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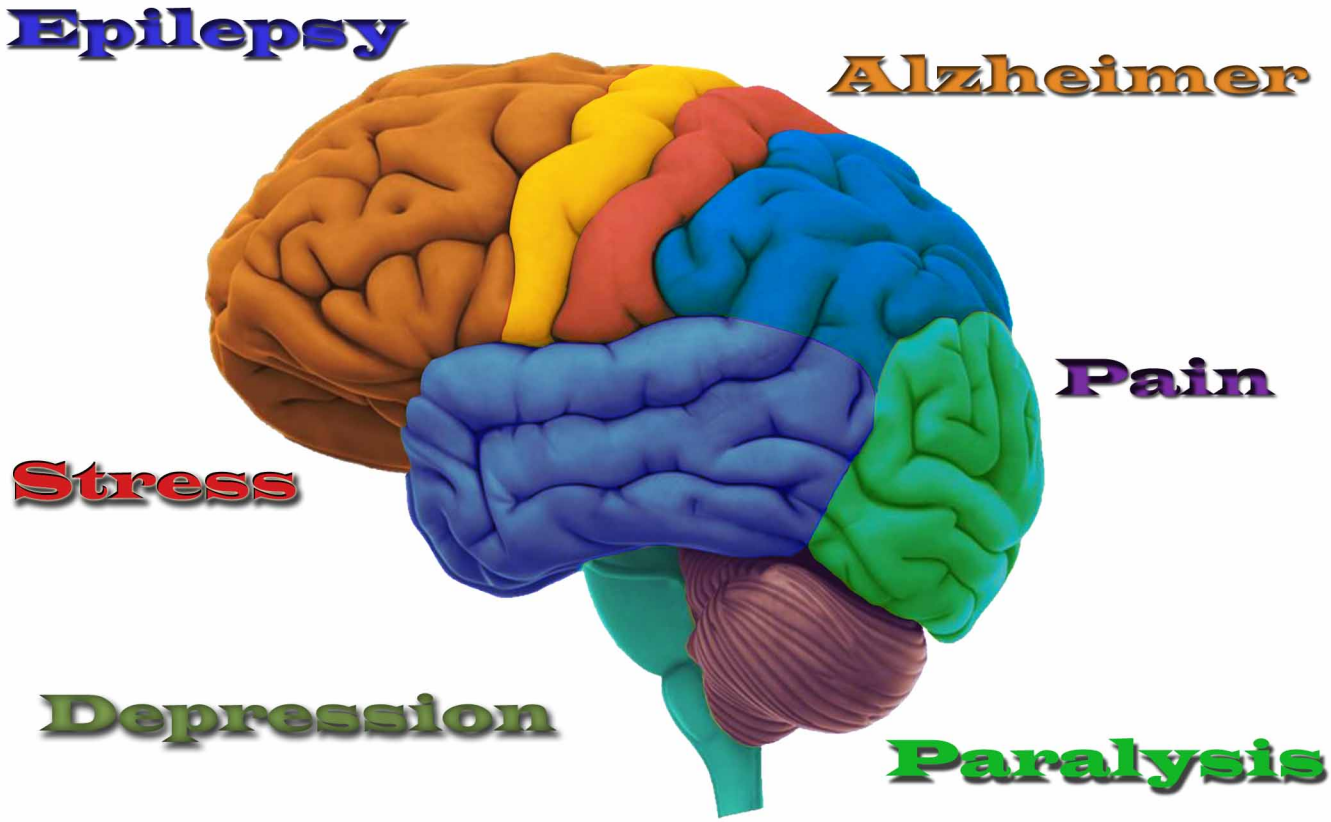

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21 - 27 June 2021 - Isparta / Turkey

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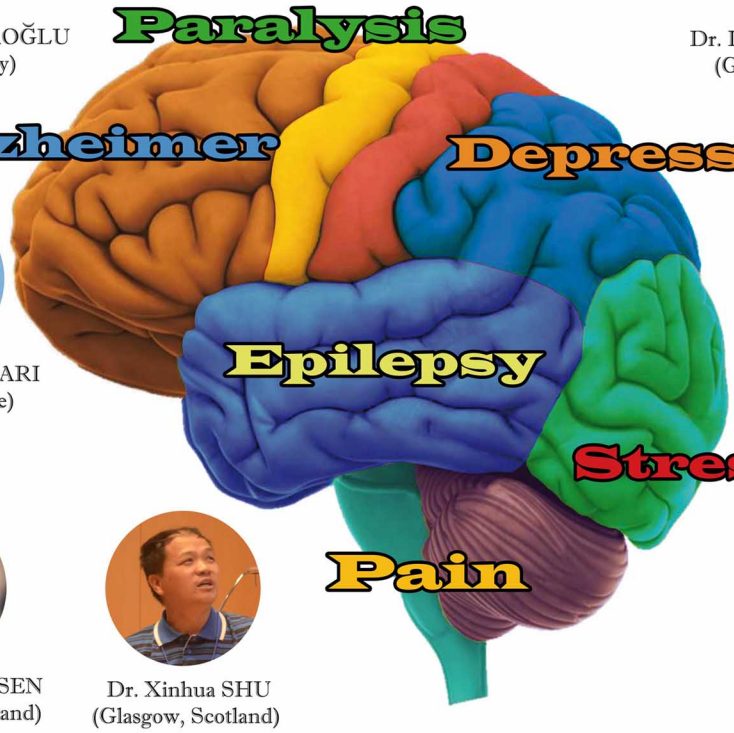

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AIM AND SCOPES
Journal of Cellular Neuroscience and Oxidative Stress is an online journal that publishes original research articles, reviews and short reviews on the molecular basis of biophysical, physiological and pharmacological processes that regulate cellular function, and the control or alteration of these processes by the action of receptors, neurotransmitters, second messengers, cation, anions, drugs or disease.

Areas of particular interest are four topics. They are;

A- Ion Channels (Na^+- K^+ Channels, Cl^- channels, Ca^{2+} channels, ADP-Ribose and metabolism of NAD^+, Patch-Clamp applications)

B- Oxidative Stress (Antioxidant vitamins, antioxidant enzymes, metabolism of nitric oxide, oxidative stress, biophysics, biochemistry and physiology of free oxygen radicals)

C- Interaction Between Oxidative Stress and Ion Channels in Neuroscience
(Effects of the oxidative stress on the activation of the voltage sensitive cation channels, effect of ADP-Ribose and NAD^+ on activation of the cation channels which are sensitive to voltage, effect of the oxidative stress on activation of the TRP channels in neurodegenerative diseases such Parkinson's and Alzheimer's diseases)

D- Gene and Oxidative Stress
(Gene abnormalities. Interaction between gene and free radicals. Gene anomalies and iron. Role of radiation and cancer on gene polymorphism)

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Biophysics	Biochemistry
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Neuroscience	Neuropharmacology

Keywords
Ion channels, cell biochemistry, biophysics, calcium signaling, cellular function, cellular physiology, metabolism, apoptosis, lipid peroxidation, nitric oxide, ageing, antioxidants, neuropathy, traumatic brain injury, pain, spinal cord injury, Alzheimer's Disease, Parkinson's Disease.

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Speakers

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Oral Presentations

SPEAKERS

Speak No. 1

Laser confocal microscope analyses in neuronal cells for investigating the TRPM2 channel

Mustafa NAZIROĞLU[1,2]

[1]Neuroscience Research Center (NÖROBAM), Suleyman Demirel University, Isparta, Turkey

[2]Drug Discovery Unit, BSN Health, Analyses, Innovation, Consultancy, Organization, Agriculture, Industry LTD, Isparta, Turkey

The confocal laser scan microscope (CLSM) imaging technique is a most valuable fluorescence technique in the cells and neurons. As compared to the electron microscopy technique, the imaging technique of CLSM is poor. However, the CLSM analyses needs less specimen as compared to the analyses of the electron microscopy. In the CLSM analyses, it is possible obtaining three-dimensional (3D) live imaging. In addition, measuring the dynamic cellular and molecular processes such as measurement of cytosolic free Ca^{2+} (cCa^{2+}) concentration and apoptosis in the cells and neurons are possible. In the Ca^{2+} imaging processes of CLSM, the cells and neurons are incubated by several florescent dyes such as Flu-3-AM and Fluo-8. The stains were used for the measurement of transient receptor potential (TRP)-dependent Ca^{2+} influx (Güzel et al. 2021; Özkaya et al. 2021).

The increase of cCa^{2+} influx is induced by the activation of several channels such as voltage gated calcium and chemical gated calcium channels. In addition to the well-known cation channels, TRP superfamily was discovered within the last decades. The superfamily is containing 28 members in mammalian. A member of the TRP superfamily is TRP melastatin 2 (TRPM2). The stimulation of ADP-ribose and oxidative stress induces the activation of TRPM2 channels in several neurons and cells (Perraud et al 2001; Nazıroğlu and Lückhoff 2008). For investigation of TRPM2, the calcium imaging by using the CLSM is a most valuable technique. In our experiments, we have been used the Fluo-3-AM and Fluo-8 dyes for the investigation of TRPM2-dependent Ca^{2+} influx in several neurons such as dorsal root ganglion, hippocampus, and microglia.

In conclusion, the CLSM is a valuable imaging technique for the investigation of TRPM2 channels.

Keywords: Confocal laser scan microscope; TRPM2 channels: Neurons

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SPEAKERS

Speak No. 2

TRPM7 in the nervous system in health and disease

Cui CHEN, Bingqing GUO, Wei LI, Nashat ABUMARIA
State Key Laboratory of Medical Neurobiology and MOE Frontiers Center for Brain Science, Institutes of Brain Science, Fudan University, Shanghai 200032, China.

TRPM7 chanzyme is a unique divalent cation ion channel that includes a serine-threonine α-kinase domain on its C-terminal. It is believed to mediate several biological processes including Zn^{2+} and Mg^{2+} homeostasis. In the central nervous system, following certain pathological triggers, TRPM7 mediates neurotoxicity, neuro-injuries, and neuronal death. This prompted neuroscientists and neurologists to propose blocking TRPM7 as a rational therapeutic strategy to prevent neuronal death and tissue damage following ischemic/traumatic brain injuries. However, the TRPM7 role in the central nervous system under physiological conditions remains unclear. We found that TRPM7 is an important regulator of synaptic and cognitive functions. Mechanistically, memory, synapse density, and synaptic plasticity were found to depend on the α-kinase domain, but not on the ion channel part of TRPM7. The α-kinase was found to regulate synapse density/plasticity by directly interacting with, and phosphorylating (inhibiting) cofilin; the cytoskeleton and/or spine density regulating protein (Liu et al. 2018). To further define mechanisms by which the α-kinase may contribute to regulating synaptic and cognitive functions, we applied a proteomics approach to identify the α-kinase interacting proteins in different cellular compartments. We found that the α-kinase is part of several large complexes of proteins, many of which function in regulating certain cellular processes including cytoskeletal organization. In the light of new findings from our lab, we will briefly provide new mechanistic insights into the role of TRPM7 in the brain under physiological and pathological conditions. New strategies on how to target TRPM7 to treat neurological and neurodegenerative disorders will be discussed as well.

Keywords: TRPM7; Neuron; Neurodegenerative diseases.

Acknowledgement: Supported by the Natural Science Foundation (NSF) of China, Fudan University-Shanghai Institute of Materia Medica Chinese Academy of science joint Grant and NSF of Shanghai Grant.

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SPEAKERS

Speak No. 3

Primary Cell Culture model: An excellent tool to study the effects of Viral Infection of CNS

Anirban BASU
National Brain Research Centre, Manesar, Haryana, India.

Through this workshop, participants will be introduced to the basics of neuro-cytobiology. The focus of our research group is on bridging the gap between our current understanding of Viral infections of Central Nervous System(CNS) and developing subsequent therapeutic strategies to combat these neurotropic viral infections. Our CNS is comprised of basic units of specialised cell types called glia and neurons. Glia are a diverse family of cells that perform a variety of supportive functions throughout our nervous system. Neurons, with their extensive cellular structure called dendrites and axons, produce unique electrical events and use a highly evolved system for communicating with one another. Our group has been able to successfully establish primary culture models by isolating these cell types from the mouse model (BALB/c) and culture them aseptically in a laboratory setting, primarily to get a deep insight upon Viral infections in CNS such as the ones cause by Japanese Encephalitis Virus (JEV) and West Nile Virus (WNV). These primary culture models provide more relevant and reliant results in comparison to the cell lines. Thus, it is an important model to study the synergistic effects of the neurotropic viral infections. Apart from the primary culture, whole brain sections are also used to study and visualise the extent of damage caused by these neurotropic viral infections.

SPEAKERS

Speak No. 4

Clues of Western blot in neuronal cells

Denis ROUSSEAU
LMGP – IMBM, UMR 5628, Institut National Polytechnique PHELMA 3, parvis Louis Néel, BP257, Grenoble Alpes University, Grenoble Cedex 1, France

A valuable technique in the imaging neuronal cells is Western blotting. The results of Western blot indicate specific proteins from the total proteins of neurons. There are three essential steps in the Western blot analyses, namely separation, transfer, and identification of target proteins by using the primary and secondary antibodies of specific proteins. Last, the bands were visualized in a dark room or device. In the presentation, I will summarize the technique in the neuronal cells. In addition, I will give clues of the Western blot analyses.

Keywords: Western blot; Antibodies; Neurons.

SPEAKERS

Speak No. 5

Principles of Ca^{2+} imaging using low-affinity indicators

Marco CANEPARI
Equipe MOTIV, Laboratoire Interdisciplinaire de Physique (LIPhy), Université Grenoble Alpes, France

In this lecture I will introduce the principles of Ca^{2+} imaging using low-affinity indicators and its applications to monitor Ca^{2+} dynamics under physiological conditions in native systems, i.e. neurons in *ex-vivo* or *in vivo* preparations. First, I will analyse in detail the issue of competition of the Ca^{2+} indicator with the endogenous Ca^{2+} buffers expressed by the cell and how Ca^{2+} imaging can be performed to monitor the free Ca^{2+} concentration without perturbing the physiological Ca^{2+} homeostasis. Second, how will show how the extremely fast kinetics of low-affinity indicators can be used to monitor fast Ca^{2+} currents to disclose the real kinetics of native voltage-gated Ca^{2+} channels, in particular by combining Ca^{2+} imaging with membrane potential imaging. I will finally extend these concepts to Na^{+} imaging to monitor in detail the origin of an action potential and how combining imaging techniques with neuronal computation allows extracting the ensemble of ionic currents.

SPEAKERS

Speak No. 6

A mouse model for age-related macular degeneration

Xinhua SHU[1,2,3]

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[2]Department of Vision Science, Glasgow Caledonian University, Glasgow, UK

[3]School of Basic Medical Sciences, Shaoyang University, Shaoyang, P.R. China

SPEAKERS

Speak No. 7

Voltage gated sodium channels and epilepsy

Simon HEBEISEN
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Epilepsy is the fourth most common neurological disorder and affects people of all ages. Medication for epilepsy is often life-long and has a major impact on the quality of life - mostly being related to substantial adverse effects. Therefore, over 30% of people with epilepsy do not achieve sufficient seizure control whilst effective medication being available.

Ion channels are often primary targets of anticonvulsant drugs. They can either act as blockers for voltage gated sodium and calcium channels or as activators for potassium or chloride channels. Additionally, modulators of ligand gated ion channels ($GABA_A$ or Glutamate receptors) are frequently used to treat epilepsy.

Employing a panel of functional electrophysiological assays using fluorescence based methods and patch-clamping on a broad range of voltage and ligand gated ion channels, we were able to successfully screen for drugs with a beneficial action profile. In successful leads we found drugs that selectively interacted with TTX sensitive, neuronal voltage gated sodium channels. Activation and fast inactivation were unchanged, while an increased affinity in the slow inactivated state was observed. This is a modern mode of action for anticonvulsive drugs. In contrast, traditional anticonvulsant drugs often show their major effects on the fast inactivated state of voltage gated sodium channels. One of the tested drugs showed substantial shifts of the voltage dependence of the slow inactivation only for $Na_V1.2$ and 1.6. This favours this drug for treating patients with diseases with compromised $Na_V1.1$ function in interneurons, such as Alzheimer's disease.

For further improvement of anticonvulsants interacting with ion channels as primary targets, compound libraries are screened to identify drugs with multiple ion channel effects like blockers of TTX sensitive Na_V channels and T type calcium channels. For this purpose, assays need to be improved and new assays need to be developed, to be able to reliably differentiate effects on ion channels in certain states and at high throughput.

Keywords: Epilepsy, voltage gated sodium channels, state dependent inactivation, patch-clamp technique

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Oral Presentations

Oral Presentation 1

Interactions between TSPO and calcium signaling in retina

Dilek ÖZKAYA
Department of Ophthalmology, Faculty of Medicine, Suleyman Demirel University, Isparta, Turkey

A reason of blindness in the elderly people is age-related macular degeneration (AMD) disease. The etiology of dry AMD has not been clarified yet. However, accumulation data indicate that excessive mitochondrial reactive oxygen species (mROS) generation in the membranes of retinal mitochondria has a main role in the etiology of dry AMD disease (Dimitrova-Shumkovska et al. 2020).

The overload calcium ion (Ca^{2+}) is the main reason of the excessive generation of mROS in the retina, because its influxes into mitochondria via the outer membrane of mitochondria induces increase of the mitochondrial membrane depolarization. The expression level of 18 kDa mitochondrial translocator protein (TSPO) was high in the outer membrane of mitochondria in the cells of retinal pigment and neuronal cells (Dimitrova-Shumkovska et al. 2020; Rashid et al. 2020).

A calcium ion permeable transient receptor potential (TRP) channel is TRP melastatin 2 (TRPM2). In retinal pigment cells, it was reported that the activation of TRPM2 is responsible from the upregulation of Ca^{2+} concentration, apoptosis, mitochondrial membrane depolarization, and mROS (Özkaya et al. 2021). In a study, presence of a direct relationship between the generation of mROS via the activation of TRPM2 was also reported (Özkaya et al. 2021). In the current presentation, I will summarize recent developments on TSPO and calcium signaling in the retinal cells. I will focus on the involvement of TRPM2 channel in the TSPO gene-induced retinal oxidative injury.

In conclusion, current literature data indicate that the presence of TSPO increased apoptosis and mROS via stimulation of TRPM2 in the retinal cells. It seems that the deletion of TSPO decreases mROS-mediated oxidative cytotoxicity via the modulation of calcium signaling in the cells of retina

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Oral Presentations

Oral Presentation 2

Recent developments on the chemotherapeutic agents-induced oxidative injury in optic nerve

Mehmet ARGUN
Department of Ophthalmology, Faculty of Medicine, Suleyman Demirel University, Isparta, Turkey

Chemotherapeutic agents include several chemicals such as cisplatin, 5-fluorouracil, and oxaliplatin. The agents have been using for the treatment of several cancer types such as breast, prostate, and neuronal metastasis. However, there are considerable dose-limiting side actions of the agents in human. For example, the treatments of cisplatin and 5-fluorouracil induced significant visual injuries in the optic nerve (Claus et al. 2019).

The etiology of the chemotherapeutic agent should be clarified in order to allow the discovery of new therapeutic drugs to modulate the chemotherapeutic agent-induced optic nerve oxidative damage. The results of recent studies indicate the involvement of chemotherapeutic agents-induced oxidative stress in the optic nerve oxidative injury in the rats (Icel et al. 2018; Taşlı et al. 2018; Özkaya and Nazıroğlu 2020).

Oxidative stress includes several reactive oxygen species (ROS) such as superoxide and hydroxyl radicals. The generation of ROS is well known to be related with several physiological neuronal activities, including mitochondrial function. The rich polyunsaturated fatty acids (PUFAs) contents of cells are the main targets of oxidative injury. The neurons, including optic nerve have rich PUFA content and they are principal targets of ROS. The ROS are scavenged by the antioxidants. For example, superoxide radicals are converted to hydrogen peroxide by the catalytic action of superoxide dismutase. The hydrogen peroxide is converted to water by the catalytic actions of catalase and glutathione peroxidase. Hence, the decrease of the antioxidants such as glutathione and glutathione peroxidase were reported in the cisplatin-induced optic nerve injury of rats, although the decreases of antioxidants are modulated by the antioxidant treatments such as curcumin, Pycnogenol, and rutin (Icel et al. 2018; Taşlı et al. 2018; Özkaya and Nazıroğlu 2020). In the oral presentation, I will summarize recent developments on the chemotherapeutic agents-induced oxidative injury in optic nerve.

In conclusion, current literature data indicate that oxidative stress has a main role on the etiology of chemotherapeutic agent-induced optic nerve injury in the experimental animals. The treatment of antioxidant has potential strategy to the modulate chemotherapeutic agents-mediated oxidative injury in the optic nerves of cancer patients undergoing chemotherapy.

Keywords: Antioxidants; Chemotherapeutic agents; Optic nerve injury; Oxidative stress

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Oral Presentations

Oral Presentation 3

The levels of female hormones and uterus antioxidants are affected by the frequencies of mobile phones and Wi-Fi: A literature review

Dilay KARADEMİR
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The devices of mobile phones and Wi-Fi have been using in several places such as home, work, school, and streets. The Wi-Fi devices induces electromagnetic radiation (EMR) at a frequency of 2450 MHz. The generations of second (2G), third (3G or UMTS), and fourth (4G or LTE) mobile phones induce EMR frequencies between 900-2600 MHz. The accumulating evidence in humans indicates that there are serious potential health risks associated with public exposure to the EMR. The experimental animal studies indicate serious risks of 900 MHz EMR from cell phones on the decreases of female hormones such as prolactin, luteotropic hormone, follicle-stimulating hormone (FSH), estrogen, and progesterone (Al-Akhras et al. 2001; Kliukiene et al. 2004; Yüksel et al. 2016). However, there are conflicting results on the subject in the literature. Therefore, the data on the influence of EMR on the female hormone levels in human and rodents are controversial. First aim of the oral presentation is reviewing the results of the EMR exposure on the female hormones in the human and rodents.

In our body, the reactive oxygen species (ROS) are generated by the several physiological functions such as phagocytosis and ATP generation (mitochondria). During the killing bacteria and viruses, the phagocytic cells such as neutrophils, microglia, and monocytes generate the ROS. However, the excessive generation of ROS has adverse action to several normal tissues, including uterus (Yüksel et al. 2016). The accumulating evidence indicates that the exposure of EMR from Wi-Fi and cell phones induces the excessive generation of ROS in uterus. In the second aim of the current presentation, I will summarize recent development on the EMR-induces ROS generation in the uterus.

In conclusion, present literature data indicate that there is a serious risk of EMR from cell phones and Wi-Fi on the female hormones and uterus in human.

Keywords: Female hormones; Oxidative stress; Uterus; Electromagnetic radiation

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Oral Presentations

Oral Presentation 4

An interaction between fibromyalgia and oxidative stress-induced Ca^{2+} influx

Şeyma TAŞTEMUR
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Fibromyalgia is characterized by a chronic pain condition. About 2% of the adult population are suffering from the fibromyalgia. In the treatment of fibromyalgia, anticonvulsants, physiotherapy, and antidepressant therapy have been using. However, these treatments cannot fully treat the disease because the etiology of fibromyalgia has not been fully clarified yet. Proposed mechanisms in the etiology of fibromyalgia are overload Ca^{2+} influx and excessive reactive oxygen species (ROS) generation.

Most of body functions such as cell proliferation, muscle contraction, and muscle cell death are controlled by the concentration of intracellular free calcium ion (Ca^{2+}). The Ca^{2+} passes the cell membrane via the activation several calcium channels such as voltage gated calcium and TRP cation channels. The overload increase of Ca^{2+} induces several pain attacks, including the pain of fibromyalgia. Recent data indicated involvement of voltage gated Ca^{2+} and TRP channels in the etiology of experimental fibromyalgia (Yüksel et al. 2017; Murasawa et al. 2021).

Oxidative stress occurs during the several physiological and pathophysiological functions. For instance, engulfed bacteria and viruses are killed in the phagocytic cells such as neutrophils and monocytes using the ROS. If the excessive generation of ROS would be not controlled by antioxidants, it induces adverse action in normal cells (Hargreaves and Mantle 2021). The ROS have also adverse action on the calcium channels such as voltage gated calcium and TRP cation channels (Yüksel et al. 2017). In turn, the increase of ROS-induced overload Ca^{2+} influx via the activation of the channels induces excessive generation of mitochondrial ROS. Lastly, the overload Ca^{2+} influx induces the hyperalgesia of fibromyalgia. In the oral presentation, I will review the present data on oxidative stress and Ca^{2+} influx in the experimental fibromyalgia.

In conclusion, it seems that the oxidative stress-induced overload Ca^{2+} influx has a main role in the etiology of fibromyalgia. The inhibition of the overload Ca^{2+} influx may be a new strategy for the treatment of fibromyalgia.

Keywords: Calcium ion influx; Fibromyalgia; Oxidative stress; Pain

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Oral Presentations

Oral Presentation 5

Involvement of TRPM2 Channel in Microglia Cell Activation: A review of literature

Kenan YILDIZHAN[1], Mustafa NAZIROĞLU [2,3,4]

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Microglia cells are the immune cells of the central nervous system (CNS). It is known that activation of microglia increases depending on pathological conditions in the CNS. While some phenotypic changes come about in activated microglia the number of cells upsurge at the same time. Moreover, they migrate to the site of injury, and secrete pro-inflammatory and anti-inflammatory cytokines, chemokines, growth factors, and oxidative stress-inducing molecules. (Malko et al. 2019). However, disruption or abnormality in microglia cell activation can lead to damage in many different diseases of the CNS, including ischemia, traumatic brain injury, Alzheimer's disease, Parkinson's disease, multiple sclerosis, and psychiatric disorders. Therefore, it is very important to understand activation mechanisms of the microglia cells.

Intracellular Ca^{2+} is a universal and vital signaling molecule in the almost all mammalian cells. The TRPM2 cation channel is a Ca^{2+} permeable cation channel. The TRPM2 channel is activated by ADPR, Ca^{2+}, reactive oxygen species (ROS), and reactive nitrogen species, and is inhibited by several inhibitors such as protons (acid pH), N-(p-amylcinnamoyl) anthranilic acid (ACA), 2-aminoethyl diphenylborinate (2-APB), and adenosine monophosphate (Naziroglu and Luckhoff, 2008). In a study, it has been reported that TRPM2 channels are naturally expressed in the microglia cell membrane and that TRPM2 translocation to the plasma membrane during microglial activation in response to stimuli (Miyake et al. 2014). Hence, Western blot analyzes show that the TRPM2 channel is highly expressed in the microglia (Akyuva et al. 2020).

Consequently, in the future, microglia cells and TRPM2 channel associated further studies will be important to understand the activation mechanisms of microglia cells, whose etiology is not understood, and excessive activation is observed, especially Alzheimer's and Parkinson's Diseases. Thus, we think that the TRPM2 channel will provide a therapeutic approach as a pharmacological target in controlling microglia cell activation in the process of neurodegenerative damage.

Keywords: Microglia, TRPM2 channel, Neurodegeneration, Oxidative stress, Calcium signaling

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Oral Presentations

Oral Presentation 6

Recent development on the TRP channels in the experimental migraine

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Migraine is a moderate or severe headache disorder accompanied by various combinations of neurological, gastrointestinal and autonomic changes, and it is a highly prevalent disease that reduces the quality of life and work force of the individual. The attacks are similar and are accompanied by transient neurological symptoms, headache, and gastrointestinal symptoms (Patterson and Silberstein, 1993). The occurrence of migraine pain and the subsequent neurogenic inflammation, vasodilation and activation of nociceptive trigeminovascular pathways maintain their importance. Although the cause of migraine attacks is not fully understood, it is thought that the activation of pain fibers that innervate meningeal nociceptors is very important in the onset of pain (Pietrobon and Striessnig, 2003).

Migraine (GTN)-induced excessive Ca^{2+} influx via activation of cell membrane channels, including transient receptor potential (TRP) channels, induces excessive mitochondrial reactive oxygen species (mROS) generation, cell death, and apoptosis in neuronal cells. Maintaining the integrity of the mitochondrial membrane is essential to avoid apoptosis. An increase of TRP melastatin 2 (TRPM2) channel activation, a member of the TRP superfamily, causes the increase of Ca^{2+} uptake into mitochondria. In turn, this leads to excessive generation of ROS via the increase of mitochondrial membrane depolarization, resulting in apoptosis, cell death, and down-regulation of survival signaling (Liu et al. 2020). It has been shown that cytosolic Ca^{2+} increase mediated by TRPM2 channel activation, causes an increase in caspase 3 and caspase 9 activities through an increase in mitochondrial membrane depolarization in nerve cells such as hippocampus, dorsal root ganglion (DRG), and microglia, although it is inhibited by chemicals such as N-(p-amylcinnamoyl) anthranilic acid (ACA), and 2-aminoethyl diphenylborinate (2APB) (Yazğan and Nazıroğlu, 2017; Yıldızhan and Nazıroğlu, 2020).

Glutathione (GSH) deficiency also causes cytosolic (cROS), and mROS mediated neurotoxicity. It includes the oxidation of the cysteine redox system, which is required for TRPM2 activation (Yıldızhan and Nazıroğlu, 2020). The reduction of members of the cysteine redox system, such as GSH, and selenium, with high cROS, and mROS concentrations leads to an imbalance in neuronal cysteine homeostasis, a decrease in neuronal GSH concentrations, and increased mROS formation. It has been reported that plasma GSH concentration decreases in experimental animals, headache, and migraine patients, and TRPM2 activation induced by GSH reduction resulted in increased oxidative neurotoxicity in nerve cells (Nazıroğlu et al. 2015; Togha et al. 2019).

In summary, while increased cROS and mROS levels cause migraine headaches, it suggests that excessive oxidative stress is a cause of migraine and causes a decrease in antioxidant levels. To further clarify the issue, further studies on migraine (GTN)-induced oxidative stress in experimental animal and human cell samples are needed.

Key words: Migraine; TRPM2 channel; Trigeminal ganglia; Oxidative stress.

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Oral Presentations

Oral Presentation 7

Involvement of TRPM2 in the etiology of Alzheimer's disease: A literature review

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A member of neurodegenerative diseases is Alzheimer's disease (AD). The incidence of AD is high in several countries, including USA. About 6.2 million 65 and older people in the USA are suffering from the AD. The AD results in dementia formation. Hence, the incidence of dementia is high in the patients with AD. In the etiology of AD, there is an abnormal build-up of proteins in the brain cells. The proteins of amyloid beta are well-known proteins in the plaques around brain cells of patients with the AD. The tau proteins in the deposits of tangles within the brain cells also act essential role in the etiology of AD. In addition to the proteins of amyloid beta and tau, the involvements of oxidative stress and excessive Ca^{2+} influx into the brain cell were indicated by the results of recent studies (Fonfria et al. 2005; Övey and Nazıroğlu 2015).

Transient receptor potential (TRP) superfamily contains several calcium permeable cation channels. A member of the TRP superfamily is TRP melastatin 2 (TRPM2). The channel is activated by several stimuli such as NAD^+, oxidative stress, and ADP-ribose (Perraud et al. 2001; Nazıroğlu and Lückhoff 2008). The involvement of TRPM2 in the etiology of several diseases was shown by the results of recent papers. In addition, there are some clues of the involvement of TRPM2 in the etiology of experimental AD (Fonfria et al. 2005; Övey and Nazıroğlu 2015). The treatment of antioxidants modulated AD-induced oxidative neurotoxicity via the inhibition of TRPM2 channel (Övey and Nazıroğlu 2015). In the oral presentation, we will review the recent data on the TRPM2 channel in the AD.

In summary, it seems that there is an essential role of TRPM2 channel in the etiology of AD, and the channel is a potential target for the treatment of AD.

Keywords: Alzheimer's disease: Beta amyloid plaque; TRPM2 channel: Neurodegeneration: Oxidative stress.

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Oral Presentations

Oral Presentation 8

In vivo antioxidative activities of ellagic acid in indomethacin-induced gastric injury related oxidative stress

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High-dose and/or long-term use of non-steroidal anti-inflammatory drugs is known to cause damage to the gastrointestinal tract and stimulate the production of reactive oxygen species (ROS) (McCarthy 1995, Vaish et al. 2013). The amount of ROS produced should be balanced with the antioxidant system in the cell. If the increase in the ROS level cannot be balanced, it may cause oxidative stress, which has an important role in the pathophysiology of diseases (Kükürt 2020, Kükürt et al. 2020, 2021). Ellagic acid is an effective natural herbal phenolic compound with free radical scavenging and antioxidant effects (Ippoushi et al. 2009). In this study, it was investigated that the effect of ellagic acid on total oxidant/antioxidant levels in gastric damage induced by indomethacin in mice.

Twenty-eight male *Swiss albino* mice were divided into four equal groups as follows: Control, Indomethacin (25 mg/kg), Ellagic acid (10 mg/kg) and Indomethacin+Ellagic acid. The levels of plasma total antioxidant and oxidant capacity were analyzed by using a spectrophotometric method. I observed that indomethacin increased the total oxidant capacity levels. In addition, it has been observed that ellagic acid has an antioxidant effect. It was observed that ellagic acid had a protective effect against oxidative stress in the indomethacin + ellagic acid group.

As a result, it was seen that ellagic acid had a protective effect against the oxidative stress caused by indomethacin. It was concluded that ellagic acid can be used as a therapeutic and protective agent in cases that cause oxidative stress due to its antioxidant properties.

Keywords: Ellagic acid; Indomethacin; Oxidative stress; Total Antioxidant/oxidant capacity

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Oral Presentations

Oral Presentation 9

In vitro models for experimental neurodegenerative diseases: focus on cell culture systems

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Neurodegenerative diseases are divided into four main groups as Alzheimer's disease, Amyotrophic Lateral Sclerosis, Huntington's disease, and Parkinson's disease, which are considered to be as neurological diseases. Among these diseases, only the prevalence of Alzheimer's disease and its related complications have more than doubled in the last years (2000-2015).

As an umbrella term, neurodegeneration, the most important difference that distinguishes neurodegenerative diseases from other neurological diseases. It is basically caused by the presence of a genetic defect in a chromosome or changings in protein architecture resulting the mutant protein aggregation. Therefore, other causes affecting the nervous system such as multiple sclerosis, hypoxia and metabolic factors are not included in the neurodegeneration framework. Irreversibly destructions of neurons by mutant proteins and mitochondrial dysfunction are two main pathways of neurodegeneration. Understanding of the neurodegeneration on cellular and molecular basis is of great importance in the development of new treatment strategies, since many neurodegenerative diseases do not have a cure. Although the therapeutic approaches developed to date can suppress the progression of the disease in individuals, they are insufficient to reduce the prevalence.

Cell culture systems are widely used in the modeling of systemic diseases in *in vitro* conditions because of their basic, sustainable, economical and optimized outputs. Moreover, *in vitro* model approaches are among the methods that are frequently used in the investigation of neurological diseases at cellular and molecular levels. An increasing number of researchers develop new *in vitro* models, mimicking neurodegenerative diseases and trying to better understand the processes of neural degeneration. In summary, I will discuss recent developments and methods about 2D and 3D cell culture models for neurodegenerative disease studies, methodological procedures and future perspectives from our previous work and literature.

Keywords: Neurodegenerative diseases; neuronal cell lines; *in vitro* models.

Oral Presentations

Oral Presentation 10

Epilepsy and TRPV1: A review of literature

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Epilepsy is a neurological disease of the central nervous system. The prevalence of epilepsy is about 2-3% in the population. The epilepsy is characterized by the seizures. The symptoms of epilepsy include several symptoms such as confusion, uncontrollable jerking movements of the arms and legs, and loss of consciousness or awareness. There are different types of epilepsy. In the etiology of epilepsy, several factors were proposed by the researchers. The excessive Ca^{2+} influx has a main role in the seizure of epilepsy. There are several drugs for the treatment of epilepsy, but they have limited action in the treatment of some types of epilepsy.

TRPV1 channel is a member of the TRP superfamily. TRPV1 is a Ca^{2+} permeable ion channel within the TRP superfamily. The TRPV1 are activated in neuronal cells by several stimuli such as hot chili pepper component (capsaicin), acidic pH ($\leq$ 5.5), and heat ($\geq$ 43 °C). The involvements of the calcium channels such as chemical and voltage gated were deeply indicated in the studies of cell culture, experimental animals, and human. However, the recent data indicated involvement of TRPV1 in the etiology of epilepsy. In addition, the administration of TRPV1 agonist (capsaicin) accelerated the seizures of epilepsy, although the pretreatments of TRPV1 antagonists (capsazepine and AMG9810) inhibited the formation of epileptic seizures in the rodents (Nazıroğlu 2015; Mohandass et al. 2020; Gladkikh et al. 2021). However, there are conflicting results on the subject, and the modulator role of TRPV1 in the formation of epileptic seizures in the pentylenetetrazol-induced kindling model in mice (Suemaru et al. 2018).

In conclusion, it seems that TRPV1 has an essential role in the etiology of epilepsy. The inhibition of TRPV1 may be a new strategy for the treatment of epilepsy.

Keywords: Epilepsy; TRPV1 channel; Hippocampus; Calcium signaling

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Oral Presentations

Oral Presentation 11

The potential anticancer action of Clostridium botulinum neurotoxin A: A review of literature

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The Clostridium botulinum neurotoxin A (BotxA) is a polypeptide, and it is produced by the Clostridium botulinum bacteria. Using the BotxA neurotoxins is increased by the the progress of research in the last decades. At the neuromuscular junction, a protease content of BotxA blocks the acetylcholine release from the vesicles of neurotransmitters. In addition, the treatment of BotxA is extensively being used as therapeutics against in several diseases such as hyperkinetic movement, pain, epilepsy, and glandular hyperactivity disorders (Mittal and Jabbari, 2020). In addition to the therapeutic actions of BotxA, its anticancer action in several cancer types such as breast cancer and glioblastoma (Nam et a. 2012; Akpınar et al. 2020; Mittal and Jabbari, 2020). It is well-known that the excessive generation of Ca^{2+} induces the generation of reactive oxygen species (ROS) and the induction of apoptosis and cancer cell death via the activation of caspase -3 and -9. The increase of apoptosis via the increase of Ca^{2+} influx induces anticancer action. The proposed mechanism of BotxA on the anticancer action in the several cancer types, including glioblastoma and neuroblastoma cells is the induction of apoptosis via the increase of the cytosolic Ca^{2+} influx (Nam et a. 2012; Akpınar et al. 2020). In the oral presentation, I will review proposed mechanisms on the anticancer action of BotxA in the several cancer types, including the glioblastoma and neuroblastoma cells.

In conclusion, it seems that BotxA has a potential anticancer action via the increase of apoptosis but the decrease of cancer cell proliferation in the cancer cells.

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Oral Presentations

Oral Presentation 12

Dexmedetomidine modulates the cerebral ischemia via inhibition of TRP channels: A review of literature

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Dexmedetomidine (DXM) is a major agent for long-term sedation in intensive care patients because it causes a quick response. DMX has also potent α2-adrenoceptor stimulator property. The protective action of DXM against cerebral and kidney ischemia/reperfusion injury was reported in the experimental animals (Cekic et al. 2014; Akpınar et al. 2016).

The several pathological and physiological processes in the body of human and animals induce the excessive generation of reactive oxygen species (ROS). The ROS are including several reactive free oxygen radicals such as superoxide and hydroxyl radical, and their generations are high in the ischemia/reperfusion injury. The brain is very sensitive to the excessive generation of ROS because of three reasons. (1) The polyunsaturated fatty acids are the main targets of ROS, and the polyunsaturated fatty acid content of brain is high. (2) The oxygen consumption rate in the brain is high. (3) The antioxidant defense system in the brain is low. Hence, the treatments of antioxidants induce the protective action against to the cerebral ischemia (Cekic et al. 2014; Akpınar et al. 2016). The antioxidant property of DXM was reported in rats (Cekic et al. 2014; Akpınar et al. 2016).

The increase of cytosolic free calcium ion (cCa^{2+}) concentration is caused by the generation of ROS (Long et al. 2019). The channels of chemical gated and voltage gated have main roles on the Ca^{2+} influxes in the cell membranes of neuron and brain. The superfamily of transient receptor potential (TRP) family with 28 members is also Ca^{2+} permeable channels in mammalian. Some TRP channels such as TRPM2 and TRPV1 are activated by ROS. The results of a recent study reported modulator role of DXM against cerebral ischemia-induced ROS via the inhibition of TRPM2 and TRPV1 activations in the hippocampus of rats (Akpınar et al. 2016). In the presentation, I will review the novel effects of DXM against to the cerebral ischemia by the modulation of TRP channels.

I concluded that cerebral ischemia-induced ROS and cCa^{2+} signaling were modulated by DXM via the inhibition of TRP channels. Hence, it seems that DXM is a potential agent for the treatment of cerebral ischemia.

Keywords: Brain; Dexmedetomidine; Ischemia/ reperfusion injury; Oxidative stress; TRP channles.

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