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# 1st INTERNATIONAL NEURONAL ENERGY DYNAMICS CONGRESS

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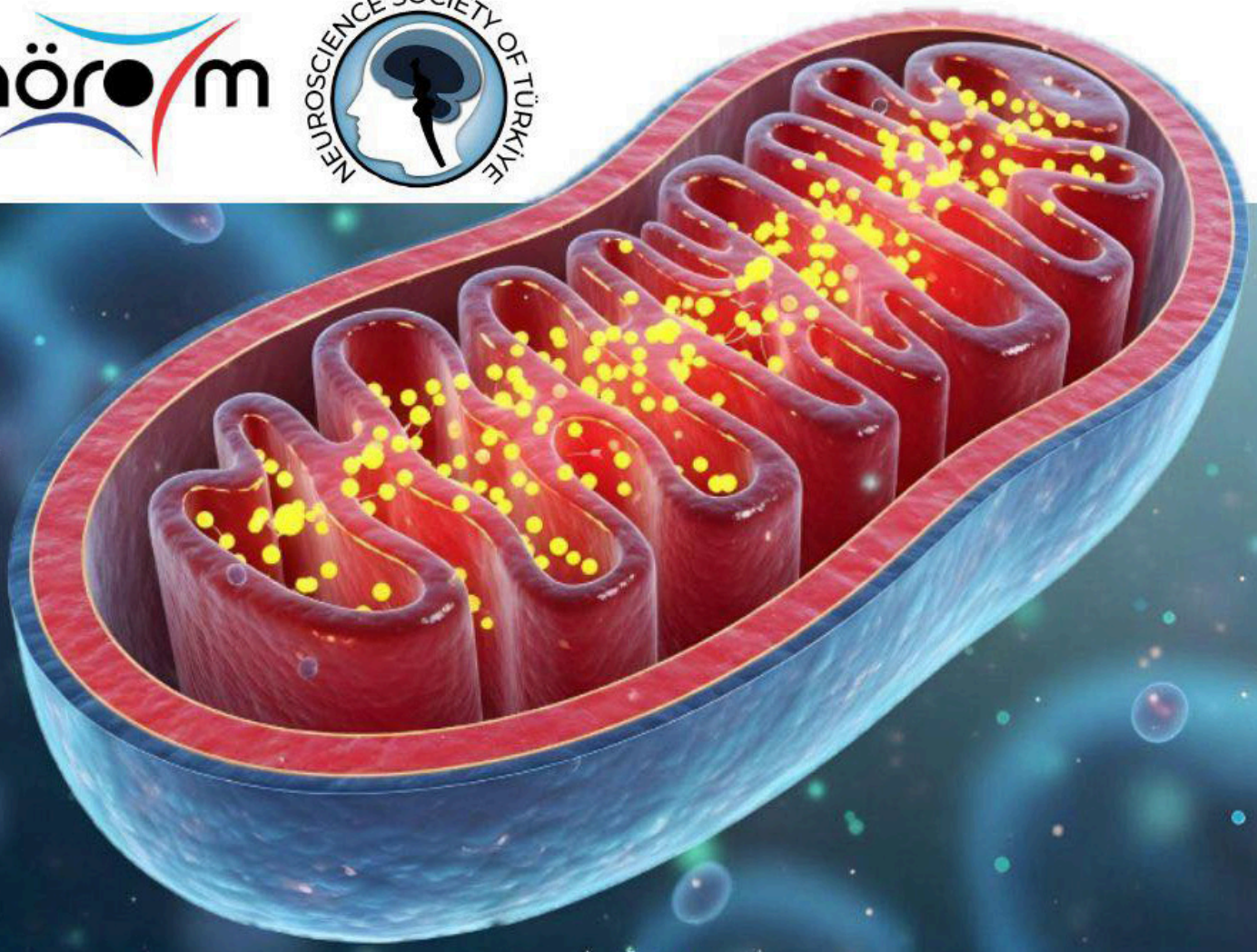

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## CONTENTS

SPEECH TEXTS

## Immunohistochemical and Ultrastructural Evaluation of Median Eminence Tanycytes in High-Fat Diet and High-Fructose Water-Induced Metabolic Syndrome Models

Ahmet Cabir[1,2], Feyzullah Beyaz[2]

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**Objective:** This study aimed to investigate immunohistochemical and ultrastructural alterations in median eminence tanycytes in metabolic syndrome models induced by a high-fat diet (HFD) and high-fructose water (HFW).

**Methods:** Thirty Wistar Albino rats were divided into control, HFD, and HFW groups. After eight weeks, median eminence sections were immunostained for GFAP, leptin receptor (LepR), insulin receptor (IR), and BDNF. Blood samples collected prior to sacrifice were analyzed for lipid profile (triglycerides, cholesterol, HDL). Image analyses were performed using Fiji (ImageJ), and statistical evaluation was conducted with GraphPad Prism 10.6. Ultrastructural tanycytes morphology was examined using scanning electron microscopy.

**Results:** GFAP immunoreactivity increased progressively across groups (C < HFD < HFW, $p < 0.05$). IR expression was highest in HFD, while LepR expression was significantly elevated in HFD but moderate in HFW (HFD > HFW > C, $p < 0.05$). BDNF expression decreased in both models, reaching its lowest level in HFW (C > HFD > HFW, $p < 0.05$).

**Conclusion:** Both HFD and HFW water induced glial activation, receptor alterations, and immunstaining alterations in median eminence tanycytes. These findings were consistent with serum lipid levels, indicating a systemic–central correlation. Fructose exerted stronger effects, suggesting greater metabolic stress and reduced neurotrophic support.

The observed microstructural damage and receptor alterations indicate impaired tanycyte-toneuron metabolic communication, potentially affecting neuronal energy balance.

**Keywords:** Median eminence, tanycyte, high-fructose water, high-fat diet, leptin receptor

## A Modular Dual-Refuge System for Real-Time Investigation of Multisensory Integration in Weakly Electric Fish

Alp Demirel, İsmail Uyanık

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**Objective:** Animals continuously integrate sensory information from multiple modalities to generate coherent behavioral responses. Weakly electric fish provide a valuable model to study multisensory integration. The objective of this study is to design a customizable, modular, and real-time experimental system that enables independent manipulation of visual and electrosensory stimuli to examine how sensory salience influences multisensory integration.

**Methods:** We developed a nested refuge structure composed of an inner transparent refuge, which provides electrosensory cues but no visual information, and an outer opaque refuge, which offers visual cues while blocking electrosensory signals. Each refuge is driven by a separate linear actuator, allowing precise and independent motion control. The system's modular design enables flexible adjustment of sensory configurations, and real-time control software allows dynamic stimulus generation and closed-loop experimentation. Trials were conducted with *eigenmannia virescens* (n = 5) performing refuge-tracking behavior.

**Results:** Preliminary findings indicate that sensory salience dynamically modulates the relative weighting between electrosensory and visual modalities. Under reduced visual contrast, fish rely more heavily on electrosensory feedback, exhibiting adaptive sensory reweighting. The observed behavior reflects a weighted combination of modalities, where contributions scale with cue salience, but the combined effect is sub-additive.

**Conclusion:** The proposed dual-refuge system provides a modular, real-time, and customizable platform to study multisensory integration and sensory reweighting in weakly electric fish. This setup enables flexible, high-resolution behavioral experiments for future investigations of neural mechanisms underlying adaptive sensory processing. Ongoing work aims to model the observed behavior as a weighted combination of cues.

This research is supported by the TUBITAK project number 123E155.

**Keywords:** Multisensory integration, sensory salience, sensory reweighting, weakly electric fish, real-time behavioral control

SPEECH TEXTS

## A Bioinspired Bioelectric Sensing Catheter System Forfluoroscopy-Free Imaging

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**Objective:** Minimally invasive treatments rely on fluoroscopy for catheter localization, exposing patients and staff to harmful ionizing radiation. We introduce a neuro-inspired system drawing from the highly sensitive electrolocation strategy of weakly electric fish. The core objective is to validate this non-ionizing method, which utilizes bioimpedance to mimic the fish's real-time sensing of its environment. This aims to provide a safer, more efficient alternative to conventional guidance.

**Methods:** The methodology involved fabricating detailed vascular models simulating key pathologies (stenosis, occlusion, bifurcation). We constructed catheters with integrated, custom electrode spacings connected to a high-gain, low-noise acquisition circuit. Validation experiments were conducted by advancing the catheter through the saline-immersed models while synchronously recording the bioimpedance signal.

**Results:** Results demonstrated that the bioimpedance signal systematically correlated with vascular anomalies: narrowing increased the signal, while bifurcation caused a decrease. Crucially, we found that the measured voltage was inversely proportional to the vessel cross-sectional area, confirming the principle of using localized impedance measurements for precise positional feedback and pathology detection in a fluid environment.

**Conclusion:** This research successfully validates a radiation-free, bioimpedance-based approach for precise intravascular localization. By translating a fundamental neural sensing strategy into a robust technological platform, this work introduces a viable new technique for advanced neuro-interventional procedures. This technology offers a compelling alternative to X-ray guidance during delicate surgeries, specifically cerebral aneurysm coiling. This study was supported by TÜSEB (Project No: 39026).

**Keywords:** Electric fish, bioimpedance, catheter, intravascular diagnosis

## Comparison of the Efficacy of Two Different Rapid Tissue Clearing Methods in Formalin-Fixed Paraffin Embedded Tissues

Gülşah Gürbüz Alver[1], Savaş Aktaş[1], Ayla Batu Öztürk[1], Nail Can Öztürk[2]

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**Objective:** Conventional histological techniques typically provide two-dimensional views of paraffin-embedded tissues. In contrast, tissue clearing recognized as a newgeneration histological approach enables detailed three-dimensional visualization and analysis. Although several studies describe the applicability of clearing techniques to formalin-fixed paraffin-embedded (FFPE) tissues, no data exist on the performance of rapid methods such as the ultrafast optical clearing method with simple (FOCMS) and the m-Xylylenediamine-based aqueous clearing system (MACS). This study aimed to evaluate the effectiveness of FOCMS and MACS for optical clearing of FFPE tissues.

**Methods:** Adult female Wistar rats (n = 12) which approved by Mersin University ethics committee for animal experiments (2024/07) were divided into two groups: paraformaldehyde-perfused fresh tissue (PPFT, n = 6) and FFPE (n = 6). Brain, kidney, and liver samples were divided into 1 mm thick sections and cleared using FOCMS and MACS methods. Before and after clearing, transparency, clearing time, linear expansion, absorbance, transmittance (%), and imaging depth (μm) were quantified via ELISA reader, light and confocal microscopy. In addition, 5hmC-immunlabeled brain slices were examined by confocal microscopy.

**Results:** The shortest clearing time observed in brain tissues using MACS (40 min), while the longest time observed in liver tissues using FOCMS (7 hr). Both FOCMS and MACS methods increased linear expansion, transmittance, and imaging depth in PPFT and FFPE tissues. Transparency levels were higher in PPFT than FFPE samples, yet FFPE tissues also showed marked improvement after clearing. MACS achieved higher transparency and imaging depth compared with FOCMS among all tissue types.

**Conclusion:** Rapid clearing methods such as FOCMS and MACS markedly enhance the three-dimensional visualization of paraffin-embedded archival tissues. Further optimization may facilitate their broader application to FFPE histopathology. This study was supported by the Mersin University Scientific Research Projects (MEÜ-BAP) unit Project No: 2024-TP2-5033, MEÜ-BAP (Project No: 2021-1-TP2-4269) and TÜBİTAK (Project No: 118C299).

**Keywords:** Rapid tissue clearing, FOCMS, MACS, FFPE, paraffin-embedded tissue

SPEECH TEXTS

## Investigation of the Neuroprotective Effects and Circadian Rhythm Modulation of Safranal in an in vitro Parkinson's Model

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**Objective:** Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by dopaminergic neuron degeneration, oxidative stress, and mitochondrial dysfunction. While Levodopa is the primary symptomatic treatment, its long-term use causes side effects. Safranal, a bioactive compound from *Crocus sativus*, possesses antioxidant and neuroprotective properties. This study aims to investigate the neuroprotective potential of Levodopa and Safranal, individually and in combination, and their impact on circadian rhythm genes in an *in vitro* PD model.

**Methods:** SH-SY5Y neuroblastoma cells were exposed to 6-hydroxydopamine (6-OHDA) to induce neurotoxicity. Neuroprotective effects of Levodopa and Safranal were assessed via cell viability and cytotoxicity assays. Molecular effects were evaluated by analyzing circadian rhythm gene expression, mitochondrial membrane potential (MMP), caspase-3/7 activity, and autophagy. Potential synergistic interactions were examined using combination index (CI) analysis.

**Results:** 6-OHDA significantly reduced cell viability and mitochondrial function. Pretreatment with Levodopa and Safranal partially restored viability. Notably, the combined treatment significantly enhanced cell survival, preserved MMP, and reduced caspase-3/7 activity more effectively than monotherapies. While 6-OHDA downregulated *Per1, Clock, Bmal1,* and *Cry1* mRNA levels ($p < 0.05$), the combination treatment significantly upregulated these genes. CI analysis confirmed a synergistic interaction between Levodopa and Safranal against 6-OHDAinduced cytotoxicity.

**Conclusion:** Levodopa and Safranal exhibited dose-dependent neuroprotective effects. Their combination markedly enhanced neuroprotection by preserving mitochondrial function, inhibiting apoptosis, and modulating circadian genes. Findings highlight Safranal as a promising therapeutic candidate for counteracting PD-associated neurodegenerative mechanisms.

**Keywords:** Parkinson's disease, safranal, SH-SY5Y, 6-OHDA, neuroprotection, circadian rhythm

## Bridging Reproducibility and Accessibility in EEG-Based Brain–Computer Interface Research: A Systematic Mapping Study

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**Objective:** This study aims to provide a systematic mapping of electroencephalography (EEG)-based brain–computer interface (BCI) research in order to identify current trends, reproducibility limitations, and accessibility gaps, and to define a structured pathway for reproducible and software-oriented BCI development.

**Methods:** A systematic mapping study was conducted on 281 EEG-based BCI articles published between 2011 and 2025. Each study was analyzed according to BCI paradigm, methodological approach, dataset availability, source code sharing, and hardware type. In addition, consumer-grade EEG devices including OpenBCI, Emotiv, and Muse were comparatively evaluated in terms of signal quality and accessibility.

**Results:** Ten major research clusters were identified, with a strong emphasis on speller systems and motor imagery paradigms. Only 15% of the reviewed studies publicly shared their datasets, and fewer than 10% provided access to source code, indicating a substantial reproducibility gap. Recurrent technical challenges included signal noise, limited generalization, and insufficient real-time validation. Consumer-grade EEG devices demonstrated improved accessibility but variable signal quality depending on paradigm type.

**Conclusion:** EEG-based BCI research shows rapid growth but remains constrained by limited openness and reproducibility. The findings highlight the need for standardized, transparent, and software-oriented development practices. Conceptual paradigm-based flowcharts are proposed to support reproducible BCI software design and to assist researchers in developing reliable and affordable EEG-based applications.

**Keywords:** EEG, brain–computer interface, reproducibility, systematic mapping study, open science

SPEECH TEXTS

## Adaptive Sensory Weighting and Motor Strategies in Weakly Electric Fishes Under Varying Environmental Conditions

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In refuge-tracking tasks, weakly electric fish rely on the integration of visual and electrosensory cues to guide movement. How different species balance these sensory inputs and adapt their motor strategies under varying environmental uncertainty remains poorly understood. Here, we aimed to compare refuge-tracking performance across sensory conditions in two weakly electric fish species, *Apteronotus albifrons* and *Eigenmannia virescens*.

We quantified refuge-tracking behavior in *A. albifrons* (n = 5) and *E. virescens* (n = 5) while a refuge was driven by a sum-of-sines trajectory. Sensory conditions were systematically manipulated by varying water conductivity, illumination, and refuge structure (window presence and refuge length). Tracking performance was assessed using four complementary behavioral metrics: two time-domain measures (root mean square error; trial-to-trial variability) and two frequency-domain measures (frequency tracking error; mean active sensing power).

Our findings show that *A. albifrons* consistently outperformed *E. virescens* across all error metrics, with performance differences primarily arising at low refuge motion frequencies. At higher frequencies, tracking accuracy declined in both species, eliminating the performance gap. Additionally, *A. albifrons* exhibited lower trial-to-trial variability and more stable tracking, with stability predominantly influenced by illumination and refuge length.

These results demonstrate species-specific strategies for integrating sensory information during refuge tracking and highlight how neural control systems adapt motor behavior to the statistical structure of the sensory environment. This comparative framework provides a foundation for mechanistic models of active sensing and sensorimotor control in weakly electric fish.

This work was supported by The Scientific and Tecnhological Research Council of Türkiye (TÜBİTAK) under grant number 120E198 awarded to Dr. İsmail Uyanık.

**Keywords:** Multisensory integration, active sensing, sensorimotor control, refuge tracking, weakly electric fish

## Investigating Multisensory Integration in *Eigenmannia virescens* by Manipulating Sensory Salience

E. Ceren Rutbil[1], Gürkan Çelik[1], Osman Kaan Karagöz[2], İsmail Uyanık[1]

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**Objective:** Multisensory integration (MSI) enables animals to improve their perception of the world by combining different sensory inputs from multiple sources based on their reliabilities. Our goal is to investigate how the central nervous system integrates sensory information gathered from the environment.

**Methods:** We studied MSI in the weakly electric fish *Eigenmannia virescens* (n = 5; age 18–24 months; total length 10–15 cm) during refuge-tracking behavior. *Eigenmannia* tends to track the longitudinal movements of a refuge in which it hides by combining visual and electrosensory information. We developed an experimental setup consisting of a translucent refuge and a projection system to provide controlled visual stimuli. Moreover, each sensory salience was independently manipulated: electrosensory salience was varied by adjusting water conductivity using biocompatible salt mix, and visual salience was manipulated by projecting light stripes onto the refuge. All experiments were conducted in darkness under various salience conditions.

**Results:** Our analysis indicates that combined sensory cues improved tracking behavior and responses to stimuli at a frequency of 0.25 Hz. A two-way ANOVA was performed to determine statistical significance and revealed that the addition of visual cues significantly reduced phase difference, RMSE, and variability ($p < 0.05$).

**Conclusion:** This study demonstrates the role of MSI in Eigenmannia virescens and how different sensory cues influence refuge-tracking behavior. These findings contribute to a better understanding of the mechanisms underlying multisensory integration.

This work was supported by Health Institutes of Türkiye (TUSEB) under grant number TUSEB16548.

**Keywords:** Multisensory integration, sensory saliance, weakly electric fish

SPEECH TEXTS

## Active Sensing Strategies of Weakly Electric Fish Under Varying Flow Conditions

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**Objective:** Weakly electric fish possess a sophisticated multisensory system that integrats es electrosensory, visual, and mechanosensory inputs, allowing them to perceive their fsurroundings even under low-visibility conditions. This study aimed to determine how ambient flow modulates active sensing strategies in *Apteronotus albifrons*.

**Methods:** Behavioral experiments were conducted in a custom-built flow tunnel (25 × 50 cm) providing precise control of water velocity and refuge motion. Four adult *A. albifrons* freely tracked a linearly actuated refuge moving with a multifrequency sinusoidal trajectory. Four flow speeds (0, 4.5, 11.16 cm/s), two illumination levels (light/dark), and two refuge types (windowed/nonwindowed) were tested. Active sensing was quantified as movement power outside the stimulus frequencies, termed mean active sensin power.

**Results:** Technological Research Council of Türkiye (Grant No. 120E198) awarded to İ. Uyanık. E.Y. Aydın was additionally supported by TÜBİTAK through the 2211.

**Conclusion:** *A. albifrons* dynamically adjusts its active sensing behavior to counteract sensory degradation in flowing water. This flownu—dependent flexibility highlights the cadaptive reorganization of multisensory control and offers valuable design insights for l bioinspired underwatt er sensing systems. This research was supported by the Scientific

**Keywords:** Active sensing movements, behavioral neuroscience, weakly electric fish

## Computational Framework for Sensory Cue Reconstruction Using Multiple Leaky Integrate-and-Fire Neurons

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**Objective:** This study aims to develop a computational framework for modeling neural coding processes by simulating neuronal responses using the Leaky Integrate-and-Fire (LIF) model. The main objective is to examine how sensory information can be reconstructed from multiple neurons that encode the same input through distinct spiking characteristics.

**Methods:** A population of simulated neurons with different intrinsic properties is modeled using the LIF approach to capture spiking dynamics. Poisson process noise is added to the spike trains to introduce variability. Tuning curves are then extracted by applying sensory inputs with varying amplitudes, revealing the relationship between firing rate and input magnitude. To suppress impulsive noise in the firing rates, the Maximum Correntropy Kalman Filter is applied, which enhances the reconstruction accuracy. Finally, a likelihood-based population decoding method is used to reconstruct the underlying sensory input from the collective spike activity.

**Results:** Simulation results show that spike information from LIF neurons encoding the same sensory input with different spiking dynamics can be effectively combined to achieve high-precision reconstruction. In the proposed framework, two sets of ten LIF neurons are implemented to encode the positive and negative components of the sensory input. The reconstructed signal achieves a Normalized Root Mean Square Error of $8 \times 10^{-2}$, indicating successful reconstruction.

**Conclusion:** The proposed framework provides an effective means of modeling and decoding neural activity. It offers insights into the mechanisms of neural coding and demonstrates potential applications in brain–computer interface systems. This work is supported by the TÜBİTAK project No. 123E155.

**Keywords:** Leaky Integrate-and-Fire, neural coding, population decoding, cue reconstruction, maximum correntropy kalman filter

SPEECH TEXTS

## The Impact of Transcranial Magnetic Stimulation on Brain Morphometry in Early Stroke Rehabilitation Using the Bobath Approach: A Pilot Study

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**Objective:** This pilot study aimed to compare the effects of inhibitory and excitatory repetitive Transcranial Magnetic Stimulation (rTMS) protocols, applied in addition to the Bobath approach, on early rehabilitation of hemiparetic stroke patients with upper extremity motor deficits due to subcortical lesions.

**Method:** Eight patients diagnosed with early-stage subcortical stroke in the neurology clinic were included in the study. The study consisted of three groups: (1) sham rTMS, (2) ipsilateral excitatory rTMS, and (3) contralateral inhibitory rTMS. Each patient received 15 sessions of rTMS applied to the primary motor cortex. Immediately after the rTMS sessions, all groups underwent physiotherapy techniques based on the Bobath approach, which is founded on neurodevelopmental principles aiming to improve postural control, reduce abnormal movement patterns, and promote functional movements. Pre- and post-treatment clinical motor assessment scales were used to evaluate the patients' upper extremity motor functions, and structural brain images were recorded on the same day. Pre- and post-treatment gray matter volume changes were assessed for the whole brain using voxel-based morphometry (VBM) and region-of-interest -based analyses. VBM analyses were performed using Computational Anatomy Toolbox-12 and Statistical Parametric Mapping-12 software implemented in MATLAB. Additionally, correlations between brain regions showing significant changes and demographic variables were calculated.

**Results:** Although the clinical evaluation results were not statistically significant when comparing pre- and post-treatment outcomes, it was demonstrated that all rTMS groups (placebo, excitatory, and inhibitory) applied combined with Bobath therapy supported post-stroke recovery and induced positive changes in mobility and upper extremity motor functions. In the VBM analyses, although not statistically significant, a trend toward decreased gray matter volume in the ipsilesional superior frontal gyrus was observed in the inhibitory rTMS group after treatment compared to before treatment, whereas the placebo and excitatory rTMS groups showed a trend toward increased volume ($p = 0.09$). The results obtained from other investigated motor regions were also not statistically significant.

**Conclusion:** As a result of the combined application of the Bobath approach and rTMS, an improvement in clinical outcomes and a trend toward opposite-direction volumetric changes in structural brain measures were observed during early-stage stroke rehabilitation depending on the mode of rTMS, inhibitory vs excitatory; however, in this pilot study, no statistically significant differences were found between the excitatory and inhibitory rTMS protocols. Larger-scale studies conducted during the acute and early subacute phases - when post-stroke neuroplasticity is at its peak-will better elucidate the morphometric effects of such multifaceted interventions. This study provides important preliminary findings that highlight the potential contributions of rTMS in early stroke rehabilitation and may serve as a foundation for future research.

**Keywords:** Stroke, early rehabilitation, bobath concept, transcranial magnetic stimulation, motor function

## Mitochondrial Myopathy Due To Thymidine Kinase 2 Deficiency: Clinical Spectrum and Therapeutic Implications From A Case Series

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**Objective:** Thymidine kinase-2 deficiency (TK2d) is a rare autosomal recessive mitochondrial myopathy caused by impaired phosphorylation of deoxythymidine and deoxycytidine, leading to mitochondrial DNA (mtDNA) depletion/deletions, defective oxidative phosphorylation, and cellular energy failure. While no approved therapies currently exist, recent evidence suggests that oral pyrimidine nucleoside supplementation may restore mtDNA and improve outcomes. We aimed to describe the clinical, biochemical, genetic characteristics of five patients with TK2d, treated under an international early access program, and to discuss mechanisms of potential therapeutic strategies.

**Methods:** We retrospectively reviewed clinical and follow-up data, laboratory findings, genetic results of five patients with TK2d.

**Results:** Four early-onset patients, all diagnosed genetically with TK2d, presented between 12-20 months with hypotonia, motor regression, bulbar/respiratory dysfunction. Three infants required invasive ventilation. Within 3-8 weeks of oral nucleoside therapy, respiratory symptoms resolved, tracheostomies were closed. Over a follow-up period of 18 months-6 years, all achieved independent ambulation. In the fourth patient, who had lost ambulation by 17 months, nucleoside therapy was recently initiated, clinical response is under follow-up. The fifth case, a 22-year-old woman with gradual proximal weakness since infancy, developed dysphagia and hypoventilation requiring gastrostomy and nocturnal non-invasive ventilation during adolescence. Genetic testing confirmed homozygous pathogenic variant in TK2. After six years of nucleoside therapy, her disease course has slowed and shows relative stabilization.

**Conclusion:** TK2d demonstrates how impaired mitochondrial nucleotide salvage results in energy failure with heterogeneous clinical outcomes. Early recognition is essential, as pyrimidine nucleoside therapy offers a promising therapeutic strategy together with multidisciplinary supportive care.

**Keywords:** TK2 deficiency, mitochondrial myopathy, pediatric neurology, nucleoside therapy

SPEECH TEXTS

## A Modular Biaxial Cell-Stretching Platform for Physiologically Relevant Strain Application and Yap-Mediated Mechanotransduction in Human Myoblasts

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**Objective:** Replicating native mechanical environments is essential to understand how biomechanical stimuli regulate neuromuscular development, regeneration, and disease. We developed a compact, modular biaxial cell-stretching platform that delivers reproducible cyclic strain to adherent cells with engineering-grade control and biological compatibility.

**Methods:** The system uses a polydimethylsiloxane membrane actuated by two orthogonally arranged high-torque stepper motors and monitored by embedded soft strain sensors to promote uniform deformation across a 12 × 12 mm culture region. Square and triangular strain waveforms (5–20% amplitude; 0.1–2 Hz) were generated with closed-loop control. Biological compatibility was evaluated using C2C12 murine myoblasts and immortalized human myoblasts (n = 3 independent experiments). Human myoblasts were subjected to 10% cyclic biaxial strain at 0.2 Hz for 5 h, followed by expression analysis of Yes-associated protein/transcriptional co-activator with PDZ-binding motif (YAP/TAZ) downstream targets.

**Results:** The platform achieved < 2% steady-state strain error across the tested range and maintained performance across membrane stiffness conditions. C2C12 proliferation was comparable to conventional culture dishes, while human myoblast viability remained > 67% after 48 h of continuous culture. Cyclic stretching significantly increased C-MYC (1.7 ×), MYL9 (4.8 ×), DIAPH1 (1.9 ×), and ANKRD1 (2.0 ×) versus static controls ($p < 0.001$).

**Conclusion:** The device delivers physiologically relevant biaxial strain and elicits authentic mechanotransductive signaling, supporting high-confidence mechanobiology studies in neuromuscular research. This study was supported by the Scientific Research Projects Coordination Unit of Hacettepe University (TOA-2023-20338).

**Keywords:** Mechanotransduction, mechanobiology, biaxial cell stretching

## Multimodal Cue Integration During Target Tracking in Freely Swimming Zebrafish

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**Objective:** Animals are routinely exposed to multi-modal sensory streams that vary in velocity, reliability, and noise. To act robustly, nervous systems must weigh and combine these cues to guide behavior. We investigated how visual and mechanosensory cues are integrated during target tracking in positive rheotaxis—a station-holding behavior of zebrafish (*Danio rerio*).

**Methods:** We built a laminar flow tunnel with two actuators delivering mechanosensory and visual stimuli independently, allowing unrestricted swimming. Mechanosensory cues were produced by a transparent D-shaped plexiglass tube that is optically invisible in water. Visual cues were produced by a blue-neon strip LED mounted in the tube that moved without creating water vibrations. The two actuators translate the tube and the LED synchronously or asynchronously, thereby enabling precise control of single- and multi-sensory conditions as well as sensory conflict. Eight adult zebrafish performed repeated tracking trials across five stimulus sets (single frequencies 0.05 Hz and 0.125 Hz, 0.05+0.125 Hz, and cross-modal combinations). The behavior of the fish was analyzed using a closed-loop systems framework, whereby the fish's motion was designated as the output and the stimulus motion as the input.

**Results:** Mechanosensory input exerted a predominant influence on target tracking. Visual cues alone were generally insufficient to elicit target tracking relative mechanosensory input. In the multisensory integration scenario, the target tracking performance improved significantly.

**Conclusion:** During rheotactic target tracking, zebrafish prioritize mechanosensory input as the primary stabilizing cue, while visual input provides complementary refinement that improves accuracy and reduces lag under multisensory stimulation. Our experimental setup provides a generalizable tool for dissecting multisensory integration in freely swimming vertebrates.

This study was supported by the Scientific and Technological Research Council of Türkiye (TÜBİTAK) under project number 120E054.

**Keywords:** Rheotaxis, multisensory integration, zebrafish, closed-loop systems

SPEECH TEXTS

## Low-Latency Multi-Notch Filtering for Active Sensing in Weakly Electric Fish

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**Objective:** Weakly electric fish behave approximately linear time-invariant during refuge tracking, producing responses only at stimulus frequencies. When electrosensory feedback is reduced, animals switch to active sensing, modulating electromotor output; this violates linearity and yields responses at non-stimulus frequencies.

**Methods:** We previously developed an adaptive notch filter that attenuates the behavioral response at a single carrier frequency, reducing closed-loop feedback and inducing active sensing. Here we generalize to multiple components and present a low-latency, stable multi-notch closed-loop method that simultaneously suppresses several frequencies. The system combines online frequency tracking, per-component adaptive notch updates, and amplitude limiting to maintain stability. We tested the method in MATLAB on refuge motions containing two–five sinusoids. Filter vector parameters are precomputed during initialization, and only the vector product is computed at each sample.

**Results:** Simulations show large attenuation at suppressed components while preserving gain and phase for unsuppressed or adjacent-band components. We also compared against a standard fast Fourier transform notch. Across 0.3–1.3 Hz, our method matched spectral suppression while operating with O(n) complexity and negligible delay. A header-only C++ implementation supports integration with middleware (e.g., Robot Operating System 1) and real-time deployment; Python bindings expose the same API.

**Conclusion:** In sum, we provide a general, low-latency, stable, and scalable framework for multi-frequency notch filtering that enables controlled transitions from stimulus-driven linearity to task-dependent nonlinear active sensing. Next, we will integrate the system in vivo and test whether multi-component suppression reliably elicits active sensing.

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**Keywords:** Active sensing movements, weakly electric fish, adaptive notch filter, multi-notch filter, closed-loop control

## Xenogenic Neural Stem Cell-Derived Extracellular Vesicles Drive Metabolic Remodeling and Neural Differentiation in Human Mesenchymal Stem Cells

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Exosomes are nanoscale extracellular vesicles that regulate intercellular communication through the transfer of metabolic and regulatory cargo. This study examines whether exosomes derived from rat subventricular zone neural stem cells (rSVZ-NSCExo) can direct human mesenchymal stem cell (hMSC) fate by reprogramming cellular energy metabolism toward a neurogenic profile. Comparative miRNA profiling demonstrated a high degree of similarity between rSVZ tissue and rSVZ-NSCExo, with 684 shared miRNAs identified. Among 728 rat-origin miRNAs, 28 miRNAs were significantly up- or downregulated in both groups (≥ 2-fold change, $p \leq 0.05$), indicating preservation of the endogenous rSVZ miRNA signature. In hMSCs treated with rSVZ-NSCExo (100 µg $mL^{-1}$), 54 miRNAs were significantly dysregulated compared with non-induced controls. The top 20 altered miRNAs, including miR-3178, let-7b, miR-222, and miR-24, are associated with mitochondrial activity, oxidative phosphorylation, and lipid metabolism. Non-targeted metabolomics using GC-MS and LC-qTOF-MS detected 16,351 mass features. A total of 92 metabolites were identified by LC-MS/LC-MS/MS and 62 metabolites by GC-MS. Dose-dependent (10–100 µg $mL^{-1}$) and time-dependent (1, 3, 5, and 10 days) analyses revealed significant metabolic remodeling (PLS-DA and ANOVA, $p < 0.05$). Affected pathways included glutamate metabolism, the TCA cycle, amino acid turnover, glycerophospholipid metabolism, dopamine signaling, and sphingolipid *de novo* biosynthesis. Network analysis identified dopamine, pyruvate, taurine, and amino acids as central metabolic hubs. Overall, this study introduces a novel exosome-based platform capable of guiding mesenchymal stem cells toward neural-specific phenotypes, offering a promising and physiologically relevant approach for *in vivo* nerve regeneration applications.

SPEECH TEXTS

## Independent Stimulation of Visual and Electrosensory Modalities in Weakly Electric Fish

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**Objective:** Weakly electric fish (*Eigenmannia virescens*) rely on both visual and electrosensory cues to interact with their environment during behaviors such as navigation and refuge tracking. However, isolating the contribution of each sensory modality remains challenging. This study aimed to develop and validate an experimental framework that enables independent stimulation of visual and electrosensory inputs.

**Methods:** We designed a dual-refuge system consisting of an inner agarose refuge dyed with ferric oxide ($Fe_2O_3$) that provides a visual cue while remaining electrically neutral, and an outer aluminum refuge that provides an electrosensory cue while remaining visually hidden, as it was fully occluded by the inner agarose refuge. Experiments were conducted in complete darkness using three adult *Eigenmannia virescens* (n = 3). Each fish performed ten trials under three conditions: movement of the outer refuge only, movement of the inner refuge only, and no refuge movement. Fish tracking responses were quantified in the frequency domain and compared statistically against the no-movement control.

**Results:** A significant tracking response was observed exclusively when the outer (electrosensory) refuge was moved. In contrast, movement of the inner (visual) refuge did not evoke systematic tracking, indicating the absence of salient electrosensory cues. Statistical comparisons confirmed that responses during inner-refuge motion did not differ from baseline across all fish.

**Conclusion:** These results demonstrate effective isolation of visual and electrosensory modalities using the proposed dual-refuge system. This framework provides a robust foundation for future studies on sensory reliability, sensory conflict, and dynamic sensory reweighting during active multisensory behavior. This work was supported by The Scientific and Technological Research Council of Türkiye (TÜBİTAK) under Grant No. 123E155 and No. 125E097.

**Keywords:** Weakly electric fish, multisensory integration, sensory isolation, electrosensation

## Evaluation of Morphometric Changes in the Brain with Cranial MR Segmentation Analysis After COVID Infection

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**Objective:** Our aim in this study was to identify anatomically the potential volumetric changes in intracranial structures in individuals with a prior Coronavirus Disease 2019 (COVID-19) infection who still complain of persistent headaches. This will pave the way for future studies to identify the potential source of headache, its relationship to symptoms, and the appropriate treatment method.

**Methods:** This retrospective study was conducted on 25 patients aged 18-50 who had mild to moderate COVID-19 and underwent a cranial magnetic resonance imaging (MRI) for any neurological indication, particularly headache, within three to six months of the initial diagnosis, and 25 controls who had not experienced COVID-19. Age and gender information was entered into the T1-weighted MRI images and uploaded to VolBrain, an online automated brain segmentation application. The volumes of cortical and subcortical structures and their ratios to the total intracranial space were obtained.

**Results:** The mean age of all participants was 31.5 ± 8.345 years. The percentage of white matter was higher and the percentage of cerebrospinal fluid was lower in the COVID-19 group (<0.001). In the COVID-19 group, total cerebrum, cerebrum white matter, cerebellum white matter, brainstem, rightleft and total lateral ventricular volume percentages were found to be statistically significantly higher ($p < 0.05$). Globus pallidus, hippocampus, amygdala and accumbens volume percentages were found to be lower in patients in the COVID-19 group ($p < 0.05$).

**Conclusion:** Understanding the changes in the volumes of intracranial structures after COVID-19 may be helpful in determining the source of prolonged neurological symptoms, especially headache, and in treating these symptoms.

**Keywords:** Brain volume, COVID-19, cranial MRI, headache, segmentation, VolBrain

SPEECH TEXTS

## Multisensory Salience Shapes Zebrafish Target-Tracking Performance During Rheotaxis

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Effective navigation in flowing water requires zebrafish (*Danio rerio*) to integrate mechanosensory and visual cues; however, how the salience of each cue shapes this multisensory control remains unresolved. We addressed this using a custom swim-tunnel assay where a transparent D-shaped tube perturbed laminar flow to engage the lateral line, while an internal red rod provided a concurrent visual reference. Cue salience was parametrically varied across three dimensions: (1) ambient illumination (light vs. dark), (2) presence of the outer transparent tube, and (3) diameter of the inner red rod. Adult zebrafish were tested as the nested tube oscillated sinusoidally at fixed frequencies. Analyses of trajectories, tracking accuracy, and frequency-response characteristics revealed a clear monotonic relationship: conditions improving the clarity or availability of either modality produced significantly tighter phase-locked tracking and higher overall gain. Conversely, reducing visual or mechanosensory clarity impaired performance, highlighting the complementary roles of these channels. These findings indicate that zebrafish rheotaxis is dynamically weighted by the perceived reliability of each input stream, offering a tractable model for salience-dependent cue weighting in vertebrate sensorimotor integration. This study was funded by TÜBİTAK under Grant 120E054.

**Keywords:** Multisensory integration, zebrafish, rheotaxis

## The Possible Effects of Baclofen on Mitochondrial Function

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**Objective:** Baclofen, a γ-aminobutyric acid type B receptor agonist, is widely used to manage spasticity and movement disorders. However, its limited efficacy in mitochondrial-related movement disorders and side effects such as muscle weakness suggest a role for mitochondria in mediating both therapeutic and adverse outcomes. This study aimed to investigate the molecular and biochemical effects of baclofen on mitochondrial function and stress responses *in vivo*.

**Methods:** Five C57BL/6J male mice were administered saline or 25 mg/kg/day baclofen via oral gavage for four weeks. Motor performance and muscle strength were assessed using activity cage, treadmill, grip strength, and RotaRod tests. Brain, kidney, and skeletal muscle tissues were analyzed by qPCR and Western blotting for markers of mitochondrial integrated stress response (ISRmt), biogenesis and autophagy. Oxygen consumption rates were measured in isolated brain mitochondria, and circulating cell-free mitochondrial DNA levels (cf-mtDNA) were quantified from plasma.

**Results:** Baclofen induced distinct tissue-specific mitochondrial alterations. In the brain, elevated ISRmt markers and autophagy indicated enhanced stress adaptation. In the kidney, baclofen increased ISRmt and mitochondrial biogenesis, potentially supporting renal energy metabolism. Conversely, skeletal muscle showed reduced biogenesis, consistent with muscle weakness. Plasma cf-mtDNA levels increased significantly, indicating systemic mitochondrial stress. Despite these molecular changes, no major phenotypic deficits were observed.

**Conclusion:** Baclofen exerts complex and tissue-dependent effects on mitochondrial function. While promoting adaptive mitochondrial responses in the brain and kidney, baclofen appears to impair skeletal muscle metabolism. Understanding these mechanisms could provide new insights into the baclofen's therapeutic actions and side effects in neurological disorders.

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**Keywords:** Baclofen, mitochondria, stress response, ISRmt, cell-free mtDNA

SPEECH TEXTS

## Mechanistic Evaluation of Hypoxia-Induced Cellular Aging by miR-34a Using *in silico* Analysis

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**Objective:** Cellular senescence denotes a stable arrest of the cell cycle accompanied by loss of normal proliferative capacity. Increasing evidence indicates that microRNAs act as key epigenetic modulators of aging. This study used an *in silico* approach to clarify how miR34a may link hypoxia to senescence.

**Methods:** A total of 112 miR-34a target genes with experimental support were retrieved from miRTarBase. Functional enrichment was carried out in Enrichr using Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) libraries, and a protein–protein interaction network was generated. GenAge and GeneCards were queried to compare miR-34a targets with aging- and hypoxia-related genes. Transcription factor regulators were identified by ChIP-X Enrichment Analysis 3 and summarized as a network map.

**Results:** GO terms enriched among miR-34a targets highlighted processes central to aging biology, including regulation of the cell cycle, apoptotic signaling, transcriptional control and responses to DNA damage. KEGG pathways reflected cellular senescence, p53 signaling, hypoxia-driven adaptation and DNA repair cascades. GenAge comparison indicated that 38 targets were linked to aging and 31 to hypoxia ($p < 0.05$). Integration with hypoxia-induced gene expression data yielded 10 shared genes, including *TP53*, *CDK6*, *CCND1*, *SIRT1*, *E2F3*, *BCL2*, *MYC*, *CDK4*, *FOXO3* and *NOTCH1*.

**Conclusion:** Our *in silico* findings suggest that miR-34a participates in both hypoxic signaling and cellular senescence through this core gene set. These results underscore the importance of miR-34a in hypoxia-associated aging and point to potentially druggable regulatory pathways, which require experimental validation.

**Keywords:** Hypoxia, *in silico* analysis, miR-34a, cellular aging

## Neurodegenerative Impact of Microbial Extracellular Vesicles on Brain Organoids

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The etiology of many neurological disorders is multifactorial and not yet fully understood. In addition to known genetic factors, numerous environmental elements such as gut microbiota dysbiosis are also considered. Inflammatory disorders in the gut are associated with neuroinflammation, earlier onset of dementia, and increased risk of Parkinson's disease. The gut microbiota affects the central nervous system and plays an essential role in the pathogenesis of neurodegenerative disorders, including Parkinson's and Alzheimer's diseases, multiple sclerosis, amyotrophic lateral sclerosis, and autism spectrum disorder. Human gut microbes influence the gut–brain axis through various mechanisms, including nutrient absorption. Growing evidence highlights microbial extracellular vesicles (EVs) as key mediators in this bidirectional communication. EVs are nano-sized, double-membraned vesicles secreted by both Gram-negative and Gram-positive bacteria. They contain lipids, proteins, and nucleic acids and can cross biological barriers. Gram-negative bacteria release outer membrane vesicles, while Gram-positive bacteria release cytoplasmic membrane vesicles. Brain organoids derived from human pluripotent stem cells provide an *in vitro* platform that mimics human brain development and structure, offering an alternative to animal models for disease modeling. This study aims to explore microbial EV–induced neuropathological mechanisms in human brain organoids, providing insights into microbiota– brain communication that may inform future therapeutic strategies.

**Keywords:** Microbial extracellular vesicles, brain organoids