates at the end of the experiment, the samples were collected at the 12th and 24th hours and the glucose amounts were calculated. Then, IR and changing intracellular glycogen amounts depending on the application of jaceosidin were shown by PAS staining.
Results: In the cytotoxicity analysis, it was observed that the toxicity of jaceosidin increased significantly after 40µM dose. Therefore, 40µM was chosen as the high dose in our study. When glucose consumptions were compared after the IR model, it was observed that jaceoside increased glucose consumption significantly at 40, 30 and 20µM doses compared to the control. It was determined that glucose consumption was the highest, especially at a dose of 30µM.
Conclusions: It has been shown that jaceoside both increases glucose consumption and prevents the deterioration of glycogen synthesis in HEPG2 cells with IR.

Keywords: Insulin resistance, HepG2, Jaceosidin

ENZYMATIC AND HISTOPATHOLOGICAL CHANGES IN RAT LIVER EXPOSED TO PRE-AND POSTNATAL RADIOFREQUENCY ELECTROMAGNETIC FIELD: A GENERATION STUDY

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Abstract

Aim: The effects of devices emitting electromagnetic field (EMF) on human health have become the subject of intense research among scientists due to rapid increase in their use. Humans are particularly attracted to use of devices emitting EMF. Therefore, this study was investigated the effects of liver development in the fetus, changes histopathological and enzymatic in female and male rats after exposed to pre and postnatal 2450-MHz continuous wave (CW) radiofrequency radiation (RFR) over four generations.

Material and Methods: Four groups; sham, irradiated female, irradiated male, irradiated male and female, with each consisting of four rats (one male/three females) were created. Rats in the exposure groups were whole-body exposed to 2450-MHz CW-RFR for 12h/day during the experiment. Irradiation started one month before fertilization in experimental group. On 18th day of the gestational period, one pregnant rat from each group was decapitated under general anesthesia and the fetuses were taken. The remaining two pregnant rats completed the normal gestation period. When offspring were two months old, four rats, one male and three females, were allocated for the second-generation study. Next generation animals were also experienced the same processes as first-generation rats. This study was evaluated development of liver in fetuses and histopathological changes using haematoxylin eosin staining, and enzymatic changes in liver of adult rats using ELISA.

Results: We were observed increase in MDA levels and decrease in SOD and CAT activities in adult rat's 2nd and 3rd exposure groups of the third and fourth generation. The livers of adults and fetuses were normal histology in control group. Hemorrhage, hepatocyte degeneration and necrotic areas with some cytoplasmic vacuolizations were observed in all exposure groups, especially in 3rd and 4th generation livers of both fetuses and adults.

Conclusions: The data show RF-EMA causes oxidative stress and histopathological changes in liver.

Keywords: Liver, Fetus, 2450 MHz continuous wave, Generation, Oxidative stress

INVESTIGATION OF THORAX DEFORMITIES IN DIFFERENT CLINICAL TYPES OF PATIENTS WITH CEREBRAL PALSY

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Abstract

Aim: Cerebral Palsy (CP) is associated with non-progressive disorders in the developing fetal or infant brain. It causes activity limitation and a group of permanent problems in the development of movement and posture. The aim of this study is to evaluate thorax deformities, anthropometric values and independence levels in different clinical types of CP and to associate them with the healthy group.
Material and Methods: For this study, 40 healthy and 133 CP patients aged 6-12 years have been evaluated so far. Ethics committee approval was obtained for the study and an informed consent form was signed. Demographic information, thorax assessment, anthropometric measurements and GMFCS were examined in the study. Anthropometric set and tape measure were used for the study.
Results: The evaluated individuals, 40 were healthy (20 women, 20 men) and 133 were patients with CP (52 women, 81 men). The women were 32 spastic, 5 ataxic, 5 dyskinetic and 10 hypotonous. The men were 61 spastic, 5 ataxic, 5 dyskinetic and 10 hypotonous. The patients were 55 born normal, 78 cesarean, 43 premature and 90 born mature. The evaluated of Thorax had 8 kyphosis, 30 scoliosis, 6 lordosis, 8 round back, 6 straight back, 18 pectus excavatum and 11 pectus carinatum deformities. Considering the independence values, there are GMFCS I 28, II 37, III 25, IV 10 and V 35 people.
Conclusions: CP is one of the most common diseases of childhood. Secondary problems often accompany CP. Mental retardation, epilepsy, malnutrition, pulmonary and postural problems are some of them. It has been observed that CP has lower respiratory functions compared to individuals with normal development. Respiratory muscle strength and chest mobility are closely related to posture, and disorders such as kyphosis, scoliosis or kyphoscoliosis are observed with CP. As a result, CP is not only a neuromuscular disease, but also brings with many problems. For this reason, when evaluating patients should be a holistic approach, multidisciplinary and secondary problems that may occur should be prevented. Nourices should be informed about CP and the quality of life of patients should be increased as much as possible.

Keywords: Cerebral palsy, Thorax, Deformity

PHOTODYNAMIC INACTIVATION OF LEISHMANIA TROPICA PROMASTIGOTES BY MALACHITE GREEN: AN IN VITRO STUDY

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Abstract

Aim: Leishmaniasis is one of the vector-mediated infectious disease and contains a series of diseases caused by protozoan parasites of the Leishmania genus. Nowadays, alternative treatment options are being developed, and Photodynamic therapy (PDT) is one of the novel approaches to eradicating parasites. PDT is based on the principle that the photosensitizer selectively accumulated in the target tissue is exposed to a visible light of a suitable wavelength. To determine and understand the mode of action of malachite green mediated PDT, we investigated the cell death mechanisms caused by L.tropica promastigotes.

Material and Methods: Parasites were incubated with 0.19, 0.39, 1.56, 3.25 and 6.25 µM of malachite green (MG) for one hour and subjected to 46.4 J/cm2 light irradiation. Morphological changes were analyzed by Giemsa staining and Scanning electron microscopy. Afterwards, physiological (mitochondrial membrane potential, cell volume, Annexin V binding, cell cycle) changes triggered by MG mediated PDT in L.tropica promastigotes were investigated using flow cytometry.

Results: MG mediated photodynamic therapy at 1.56 and 3.125 µM decreased the viability of the L.tropica promastigotes.Polarization in the mitochondrial membrane of healthy promastigotes caused an change in the direction of depolarization in MG+PDT treated promastigotes. The percentage of Annexin V+ apoptotic cells was found to be 2% in the untreated control group, and 31.4% (1.56µM) to 41.4% (3.125 µM) in the MG+PDT-treated group. L.tropica promastigotes was bloked in G0/G1 phase. The morphology of the parasite was affected at the 1.56 and 3.125 µM MG+PDT, resulting in rounded cells with loss of flagellum and irregular shape.

Conclusions: This study demonstrated antileishmanial effects through mitochondrial dysfunction, cell cycle arrest, and cell death to parasites. Our findings support that MG mediated PDT may represent a new treatment option for Cutaneous Leishmaniasis.

Keywords: Leishmania tropica, Malachite green, Photodynamic therapy, Apoptosis

DETERMINATION OF THE EFFECT OF VITAMIN D ON THE SENSE OF SMELL

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Abstract

Aim: Vitamin D is the only vitamin that can be synthesized in the human body. Apart from its effect on calcium-bone balance, the role of vitamin D in regulating many cell functions has been studied. Vitamin D receptors have been identified in the olfactory system. Therefore, we think that vitamin D may affect olfaction. We aimed to investigate the effects of blood vitamin D levels on the sense of smell.

Material and Methods: Volunteers were divided into two groups those with 25-hydroxy vitamin D blood levels (electrochemiluminescence method) below 30ng/ml and above. Volunteers with values below 30ng/ml received 8 weeks of orally ergocalciferol 50000 IU/week. Volunteers underwent a smelling test, which included the butanol test and odor recognition (Connecticut olfactory test). It was investigated whether there was a difference between groups and pre-and post-treatment test scores of the 1st group.

Results: Each group consisted of 20 people. The 25-hydroxy vitamin D levels of volunteers in the first group ranged between 3-22,8ng/ml. Odor scores were 2,5-6 for right and 3-6 for left. The 25-hydroxy vitamin D levels of volunteers in the second group ranged between 30-48,7ng/ml. Scores ranged from 5,5-7 for right and 5,5-7 for left. Post-treatment, scores of the 1st group were between 5,5-7 for right and 6-7 for left. Pre-treatment scores of the 1st group were found to be significantly lower than the 2nd group ($p<0.05$). After treatment, the scores of the groups were similar($p>0.05$) and the scores of the 1st group were significantly higher than pre-treatment($p<0.05$).

Conclusions: Vitamin D deficiency can cause olfactory dysfunction, which can reverse with treatment.

Keywords: Olfactory, Replacement, Deficiency

EFFECT OF CAFFEINE ON HIPPOCAMPAL SNAP25 AND GFAP IN A SOCIAL ISOLATION STRESS

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Abstract

Aim: Caffeine is the most popular psychostimulant substance consumed worldwide. Caffeine's neurochemical effects on social isolation stress are little known. In this study, the possible effect of caffeine against social isolation (SI) stress in early life was investigated with hippocampal synaptic vesicle protein SNAP25 and astrocyte marker GFAP.

Material and Methods: 21-day old Wistar albino male rats (n=32) were divided into 4 groups as: control group (C); caffeine group (Cf); SI group and SI+Cf group (SICf). Caffeine (0.3 g/L) was added to the drinking water of the experimental animals for 4 weeks. SI stress was induced by rats housed alone in a standard cage. After the 4-week experimental procedure, learning and memory performance were assessed with the Morris Water Maze Test (MWMT). Hippocampal SNAP 25 and GFAP gene expression levels were investigated by RT-PCR method.

Results: According to our MWMT findings, the time spent in the quadrant where the platform was lifted was shorter in the SI group compared to the C group ($p<0.05$). Hippocampal SNAP25 gene expression was lower in the Cf and SICf groups than in the C group ($p<0.05$). The GFAP gene expression level was higher in the SICf group than in the C group ($p<0.05$).

Conclusions: SI stress has a negative effect on hippocampal memory. Caffeine lowers hippocampal SNAP25 gene expression, and together with SI, caffeine increases GFAP gene expression. Caffeine induces neurochemical changes in the hippocampus, without affecting memory function. This study was supported by Adiyaman University (grant number, TIPFMAP/2021-0002).

Keywords: Caffeine, Social isolation, Hippocampus

DNA TENSION MAY INCREASE CRISPR-CAS9 AND SGRNA DISSOCIATION/ASSOCIATION RATE

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Abstract

Aim: CRISPR/Cas9 offers a two-component system for double stranded DNA cleavage. Cas9 is the enzymatic component with two nuclease domains for cleaving the DNA strands. Single guide RNA (sgRNA) is the RNA component which associates with the Cas9 enzyme for the target detection. After Cas9 and sgRNA are associated, they form a stable Cas9/sgRNA complex to interrogate the DNA sequences. Once the complementarity of guide RNA and target DNA is maintained, DNA cleavage occurs. CRISPR systems are mainly derived from bacteria. Unlike prokaryotic DNA, eukaryotic DNA face mechanical tension during various cellular processes like compaction, extraction, replication, transcription, or chromatin remodeling. The energetic profile of CRISPR/Cas9 cleavage suggests that mechanical tension on the DNA can alter the reaction kinetics. However, the stability of Cas9/sgRNA complexes when targeting DNA with mechanical tension remains unknown. Here I show that the stability of the Cas9/sgRNA complex are reduced in the presence of a mechanical tension on the target DNA.

Material and Methods: I employed a single-molecule technique to monitor two types of target DNA in the same microchamber: relaxed and mechanically stressed DNA. The target DNA molecules were attached to the surface and labeled with either fluorescent polystyrene beads or magnetic beads. Initially, only Cas9/sgRNA complexes to target DNA with tension were introduced. Later, sgRNA for relaxed DNA target without Cas9 molecules were introduced.

Results: Shortly after adding the new sgRNA, I observed the cleavage process of the relaxed DNA tethers. In contrast to the reported stability of Cas9/sgRNA complex, this outcome suggests a faster sgRNA switching in the presence of a mechanical tension on the target DNA.

Conclusions: This observation has many implications for the CRISPR/Cas9 gene-editing technique. As an example, it is possible to target more than one gene by supplying only relevant sgRNAs with a limited amount of Cas9 enzymes.

Keywords: CRISPR, Single-molecule biophysics, DNA mechanics, Gene-editing

EFFECTS OF THYMUS VULGARIS OIL ON SODIUM HYPOCHLORITE TOXICITY IN RATS

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Abstract

Aim: Sodium hypochlorite (NaOCl) is a chemical compound used as a disinfectant and bleaching agent in the food industry, healthcare, drinking water treatment, endodontic treatment. Due to its strong oxidizing properties, NaOCl has been shown to cause gastrointestinal, hematological, and pulmonary toxicity in long-term exposure as a result of inhalation. In this study, we aimed to demonstrate the pulmonary toxicity associated with exposure to two doses of NaOCl, potential damage mechanisms, and effect of thymus vulgaris oil (TVg), which has antimicrobial and anti-inflammatory effects.

Material and Methods: In the study, 6 groups were formed with 5 rats in each group. Rats were exposed to inhalation (control, TVg, 4% NaOCl, 15% NaOCl, 4% NaOCl+TVg and 15% NaOCl+TVg) for 30 min with nebulizer. At the end of the inhalation process, blood and diaphragm muscle was taken for biochemical analyzes and recordings of contraction responses, respectively.

Results: Decrease in diaphragm muscle maximum contraction force (Pm) was detected in 4% NaOCl at 100 Hz and 1 Hz stimulation at 15% NaOCl compared to control ($p<0.05$). It was found that TVg improved these reductions in Pm. At 80 and 100 Hz frequencies, a significant increase ($p<0.05$) was observed in 15% NaOCl compared to 4% NaOCl. There was no significant difference between groups at 10, 20 and 40 Hz. There was no significant difference between groups for serum TNF-α parameter, but serum LDH level was higher in all groups compared to the control ($p<0.05$).

Conclusions: It can be said that both doses of NaOCl affect the diaphragm muscle, which is important in respiration, and TVg has a positive effect. Also, this study shows that the large reserve capacity for diaphragm muscle force generation allows for higher-force motor behaviors. However, detailed studies are needed to understand which compensation mechanisms are involved in the emergence of results.

Keywords: Sodium hypochlorite, Inhalation, *Thymus vulgaris*, Toxicity

THE EFFICACY OF SOME PHARMACOLOGICAL AGENTS WITH SUPPRESSIVE PROPERTIES AGAINST SOCE

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Abstract

Aim: The store operated Ca^{2+} entry (SOCE) represents an important route for generating cellular Ca^{2+} signals that are implicated in physiological and various pathological scenarios. Abnormal SOCE seem to underlie several diseases that notably include cardiomyopathy, allergy, inflammation, and cancer. Therefore, any modulator of this pathway is likely to have significant impact in cell biology under both normal and abnormal conditions. In this study, the effects, and modes of action of some of the most used chemicals known as SOCE inhibitors at the point of suppressing SOCE were investigated.

Material and Methods: The effects of some SOCE blockers such as PYR6, Synta66, BTP2 and GSK7976 against SOCE were investigated in whole cell configuration by the patch clamp method. Ca^{2+} release activated Ca^{2+} current (ICRAC) was measured using voltage ramps (−100 to +100 mV in 50 ms) applied every 2 s. The current amplitude was normalized to cell size and shown as current density, pA/pF. Rat basophilic leukemia cells (RBL) were used in this study. Cells were pre-treated with each drug for ~20 min prior to recording for each experiment.

Results: According to the findings, it was seen that Synta66 and PYR6 blocked SOCE entry statistically significantly both intracellularly and extracellularly. On the other hand, GSK7976 and BTP2 could only significantly block these currents extracellularly.

Conclusions: The activities of some of the regulators of SOCE, which are known to be an important Ca^{2+} pathway not only in non-excitable cells but also in excitable cells, are summarized in this study. According to the findings, Synta66 and PYR6 can suppress SOCE entry through both Stim molecules and Orai channels, while GSK7976 and BTP2 can only inhibit Orai channels from outside the cell. Findings obtained in this study will make important contributions to the manipulation of the SOCE mechanism in both physiological and pathophysiological conditions.

Keywords: SOCE, Stim1, Orai1, Ca^{2+} Channels

THE EFFECT OF 5G (6 GHZ) RADIOFREQUENCY ELECTROMAGNETIC FIELD ON VITALITY AND APOPTOSIS IN RAT BLOOD CELL

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Abstract

Aim: In our study, we aimed to investigate the effect of 6 GHz radiofrequency electromagnetic field (RF- EMF) on the ratio of vitality, apoptotic (the early, the late) and necrotic in rat blood cells. Since the new technological devices will be adapted in the mid band range 5G, 6GHz RF-EMF were used in the present study.

Material and Methods: In our study, 10 Wistar Albino male rats were used weights range between 250-300g. Before RF-EMF applications, blood samples were collected from all rats by cardiac puncture method (1cc). These rats were selected as the control groups (0.day). The same rats, after 4-day adaptation period by placing in the special application cage were exposed to the 6 GHz RF-EMF application for 4 hour/day for 6 weeks. After RF-EMA applications, blood samples (1cc) were re-collected from the same rats. These rats were selected as the radiofrequency radiation (RFR) groups (42.day). Blood samples both groups worked at the same day. Flow cytometric analysis in which annexin-V kit used, was performed to determine the percentage the ratio of viable cell, the early apoptotic cell, the late apoptotic and necrotic cell.

Results: The ratio of % viable cells were increased in the RFR group by compared to the control group, and this difference was statistically significant. The ratio of % cells in the early apoptotic and necrotic decreased statistically significant in the RFR group by compared to the control group. In addition, there were no statistically meaningful differences between RFR and control group by compared to the ratio of % cells in the late apoptotic.

Conclusions: The results of the present study clearly showed that 6 GHz RF-EMAs emitted from new generation 5G systems had no adverse effects on vitality and apoptosis in rat blood cells.

Keywords: 5G, Cell, Vitality, Apoptosis

THERAPEUTIC EFFECTS OF TRANSCRANIAL DIRECT CURRENT STIMULATION ON THE GLUTAMATERGIC PATHWAY IN AN EXPERIMENTAL MODEL OF CEREBRAL

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Abstract

Aim: Cerebral ischemia occurs as a result of obstruction of some or all of the arteries feeding the brain, resulting in significant impairments in both motor and cognitive functions. In our study, we aimed to investigate the effects of Transcranial Direct Current Stimulation(tDCS) application on learning and memory and molecular mechanisms of rats with focal cerebral ischemia.

Material and Methods: 30 male Wistar rats, each of which weighs 290-310 g, were divided into three groups as Sham, Ischemia/Reperfusion (IR) and IR+tDCS groups, with 10 rats in each group. The IR model was created by MCA's 90-minute occlusion. tDCS treatments were applied 0.5 mA 30 minutes a day for 2 days after IR. Novel object recognition was used to evaluate learning and memory, and open field test was performed to evaluate locomotor activity. Glutamate, Ca2+ and N-Methyl-D-Aspartate (NMDA)levels in hippocampus tissues were evaluated. Statistical analyzes were performed by One-Way ANOVA test.

Results: Increase was observed in IR+tDCS an group compared to IR group while significant decrease was observed in IR group compared to Sham in the behavioral experiments data($p<0.05$). While glutamate, Ca^{2+} and NMDAR levels, were significantly higher in IR group compared to Sham group($p<0.001$), it was found to be significantly lower in IR+ tDCS group compared to IR group($p<0.05$).

Conclusions: In our study, it was concluded that post-IR tDCS application improves learning and memory disorders and has a neuroprotective effect on learning and memory by regulating glutamate and Ca2+ levels, which play a role in hippocampal glutamatergic cell death as a result of excitoxicity.

Acknowledgement: Our project was supported by TÜBİTAK 2209-A University (Project number: 1919B012103317).

Keywords: Glutamate, Ischemia reperfusion, Learning and memory, tDCS

EARLY DIABETES ESTIMATION WITH MACHINE LEARNING

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Abstract

Aim: In this study, it is aimed to realize the early diagnosis of diabetes by using machine learning, which is one of sub-units of artificial intelligence, and clinical data.

Material and Methods: UCI (University of California Irvine) data set used in this study. The data set include 286 patient and 179 healthy person's different feature like Pre-breakfast blood glucose measurement, Typical exercise activity. These 20 different parameters are important for early diabetes estimation. These data sets were coded in the system created through MATLAB program and the optimum result was achieved. An Artificial Neural Network (ANN) model was created, and disease prediction classification was made. MATLAB classification functions such as SVM (Support Vector Machine), DT (Decision Trees) were also used in classification. Results were evaluated by obtaining ANN Model, Confusion matrix, ROCcurve, Accuracy and sensitivity ratios.

Results: It was observed that data set we used in our study was not evenly distributed. In this case, data set balancing was performed for artificial intelligence to give more reliable results. The system was tested by training ANN model we created with training data set. Here, training-test ratios (60%-40%), hidden layers (3 pieces) and number of neurons (15, 25, 10) were optimized, showing a high accuracy rate of 98%. In addition, it was seen that best classification algorithm was DT classification. It has been determined that each new data to be entered here increases sensitivity and specificity of system it is aimed to develop data set

Conclusions: In our study, it was concluded that with machine learning the early diabetes estimation can be realized. In this case it will be helper for prevent the future damages of diabetes.

Keywords: Artificial intelligence, Machine learning, Diabetes

AN INVESTIGATION INTO THE EFFECT OF THE DIFFERENT VINCULIN ISOFORMS IN THE MORPHOLOGY OF H9C2 CELLS

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Abstract

Aim: Cardiomyopathy is a prevalent form of cardiac disease that affects the heart muscle. One of the genes related with both dilated and hypertrophic cardiomyopathies is VCL, which encodes the adaptor protein vinculin (Vcl) that links the actin cytoskeleton to the adhesion receptors. Vcl is ubiquitous in focal adhesions that transmit force from the extracellular matrix to the cytoplasm. Metavinculin (MVcl), a muscle-specific isoform of vinculin, is also present in cell adhesion sites, such as costameres, intercalated discs, and thick plaques, alongside Vcl. Despite the fact that the function of MVcl in muscle cells is unknown, point mutations in the insert region have been linked to cardiac disease. The aim of this study was to investigate how MVcl affects actin cytoskeleton and focal adhesions in a cardiac muscle cell line.

Material and Methods: H9C2 cells were transfected with mEmerald-Vinculin-N-18 (Addgene) expression plasmid, using Lipofectamine 3000. MVcl-GFP and Vcl-GFP expressing cells were examined by confocal microscopy and focal adhesion analysis were performed. Western blot studies were conducted to detect variations in the protein levels of focal adhesion proteins and Vcl-binding partners, such as focal adhesion kinase (FAK) (125 kDa), Talin-1 (270 kDa), and -Actinin (100 kDa).

Results: We detected no statistically significant difference between the computed mean focal adhesion areas of MVcl- and Vcl-transfected cells. However, MVcl-transfected cells had a greater surface area than Vcl-transfected cells. According to our findings, there were no significant variations in focal adhesion protein levels between control and vinculin isoform-expressing cells.

Conclusions: In conclusion, focal adhesion analysis methods were successfully applied to H9C2 cells and the effects of Vcl and MVcl on cytoskeletal organization were observed. This work was supported by The Scientific and Technical Research Council of Türkiye (Tübitak grant number 118Z149)

Keywords: Vinculin, Metavinculin, Hypertrophy, Focal adhesion, Cardiomyopathy

ASSOCIATIONS OF IL-6 POLYMORPHISMS AND HAPLOTYPES WITH OBESITY IN A TURKISH POPULATION

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Abstract

Aim: Chronic inflammation plays an important role in the pathogenesis of obesity, which is the most common disease worldwide. Therefore, in this study we aimed to investigate the possible effects of a cytokine, IL-6, rs2069827 (-1363, G/T), rs1800797 (-597, G/A) and rs1800796 (-572, G/C) polymorphisms on the development of obesity.

Material and Methods: 60 patients diagnosed with obesity and 59 healthy controls who applied to Kerolight Healthy Nutrition and Diet Counseling Center were selected for the study. Informed consent form and blood samples were taken from each individual, and genomic DNA isolations were made with the classic phenol-chloroform method. The presence of polymorphisms of IL-6, rs2069827 (-1363, G/T), rs1800797 (-597, G/A) and rs1800796 (-572, G/C) were determined by using and polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method. The odds ratio (OR), the frequencies of the genotype and alleles, LD and haplotype analyzes were obtained with the Arlequin (ver 3.1) and Haploview (ver 4.2) programs.

Results: According to the genotype and allele distribution between patients and controls, we determined that IL-6, rs1800796; G allele (OR: 2.4160, %95CI:1.3816-4.2246, p: 0,0020) and GG genotype may contribute to the development of obesity. When genotype and allele frequencies were evaluated between obese women and control women, a statistically significant difference was found in rs1800796. Haplotype results showed that haplotype GGG (61,66%) has the highest frequency in obese patients than in controls.

Conclusions: We consider that the IL-6 rs1800796 polymorphic locus may be a valuable marker for obesity. Considering the roles of IL-6 in obesity, studying different polymorphic loci in different populations, and determining the clinical features of obesity are important for our understanding of disease development and susceptibility.

Keywords: Obesity, IL-6, Polymorphism, Haplotype

EVALUATION OF THE EFFECT OF CAFFEINE CONSUMPTION ON COGNITIVE FUNCTIONS BY ELECTROENCEPHALOGRAPHY IN UNIVERSITY STUDENTS

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Abstract

Aim: It was aimed to evaluate the effect of caffeine consumption on cognitive functions of university students with electroencephalography (EEG).

Material and Methods: For this purpose, 37 students participated. The participants were divided into two main groups: consuming less than 3 mg/kg/day of caffeine (less than a 150 ml cup of coffee) (low caffeine consumption group) (LC) and consuming more than 3 mg/kg/day of caffeine (high caffeine consumption group) (HC). On the first day for both groups, MOCA test was applied, and EEG was recorded with eyes open/closed. Seven days later, both groups separated as caffeinated and decaffeinated coffee drinkers (LC+Caff, LC+Decaff, HC+Caff, HC+Decaff). A second MOCA test and EEG recording was performed approximately one hour after drinking coffee.

Results: It was determined that, the MOCA test score increased significantly in the second measurement compared to the first one in HC+Decaff. The cognitive performance increased in decaffeinated coffee drinkers, so it was interpreted as a placebo effect. In the data obtained from the second eyes closed EEG recording, there was a significant decrease on the power of alpha1 and alpha2 waves in HC+Caff compared to HC+Decaff. That situation is thought to be caused by the stimulating and attention-enhancing effect of caffeine. It was observed that from the second eyes open EEG recording, the power of delta waves decreased and the power of beta1 and beta2 waves increased significantly in LC+Caff compared to LC+Decaff. It is thought that the increase in brain activity is caused by the stimulating effect of caffeine. The increase in brain activity supports the increase in the MOCA test scores.

Conclusions: We observed that the neurophysiological changes caused by caffeine can be quantitatively examined by EEG. Also, the stimulant effect of caffeine can improve cognitive functions, but the habit and amount of caffeine can affect this situation.

Keywords: Caffeine, Cognitive process, Electroencephalography, Neurophysiology

EFFECT OF SOLVENT ON MOLECULAR INTERACTIONS: NAD – DIPHTHERIA TOXIN CASE

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Abstract

Aim: The aim of the work is understanding the solvent effect on the relation of Diphtheria Toxin (DT) and Nicotinamide adenine Dinucleotide (NAD) via Differential Scanning Calorimetry (DSC).

Material and Methods: Diphtheria toxin was purchased from Sigma and compared to the toxin which synthesized in Refik Saydam Hygiene Institute Center. NAD was purchased from Sigma also. DSC analyses conducted between 25 – 120 °C with 2 °C/min heating rate under nitrogen atmosphere with 3 mL/min flow rate with Shimadzu, DSC 60+ device. To test solvent effect, NAD samples dissolved in distilled water, PBS, 2%, %10, and %100 DMSO then incubated with DT for 24 hours. Afterwards, analyzed with DSC.

Results: According to the DSC thermograms, denaturation of protein structure of NAD and DT is observed with increasing DMSO rate in the solvent. Additionally melting points of reactions occurred in distilled water, PBS, 2%, 10%, and 100% are calculated around 69 °C, 66 °C, 63 °C, 65 °C, and 108 °C, respectively. Gibb's free energy is also calculated and resulted in increasing behavior in the previous order respectively. Melting points of NAD and DT is calculated as 65 °C and 75 °C when dissolved in distilled water.

Conclusions: In the results, the reaction that took place in 100 % DMSO solvent had the largest ΔG value, followed by the reactions in solvents consisting of 10 % DMSO, 2 % DMSO, PBS and distilled water, respectively. These results show that increasing concentrations of DMSO breaks important protein sub-structures such as α-helices.

Keywords: Solvent effect, Nicotinamide adenine dinucleotide (NAD), Diphtheria toxin (DT), Differential scanning calorimetry (DSC), Melting point

Abstracts for Poster Presentations

THE EFFECT OF SELENIUM APPLICATION ON OXIDATIVE VALUES IN RATS EXERCISING UNTIL DEPLETION

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Abstract

Aim: In this study, it was aimed to investigate the effect of Selenium, which has an important place among antioxidants, on oxidative stress and oxidative stress-related protein expressions in various tissues of rats that were floated until exhaustion.

Material and Methods: Eighteen male Wistar-Albino rats were divided into two groups, nine in each group. For the rats to get used to swimming, the rats were floated before the experimental applications started. In the control group, once a day for 20 days; placebo (physiological saline) and 0.8 mg/kg selenium were given to the selenium group. At the end of the 20th day, the groups were floated until exhaustion. After the final float, the rats were immediately sacrificed under anesthesia. In kidney, heart and hemolysate; MDA to GSH level; CAT and GSH-Px activity were examined. The levels of HO-1 and Nrf2, which are proteins associated with oxidative stress in kidney tissue, were measured by Western blot method.

Results: The MDA level in the kidney tissue of the selenium group was significantly lower (p <0.01). GSH level and GSH-Px activity were significantly higher in the selenium group kidney tissue (p <0.05). Nrf2 and HO-1 protein levels were found to be significantly higher in kidney tissue (p <0.05).

Conclusion: As a result, it was found that selenium supplementation decreased oxidative stress in kidney tissue and increased Nrf2 and HO-1 protein levels, which are associated with oxidative response, in rats that were floated until exhaustion.

Keywords: Antioxidant, Exercise, Oxidative stress, Swimming

DETERMINATION OF THE LEVELS OF PERIPHERAL CD4$^+$ AND CD8$^+$ T CELLS IN TURKISH MYASTHENIA GRAVIS PATIENTS

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Abstract

Aim: Myasthenia gravis (MG) is a rare, autoimmune neuromuscular junction disorder. Weakness and weariness in the skeletal muscles are hallmarks of this antibody-mediated autoimmune condition. Neuromuscular transmission failure in MG is most commonly elicited by autoantibodies against the acetylcholine receptor (AChR) or the muscle-specific kinase (MuSK). Double-seronegative myasthenia gravis (dSNMG) includes patients with MG without detectable antibodies to the AChR or MuSK. Since MG is a B cell-mediated, T cell-dependent autoimmune disease, here we aimed to investigate the levels of CD4$^+$ and CD8$^+$ cells in the two subsets of the Turkish MG patients: MG patients negative for both AChR and MuSK antibodies (dSNMG) and the patients positive for at least one of the antibodies for AChR and MuSK.

Material and Methods: MG patients, who are not under therapy, were identified for their autoantibody status and subdivided into D2 and D3 groups. The patients with negative for both anti-AChR and anti-MuSK antibodies were considered in the D2 group (7 patients) and, those with positive for at least one of the autoantibodies were considered in the D3 group (7 patients). Healthy individuals (31 individuals), with matching age and gender but without any autoimmune disease, were classified as the "control group".

Results: Although the results were not significant statistically (p=0.1249), a trend toward an increase in the frequency of the CD4$^+$ cells among CD3$^+$ lymphocytes were found in MG patients with negative for both autoantibodies (D2 group; dSNMG) compared to healthy controls. A similar trend was also observed when the disease groups were compared with each other (D2 vs D3; p=0.1037)

Conclusion: The results show a modest increase in the percentage of CD3$^+$ CD4$^+$ cells in dSNMG patients. Since CD4$^+$ T cells regulate B cell antibody production, the obtained results may indicate the importance of the other autoantibodies, rather than anti-AChR and anti-MuSK, to the disease etiology.

Keywords: Myasthenia gravis, Flow cytometry, CD4$^+$ T Cells, CD8$^+$ T cells

EFFECTS OF DIFFERENT COLORED LIGHTS ON COGNITIVE PERFORMANCES AND AUTONOMIC NERVOUS SYSTEM

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Abstract

Aim: Studies in which both a psychometric cognitive test and an objective autonomic nervous system measurement are used simultaneously are rare. In this study, the aim is to determine whether the dominance of the sympathetic and parasympathetic nervous system, cognitive test accuracy and success of response time are different for red and blue lights in healthy subjects.

Material and Methods: Heart rate variability (HRV) recordings were taken via photoplethysmography while subjects were sitting for two minutes under 300 lux white, red, and blue lights given in mixed order, and immediately after this time, the PEBL Continuous Performance Test-AX was applied, which lasted for five minutes while the light was exposed.

Results: It was observed that the color of the light, red or blue, did not have a significant effect on the response inhibition or rapid response values in the cognitive test. From the electrophysiological measurement data, it was determined that the parameters of heart rate (HR), mean time between consecutive heartbeats (NNmean), standard deviation of normalized time between consecutive heartbeats (SDNN) and the root mean square of the difference between sequential heartbeats (RMSSD) are not significantly affected by light. A significant difference was found due to the change of light color for, low frequency (LF), high frequency (HF) and low frequency to the high-frequency ratio (LF/HF).

Conclusion: Discovering that there are conflicting reports in the literature, the effect of red and blue lights on cognitive performance was simply measured for the components of response inhibition and rapid response, lasting 5 minutes. It was determined that there was no effect on cognitive abilities between the lights during the measurement.

Keywords: Light effect, Autonomic nervous system, Cognitive performance

EFFECTS OF PRENATAL AND POSTNATAL EXPOSURE OF THIAMINE DEFICIENCY ON LEARNING AND MEMORY IN ADULTHOOD

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Abstract

Aim: In this study, behavioral changes in adulthood of thiamine deficiency induced rats during prenatal and lactation period were investigated.

Material and Methods: The study included 2 groups with 4 females in each group (Wistar Albino, aged 6 months). Group1 (NN): received normal diet before and after birth. Group2 (TN): received thiamine-deficient diet before birth and normal diet after birth. During the pregnancy and postnatal lactation period (mean 21 days), nutrition was continued as per the protocol for each group. At 60 days after birth, 10 rat pups were taken for experiment for each group. Open Field, Elevated Plus Maze and New Object Recognition tests were used for behavioral analysis. Total distance, average speed, number of frames entered, time spent in the outer quadrant, the time spent in open and closed arms, the discrimination index was calculated. Independent Samples T Test was used when parametric test assumptions were met, and Mann Whitney U test was used in non-parametric conditions.

Results: In TN group, number of frames entered in open field test (NN: 83,16 (51,00-100,00), TN: 64,88(51,00-90,00), $p<0.05$) and rate of time spent in the outer quadrant (NN: 40,74 ±5,05, TN: 69,23±10,59, $p<0.05$) increased. Ratio of time spent in open arm in the TN group (NN: 40,74 ±5,05, TN: 21,14±4,30, $p<0.05$) was decreased. Discrimination index was decreased in the TN (NN: 58,71(49,09-81,74), TN: 43,66(30,02-61,56), $p<0.05$) group.

Conclusion: As a result, it has been observed that malnutrition during prenatal and lactation periods may cause behavioral, learning and memory disorders in later ages. For this reason, preventing nutrient deficiencies that may occur by focusing on the early period will provide long-term and widespread benefits to individuals and societies.

Keywords: Learning and memory, Behavior, Thiamine deficiency

SIMULATION OF ARTERIAL BIOMECHANICS BASED ON A BIPHASIC MICROMECHANICAL FINITE ELEMENT MODEL

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Abstract

Aim: Arterial ageing is associated with remodeling and the loss of arterial elasticity which might lead to various cardiovascular diseases. A better characterization of the biomechanical aspects of arteries will be beneficial for a better understanding of vascular ageing. The aim of this study is to discuss the integration of matrix and fiber phases on the passive artery wall model to achieve a realistic simulation of the artery and obtain passive pressure-artery diameter relationship.

Material and Methods: Three-dimensional finite element meshes of an arterial strip were constructed using various mesh densities in the radial direction. The biphasic material having 1:1 volume fraction of the ground and fiber phases was set up to behave according to a neo-hookean and an exponential (Holzapfel, 2000) model, respectively. Different fiber lay angles (30, 45, 60) were simulated to show the effect of fiber orientation on the axial force during inflation. The contribution of ground and fiber phases on the stress components were examined separately. All simulations were performed by using the general purpose open-source finite element analysis program (FEAP, University of Berkeley).

Results: A mesh convergence analysis was performed using different mesh densities (4,8,16,32 elements in the radial direction). The axial force generated during inflation was shown to vary as a function of the fiber orientation, where larger fiber angles resulted in a stiffer axial response, and a larger axial force. In contrast, the pressure-diameter curves indicated that decreasing fiber angles resulted in stiffer circumferential response. The contribution of the fiber on the total stress components was found to be much higher than that of the ground phase.

Conclusion: These results indicate that the effect of fiber orientation can be included by using a micro-mechanical based constitutive model and might lead to a better characterization of the biomechanical aspects of arteries and a better understanding of critical parameters to define vascular ageing.

Keywords: Vascular ageing, Stiffness, Mechanistic model, Finite element analysis

PROTECTIVE ROLE OF SIRTUIN1 IN INSULIN RESISTANT CARDIOMYOCYTES

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Abstract

Aim: Sirtuins are NAD+ dependent deacetylases and regulate protein function by post-translational modification, thereby representing a metabolic sensor. It has been shown that sirtuins are involved in energy metabolism modulation, DNA repair, inflammation, oxidative stress, and apoptosis. Furthermore, SIRT1(Sirtuin1) is thought to be protected against obesity, insulin resistance, type 2 diabetes mellitus and cardiovascular diseases. However, mechanisms of SIRT1 in cardiovascular diseases has not been fully understood. Therefore, here, we aimed to investigate the role of SIRT1 on heart function in insulin resistant cardiomyocytes.

Material and Methods: We incubated the H9c2 cells with palmitic acid (PA; 50µM for 24h) to induce insulin resistant (IR) cardiomyocytes. The development of IR in H9c2 cells were verified by determining the cellular 2-DG6P uptake assays. Control and IR cardiomyocytes were incubated with EX527 (10µM;24h) or SRT1720 (1µM;24h) to inhibit or activate the SIRT1 respectively. We measured intracellular free calcium and zinc, reactive oxygen (ROS) and nitrogen species (RNS), mitochondrial membrane potential (MMP), ATP and lysine (K)- acetylation level by using electrophysiological and biochemical techniques.

Results: We observed that IR and SIRT1 inhibited groups showed significant increase in intracellular free calcium and zinc, depolarized MMP, decreased ATP production and elevated ROS and RNS level compared to control group. Moreover, total lysine (K)-acetylation level was increased in IR and SIRT1 inhibited groups. Incubation the IR cells with SIRT1 activator decreased the K-acetylation level and reversed the IR or Kacetylation induced increased ROS production, intracellular free calcium, and zinc levels, MMP and decreased ATP level without changing the RNS production.

Conclusion: Hereby, it has been found that the SIRT1 plays a protective role in the development of insulin resistance by modulating the cellular and mitochondrial function.

Keywords: Heart, Insulin resistance, Lysin acetylation, SIRT1, Mitochondria

EVALUATION OF THE EFFECT OF DONEPEZIL ON SKELETAL MUSCLE CONTRACTION RESPONSES IN FROGS

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Abstract

Aim: Donepezil is a chemical agent used in the treatment of Alzheimer's/Dementia disease, which increases acetylcholine levels by inhibiting the acetylcholinesterase enzyme that removes acetylcholine from the environment. These substances, called acetylcholine esterase inhibitors, block the activity of acetylcholinesterase, and can effectively treat the symptoms of neurodegenerative disorders by increasing the amount of acetylcholine in the central nervous system. Moreover, these agents are effective in preventing of inflammation and in angiogenesis-related muscle regeneration. Considering the studies so far, it may be claimed that acetylcholinesterase inhibitors may increase the skeletal muscle regeneration in the injured muscle. However, there are very few studies that support this hypothesis. The present study aimed to investigate the effects of donepezil on skeletal muscle contractions.

Material and Methods: In the present study, 20 Rana Macrocnemis frogs were divided equally into two main groups as control and donepezil. Skeletal muscles were isolated from experimental animal frogs using suitable surgical methods and stabilized in Ringer's solution at 4 °C for an hour. In a 10 ml organ bath, the tissue was placed between the electrodes and connected to the isometric transducer. The tone was set to 1 gram. After the one-hour stabilization period, the contraction responses (amplitudes) resulting from electrical, or acetylcholine stimulation were processed by the data acquisition system. Contractile responses were also obtained from donepezil-incubated tissue as well as the control.

Results: As a result of the analysis, it was determined that donepezil (10-7; 10-6 and 10-5 M) significantly decreased the twitch amplitude induced by 10V electrical stimulation in a dose-dependent manner when compared to control group (p <0.05). Furthermore, donepezil (10-5 M) slightly decreased the amplitude of contraction induced by acetylcholine (10-4 M).

Conclusion: The decrease caused by donepezil may indicate possible effects of the agent on cellular signaling pathways.

Keywords: Donepezil, Skeletal muscle, Contraction

DETECTION OF B-THALASSEMIA MUTATIONS USING PROBE-GATED SILICA NANOPARTICLES

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Abstract

Aim: β-thalassemia is a heterogeneous autosomal recessive hereditary anemia characterized by anomalies in the β-globin chain. Diagnosing β-thalassemia requires a comprehensive assessment combining red blood cell phenotypes, hemoglobin profiles, and DNA analysis which are costly and take a long time. The present study aimed to develop a fast, sensitive, low-cost detection assay for β-thalassemia.

Material and Methods: A rapid detection method for β-Thalassemia diagnosis was proposed using a specific mutation probe (IVS 1.1 (G>A), IVS 1.110 (G>A), and Codon 8 (-AA)) gated silica nanoparticles. This method is based on fluorescein releases from mesoporous MCM-41 type silica nanoparticles during hybridization between a conjugated single-strand of β-Thalassemia mutation oligonucleotide and β-Thalassemia single-stranded DNA samples. The nanoparticles were characterized using Dynamic Light Scattering (DLS), Fourier Transform Infrared Spectroscopy (FTIR), and Transmission Electron Microscopy (TEM) methods. Using mutation and healthy probes, cumulative fluorescein released from gated silica nanoparticles was measured at 5, 15, 30, and 60 min. The limit of detection (LOD) was calculated using the 3σ method for three mutations. Student's t-test and One-Way ANOVA were used for statistical analysis.

Results: The spherical-porous structure was shown using TEM, and the size of the nanoparticles was measured as 222.4 ± 28.32 nm. For β-Thalassemia positive conditions, the number of released fluorescein increased over time compared to healthy control probe-gated silica nanoparticles, and the optimum target detection time had been determined as 15 minutes. The limit of detection was calculated as 1.36 nM, 15 nM, 4.26 nM for Codon 8, IVS 1.1, and IVS 1.110, respectively, which makes this tool sensitive.

Conclusion: Consequently, this nanoparticle-based method could be favored for detecting β-Thalassemia and optimized for the different mutations. Thus, it could be improved for β-Thalassemia as it is faster, promising for sensitive detection, easy to operate, and less expensive than current methods.

Keywords: β-thalassemia, MCM-41, Thalassemia mutations, Silica nanoparticles

IMMUNO-DENSITY OF MUSCARINIC RECEPTORS AND KIR3.1 CHANNEL IN AUTONOMIC TISSUES UNDER DEMYELINATED CONDITIONS

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Abstract

Aim: Multiple sclerosis (MS) is a demyelinating disease of the central nervous system. Increasing evidence shows that the autonomic system is affected in MS and contributes to the pathogenesis. We aimed to investigate the effects of muscarinic ACh receptor 1 (mAChR1), mAChR2 and inwardly rectifying potassium channel 3.1 (Kir3.1) immunoreactivities on brain stem, vagus nerve and heart tissues under demyelination model.
Material and Methods: Wistar albino rats were divided into male control group (n=7), female control group (n=7), male cuprizone group (n=12), female Cuprizone group (n=12). Weights were measured throughout the model observation process. Cuprizone-induced demyelination pattern was confirmed by Luxol fast blue (LFB) staining of the brain in hippocampus (Gyrus dentatus and Cornu Ammonis) and cortex. After dissection, biparietal and occipitofrontal distances, interatrial and atrial-ventricular distances were measured. After the histopathological analysis of brain stem, vagus nerve and heart (atria and ventricle) tissues obtained from the created demyelinated model, mAChR1, mAChR2 and Kir 3.1 immuno-densities were investigated by immunohistochemical methods.
Results: Myelin staining showed significant demyelination in the hippocampus and cortex compared to the control group. Immunoreactivities of mAChR2, mAChR3 and Kir3.1 in atria and ventricles were significantly increased in cuprizone groups ($p<0.05$). In brainstem, mAChR2 and mAChR3 immunoreactivities were significantly increased in the female cuprizone group ($p<0.05$). Immuno-densities of mAChR2 and mAChR3 were significantly increased in both left and right vagus nerve for cuprizone group ($p<0.01$).
Conclusion: Our data reveal that the demyelinating model can produce significant cholinergic changes in autonomic tissues including the brainstem, vagus nerve, and heart. High immunoreactive response to demyelination at cholinergic centers may count as new target.

Keywords: Cuprizone, Acetylcholine, Inwardly rectifying potassium channels

COMPARISON OF MUSCLE ACTIVATION DURING THREE DIFFERENT UPPER BODY EXERCISES

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Abstract

Aim: Knowing the agonist muscles for exercises is a critical factor when designing training programs. The aim of this study is to investigate the muscular activation of latissimus dorsi, trapezius middle and deltoid posterior during three different upper body exercises (Lat pull down, barbell bent over row, dumbbell row).

Material and Methods: 14 healthy male subject who have at least 1 year of resistance training experience and who exercise 3 times/week joined in this study. On the first testing session, after the standardized warm up, loads that correspond to 4-6 repetition maximums were found. On the second testing session, which was done around 48 hours after the first session, electrodes were placed on the latissimus dorsi, trapezius middle and deltoid posterior muscles after the warmup and subjects performed the exercises 4-6 repetitions with the loads determined in the first session. For the electromyography (EMG) analysis, peak values were taken for maximum voluntary contractions whereas the mean values were taken for dynamic efforts. ANOVA with repeated measures was used for data analyses.

Results: The findings demonstrated that the barbell bent over row exercise activated deltoid posterior more than latissimus dorsi and trapezius middle ($p<0.001$). Additionally, the activation of the latissimus dorsi and the deltoid posterior were more than trapezius middle during lat pull down exercise ($p=0,001$). It was found that the latissimus dorsi showed more activity in the lat pull down and dumbbell row exercises compared to barbell bent over row exercise ($p<0.005$). But deltoid posterior was most active in the barbell bent over row exercise ($p=0.001$). Trapezius middle was more active in the dumbbell row and barbell bent over row exercise compared to lat pull down exercise ($p=0.001$).

Conclusion: In conclusion practitioners who want to target a certain muscle group during their training sessions might take these differences into consideration.

Keywords: Electromyography, Resistance training, Upper body exercise

ANTI-INFLAMMATORY AND ANTI-FIBROTIC EFFECTS OF VITAMIN D SUPPLEMENTATION AND SWIMMING EXERCISE IN BLEOMYCIN-INDUCED LUNG FIBROSIS IN RATS

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Abstract

Aim: With this study, in experimental pulmonary fibrosis; with vitamin D supplementation, it is aimed to reduce the formation of fibrosis and developing inflammation. In addition, it is expected to contribute to recovery by providing pulmonary rehabilitation with swimming exercise.

Material and Methods: 69 wistar albino rats were used in the present study. The rats were randomly divided into ten different groups as the control groups, the bleomycin group, the vitamin D dose group, the swimming exercise group, and the subgroups of these groups. A 6-week study schedule was designed. In order to induce pulmonary fibrosis, 2.5 mg/kg bleomycin was given as single dose intratracheal. to Rats were orally (gavage) given double dose vitamin D (200IU and 100IU) in olive oil for 6 weeks. In addition, they underwent a 30-minute swimming exercise at a suitable temperature and level in a modified tank on day. Rats were sacrificed after 28 days following bleomycin intake. Blood samples and pathology samples were also taken from rats.

Results: There was a significant increase in serum TGF- β levels in bleomycin group compared to control group (p<0.0011). However, there was a statistically significant decrease in serum TGF- β levels in 200 IU vitamin D and swimming exercise group compared to bleomycin group (p<0.0011). In fibrosis scoring, the bleomycin group had the highest fibrosis score. (p<0.005). When compared to bleomycin group, there was a statistically significant decrease in fibrosis score in vitamin D group (p<0.005).

Conclusion: During the experiment for pulmonary fibrosis induced by bleomycin, there were statistically significant decreases in inflammation and fibrosis in vitamin D and swimming exercise group compared to bleomycin group. As a result, it can be suggested that vitamin D supplementation may reduce TGF- β levels in pulmonary fibrosis, thus resulting in a decreased fibrosis.

Keywords: Pulmonary fibrosis, Vitamin D, Swimming exercise, Bleomycin

THE CHRONIC EFFECTS OF IRON OVERLOAD ON T-TYPE CA^{2+} CURRENTS IN HL-1 CELLS

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Abstract

Aim: Iron is the most abundant transition metal in the human body and plays substantial role in many physiological processes (part of the hemoglobin structure and iron containing enzymes). In human body, absorption, storage, and distribution of iron is tightly regulated. Dysregulation of iron homeostasis may lead to deposition of excess iron in vital organs including the heart. We investigate the chronic effect of iron overload on T-type Ca^{2+} currents in mice atrium derived HL-1 cells.

Material and Methods: Iron uptake into HL-1 cells was assessed by colorimetric kit (DIFE-250). Expression of Ca^{2+} channels and the effect of iron overload on the channel's expressions were assessed by reverse transcription and quantitative polymerase chain reaction respectively. Using whole cell patch clamp, voltage dependent channel currents were obtained.

Results: Iron uptake into HL-1 cells was assessed by colorimetric kit (DIFE-250). Expression of Ca^{2+} channels and the effect of iron overload on the channel's expressions were assessed by reverse transcription and quantitative polymerase chain reaction respectively. Using whole cell patch clamp, voltage dependent channel currents were obtained.

Conclusion: We conclude that, iron overload reduced T-type Ca^{2+} channel currents in a time (24 and 48 hours) and concentration (300, 600 uM) dependent manner that could potentially affect action potential. All the electrophysiological results obtained from this study will help to clarify the complex response mechanisms involved such as heart in iron toxicity.

Keywords: HL-1 cells, Iron overload, T-type Ca^{2+} channel

CO-DEVELOPMENT OF POLYCARBOLACTAN (PCL)-HYDROXYAPATITE (HA) COMPONENT NANOFIBER SCAFFOLDS WITH HEXOGONAL BORON NITRATE

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Abstract

Aim: Different strategies have been developed to repair major defects in bone. In the studies, biomineralized electrospun nanofiber scaffolds were used to mimic the natural bone extracellular matrix. This work: We added hydroxyapatite to enhance PCL functionality to nanofiber scaffolds used in tissue engineering. By adding hexagonal boron nitride (hBN) to the scaffolds, since the use of boron in non-toxic doses in bone tissue engineering provides calcium mineralization; It was designed to investigate the minimization of large bone

Material and Methods: To examine the effect of hBN on PCL scaffolds containing 8% HA, different concentrations of hBN-HA-PCL solution were prepared. The solutions contain 1 control group and 4 different concentrations. When the solutions were mixed in a magnetic stirrer and a homogeneous mixture was obtained, electro-spinning was performed by drawing the polymer solution with the help of a syringe. Chemical bonds were analyzed by Fourier transform infrared spectroscopy (FTIR). Morphological images of the scaffolds were observed using Field Emission Gun Scanning Electron Microscopy (FESGEM). Tensile tests were applied to the scaffolds in accordance with ASTMD882-10 standards.

Results: In the tensile test performed for the mechanical characterization of the scaffolds, the maximum strength of the control group was 6.147 and the stretch was 3.074, while the mechanical properties weakened as the hBN amount increased. While the fiber structure was high and thin in the control group, when 0.05% hBN was added, the fiber structure was deteriorated, but at 0.25% hBN concentration, the fiber structure was oriented in one direction and became finer. 0.5% hBN was finer in fiber structure.

Conclusion: Nanofiber composite scaffolds were produced successfully. With the addition of boron, the nanofibers became thinner and oriented. However, in terms of mechanical properties, as the hBN ratio increased, its mechanical properties weakened, and a more brittle structure was obtained.

Keywords: Electrospinning, PCL, Hydroxyapatite, Hexagonal boron nitrate.

TRACKING OF B-LACTOGLOBULIN STRUCTURE DURING SLIGHTLY-HEATED HYDROLYTIC PROCESS WITH INFRARED SPECTROSCOPY

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Abstract

Aim: Determining the structural fragments of proteins is crucial in many fields such as biotechnology, proteomics, drug, and the food industry. In the current study, we aimed to control the structural changes of β-lactoglobulin (a whey protein) due to enzymatic hydrolysis at high temperatures by using infrared spectroscopy.

Material and Methods: For the proteolytic process of β-lactoglobulin by trypsin, the initial substrate concentration was 50 mg/ml in 10 mM potassium phosphate deuterium oxide buffer at pD 7.9. The substrate/enzyme ratio of the samples was 10000/1. The substrate and enzyme mixtures were measured at 45°C for 120 min by using PerkinElmer UATR Two Fourier Transform-infrared spectrometer (FT-IR) equipped with a DTGS detector. We carried out the measurements in mid-IR range (4000-1000 cm^{-1}) with the resolution of 4 cm^{-1} and 8 scans in the transmission mode. Then, the spectral analysis was performed from FT-IR absorbance spectra with "OPUS 7.0" software.

Results: Conformational changes in β-lactoglobulin (BLG) were observed in the amide I and amide II bands due to the effect of trypsin at 45°C. The IR signals absorbing at 1660 (turn), 1650 (α-helix), 1633 (β-sheet), 1695, and 1623 cm-1 (intermolecular β-sheets) decrease while the IR signals absorbing around 1608-1560 cm-1 (carboxylate groups) increase in the presence of trypsin. Such spectral features indicate the breakdown of BLG during tryptic hydrolysis.

Conclusion: IR spectroscopic analysis allowed us not only detection of enzymatic digestion but also the determination of the structural changes and fragments in the intact protein, even at high temperatures. Functional mechanisms of proteolysis will be investigated further in detail by using biophysical/physicochemical methodologies. This work was funded by the Scientific and Technological Research Council of Türkiye through the international TUBİTAK-2532 Russia Bilateral Cooperation project (Grant#119N423 to Dr. Günnur GÜLER).

Keywords: Proteolysis, Infrared spectroscopy, Protein secondary structure

EFFECT OF ARCHIDONIC ACID ON PARKINSON'S DISEASE: *IN VITRO* STUDY

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Abstract

Aim: Parkinson's disease (PD) is a neurodegenerative disease that results from dysfunction of neurons in brain. Arachidonic acid (AA) is long-chain polyunsaturated fatty acid that is vital to many human physiological processes such as gene expression, structure, and function of membranes. AA has an important role in neuroprotection against mitochondrial dysfunction, neuroinflammation and oxidative stress in neurodegenerative diseases such as Alzheimer's and PD. In our study, effect of AA on PD will be examined.

Material and Methods: SH-SY5Y Neuroblastoma cell line was obtained from Atatürk University (Erzurum, Türkiye) Department of Medical Pharmacology. To create the PD model under cell culture conditions, doses of AA (0.01-0.1-1-10 and 100µM) were added to SH-SY5Y cells and then treated with 200µM 6-OHDA. After 24 hours, cell viability was determined with 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazoliumbromide. Total antioxidant capacity (TAC) and total oxidant status (TOS) were evaluated by their analysis. Results will be analyzed with one-way ANOVA method using SPSS.

Results: The viability was defined as 100% in control groups and other groups were rated accordingly. The survival rate was determined as 70% in group that was only exposed to 6-OHDA toxicity. At AA doses, it was found that viability decreased depending on dose. The highest viability rates were observed in AA groups exposed to 6-OHDA toxicity at 0.01 and 0. µM concentrations. These values were found to be statistically significant. Similar results were found in our TAC and TOS tests.

Conclusion: Sambra et all. suggested that AA metabolites may constitute a therapeutic target for PD, as they are widely distributed in brain, are antioxidants, and show effects that reduce oxidative stress and inflammation. Xicoy et all. they found that use of low doses of fatty acids reduced toxicity of 6-OHDA in SH-SY5Y cells. Our study is consistent with these results.

Keywords: Parkinson disease, Arachidonic Acid, Cell culture

EFFECTS OF TOXOPLASMA GONDII PARASITE ON LEARNING AND ANXIETY

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Abstract

Aim: The aim of this study is to investigate behavioral effects of Toxoplazma gondii parasite on locomotor activity, anxiety, learning and memory in bradyzoite stage.
Material and Methods: In our study, 20 male mice of Mus musculus variety albino genus, weighing 20-25 g, 4-5 weeks old, were used. The Toxoplazma gondii parasite model was created by using 48–50-hour intraperitoneal passages of Toxoplazma gondii RH Ankara strain in mice for intraperitoneal inoculation of mice and giving 5x104 tachyzoites to each mouse. No inoculation was made in control group. Locomotor activity was evaluated in open field test, anxious behavior was evaluated in elevated plus maze test, and learning behavior was evaluated in new object recognition test. Statistical analyzes were performed with Student's T test.
Results: In open field test data, compared to control group, there was a significant decrease in total number of distances taken in center and number of inter-quadrant transitions in Toxoplazma gondii group, while significant increase was observed in total number of distances taken in outer quadrants and number of transitions between quadrants($p<0.05$). In elevated plus maze test, there was a statistically significant decrease in number of entries into open arms and time spent in open arms in Toxoplazma gondii group compared to control group, while an increase was observed in number of entries into closed arms and time spent in closed arms ($p<0.05$). In new object recognition test, the time spent on new object of Toxoplazma gondii group was found to be significantly less than that of control group.
Conclusion: In our study, it has been shown that Toxoplazma gondii parasite in bradyzoite stage reduces locomotor activity, causes learning and memory impairment, and has anxiogenic effects. Our project was supported by Hitit University (Project number: TIP19001.21.007).
Acknowledgements: Thanks to Prof. Dr. Meltem Bahcelioglu for her help in the behavior experiments.

Keywords: Anxiety, Bradizoite, Learning and memory, Toxoplazma gondii

INVESTIGATION OF THE EFFECTS OF TRANSCRANIAL DIRECT CURRENT STIMULATION ON LEARNING AND MEMORY CHANGES IN EXPERIMENTAL EPILEPSY

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Abstract

Aim: Epilepsy is a serious neurological disease that causes social, psychological, and economic problems all over the world. In our study, it was aimed to investigate effects of transcranial Direct Current Stimulation (tDCS) application on neuroinflammation in rats with epilepsy model.

Material and Methods: 30 male Wistar rats weighing 250-300 g, 10 rats in each group, were divided into three groups as Control, Epilepsy and Epilepsy+tDCS groups. The epilepsy model was created by administering a single dose of 60 mg/kg Pentylenetetrazole (i.p.) to the subjects. To epilepsy+tDCS group, 30 min. on the 1st and 2nd days of the experiment. 1 mA anodal-tDCS stimulus was given. Locomotor activity nad learnin and memory was evaluated behaviorally by open field, novel object recognition and Y-maze tests. neuronal Nitric Oxide Synthases (nNOS) and glial fibrillary acidic protein (GFAP) expressions and Superoxide Dismutase (SOD), Malondialdehit (MDA), Interleukin (IL-1β) and Tumor Necrosis Factor-α (TNF-α) levels were measured in hippocampus region of brain. Statistical analyzes were performed with One Way ANOVA test.

Results: In behavioral experiments data, a significant decrease was observed in Epilepsy group compared to Control group, while a significant increase was observed in Epilepsy+tDCS group compared to Epilepsy group ($p<0.05$). Compared to control group, GFAP and nNOS expressions were increased in epilepsy group, while tDCS stimulation and GFAP and nNOS expressions were decreased in epilepsy+tDCS group. A significant decrease was observed in SOD levels in epilepsy group compared to control group, while significant increases were observed in MDA, IL-1β and TNF-α levels ($p<0.05$). There was an increase in SOD levels in treatment groups compared to epilepsy groups, while decreases in MDA, IL-1β and TNF-α levels were observed.

Conclusion: In our study, it has been shown that tDCS administration in epilepsy has therapeutic and neuroprotective effects on oxidative stress and neuroinflammation and has a reducing effect on neuroinflation. Our project was supported by Coordination Unit of Scientific Research Projects of Hitit University (Project number: TIP19001.21.003).

Keywords: Epilepsy, Learning and Memory, Neuroinflammation, PTZ, tDCS

THERAPEUTIC AND NEUROPROTECTIVE EFFECTS OF TRANSCRANIAL DIRECT CURRENT STIMULATION ON EXPERIMENTAL MODEL OF CHRONIC EPILEPSY

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Abstract

Aim: Epilepsy causes physical, psychological, social, and economic problems. In our study, it was aimed to investigate effects of transcranial Direct Current Stimulation (tDCS) application on neuroinflammation in rats with chronic TLE model.

Material and Methods: 30 male Wistar rats weighing 250-300 g, were divided into three groups as Control, Epilepsy and Epilepsy+tDCS groups. In chronic TLE model, subjects were administered 60 mg/kg i.p. PTZ on first day. Then, 35 mg/kg PTZ was injected into groups every other day until epilepsy pattern occurred. In epilepsy+tDCS group, 30 min. on days without PTZ injection. 1 mA anodal tDCS was given. Locomotor activity and learning and memory was evaluated behaviorally by open field, novel object recognition and Y-maze tests. neuronal Nitric Oxide Synthases (nNOS) and glial fibrillary acidic protein (GFAP) expressions and Superoxide Dismutase (SOD), Malondialdehit (MDA), Interleukin (IL-1β) and Tumor Necrosis Factor-α(TNF-α) levels were measured in hippocampus region of brain. Statistical analyzes were performed with One Way ANOVA test.

Results: In behavioral experiments data, a significant decrease was observed in Epilepsy group compared to Control group, while a significant increase was observed in Epilepsy+tDCS group compared to Epilepsy group($p<0.05$). Compared to control group, GFAP and nNOS expressions were increased in epilepsy group, while tDCS stimulation and GFAP and nNOS expressions were decreased in epilepsy+tDCS groups. A significant decrease was observed in SOD levels in epilepsy groups compared to control group, while significant increases were observed in MDA, IL-1β and TNF-α levels($p<0.05$). There was an increase in SOD levels in treatment group compared to epilepsy group, while decreases in MDA, IL-1β and TNF-α levels were observed. However, these changes were statistically significant only in epilepsy+tDCS group.

Conclusion: In our study, it has been shown that tDCS administration in chronic epilepsy has therapeutic and neuroprotective effects on oxidative stress and neuroinflammation and has a reducing effect on neuroinflammation (Project number: TIP19001.21.003).

Keywords: Epilepsy, Learning and memory, Neuroinflammation, PTZ, tDCS

EFFECT OF CALCIUM SENSING RECEPTOR ON T98 GLIOBLASTOMA CELLS

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Abstract

Aim: Calcium-sensing receptor (CaSR) is a G protein-coupled receptor that performs cell type-specific functions in many tissues and some cancers. Cinacalcet is designed as a calcimimetic that appears to directly mimic the action of calcium. Glioblastoma is the most common malignant primary brain tumor with a median survival of 15 months despite current treatment standards. Our studies show that it has not been fully determined whether CaSR is an oncogene or a tumor suppressor on T98G glioblastoma cells. The aim of our study was to examine the processes triggered by cinacalcet, a therapeutic CaSR allosteric activator, in T98G glioblastoma cells.

Material and Methods: T98 glioblastoma cells were obtained from Atatürk University (Erzurum, Türkiye) Department of Pharmacology. Briefly, cells centrifuged at 1200 rpm for 5 min were seeded into 96-well plates with fresh medium (antibiotic 1%, FBS 15% and DMEM) and an incubation at 5% CO2 and 37°C. When there was an 85-90% increase in cells, doses of Cinacalset (0.5, 1, 2, 4 and 8 µg/mL) were added to the well plate and allowed to incubate. After 24 hours of incubation, wells treated with 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazoliumbromide were read at 570 nm. The results were analyzed by one-way ANOVA method using SPSS, IBM 21.00 program.

Results: In our control group, the viability was evaluated as 100% and the other groups received the corresponding grades. It was discovered that when cinacalcet doses were increased, the viability of glioblastoma cells decreased compared to the control group. Statistically the lowest viability rates were discovered at doses of 4 and 8 µg/mL ($P<0.001$).

Conclusion: According to Tennakoon et al., while CaSR controls angiogenesis, cell migration, cell death, proliferation, differentiation, and tumor suppression in some cancers, it acts as an oncogene in others. Our findings showed that cinacalcet has tumor suppressive effects in T98 glioblastoma cells. We are still doing research on this topic.

Keywords: Calcium sensing receptor, T98, Glioblastoma

USING OF NANOMATERIALS IN BIOANALYTICAL APPLICATIONS AND DEVELOPMENT OF MOBILE APP-SUPPORTED COLORIMETRIC DIAGNOSTIC TESTS

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Abstract

Recently, different nanoparticles have been used to cross the blood-brain barrier, to transfer various drugs to the brain for therapeutic purposes or to image different parts of the brain, to provide rapid and sensitive infection detection. Quantum dots, gold nanoparticles, iron oxide nanoparticles, organic-inorganic hybrid nanomaterials as theranostic agents that enable both treatment and diagnosis are ideally used nanoparticles for the development of nanobio-sensors. Although designed as smart drug carrier molecules, especially gold nanoparticles are used for rapid and sensitive bio-detection or bio-diagnosis in diagnostic tests due to their unique surface plasmon resonance properties. Gold nanoparticles are used in many bioanalytical and biomedical applications due to their short time production, stable structure, easy surface modification and unique optical properties. Thus, this localized surface plasmon resonance feature of Au NPs is used as a colorimetric sensor for the determination of many molecules. As a result of unconscious use of antibiotics, frequent and long hospital stays, multi-drug resistant microorganisms pose a significant threat to public health all over the world and have increased significantly in the last 20 years. For this reason, economic, fast, and sensitive colorimetric biosensors containing plant-derived, biocompatible anthocyanin molecules, which work with different mechanisms, have been developed for the detection of microorganisms with high urease activity and the presence of resistance in common species that develop antibiotic resistance within the scope of the project. The widespread use of the developed anthocyanin-based urease test and antibiotic resistance test will provide a great opportunity for accurate, economical, and rapid diagnosis of urease-positive bacteria and multi-drug resistant microorganisms. A mobile application has been developed in order to analyze the results with precision and has been standardized for easy use in the clinic.

Keywords: Nanoparticle, Infection detection, Diagnostic kit

EVALUATION OF PULSED MAGNETIC FIELDS AND RESVERATROL ON THE CONTRACTILE PROTEIN IN DIABETIC RAT AORTA MUSCLE

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Abstract

Aim: Diabetes, an autoimmune disease, is important one of these diseases. The aim of this study was to evaluate the effects of pulsed magnetic field (PMF) and antioxidant, particularly on weight loss ratios, blood glucose levels and contractile protein calmodulin (CAM) or myosin light-chain kinase (MYLK) of aorta muscle.
Material and Methods: The experimental groups were divided into eight groups as control, experimental and exposed to magnetic field groups (C, DM, C-RSV, DM-RSV, C-PMF, DM-PMF, C-RSV-PMF, DM-RSV-PMF) Before, experimental diabetes was formed. Then antioxidant (Resveratrol;(RSV)) were injected intraperitoneally into groups determined in one month at the same time of the day. The rats in the PMF groups were exposed to horizontal pulsed magnetic field (PMF) at 50 Hz for 1h/5days/during one month. At the end of one month, all the groups were anesthetized by sodium pentobarbital and then were sacrificed under anesthesia. The thoracic aorta was dissected aorta tissue sample was used for aorta muscle CAM and MYLK assays.
Results: After four-weeks, according to C group blood glucose values of the rats in the C-PMF, C-RSV and C-RSV-PMF groups decreased. According to DM group blood glucose values of the rats in the DM-PMF, DM-RSV and DM-RSV-PMF groups decreased. According to the rats in C and DM groups, the CAM and MYLK levels decreased in C-PMF and DM-PMF. In the C-RSV and DM-RSV groups, CAM and MYLK levels was decreased according to the C and DM groups. Therefore, CAM and MYLK levels in C-RSV-PMF and DM-RSV-PMF was decreased in according to C and DM groups.
Conclusion: In conclusion, our data provide preliminary evidence on the therapeutic effects of PMF and RSV treatment, which ameliorates enhanced vascular contraction without any adverse reaction in diabetic aorta

Keywords: Blood glucose level, Diabetes, Type 1 diabetes, Resveratrol, Pulsed magnetic field

EFFECTS OF PULSED MAGNETIC FIELD ON ANTIOXIDANT ENZYMES LEVELS IN ADOLESCENCE

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Abstract

Aim: Expression levels of heat shock proteins (HSP70/72), increase in the presence of stress. The aim of our study was to examine the SOD and CAT levels in hippocampus and serum samples of adolescent rats, which were exposed to low frequency pulsed PMF (50 Hz) during their intrauterine development.

Material and Methods: Pregnant Wistar albino rats were employed in our study. Pregnant rats were divided into PMF exposed group and control group. The rats in the pulsed electromagnetic field (PEMF) group were exposed to vertical PMF throughout the pregnancy. Hippocampus tissues and serum samples were obtained during puberty only from male offspring (Control group (C); n=10, pulsed magnetic field group (PMF); n=10), which were the pups of exposed and non-exposed pregnant rats. The levels of stress proteins (HSP70/72) and antioxidant enzymes (superoxide dismutase (SOD) and catalase (CAT) were measured from the blood samples or hippocampus taken.

Results: According to our results, the HSP70 and HSP72 levels in serum samples of the offspring rats in PMF group increased in compared to control group, these increases were statistically insignificant. However, increased CAT and SOD protein expressions were observed both in hippocampus and serum samples of offspring rats in PMF group compared to control group.

Conclusion: It is expected that antioxidant enzyme (SOD and CAT) levels will decrease due to increasing stress factors (HSP70 and HSP72). Current studies have been reported that there has been a decrease in CAT and SOD levels with adult PMF exposure. According to our results, HSP70 and HSP72 heat shock proteins increased under the effect of pulsed magnetic field in serum samples of rats in PMF group. The increase in CAT and SOD protein expression in adolescent hippocampus and serum samples of offspring rats, exposed to a vertically PMF at 50 Hz frequency in intrauterine stage.

Keywords: Pregnancy Rat, Adolescence, Pulsed electromagnetic field, SOD, CAT, HSP70

EVALUATION OF THE RELATIONSHIP BETWEEN DIGITAL EYE STRAIN SYNDROME AND THE ELECTROMAGNETIC FIELD

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Abstract

Aim: This study aimed to determine the prevalence of digital eye strain syndrome among secretaries working in different departments of Adana Çukurova University Balcalı Hospital (Türkiye) and to determine its relationship with the electromagnetic field (EMF).

Material and Methods: This cross-sectional study included 143 secretaries working in different departments of the hospital. Besides eye examinations, Computer Vision Syndrome Questionnaire Scale (CVS-Q), Ocular Surface Disease Index Scale (OSDI) and Cornell Musculoskeletal System Questionnaire were applied to the participants. Low-frequency EMF measurements of the working environment were measured with a 6010 Gauss/Teslameter device and high-frequency EMF measurements with a Narda NBM-520 device. The light intensity of the environment was also measured with an LX-1102 Device

Results: The mean age of participants was 39.61 years, with a male-to-female ratio of 25.2% to 74.8%. CVS-Q scale revealed 83.9% of digital eye strain syndrome among participants. A positive, but weak correlation was found between CVS-Q and EMF, while a moderately strong, negative correlation was found between EMF measurements and Schirmer measurements of both eyes. The working environment EMF values of people with CVS were found to be statistically significantly higher ($p<0.05$). The logistic regression analysis formulated to predict digital eyestrain syndrome revealed that every 1.071 μT increase in ambient low-frequency EMF increased CVS risk 2.91 times. In the linear regression analysis, a one-unit increase in the low-frequency EMF of the environment was found to result in an increase of 0.004 units in the CVS-Q score.

Conclusion: A moderate relationship between digital eye strain syndrome and EMF was observed among people exposed to low-frequency EMF. This leads us to recommend regular measurement of EMF in working environments, developing protective behaviours (break intervals, 20-20-20 rules, etc.) for those working in risky areas, and providing necessary training for protection from non-ionizing radiation.

Keywords: Eye strain syndrome, Dry eyes, electromagnetic field, EMF, Computer vision syndrome

EFFECTS OF PTEROSTILBENE AND PULSED MAGNETIC FIELD ON CALMODULIN AND MYOSINE LIGHT-CHAIN KINASE ENZYME IN DIABETIC RATS

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Abstract

Aim: In this study, the effects of pulsed magnetic field and antioxidant PTS, which is an alternative treatment method for deformation in aortic muscles of diabetic rats, on contractile protein; calmodulin (CAM) were investigated.

Material and Methods: Sixty male Wistar Albino rats were used in this study. The rats were separated into 8 groups. The groups were named Control (C), Diabetes Mellitus (DM), Control Pulsed Magnetic Field (C-PMF), Diabetes Pulslu Magnetic Field (DM-PMF), Control-Pterostilbene (C-PTS), Diabetes-Pterostilbene (DM-PTS), Control-Pterostilbene-Pulsed Magnetic Field (C-PTS-PMF) and Diabetes-Pterostilbene-Pulsed Magnetic Field (DM-PTS-PMF). The rats determined as the diabetes groups were dissolved 45 mg/kg/ml streptozotocin (STZ) in physiological saline (SF) and injected into the tail vein as a single dose intravenously. The used PMF had 50 Hz frequency, 1.5 mT intensity and its direction was horizontal. The aorta was dissected thoracic aorta tissue sample was used for muscle contractile protein CAM and myosine light-chain kinase enzyme (MLCK).

Result: Weight gain rate of the rats in C and C-PMF groups. However, in DM and DM-PMF groups weight loss rate decreased. In C-PTS and C-PTS-PMF groups weight gain rate increased, while in the DM-PTS and DM-PTS-PMF groups weight loss rate decreased. CAM levels of the rats in the C-PTS, and DM-PTS groups decreased. Besides, MLCK levels of the rats in the C-PTS, and DM-PTS groups decreased. However, in the C-PTS-PMF and DM-PTS-PMF groups, MLCK and CAM levels decreases were statistically significant.

Conclusion: When the weight loss rates were compared in groups, it was observed that treatments of PMF and PTS slowed down the weight loss rates in the DM groups. Blood glucose levels decreased in the PMF and PMF-PTS groups, comparing to the C and DM groups. It suggests that non-invasive PMF and PTS treatments could have a positive effect on contraction of aorta muscle**.**

Keywords: Diabetes Mellitus, Pterositilbene, Pulsed Magnetic Field, Contractile Proteins

ULTRASTRUCTURAL CHANGES OF BRAIN TISSUE IN EXPERIMENTAL EPILEPTIC SEIZURES

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Abstract

Aim: Brain tissue is one of the most important target tissues to be examined in epilepsy. Therefore, in the present study, it was aimed to determine the pathologies that may occur in the brain tissue of rats, which was created an experimental epilepsy model, by electron microscopy.

Material and Methods: 24 Wistar-albino adult male rats used in this study were divided into 3 groups (n=8). Group 1 rats were control group. Pentylenetetrazole (PTZ) administrated to group 2 rats to induce the seizures with 35 mg/kg intraperitoneally injection every two days. Levetiracetam (LEV) i.p. at a dose of 108 mg/kg was given to group 3 rats before PTZ application. At the end of one month, the brain was dissected, and pathological examination was performed from the tissue The brain samples were fixed with 2.5% glutaraldehyde solution and prepared for section, after preparation 70-110 nm sections were cut with ultramicrotome and the sections were stained with uranyl acetate and lead. Then, the brain samples were examined with Transmission Electron Microscope (TEM) and the ultrastructural alterations were photographed at 80kV.

Results: Myelin sheath degeneration in the axons, vacuolar alteration in the astrocyte cell and necrosis were detected in the brain ultrastructure of Group 2. Although in Group 3 the severity of the cytopathological changes were milder than Group 2, mitochondrial deformation (cristolysis) in astrocyte cell as in the neurons and myelin degeneration in the axons were observed. No ultrastructural changes were observed in the brain of the control rats (Group 1) for 30 days.

Conclusion: Seizures may induce ultrastructural changes in brain of rats. This induction needed to have micro bio system analysis

Keywords: Seizures, Brain, Ultrastructural changes, PTZ-epilepsy model

EXPRESSION OF THE BIG POTASSIUM CHANNEL IN EPILEPTIC RATS OF BRAIN EXPOSED TO CHRONIC PULSED MAGNETIC FIELD

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Abstract

Aim: The aim of this study was to understand the expression of big potassium (BK channels) channels in epileptic seizures under magnetic field application.

Material and Methods: Forty Wistar albino adult male rats used in this study were divided into 5 groups (n=8). 1st group rats were control group. Pentylenetetrazole (PTZ) administrated to 2nd group rats to induce the seizures with 35 mg/kg intraperitoneally injection every two days. Levetiracetam (LEV) i.p. at a dose of 108 mg/kg was given to 3rd group rats before PTZ application. Pulsed magnetic field with 1.5 mT was exposed to the 4th group rats for 3 hours a day for 1 month. In addition to PTZ application, 1.5 mT pulsed magnetic field was exposed to the 5th group rats for 3 hours a day for 1 month. At the end of one month, the brain was dissected, and pathological examination was performed from the tissue. The expression of BK channels was analyzed by Western Blot and immunohistochemical method.

Results: The occurrence of epileptic seizures was proven by c-Fos staining and a significant increase in c-Fos protein expression was observed in the hippocampus and frontal cortex of the experimental groups. In the pathology analysis provided by hematoxylin-eosin staining, severe neuron degeneration was determined in the hippocampus region. BK channel expression in the frontal cortex was 2.1-fold in the PTZ (2nd) group compared to the control group; and increased significantly 1.68-fold in the magnetic field (4th) group and 2.03-fold in the PTZ+magnetic field (5th) group. In the hippocampus, however, ion channel expression was decreased in the positive control (3rd) group compared to all other groups.

Conclusion: The results of magnetic field application and BK channel are good candidates to be evaluated in the control of seizures. Results should be improved with electrophysiological ion channel current measurements.

Keywords: PTZ-epilepsy model, Magnetic field, BK channels, Seizure

HUMANIN MAY HAVE A PROTECTIVE ROLE IN STZ-INDUCED INFLAMMATION IN MICE

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Abstract

Aim: Humanin is a 24-amino acid mitochondrial DNA-encoded peptide involved in many biological processes associated with inflammatory response. Recent studies indicate presence of a strong link between mitochondrial disfunction and inflammation. Inflammation can lead to the onset and complications of diabetes. Although the curative effect of humanin on the complications of diabetes is known, its effect on inflammation after diabetes is not yet known. The aim of this study was to examine the effect of chronic humanin administration on markers of inflammation in diabetes-induced mice.

Material and Methods: Forty adult mice were randomly selected for this study. Mice were divided into four groups (ten mice in each group): control group (saline), Humanin group (4 mg/kg humanin), STZ group (150 mg/kg dose) STZ+Humanin group. After decapitation, the blood samples were centrifuged. IL-1, IL-6 and IL-10 levels were measured by ELISA method from obtained serum samples.

Results: Diabetes decreased IL-10 levels and increased IL-1B and IL-6 levels compared to control. Also, humanin decreased IL-1 and IL-6 levels, while it increased IL-10 level in the diabetic mice.

Conclusion: Our novel findings implicate that humanin may be a target molecule in preventing the development and complications of diabetes.

Acknowledgement: This study was sponsored by the Turkish Scientific Technical Research Organization (TÜBİTAK Project No: 119R084).

Keywords: Humanin, Diabetes, Inflammation

ANGIOTENSIN 1-7 PREVENTS VENTRICULAR DIASTOLIC DYSFUNCTION IN DIABETIC CARDIOMYOPATHY

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Abstract

Aim: Renin-Angiotensin-Aldosterone System (RAAS) plays a critical role in the pathophysiology of heart failure. Decreasing the production of angiotensin II (Ang II) or inhibiting its receptor activity has been shown to reverse remodeling in diabetic cardiomyopathy (DCM). Recently angiotensin 1-7 (Ang 1-7) which is produced via ACE-2 enzyme pathway was shown as a novel component of RAAS. Counter effects of Ang 1-7 opposing to Ang II caused increasing research focused on novel RAAS concepts systemic and locally at the tissue level. Hereby we investigated the effects of Ang 1-7 on diabetic alterations in cardiac functions in a rat DCM model.

Material and Methods: Diabetes was induced by application of a single dose of 50 mg/kg streptozotocin as i.p. 600 µg/kg Ang 1-7 was applied for 30 days after diabetes induction. Left ventricular functions were evaluated by pressure-volume measurement by Transonic PV Loop System (ADV500).

Results: The experimental diabetes model decreased the stroke work (SW) by causing a decrease in stroke volume (SV) and cardiac output (CO). The main reason for this is the decrease in end-diastolic volume (EDV) in diabetic conditions. In addition, pressure-volume area (PVA) and potential energy (PE) decrease in diabetes, and cardiac efficiency decrease with the change of contraction (+dP/dt) and relaxation (Tau) kinetics.

Conclusion: Ang1-7 influences recovery of cardiac function by improving SW and contractility in DCMP model. Also, Ang1-7 preserves the maintenance of ventriculo-arterial coupling by increasing ventricular compliance and decreasing arterial elastance. ACE-2 pathway may be considered a potential therapeutic target since our results claim that Ang 1-7 improves remodeling in DCM.

This study was funded by TÜBİTAK (Project No: 117S066) and Akdeniz University BAP (Grant No: TDK-2021-5449).

Keywords: Renin-Angiotensin, Angiotensin 1-7, Heart, Diabetes Mellitus, P-V Loop, Rat

INVESTIGATION OF CATECHOL-O-METHYLTRANSFERASE G-1947A GENETIC VARIANT AND ESSENTIAL HYPERTENSION RELATIONSHIP İN TURKISH POPULATION

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Abstract

Aim: Catechol-O-methyltransferase (COMT) is one of enzymes that play role in the catecholamine metabolism. This enzyme catalyzes transformation of a methyl group from S-adenosyl methionine (SAM) to catecholamine neurotransmitters dopamine, norepinephrine and epinephrine and lead to the inactivation of these catecholes. Genetic polymorphism rs4680 (Val158Met) of COMT is known as a major variant that changes enzymatic activity and association of this variant with essential hypertension (EHT) has been previously shown in several populations. Therefore, in our study, we aimed to determine distribution of this promoter variant in Turkish population and to reveal its correlation with EHT.

Material and Methods: DNA was isolated from peripheral blood samples (200 µl) of 221 patients diagnosed with essential hypertension (EHT) and 170 healthy persons without EHT, referred to the Department of Internal Medicine, Pendik Education and Research Hospital of Marmara University Medical Faculty. Real-time PCR analyzes were performed using LightCycler 96 (Roche). Distribution of genotypes and their relationship with EHT was evaluated statistically using GraphPad Prism software (v.7.0).

Results: The genotype distribution for COMT G-1947A (rs4680) variance were found as 39.8% AA, 34.3% GA, and 25.9% GG in 221 EHT patients. Corresponding values for healthy individuals were 31.1% AA, 27.1% GA and 41.8% GG. The respective frequencies between two groups were found statistically significant when compared using chi-square analysis (p=0,0038). The difference in single allele distributions (A / G) was also statistically significant, showing strong correlation with EHT (p=0,0006).

Conclusion: According to our results, G-1947A variance have a strong positive association with hypertension. Therefore G-1947A polymorphism could be an important risk marker for Turkish population.

Acknowledgement: This study was supported by Marmara University Scientific Research Projects Commission with project number SAG-C-YLP-131217-0650.

Keywords: COMT, SNP, Catecholamine, Polimorfism, Hypertension

DETERMINATION OF ANTI-CANCER PROPERTIES OF URTICA DIOICA ETHANOL EXTRACT ON HEMATOPOIETIC CELL LINES

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Abstract

Aim: Urtica dioica is a natural phytotherapeutic agent with various effects such as antioxidant, anti-inflammatory, anti-fungal, hypotensive as well as anti-carcinogenic. In recent years, phytotherapeutic approaches to reduce side effects of available chemotherapeutic agents or to find new agents with higher toxicity in cancer cells relative to healthy ones, are area of intense research. Therefore, in this study, we investigated anti-carcinogenic effects of U. dioica ethanol extract on K562 human chronic myeloid erythrocyte cell lines and on lymphocytes isolated from healthy donors (PBMC).

Material and Methods: U. dioica extract was isolated by using soxhlet extraction methodology. Anti-carcinogenic effects of the agent were analyzed with MTT assay (Cell Proliferation Kit I, Roche), Annexin V/PI (Molecular Probes A10788), mitochondrial membrane potential assay (JC-1, Abnova KA1324) and cell cycle analyses (PI staining in flow cytometer (FACS Calibur). PBMCs were prepared from healthy volunteers through Ficoll Hypaque density gradients.

Results: Data indicated that treatment with U. dioica didn't show up a dose-dependent cytotoxic effect on K562 cell line, but there was a 20% suppression at 25 µg/ml compared to PBMC ($p<0.001$). U. dioica extract yielded to an increase in apoptosis 13% and 41% for 25 µg/ml and 100 µg/ml, respectively, in comparison to untreated control cells ($p=0.033$). It has also induced cell cycle arrest at G0/G1 phase, in a dose-dependent manner. Accumulation at G0/G1 phase increased 9.6, 10 and 14% in 50, 75 and 100 µg/ml concentrations, respectively, compared to the control group ($p<0.0001$).

Conclusion: Our findings explicitly show that the total ethanol extract of U. dioica is highly effective in K562 cells on the induction of apoptosis and cell cycle arrest at reasonably low concentrations and these effects significantly pronounced compared to healthy controls.

Keywords: *Urtica dioica*, Leukemia, Apoptosis, K562, Cell cycle

THE EFFECTS ON THE TELOMERE LENGTH OF HEALTHCARE PROFESSIONALS OF DIAGNOSTIC DEVICES USING NON-IONIZING RADIATION

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Abstract

Aim: Electromagnetic radiation with 0-Hz to 1.1-THz frequencies including ultraviolet light, infrared and radio waves are defining non-ionizing radiation (NIR). With advances in technology, devices using NIR have become increasingly common in healthcare. In 2011, WHO and International Agency for Research on Cancer (IARC) classified non-ionizing radiation as a possible human carcinogen (Group 2B). Telomeres are nucleoprotein complexes comprised of tandem arrays of repetitive DNA sequence that serve to protect chromosomal termini from inappropriate degradation. However, the effects of non-ionizing radiation exposure on telomeres per se are much less well understood. Therefore, this aim of study is to investigate the effects on the telomere length of healthcare professionals of diagnostic devices using non-ionizing radiation.

Material and Methods: The control group consisted of healthy volunteers (n=8), the study group consisted of laboratory worker of microbiology (n=4), physiology(n=8), central laboratory(n=10), serology (n=8) and parasitology (n=3). 2 ml of whole blood from all consenting groups was taken into tubes with EDTA, and telomere length was evaluated from serum samples using an Absolute Human Telomere Length Quantification qPCR Assay Kit (ScienceCell). Demographic information was obtained from all groups regarding age, gender, occupational years, smoking and alcohol consumption, and whether they had any chronic diseases. Age range and professional years were tried to be equal as much as possible between the groups.

Results: Telomere length of the control group was 22.08 and non-ionizing radiation groups were 14.66 ($p<0.005$). Telomere length shorting may be associated with genomic instability, cancer, or senescence in a variety of settings.

Conclusion: The results showed the critical importance of telomere length in non-ionizing radiation response. On-ionizing radiation exposure in medical staff may be associated with increased telomere length shortening. This project supported from TUBİTAK 2209-A and ERUBAP; Project numbers: TSA-2022-11675.

Keywords: Occupational exposure, Non-ionizing radiation, Cancer, Telomere length, Medical staff

THE EFFECT OF CURCUMIN-MEDIATED SONODYNAMIC THERAPY ON LEISHMANIA TROPICA PROMASTIGOTES

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Abstract

Aim: Leishmaniasis is an infectious disease that is transmitted by Phlebotomus, 400 thousand new cases appearing every year, and approximately 350 million people are at risk, and accepted by the World Health Organization as one of the six important tropical diseases. There is a need for new treatment options in the treatment of Leishmaniasis, since there is no standard treatment scheme with few side effects. Sonodynamic therapy (SDT) is also a candidate to be one of these options. SDT is a treatment method based on the simultaneous combination of low-intensity ultrasound and a sonosensitizer, and the generation of reactive oxygen species in cells in the presence of molecular oxygen.

Material and Methods: Curcumin was used as a sonosensitizer in this study. Experimental groups were divided into the four groups: (1) Control group: No curcumin, no ultrasound; (2) treatment with all curcumin concentrations alone; (3) Curcumin mediated SDT group: ultrasound in the presence of curcumin; (4) Ultrasound treatment at 1 MHz, with a 3W/cm2 power intensity and a 50% duty cycle for 7 min (only US group.

Results: With the combination of curcumin (15.6 µM) and ultrasound (3W/cm2 intensity, 7 min), L.tropica promastigote viability was found to be significantly decreased ($p<0.001$) compared to the control group. Giemsa staining findings showed that 15.6 µM Curcumin mediated SDT induced several morphological alterations in L.tropica promastigotes typical of apoptosis. Late apoptosis was observed in 15.6 µM curcumin combined SDT treated parasites according to Annexin/PI staining.

Conclusion: This study provides new data elucidating the molecular mechanism underlying the anti-leishmanial effect of Curcumin mediated SDT. Curcumin mediated SDT has the potential to inactivate L.tropica promastigotes. However, further testing with amastigote or animal models is needed.

Keywords: *Leishmania tropica*, Curcumin, Sonodynamic therapy, Apoptosis

INVESTIGATION OF THE EFFECTS OF EXPOSURE TO PRE- AND POSTNATAL RADIOFREQUENCY RADIATION ON OSSIFICATION: A FOUR GENERATIONS STUDY

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Abstract

Aim: International Commission on Non-Ionizing Radiation Protection and World Health Organization are concerned with the bioeffects of electromagnetic field (EMF) in terms of biological health effects of radiofrequency radiation (RFR) on pregnant women and their infants. Our aim is to evaluate the effects of pre-and postnatal 2.4 GHz continuous wave (CW) RFR on cranial ossification right and left anterior-posterior extremity ossification four generations of rat fetuses.

Material and Methods: Four groups such as sham, irradiated female, irradiated male, irradiated male and female, which each consisting of four rats (a male and three female). Rats in the exposure groups were whole-body exposed to 2.4 GHz CW-RFR for 12h/day during the experiment. Irradiation started one month before fertilization in experimental group. On the 18th day of gestational period, one pregnant rat from each group was decapitated under general anesthesia and fetuses were taken. The remaining two pregnant rats completed normal gestation period. When offspring were two months old, four rats, one male and three female, were allocated for second generation study. Next generation animals were also experienced same processes as first-generation rats. Cranial ossification in all generation fetuses were measured by digital caliper. The ossification right and left anterior-posterior extremity bones in all generation fetuses were evaluated by using skeleton double staining methods.

Results: Head-tail length of exposure groups all generation was increased. Total bone length, ossification area and ossification percentage were increased significantly in exposure groups 2nd and 3rd generation. Ossification percentage of clavicula and scapula was significantly increased exposure groups of 4th generation. However, ossification percentage in the humerus, radius, and ulna were showed significant increase in exposure groups ($p<0.001$).

Conclusion: Pre-and postnatal 2.4 GHz CW-RFR exposure increases primary ossification and may change bone length and bone density rat fetuses.

Keywords: 2.4 GHz RF, Pre-and postnatal exposure, Ossification, Continuous wave, Four generation

DETERMINATION OF THE RELATIONSHIP BETWEEN TASTE SENSITIVITY AND DIETARY SODIUM INTAKE IN YOUNG ADULTS

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Abstract

Aim: Excessive consumption of sodium is a major risk factor for hypertension. Individuals with low salt sensitivity tend to increase their salt consumption to achieve delicious flavors. The study aimed to determine the relationship between salty taste sensitivity, and nutritional and anthropometric data in young adults.

Material and Methods: The cross-sectional study population consisted of a total of 99 university students, 89.9% (n=89) female and 10.2% (n=10) male, aged between 18-29 years. The socio-demographic, anthropometric, and food consumption characteristics of the participants were recorded. To evaluate the salt taste detection threshold and salt taste recognition thresholds, 8 different concentrations of solutions were prepared in the range of 2 to 256 mmol/L.

Results: The mean not perceiving the salt taste of the participants was determined as 7.4±6.6 mmol/L and the mean salt recognition threshold was 10.22±09.58 mmol/L. Most participants (42.4%) determined the salt taste detection threshold at 4 mmol/L, and 35.4% at 8 mmol/L. The salt taste recognition threshold was recognized by 29.3% of the participants at the 4 mmol/L and 25.3% at a level of 8 mmol/L. There was no significant (p>0.05) difference between the threshold for not perceiving the salt taste and the threshold for recognizing the salt taste according to gender. While no significant relationship was found between not perceiving the salt taste threshold and consumption of sodium, table salt, energy, protein, fat, and carbohydrate(p>0.05). A low-level negative linear correlation was found between body mass index (p<0.01 r: -0.26), waist (p<0.01 r: -0.26), waist/hip ratio (p<0.05 r: -0.22). No relationship was found between the salt taste recognition threshold and food consumption and anthropometric measurements (p>0.05).

Conclusion: The study shows that there is no statistically significant correlation between salt sensitivity and the amount of energy, macronutrients, sodium, and table salt contained in the diet, but there is a negative and weak relationship for anthropometric measurements.

Keywords: Dietary Sodium, Diet, Hypertension, Taste Threshold

THE ROLE OF CA^{2+}-ACTIVATED CL^- CHANNELS IN P2X7-ACTIVATED ANION PERMEABILITY

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Abstract

Aim: The P2X7 receptor is a non-selective cation channel activated by purines. It also induces a permeation pathway in the cell membrane for molecules up to 900 Da. This membrane permeability pathway is not nonselective or apoptotic. The mechanism of the formation of permeability of the receptor pore has not yet been clarified. In this study, we examined whether Ca^{2+} -activated Cl^- channels are required for P2X7-activated large membrane permeability and blebbing.

Material and Methods: We examined the effect of flufenamic acid (FFA), a Ca^{2+} activated Cl^- channel inhibitor, on P2X7-mediated fluorescent molecule uptake using fluorescence microscopy. For this, we examined the effect of FFA on different fluorescent molecules (negatively charged Lucifer Yellow and positively charged YO-PRO-1) entries in mouse macrophage-derived RAW 264.7 culture cells that endogenously express the P2X7 receptor. We calculated the ratio of cells that up took fluorescent molecules after receptor stimulation with ATP (1mM). We considered those ratios as a measure of fluorescent molecule uptakes. We calculated this ratio in different extracellular conditions (with and without Ca^{2+}).

Results: We observed YO-PRO-1 entry in both conditions with and without Ca^{2+} after receptor stimulation with ATP. As expected, FFA as a type of Cl^- channel inhibitor did not inhibit the entry of positively charged YO-PRO-1 in either case. FFA blocked Lucifer Yellow entry in Ca^{2+}-containing conditions, but not in nominal Ca^{2+}-free conditions. In addition, FFA showed basal Lucifer Yellow entry in an extracellular Ca^{2+} dependent manner.

Conclusion: We showed that P2X7 receptor activation is a complex mechanism, open to misinterpretation. For example, if only negative dye entry is investigated in conditions containing only Ca^{2+}, it will lead to misinterpretations that permeability occurs through anion channels and P2X7-activated membrane permeability requires Ca^{2+}-activated Cl^- channel activation. Our data showed that P2X7 activates multiple permeation pathways, with different Ca^{2+} requirements and sensitivity to the FFA of these permeation pathways.

Keywords: P2X7, Macrophage, Fluorescence, Membrane permeability, Cl^- channel, Glufenamic acid

A STUDY ON LONG-TERM ATR FT-IR MEASUREMENTS AT AMBIENT ATMOSPHERIC CONDITIONS

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Abstract

Aim: FT-IR devices are sensitive to the environment. Measurements are commonly performed after stabilization of the instrument, and by taking a background spectrum immediately before the actual sample measurement. These minimize environmental influences and prevent spectral distortions. A spectral signal around 1000 cm-1 emerged when testing the instrumental stability after taking a background in a day and performing measurements on the following days, by performing blank measurements without any sample on the surface. Spectral distortions were expected. However, observed signal was unlike a distortion. It was a sample signal. Investigating the nature of that signal was aimed.

Material and Methods: FT-IR spectra were obtained daily, or weekly, through ATR FT-IR measurements at one location, after taking a background. Such measurements were performed at two additional places, i.e., laboratories. Measurements were performed with Perkin Elmer's SpektrumTwo model ATR FT-IR device within the 400-4000 cm-1 (mid-IR) wavenumber range, with 4 cm-1 resolution, and by collecting 8 scans at least. Spectral intensity changes were inspected. Selected spectra were compared with a spectral library.

Results: Regional spectral signal increases were observed in all indoor environment measurements. Inspection with spectral library could not explain the nature of the signal under study. Signal under study was consistently increasing in time. That signal of interest was likely due to oxidation of the silicon carbide detector of the instrument. Namely, the signal was deemed as silicon oxide, based on literature, through raw comparison of the spectral data in the literature with the peak position and shape of the signal under study. It could not be identified through spectral library comparison due to spectral distortions, observed as the evolution of a negative absorbance signal.

Conclusion: Long-term ATR FT-IR measurements were performed at ambient indoor atmospheric conditions. Consistent emergence of a signal was observed. That signal was silicon oxide, in conclusion.

Keywords: FT-IR, Ambient atmosphere, Indoor atmosphere

STZ-INDUCED SCIATIC NERVE CONDUCTION VELOCITY AND PTEROSTIBENE EFFECTS IN RATS

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Abstract

Aim: The aim of this study is investigation of the effects of pterostilbene (PTS) (trans-3,5- dimethoxy-4-hydroxystilbene) applied at different doses in the treatment of streptozotocin- induced diabetic myopathy.

Material and Methods: In our study, 5 groups were formed with 10 rats per group. The groups are Control (C), Diabetes (DM), Diabetes+10mg/kg PTS (PTS10), Diabetes+20mg/kg PTS (PTS20), Diabetes+40mg/kg PTS (PTS40). Body weights, serum malondialdehyde (MDA), nerve conduction velocity and blood glucose levels were determined in all groups by biophysical and biochemical analyzes performed at the end of the 5-week experiment period.

Results: The weight losses were measured as 23.8% in the DM, 17.3% in the PTS10, 7.6% in the PTS20 and 1.3% in the PTS40 group. When compared to the DM group, the decrease in blood glucose level was 46.1% in the PTS10, 55.8% in the PTS20 and 63.4% in the PTS40 group. The serum insulin value reduction rate was calculated as 62% in DM, 42% in PTS10, 23.4% in PTS20 and 1.6% in PTS40 according to control group. The serum MDA increasing rate was found as 492% in DM, 229% in PTS10, 144% in PTS20 and 97% in PTS40 according to control group. Nerve Conduction Rate decreased by 52% in the DM group compared with the control group. The decrease rates in nerve conduction of PTS groups are respectively; PTS10 37%, PTS20 32% and PTS40 26% were found.

Conclusion: We believe that the therapeutic properties of pterostilbene administration are better in the treatment of diabetic diseases than other nutraceutical supplements for the time being and that deeper research should be done.

Keywords: Streptozotocin, Nerve Conduction Velocity, Pterostilbene, Blood glucose

INVESTIGATION OF ELECTRIC AND MAGNETIC FIELD POLLUTION AND ANXIETY AND DEPRESSIVE EFFECTS IN ADULT INDIVIDUALS IN ŞANLIURFA

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Abstract

***Aim*:** Electromagnetic fields (EMF) causes various health problems. There are studies showing that exposure to EMF may cause effects such as stress, depression, and insomnia. The present study aimed to investigate the EMF pollution in city center of Şanlıurfa and anxiety-depression symptoms of people who exposed to EMF.

***Material and Methods*:** EF and MF measurements were taken by Gauss/Tesla meter at ground at TEİAŞ ,44 substations (for each transformer: at 0 point, 1 and 2 meters away and the closest home/office to the transformer). These measurement points are around transformers and in TEİAŞ facility which are nearby the houses/offices.
Anxiety and depression symptoms of groups were measured by using beck anxiety inventory scale (BAI) and beck depression inventory scale (BDI). Both the experimental and control group members were required to not have a psychological disorder. The experimental group consists of individuals living in TEİAŞ lodgings, TEİAŞ employees and individuals who living close to the transformers (n=55). The control group individuals (n=50) are living outside the Şanlıurfa transformers/high transmission lines. Measured values were compared with ICNIRP and ACGIH standards and the relation between EMF pollution and anxiety-depression was evaluated statistically.

***Result*:** Average MF value of 44 transformers: at 0 metre 0.087 mT, at one meter away 0.072 mT, two meters away 0.066 mT, at closest home/office to the transformer 0.058 mT. MF and EF values at TEİAŞ: 0.13- 0.18 mT and 38,8-58,9 kV/m respectively. All measured MF values were below the standards, but EF values were within concern limit at some points. There was no statistical difference between the experimental and control groups in general

***Conclusion*:** There is no statistically convincing evidence for an association between EMF exposure and anxiety-depression symptoms ($p>0.05$). We attribute this result to the fact that our MF values are lower than the standards.

Keywords: Electromagnetic fields, Anxiety, Depression, Standards

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