

THE 3RD JOINT SATELLITE MEETING OF TURKEY CHAPTER OF SOCIETY FOR NEUROSCIENCE (SfN) & NEUROSCIENCE SOCIETY OF TURKEY (NST=TÜBAS)

SfN Turkey Chapter Satellite Meeting aims to bring together Turkish neuroscientists residing in and outside Turkey willing to improve international collaboration and to create an environment for communication of scientific ideas, achievements and funding opportunities.

Program website:

<http://www.sfn.org/Annual-Meeting/Neuroscience-2015/Sessions-and-Events/Satellite-Events>

Location: Lurie - Searle Seminar Room, 1st Floor

Robert H. Lurie Medical Research Center of Northwestern University, 303 E Superior St, Chicago, IL 60611, USA

Date: Saturday, October 17th, 2015, 8.00-12.50 AM

Organizer:

Neuroscience Society of Turkey (NST=TÜBAS) - Society for Neuroscience (SfN) Turkey Chapter

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PROGRAM - THE 3RD JOINT SATELLITE MEETING OF TURKEY CHAPTER OF SOCIETY FOR NEUROSCIENCE (SfN) & NEUROSCIENCE SOCIETY OF TURKEY (NST=TÜBAS)

Time	Event
8:00 AM	Registration and social gathering
8:30 AM	Invited Speaker: Deniz Yilmazer-Hanke, "Fear-related genes in limbic brain regions of a novel D x H recombinant inbred strain with a DBA/2J background"
9:00 AM	Bige Vardar, "Effects of bicuculline and NMDA on the vibrotactile responses of cortical neurons in the rat SI cortex"
9:10 AM	Seda Bilaloglu, "Adaptation of grip forces to tactile surfaces is based on categorization of frictional surfaces rather than on coefficient of friction"
9:20 AM	Nihan Alp, "EEG frequency tagging reveals neural integration in the perception of coordinated motion"
9:30 AM	Merve Kasap, "Role of Na ⁺ Leak Current Channel in Involuntary Movement Disorders in <i>C. elegans</i> "
9:40 AM	Sercan Deniz, "Information transfer at the mammalian cone to Off-bipolar cell synapse: impact of the synaptic anatomy on the neurotransmission."
9:50 AM	Selin Neseliler, "Brain self-control networks and weight loss in humans"
10:00 AM	Mehtap Bacioglu, "Seeded induction of α -synucleinopathy in transgenic mice"
10:10 AM	Nurgül Salli, "Gene Expression Profile in Glioblastoma Multiforme"
10:20 AM	Aslıhan Selimbeyoğlu, "Optogenetic rescue of impaired social behavior phenotype in autism"
10:30 AM	<i>Coffee Break</i>
10:50 AM	Hande Ozdinler, "Cellular and molecular basis of selective neuronal vulnerability"
11:00 AM	Munira Salim, "The effects of monosodium l-glutamate on the behavior, addiction, and pain threshold in rats"
11:10 AM	Aylin Keskin, "Risk of aggravation of neuronal dysfunction by passive immunotherapy with anti-A β antibodies"
11:20 AM	Ulaş Çiftçioğlu, "Naturalistic visual stimuli modulate neural oscillations in the ventral lateral geniculate nucleus of the thalamus"
11:30 AM	İsmail Devecioğlu, "Vibrotactile sensitivity of freely behaving rats and operant conditioning by intracortical microstimulation"

11:40 AM	Gül Erdemli, "Automated Patch Clamp Technologies for Neuroscience Drug Discovery: Challenges and Future Directions"
11:50 AM	Oya Arı Uyar, "ELK-1 as a new mitotic target"
12:00 PM	Demet Arac-Ozkan, "Structural organization of the extracellular domains of adhesion GPCRs"
12:10 PM	Cagla Burçak Akagündüz, "In vitro analysis of axolotl spinal cord in terms of regeneration"
12:20 PM	Tuba Tuylu Kucukkilinc, "Low dose bisphenol A alters acetylcholinesterase and butyrylcholinesterase gene expression levels"
12:30 PM	Tuba Sural-Fehr, "Psychosine causes cellular toxicity by down-regulating the PI3K/Akt pathway in motoneurons"
12:40 PM	Closing remarks

**ABSTRACTS OF THE 3RD JOINT SATELLITE MEETING OF TURKEY
CHAPTER OF SOCIETY FOR NEUROSCIENCE (SfN) & NEUROSCIENCE
SOCIETY OF TURKEY (NST=TÜBAS)**

INVITED LECTURE

Deniz Yilmazer-Hanke, "Fear-related genes in limbic brain regions of a novel D x H recombinant inbred strain with a DBA/2J background"

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Fear is an evolutionarily conserved emotion induced by anticipated threats. In the present study, the goal was to identify fear-related gene expression in limbic brain regions of a novel fearful D x H recombinant inbred (RI) strain with a DBA/2J background, which has been generated in our laboratory. We have combined a quantitative trait loci (QTL) analysis with genome-wide gene expression analyses to identify expression QTLs (eQTLs). Microarray analyses showed that a proportionally high percentage of genes that are differentially expressed between fearful RI and control mice are encoded by chromosomes 13 and 14. Although the percentage of genes encoded by these two chromosomes make up only 3-4 % of genes in the mouse genome (protein coding and non-coding genes), the percentage of differentially expressed genes on chromosomes 13 and 14 corresponded to 12-13% of all differentially expressed genes. The present data support the hypothesis that genes encoded by chromosomes 13/14 are cis-acting eQTLs that may be responsible for the fear-related differences between fearful RI and control DBA/2J mice (funded through NIH-NIGMS 8P20GM103471-09 and State of Nebraska LB692 funds to DYH).

Bige Vardar, "Effects of bicuculline and NMDA on the vibrotactile responses of cortical neurons in the rat SI cortex"

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We previously found that bicuculline ($GABA_A$ receptor antagonist) and NMDA had contradictory, i.e. increasing and decreasing, effects on the average spike rates of neurons from the hindpaw representation in the rat SI cortex. We studied this in more detail by classifying neurons based on location (layers III, IV, V) and spike shape (regular-spiking (RS), fast-spiking (FS), and intrinsically bursting (IB)). We recorded single-unit spike activity during and after drug microinjection from 30 tactile neurons in 9 anesthetized Wistar albino rats. A combination electrode (5 injection barrels + 1 carbon-fiber electrode for recording) was used for applying aCSF (sham condition), 200 μ M bicuculline, and 10 μ M NMDA by a pneumatic microinjection pump (5 pulses of \sim 8 nL volume). After mapping the receptive field of each neuron, vibrotactile stimuli (bursts of 5-, 40-, and 250-Hz sinusoidal displacements; duration: 0.5 s; amplitude range: 33-158 μ m) were applied on the glabrous skin of the hindpaw. Intracortical drug injection preceded the tactile stimulus. Average firing rates were calculated for the baseline before the stimulus (R_b) and for the entire stimulus duration (0.5 s) (R_d). 3-way ANOVAs (factors: stimulus frequency, cortical layer, drug vs. sham) showed significant main effects of vibrotactile frequency on R_d (p 's = 0.001 and 0.046 for bicuculline and NMDA respectively). However, due to the large variation of responses, significant drug effects were not found in ANOVA. Therefore, we analyzed R_d based on paired comparisons between the drug and sham conditions at each frequency. Bicuculline significantly increased R_d at 5 and 250 Hz (paired t -test; p 's = 0.010), but not at 40 Hz. On the other hand, NMDA significantly increased R_d only at 40 Hz (paired t -test; p = 0.020). For both drugs, $R_d - R_b$ was mostly not affected, which shows that background firing rate somewhat also increased with drug application. For both drugs and at all frequencies, R_d was significantly increased in RS neurons ($n=14$). However, R_d of presumably inhibitory FS neurons ($n=11$) was not significantly affected by drug application. These results suggest that vibrotactile responses of the SI cortical neurons are influenced by complex excitatory and inhibitory interactions which are difficult to predict just by considering the established roles of the applied drugs.

Support: Boğaziçi University BAP project: 13XP8

Seda Bilaloglu, "Adaptation of grip forces to tactile surfaces is based on categorization of frictional surfaces rather than on coefficient of friction"

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Adaptation of fingertip forces to the friction at the grip surface is necessary to prevent use of inadequate or excessive grip forces. The purpose of this study was to understand the interaction between the frictional surfaces and the fingertip grip surface during grasping and lifting. The coefficients of friction (COF) of 18 different frictional surfaces were obtained by dragging the textured surface affixed to a standard mass across a standard surface on a tabletop. The COF ranged from 0.36 to 1.17 (mean=0.73). Ten subjects without neurologic deficits then grasped and lifted an instrumented grip device with the 18 different surfaces 7 times for each surface with bare hands and with a thin layer of tegaderm applied to the fingertip (to control for subject-level variability in fingertip moisture and skin texture). There were no significant differences in 2-point discrimination or pressure sensitivity threshold between barehands and tegaderm, but tegaderm impaired static tactile discrimination. The COF during interaction of the frictional surface with the fingertips was measured as the slip ratio (grip force/ load force at the moment of slip). As expected, there was greater between-subject variability in the slip ration with bare hands (ICC=0.67) than with tegaderm (ICC=0.63). However, instead of a monotonic change in the slip ratios with the COF of the textured surfaces (measured against a standard surface), the slip ratios clustered into smooth and rough categories both with bare hands and tegaderm. We therefore collapsed all the smooth and rough surfaces (9 each) and further examined the adaptation of fingertip grip force rates (PGFR) to the frictional surface. We found that the average PGFR was significantly higher for the smooth surfaces compared with the rough surfaces ($b=-5.75$, $p<0.001$) with bare hands but not with tegaderm ($b=-1.26$, $p=0.1932$). The PGFR did not vary with the COF. These results suggest that the tactile surfaces are categorized broadly as smooth and rough, and the adaptation of fingertip forces is based on this broad categorization rather than on the coefficient of friction of the tactile-surfaces per se. Using tegaderm to remove subject-level variability in fingertip moisture and skin texture effectively impairs tactile discrimination and adaptation of grip forces. The receptors on the skin surface necessary for tactile discrimination are also necessary for grip force adaption.

Nihan Alp, "EEG frequency tagging reveals neural integration in the perception of coordinated motion"

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Gestalt psychologist pointed out non-linear interactions between parts by stating that "The whole is different than the sum of its parts", but current methods have not been able to pinpoint how non-linear interactions occur at the neural level. To be able to investigate the neural interactions, it is important to use an approach that allows distinguishing the neural activities representing the organized whole from those corresponding to individual elements. The frequency tagging technique takes advantage of the fact that presenting a periodic visual stimulus to the human brain yields periodic responses directly related to the frequency of stimulation. Moreover, it disentangles objectively the contribution of different frequency components to the brain's overall responses by producing non-linear intermodulation components (IMs: $f_1 \pm f_2$). Therefore, application of this technique in vision science opens up a new and objective way to investigate interactions at the neural level.

Here we used the point-light display (PLD), which is one of the most frequently used stimuli to investigate the interaction between form and motion. In a PLD, the motion of the individual dots, their specific configuration, and the spatiotemporal dynamics of their trajectories together give rise to the perception of a human figure carrying out a particular action. We combine multiple PLDs presented simultaneously to investigate the mechanisms that are involved in processing coordinated movements and to identify the neural activity that is specific for the perception of globally coordinated movements. For this purpose, the frequency-tagging technique was applied in combination with EEG recording. In the experimental condition, the motions of the PLDs were coordinated as in a group of dancers. In three control conditions, the coordinated motions, the perception of biologically plausible motion, or both were diminished, respectively. Frequency tagging was implemented by modulating the luminance intensity of the point lights with different frequencies for the different dancers (PLD1= f_1 and PLD2= f_2). Fast Fourier Transform was applied to investigate the effect of coordinated motion. Hence, comparing IM effects between the experimental condition (coordinated motion) and the control conditions allows us to analyze the interaction and integration of the biological motions among the dancers, hence enabling us to identify neural activities and cortical areas that are involved in the perceptual integration of coordinated biological motion.

Merve Kasap, "Role of Na⁺ Leak Current Channel in Involuntary Movement Disorders in *C. elegans*"

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The human sodium leak current channel (NALCN) is implicated in many genetic forms of the movement disorders such as dystonia and dyskinesia. Mutations in NALCN cause similar abnormalities in mice, *Drosophila* and *C. elegans*. Reduced NALCN expression in *Drosophila* altered locomotive behavior and circadian rhythms although the flies were viable and fertile. Also, they displayed a narrow abdomen phenotype with 'hesitant walking' and had altered sensitivities to general anesthetics such as halothane. Loss-of-function mutation in *C. elegans* NALCN caused animals to move extremely slowly and when touched on the tail they showed a fainting or freezing response similar to frozen gait in Parkinson's disease patients. Gain-of-function mutation in NALCN caused an extremely active phenotype; worms showed excess coiling, turns and reversals similar to dystonia and dyskinesia. We think that mutations in NALCN disrupt the depolarization-repolarization balance by changing the relative concentrations of sodium, calcium and potassium inside the cell. Previously, we showed that it is possible to correct movement of NALCN loss-of-function animals with nicotine and K⁺ channel blockers. Therefore, we hypothesized that we should be able to correct movement in gain-of-function (*gf*) mutant animals [*unc-77 (e625)* allele] with a similar strategy. In order to evaluate the movements of the worms, we observed spontaneous movement, startle response and foraging (food seeking) behavior. Our studies with potassium channel activators on *gf* animals remain inconclusive except 2-aminoethoxydiphenyl borate (2-APB). 2-APB is a pharmacological agent with various actions such as such as inhibiting inositol trisphosphate receptors, transient receptor potential channels, and gap junctions; and modifying store-operated calcium channels function. Beside 2-APB, we discovered several pharmacological agents such as nimodipine, flunarizine and ethoxzolamide that improve or correct the movement of *gf* animals in the foraging assay. These drugs potentially share a common mechanism of action by regulating calcium flux. We hope to discover specific pharmacological agents that target the NALCN. Drugs that can correct behavioral deficits caused by NALCN mutations may be useful for the treatment of human movement disorders.

Sercan Deniz, "Information transfer at the mammalian cone to Off-bipolar cell synapse: impact of the synaptic anatomy on the neurotransmission."

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Thanks to its localization and organization, the retina is an excellent model for the study of neurotransmission. It features many characteristic mechanisms found in other brain regions, within a highly organized and well-defined neuronal network.

An important feature of retinal neurotransmission is the parallel processing of visual information. During a step of light, cone photoreceptors have temporally similar responses, whereas the responses of the 15 to 20 types of retinal ganglion cells are temporally diverse. Parallel processing starts at the first synapse of the retinal network, when an individual cone photoreceptor signals to more than 12 distinct bipolar cells. These bipolar cell types are distinguished by the glutamate receptors they express at their dendritic terminals, and by making characteristic numbers of contacts with a cone at either basal or invaginating synaptic contacts. Our goal is to understand in which extent these anatomical differences between bipolar cell types impact on the statistical properties of signaling. We recorded in voltage clamp from a presynaptic cone and a postsynaptic cone bipolar cell and measured the reproducibility of the synaptic response. Paired recordings were obtained from slices of the cone dominant ground squirrel retina. The input voltage clamp command to the cone was a 16 s white noise stimulus consistent of four 4 s repeats. The stimulus contained frequencies at equal power between 0-100 Hz with a mean of -42 to -51 mV and a standard deviation of 2.5 mV. We used the frequency-dependent bipolar cell response mean and variance to calculate the Signal to Noise Ratio (SNR) and information rate for each synapse. Cone to bipolar cell pairs intracellularly labeled during recording were processed for immunohistochemistry and contact counting. We found that information rate differed between the OFF-bipolar cell types. Overall, the bipolar cells that make the largest number of contacts with a cone have the highest information rates. This is in line with the general idea that more contacts enable the bipolar cell to sample release from more ribbons, which in turn provides a better estimate of the cone signal. Surprisingly, although making the fewest contacts overall, the cb1a cell had almost a 3-fold higher information rate on a per contact basis. The reasons for this increase are unknown.

The results show that the cone signal undergoes a different resampling at the cone synapse in the different types of Off cone bipolar cells, and suggest a specialized function for cb1a cell contacts that remains to be determined.

Selin Neseliler, "Brain self-control networks and weight loss in humans"

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While for most adults, dieting does not result in sustainable weightloss, successful weight losers can be predicted by the initial weight loss at 1 month. We used fMRI to investigate how the neural response to food cues changes as weightloss progresses over three months. 24 adults enrolled in a three month weight loss program based on calorie restriction (mean BMI: 30.1 ± 3.2 , range: 25-37). The average BMI of the participants decreased over the 3 month period from 30.1 to 28.6 ($F(1.2, 21.4) = 32.7$, $p < 0.001$). Subjects underwent fMRI prior to dieting, at 1 month, and at 3 months, while viewing and rating food and scenery images. fMRI response for food cues was contrasted to scenery cues. Compared to the baseline, at 1 month, participants showed reduced activation in the ventromedial prefrontal cortex, a brain region that has been implicated in encoding stimulus value. In addition, there was a correlation between weight lost and increased activation in a frontoparietal network that has been implicated in cognitive control. Despite continuous weight loss, at three months the activity of the brain regions associated both with the reward value and with cognitive control returned to baseline. Behavioral results followed a similar pattern: at 1 month participants rated food cues, but not scenery cues, as less wanted. At 3 months, the rating for food cues returned to baseline ($F(2,42) = 6.9$, $p = 0.002$). The initial weightloss is associated with greater activity in regions implicated in cognitive control and reduced activity in regions associated with stimulus value. This response returns to baseline at 3 months despite continuous weightloss. This change may contribute to reduced control over food intake and to subsequent weight regain in longterm.

Mehtap Bacioglu, "Seeded induction of α -synucleinopathy in transgenic mice"

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Aggregation of misfolded proteins is a common feature of many neurodegenerative diseases (Jucker & Walker, Nature, 2013). Parkinson's disease (PD) is characterized by intracellular deposits of aggregated α -synuclein in the form of Lewy bodies and Lewy neurites, which appear in a stereotypical manner in the brains of PD patients (Goedert et al, Nature Reviews Neurology, 2013). The mechanism underlying the formation and spreading of α -synuclein pathology is still puzzling. Inoculation studies, where α -synuclein lesions are induced in susceptible hosts, suggest that α -synuclein behaves in a prion-like manner by templating misfolding of soluble α -synuclein into insoluble aggregates (Luk et al, PNAS, 2009).

Here we report that α -synuclein aggregation can be induced in different α -synuclein transgenic mouse models following intracerebral injections of dilute mouse brain extracts containing aggregated α -synuclein. The brain extract-induced α -synuclein lesions show similar properties as the α -synuclein lesion in PD patients such as α -synuclein phosphorylation and abundant β -sheet structure. In addition, the induced α -synuclein aggregates are accompanied by microglia activation and astrogliosis. In contrast, the injection of control mouse brain extracts, i.e. without aggregated α -synuclein does not induce any α -synuclein pathology. Moreover, we provide *in vivo* evidence that the injected α -synuclein material is taken up by cells shortly after the injection.

In conclusion, our data contributes to the growing evidence of a prion-like mechanism of α -synuclein aggregation. The experimental model system described here will be instrumental to study the commonalities and differences between PD, other synucleinopathies, and prion diseases.

Nurgül Salli, "Gene Expression Profile in Glioblastoma Multiforme"

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The most aggressive type of brain tumor is glioblastoma multiforme (GBM). Currently, temozolomide (TMZ), combined with radiation, is the most effective therapy for GBM, but chemoresistance, that occurs in tumors, limits the efficacy of this treatment. To understand the molecular and cellular processes that underlie temozolomide resistance in GBM tumors we investigated alterations in protein expression, gene expression in primary GBM tumors from patients with different survival phenotypes (primary tumors for which there was not tumor recurrence after TMZ treatment) and patient primary tumors for which there was tumor recurrence. After proteomics analysis 92 spots out of over 2200 protein spots were found to be differentially-expressed. Of these, 16 up-regulated proteins and 15 down-regulated spots were chosen for identification by mass spectrometry. Individual specimens subjected to gene expression analysis Gene expression of Vimentin (VIMA) (P=0.01)(1.8 fold decreased in proteomics), LIM and SH3 domain protein (LASP1) (P=0.01) (1.9 fold decreased in proteomics), AnnexinA2 (ANXA2) (p=0.01) (3.2 fold decreased in proteomics) and AnnexinA5 (ANXA5)(P=0.01) (4.4 fold increased in proteomics), Coactosin-like protein (COTL1) (0.05) (3.5 fold increased in proteomics) , S100 calcium binding protein A9 (S10A9)(P=0.04) (3.7 fold increased in recurrent patients' primary tumor in proteomic) were found significantly different.

Multidrug resistance gene (MDR1) (P=0.02), UDP-glucose ceramide glucosyltransferase (UGCG) (p=0.02), C-X-C chemokine receptor type 4 (CXCR4)(P=0.04) gene expression elevated in the recurrent tumor specimens in the targeted genes. These results suggest that VIMA, LASP1, AnnexinA2, AnnexinA5, COTL1, S10A9, MDR1, UGCG and CXCR4 were significantly plays role on recurrence of GBM tumors.

Aslihan Selimbeyoğlu, "Optogenetic rescue of impaired social behavior phenotype in autism"

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Altered cellular excitatory/inhibitory (E/I) balance is emerging as a common pathophysiological characteristic that could link diverse autism-associated genetic variations in mouse models. To understand possible disease relevance, it may be of great interest to identify specific cells and circuits within which such E/I imbalance changes could cause autism-related phenotypes in real time. Increased excitability in medial prefrontal cortex (mPFC) pyramidal (PYR) neurons was previously found to reduce social interaction in mice, which can be partially recovered by simultaneous compensatory excitation of inhibitory parvalbumin (PV) neurons. Here, we investigate the role of real-time changes in E/I balance in a clinically-inspired CNTNAP2 KO mouse line with decreased cortical PV neurons and impaired social behavior. We crossed CNTNAP2 mice with PV::Cre mice, and expressed bistable SSFO channelrhodopsin in PV cells. Without stimulation, CNTNAP2 KO mice spent less time engaging socially than WT (n=7 WT, n=11 KO, p<0.05). Increasing PV cell excitability reversed the impaired social behavior (n=11 KO no-stim, n=6 KO stim, p<0.05) in KOs while not affecting WT littermates (n=9 WT no-stim, n=7 WT stim, p>0.05). We did not find any differences in novel object interaction between WT and KOs, and the SSFO stimulation did not affect object interaction (n=4 WT, n=6 KO, p>0.05, for both stim and no-stim). The phenotype could be largely traced to decreased mean interaction time in the initial KO social bouts (n=6 KO, n=5 WT, p<0.01); additionally, WT social bout length decayed exponentially during the course of the test, while KO's did not (n=5 WT R²=0.88, n=6 KO R²=0.10). We further dissected real-time activity in mPFC by using fiber photometry to simultaneously record from PV and PYR neurons expressing *ef1a-DIO-GCaMP6f* and *CKIIa-RCaMP2*, respectively. Both types of neurons responded to novel social and object stimuli in a time-locked manner, with similar peak fluorescence changes (peak dF/F for social vs object; n=5 WT p>0.05, n=6 KO p>0.05). On the other hand, within-bout fluorescence changes were different for WT and KO mice during the initial bouts. Peak fluorescence signals were significantly different at the end of the bout compared to the beginning for WT social but not object interactions; in contrast these signals were similar for KOs (first vs last 0.25 s; n=5 WT p<0.01 for social, p>0.01 for object; n=6 KO p>0.01 for both social and object), suggesting that the KOs process social stimulus similarly to objects. Together these results illustrate the role of real-time balance between mPFC PV and PYR cells in modulating social behavior relevant to autism pathophysiology.

P. Hande Ozdinler, "Cellular and molecular basis of selective neuronal vulnerability"

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In neurodegenerative diseases, a select set of neuron population display early vulnerability and undergo selective neurodegeneration. Understanding the cellular and molecular basis of this selective vulnerability is an important quest. We focus our attention to motor neuron diseases and try to understand why motor neurons in the cerebral cortex progressively degenerate while other neuron populations remain relatively intact. Here, I will discuss the recent findings and the current understanding of selective vulnerability in diseases.

Aylin Keskin, "Risk of aggravation of neuronal dysfunction by passive immunotherapy with anti-A β antibodies"

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Amyloid- β (A β) has an essential role in the pathogenesis of Alzheimer's disease (AD). Large phase III clinical trials of passive immunotherapy aiming at the removal of A β from the brain have ended with no clinical benefit, however the reasons for this failure are largely unknown. Here, we employed in vivo two-photon calcium imaging with single cell-resolution to analyze the function of layer 2/3 cortical neurons in two different transgenic mouse models of AD, the PDAPP and the Tg2576 models. In both mouse models, we found a massive increase in the fractions of abnormally hyperactive neurons (19.5 % in PDAPP and 31.1 % in Tg2576 mice as compared to 2.9 % in wild-type mice). This increase in the fractions of hyperactive neurons was in line with previous results obtained in the APP23xPS45 mouse model (Busche et al., *Science*, 2008; Busche et al., *PNAS*, 2012). Next, we monitored the activity status of the cortical neurons in PDAPP and Tg2576 mice that were passively immunized with monoclonal antibodies against A β (PDAPP mice were immunized with 3d6 and Tg2576 mice were immunized with β 1 mouse monoclonal antibody). We found in both AD models that the fractions of hyperactive neurons increased substantially (17.9 % in controls vs. 52.4 % in 3d6-treated PDAPP mice and 31.1 % in controls vs. 59.5 % in β 1-treated Tg2576 mice). Furthermore, in a fraction of treated animals we found an abnormal synchronicity of hyperactive neurons. In summary, our results demonstrate negative functional consequences of passive immunotherapy with anti-A β directed monoclonal antibodies, which may be a cellular mechanism for the lack of positive cognitive effects of such antibodies in recent clinical trials. Moreover, the results emphasize the need to incorporate functional in vivo assays in the development and evaluation of therapies for AD.

Ulaş Çiftçioğlu, "Naturalistic visual stimuli modulate neural oscillations in the ventral lateral geniculate nucleus of the thalamus"

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There are two main routes from the eye to the brain in mammals. The pathway from the retina to the superior colliculus (SC) is directly involved with sensorimotor tasks and the pathway from the retina to the lateral geniculate nucleus of the thalamus (LGN) is associated with form vision. However the LGN is not a homogeneous structure and comprises a dorsal and a ventral subnucleus, the dLGN and the vLGN respectively. While the dLGN projects directly to the neocortex, the evolutionarily older vLGN connects with subcortical structures that coordinate movement, the SC, for example.

The dLGN, which has been studied in depth, is much larger than its ventral counterpart, whose small size creates a challenge for electrophysiological studies in vivo. In mice, however, the two subnuclei are roughly the same size and are thus equally accessible. We have taken advantage of this species difference to explore the structure and function of the vLGN in the whole animal, using techniques of whole-cell recording with dye-filled electrodes in vivo in addition to computational analyses.

Recently, we compared the two divisions of the murine LGN and found that neurons in the vLGN had receptive fields several times larger than those of relay cells in the dLGN, along with broader dendritic arbors. These findings were in keeping with the idea that the vLGN does not play a dominant role in form vision. Our next step was to compare neural coding in the vLGN with that in sensorimotor structures it connects to, using the literature about the SC as a starting point. In particular, experiments in both awake (Brecht et al., 2004) and anesthetized animals (Stitt et al., 2013; Sridharan et al., 2011) show that neurons in the SC encode visual stimuli in two ways, as a conventional rate code and also by means of gamma oscillations. We began our analysis using full field stimuli of different luminance values. Approximately a third of the cells in the vLGN responded both with an increase in firing rate and the initiation of gamma oscillations. The strength and frequency of the oscillations remained fairly constant once the threshold luminance value was reached. To determine if these oscillations might play a role in natural vision, we recorded responses to movies and found that gamma oscillations occurred during some image sequences. The strength of the oscillations decreased with increasing stimulus contrast. These oscillations might help coordinate activity between the vLGN and subcortical visual motor networks in the execution of motor tasks.

İsmail Devecioğlu, "Vibrotactile sensitivity of freely behaving rats and operant conditioning by intracortical microstimulation"

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The vibrissal system has been widely studied in awake behaving rats. However, humans do not have vibrissae. The mechanoreceptors in the glabrous skin of the fore- and hind-paws of rats are similar to those in humans. We measured the psychophysical sensitivity of 5 Wistar albino rats which were trained to detect the absence or the presence of tactile vibrations (duration: 0.5 s) applied to the volar surface of their hind-paws in a novel operant chamber designed for this purpose (Devecioğlu and Güçlü, *J Neurosci Methods*, 242: 41-51, 2015). Rats reported whether they felt the vibration or not by pressing the right or the left lever, respectively. Accuracies and conditional probabilities (hit rate, $p(h)$, and false-alarm rate, $p(f)$) were recorded. By using method of constant stimuli, we tested 3 frequencies (40 Hz, 60 Hz and 80 Hz) and 6 intensity levels (3-200 μm). Each condition was repeated 4 times. Psychometric curves were fitted to corrected hit rates. On the psychometric curves, 50% probability was measured as the threshold of detection. The subject averages at each frequency were as the following: 40 Hz, 25.55 dB \pm 2.52; 60 Hz, 21.37 dB \pm 1.94; 80 Hz, 18.73 dB \pm 1.86 (dB ref 1 μm). This decreasing trend is consistent with data from humans. 3 out of 5 rats were implanted with microwire arrays in the hind-paw representation of the somatosensory cortex. The rats were trained to detect the absence or the presence of biphasic (cathodic phase first), charge-balanced current pulses (phase duration: 600 μs , inter-phase interval: 53 μs) injected into the cortex. We tested electrical stimulation (6 current amplitudes: 2.5-40 μA) at the same frequencies used in tactile experiments. The average electrical detection thresholds decreased as the frequency increased as in the tactile experiments: 40 Hz, 22.90 dB \pm 1.92; 60 Hz, 18.98 \pm 1.3; 80 Hz, 18.15 \pm 0.7 (dB ref 1 μA). These results indicate that intracortical microstimulation generates neural activity which results in similar psychophysical performance as in the tactile experiments. We are working to utilize this principle in somatosensory neuroprostheses.

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Gül Erdemli, "Automated Patch Clamp Technologies for Neuroscience Drug Discovery: Challenges and Future Directions"

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Ion channels are integral membrane proteins allowing the movement of ions across cell membranes. They play key roles in many diverse cellular functions and represent a target class with significant potential for drug discovery for a wide range of human diseases. Although within the last decade significant progress has been made, ion channels remain significantly under-exploited as therapeutic targets. Despite the large investment in ion channel screening, the promise of improved second generation ion channel drugs is yet to be fulfilled. This is at least partly due to limitations in high throughput assay technologies that support screening and lead optimization. With significant advancements in automated patch clamp systems and alternative screening technologies, however, some of these limitations can be addressed to allow ion channel drug discovery to reach its potential. In this presentation, the automated patch clamp technologies commonly utilized for ion channel drug discovery will be reviewed and their implementation to drug discovery will be discussed with examples.

Oya Arı Uyar, "ELK-1 as a new mitotic target"

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The ternary complex factor Elk-1 is a transcription factor and a proto-oncogene that involved in numerous biological processes such as survival, differentiation, proliferation, angiogenesis and apoptosis. Since Elk-1 is stimulated by external growth signals and has a role in activation of immediate early gene transcription, it has been related to cancer formation. Elk-1 is known to be phosphorylated by PKC, MAPK and PI3K pathways in various brain tumors. Increased Threonine 417 phosphorylation of Elk-1 has been observed in brain tissues from patients with neurodegenerative diseases. The interaction between Elk-1 and neuronal microtubules and microtubule based motor proteins, dynein and kinesins has also been elucidated in brain tumour model cells such as glioma, glioblastoma and neuroblastoma. Confocal microscopy analyses revealed that serine 383 phosphorylated Elk-1 is found at the nucleus during interphase and through prophase to metaphase predominantly localizes to the spindle poles. In anaphase, Elk-1 accumulates both at the spindle poles and midzone and Elk-1 relocates to the spindle midbody when cells proceed to the cytokinesis. The interaction of Elk-1 with dynein and kinesin motors indicates that this mobility of Elk-1 during mitosis is realized through motor proteins. In addition to microtubule motor proteins, Elk-1 also interacts with the cell cycle kinase Aurora-A and when Aurora inhibitors are used, P-S383-Elk-1 fails to localize to the poles and remains associated with DNA. The mitotic spindle localization of a transcription factor and its interaction with motor proteins and mitotic kinase Aurora-A is particularly interesting. Our *in silico* analysis has revealed several putative sites for phosphorylation by mitotic kinases such as Cdks, Plks and Aurora kinases. Mitotic kinases have pivotal roles during regulation of cell cycle progression, centrosome maturation and microtubule dynamics and any abnormalities in these processes resulted in the formation and progression of tumors. Investigation of the interaction between Elk-1 and such mitotic kinases is supposed to help to understand the possible mitotic role of Elk-1 and its effects in brain tumor cells.

Demet Arac-Ozkan, "Structural organization of the extracellular domains of adhesion GPCRs"

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Adhesion GPCRs are key signaling molecules and are involved in essential neuronal functions. They have large extracellular regions decorated by numerous adhesion domains and a conserved GPCR Autoproteolysis Inducing (GAIN) domain that mediates self-cleavage of the receptor. Discovery of the novel GAIN domain and determination of its high-resolution crystal structures revealed the mechanism of self-cleavage and provided the great hints as to why these receptors are regulated by tethered agonists hindered within the GAIN domain. The talk will focus on our recent unpublished data on further structural/functional understanding of the extracellular domains of select adhesion GPCRs that are essential for different functions in the brain such as cortex development and synapse maturation. Our studies revealed unpredicted domains in the extracellular regions, identified the conserved surfaces of these domains, and shed light on the atomic details of how these domains interact with their extracellular ligands to regulate receptor function. In addition, we engineered and determined the structures of synthetic proteins that specifically and tightly bind to the extracellular domains of adhesion GPCRs to be used as potential lead compounds for future drug discovery. These structural studies serve as a starting point to understand and dissect the distinct roles of these domains in the functions of adhesion GPCRs.

Cagla Burçak Akagündüz, "In vitro analysis of axolotl spinal cord in terms of regeneration"

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Ambystoma mexicanum (Axolotl), an aquatic salamander originating from Mexico. With their unique capacity in comparison to other amphibians, axolotls are known to reach adulthood without metamorphosis keeping their high regenerative capacity throughout their lifetime. This unique feature makes them a demanding model organism for regenerative and restorative neuroscience.

Studies demonstrate that axon regrowth and cellular differentiation occur and continue throughout lifetime of an axolotl even though axolotl is taxonomically closest relative of human among other amphibians. Due to this reason, the cellular mechanism behind the regenerative capacity of axolotl nervous system can shed light to mammals'.

Medipol / REMER houses a large axolotl husbandry and breeding facility. Many groups do extensive research on systems biology and neuroscience of this unique animal. Our research group is specifically focused on spinal cord injury in axolotl. We are currently working on a paralysis inducing injury model and cell culture. We mainly use immunocytochemistry to explore cell diversity, morphology and function of 3 significantly different groups; uninjured control spinal cord cells, spinal cord cells plated on 7th day post-injury (DPI7) and spinal cord cells plated on 14th day post-injury (DPI14).

Tuba Tuylu Kucukkilinc, "Low dose bisphenol A alters acetylcholinesterase and butyrylcholinesterase gene expression levels"

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BPA is an endocrine disruptor chemical commonly used in industry that is reported to be toxic on reproductive, immune and nervous systems. Acetylcholinesterase (AChE) is a widely distributed enzyme whose main role is termination of nerve transmission by hydrolyzing acetylcholine. It is documented that stress, increased apoptosis, neurological diseases like Alzheimer's and epilepsy, disruption in blood brain barrier integrity may change the mRNA expressions and protein concentration of AChE. Non cholinergic functions of AChE including cell growth and differentiation, tumorigenesis, hematopoiesis are also well documented. Over the last decade, its potential role in apoptosis and necroptosis was reported. On the other hand acetylcholine, the substrate of AChE, inhibits proinflammatory cytokine production via TNF alpha which is known as "cholinergic anti inflammatory pathway" in literature. AChE is thought to be the connection of BPA toxicity between nervous and immune systems.

Preliminary data generated by our group shows that BPA inhibits AChE in vitro and changes AChE gene expression in SHSY5Y at 48 hours (1). Considering our preliminary data BPA is expected to effect anti inflammatory pathway due to altered AChE level. For this purpose SHSY5Y cells were treated with BPA at 1pM and 1nM doses for 0-12 hours and TNF- α level, caspase 8 and AChE activities were investigated.

The results demonstrate that low dose treatment of BPA remarkably reduce caspase 8 levels at 2 hours and suppresses TNF α levels at 4 hours. Together our data enlightens effects of BPA on cholinergic anti inflammatory pathway via TNF α link .

Tuba Sural-Fehr, "Psychosine causes cellular toxicity by down-regulating the PI3K/Akt pathway in motoneurons"

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Deficiency of the lysosomal galactosyl-ceramidase (*GALC*) enzyme results in the accumulation of the toxic lipid psychosine, and is the underlying cause for the hereditary Krabbe's disease. Psychosine causes fast axonal transport defects through abnormal activation of *GSK3b* and results in a dying-back pathology in neurons. However, the exact mechanism leading to this activation and the associated cellular toxicity is unknown. We previously showed that psychosine preferentially accumulates in lipid rafts within cell membranes disrupting their structure. Lipid rafts are essential platforms for cellular signaling pathways, therefore we hypothesized that psychosine accumulation would lead to a deregulation of intracellular signaling pathways affecting key mediators of integrity in neuronal axons. Using the neuronal-like NSC34 cell culture system, we have systematically analyzed the downstream effects of psychosine, particularly on cellular signaling. We have found that exogenous psychosine administration causes a significant downregulation of the PI3K/Akt and MAPK pathways downstream of the IGF receptor. Inhibition of phospho-Akt takes place mainly at the plasma membrane and can be fully recovered through either stimulation of the IGF receptor by IGF-1, or using a small molecule activator (*SC-79*) of Akt, implying that the shortterm effects of psychosine toxicity may be reversible.

We conclude that the mechanism of psychosine toxicity in motoneurons goes through modulation of the cell's ability to sense growth factor availability in its environment and appropriately adjust its intracellular response. This effect possibly goes through perturbing the structure within membrane lipid rafts, thereby altering associated survival signals that depend on them, such as Akt activation coupled to IGF receptor signaling. Therefore, the use of Akt activators such as IGF-1 or *SC-79* may represent potential therapies to alleviate the aspects of this disease regulated by this pathway.

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