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Mobile brain imaging in butoh dancers: from rehearsals to public performance

Dissecting the neurobiology of dance would shed light on a complex, yet ubiquitous, form of human communication. In this experiment, we sought to study, via mobile electroencephalography (EEG), the brain activ...

Constantina Theofanopoulou, Sadye Paez, Derek Huber, Eric Todd, Mauricio A. Ramírez-Moreno, Badie Khaleghian, Alberto Muñoz Sánchez, Leah Barceló, Vangelina Gand and José L. Contreras-Vidal

BMC Neuroscience 2024 25:62

Research | Published on: 6 November 2024

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The cognitive neuroscience and neurocognitive rehabilitation of dance

Creative movement, in the form of music- and dance-based exercise and rehabilitation, can serve as a model for learning and memory, visuospatial orientation, mental imagery, and multimodal sensory-motor integr...

Madeleine Eve Hackney, Agnieszka Zofia Burzynska and Lena H. Ting

BMC Neuroscience 2024 25:58

Review | Published on: 6 November 2024

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APOE4 rat model of Alzheimer's disease: sex differences, genetic risk and diet

The strongest genetic risk factor for Alzheimer's disease (AD) is the $\epsilon 4$ allele of apolipoprotein E (*ApoE* $\epsilon 4$). A high fat diet also adds to the risk of dementia and AD. In addition, there are sex differences as w...

Bradley Colarusso, Richard Ortiz, Julian Yeboah, Arnold Chang, Megha Gupta, Praveen Kulkarni and Craig F. Ferris

BMC Neuroscience 2024 25:57

Research | Published on: 6 November 2024

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ZA-II-05, a novel NMDA-receptor antagonist reverses vanadium-induced neurotoxicity in *Caenorhabditis elegans* (*C. elegans*)

Vanadium is a widely used transition metal in industrial applications, but it also poses significant neurotoxic and environmental risks. Previous studies have shown that exposure to vanadium may lead to neurod...

Amany Ladagu, Funmilayo Olopade, Paul Chazot, Taiwo Elufioye, Toan Luong, Madison Fuller, Ethan Halprin, Jessica Mckay, Zeynep Ates-Alagoz, Taidinda Gilbert, Adeboye Adejare and James Olopade

BMC Neuroscience 2024 25:56

Research | Published on: 28 October 2024

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Structural and functional sex differences in medial temporal lobe subregions at midlife

Research has increasingly recognized sex differences in aging and Alzheimer's Disease (AD) susceptibility. However, sex effects on the medial temporal lobe (MTL), a crucial region affected by aging and AD, rem...

Marie Caillaud, Isabelle Gallagher, Janelle Foret and Andreana P. Haley

BMC Neuroscience 2024 25:55

Research | Published on: 25 October 2024

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Exploring sex differences in auditory saliency: the role of acoustic characteristics in bottom-up attention

Several cognitive functions are related to sex. However, the relationship between auditory attention and sex remains unclear. The present study aimed to explore sex differences in auditory saliency judgments, ...

Naoya Obama, Yoshiki Sato, Narihiro Kodama, Yuhei Kodani, Katsuya Nakamura, Ayaka Yokozeki and Shinsuke Nagami

BMC Neuroscience 2024 25:54

Research | Published on: 24 October 2024

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Retraction Note: MicroRNA expression profile of the hippocampus in a rat model of temporal lobe epilepsy and miR-34a-targeted neuroprotection against hippocampal neurone cell apoptosis post-status epilepticus

Kai Hu, Yuan-Yuan Xie, Chen Zhang, Dong-Sheng Ouyang, Hong-Yu Long, Dan-Ni Sun, Li-Li Long, Li Feng, Yi Li and Bo Xiao

BMC Neuroscience 2024 25:53

Retraction Note | Published on: 17 October 2024

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Tinnitus is associated with increased extracellular matrix density in the auditory cortex of Mongolian gerbils

Most scientists agree that subjective tinnitus is the pathological result of an interaction of damage to the peripheral auditory system and central neuroplastic adaptations. Here we investigate such tinnitus r...

Konstantin Tziridis, Antonia Maul, Jwan Rasheed, Patrick Krauss, Achim Schilling and Holger Schulze

BMC Neuroscience 2024 25:52

Research | Published on: 17 October 2024

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Making sense together: dance improvisation as a framework for a collaborative interdisciplinary learning processes

This editorial outlines the outcome of an interdisciplinary session on collective sense-making through dance improvisation, which took place during the ‘Neural and Social Bases of Creative Movement’ workshop. ...

Lisa Nelson, Julien Laroche, Nara Figueiredo, João Fiadeiro, Joseph Dumit and Asaf Bachrach

BMC Neuroscience 2024 25:51

Editorial | Published on: 16 October 2024

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Correction to: Simulated complexes formed from a set of postsynaptic proteins suggest a localised effect of a hypomorphic Shank mutation

Marcell Miski, Áron Weber, Krisztina Fekete-Molnár, Bence Márk Keömley-Horváth, Attila Csikász-Nagy and Zoltán Gáspári

BMC Neuroscience 2024 25:50

Correction | Published on: 9 October 2024

 The [original article](#) was published in *BMC Neuroscience* 2024 **25**:32

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Neuroprotective effects of psilocybin in a rat model of stroke

Psilocybin is a psychedelic 5HT2A receptor agonist found in “magic mushrooms”. Recent studies have indicated that 5HT2A agonists, such as dimethyltryptamine, given before middle cerebral artery occlusion (MCAo...

Seong-Jin Yu, Kuo-Jen Wu, Yu-Syuan Wang, Eunkyung Bae, Fabio Chianelli, Nicholas Bambakidis and Yun Wang

BMC Neuroscience 2024 25:49

Research | Published on: 8 October 2024

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Vocal usage learning and vocal comprehension learning in harbor seals

Which mammals show vocal learning abilities, e.g., can learn new sounds, or learn to use sounds in new contexts? Vocal usage and comprehension learning are submodules of vocal learning. Specifically, vocal usa...

Diandra Duengen, Yannick Jadoul and Andrea Ravignani

BMC Neuroscience 2024 25:48

Research | Published on: 4 October 2024

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Tactile stimulation designs adapted to clinical settings result in reliable fMRI-based somatosensory digit maps

Movement constraints in stroke survivors are often accompanied by additional impairments in related somatosensory perception. A complex interplay between the primary somatosensory and motor cortices is essenti...

Till Steinbach, Judith Eck, Inge Timmers, Emma E. Biggs, Rainer Goebel, Renate Schweizer and Amanda L. Kaas

BMC Neuroscience 2024 25:47

Research | Published on: 1 October 2024

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Distinct connectivity patterns in bipolar and unipolar depression: a functional connectivity multivariate pattern analysis study

Patients with bipolar disorder (BD) and major depressive disorder (MDD) exhibit depressive episodes with similar symptoms despite having different and poorly understood underlying neurobiology, often leading t...

Martin Pastrnak, Monika Klirova, Martin Bares and Tomas Novak

BMC Neuroscience 2024 25:46

Research | Published on: 27 September 2024

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Thymoquinone ameliorate oxidative stress, GABAergic neuronal depletion and memory impairment through Nrf2/ARE signaling pathway in the dentate gyrus following cypermethrin administration

Exposure to chemical toxins, including insecticides, harms bodily organs like the brain. This study examined the neuroprotective of thymoquinone on the cypermethrin's harmful effects on the histoarchitecture o...

Abubakar Lekan Imam, Akeem Ayodeji Okesina, Fatimo Ajoke Sulaimon, Aminu Imam, Ruqayyah Yetunde Ibiyeye, Lukuman Aboyeji Oyewole, Sikiru Abayomi Biliaminu, Monsur Shehu, Abdulhameed Oluwatomi Alli, Oluwatosin Olasheu Omoola and Salihu Moyosore Ajao

BMC Neuroscience 2024 25:45

Research | Published on: 27 September 2024

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Dorsal root ganglion inflammation by oxaliplatin toxicity: DPEP1 as possible target for peripheral neuropathy prevention

Peripheral neuropathy (PN) constitutes a dose-limiting side effect of oxaliplatin chemotherapy that often compromises the efficacy of antineoplastic treatments. Sensory neurons damage in dorsal root ganglia (D...

Karen Álvarez-Tosco, Rebeca González-Fernández, María Ángeles González-Nicolás, Rita Martín-Ramírez, Manuel Morales, Ricardo Gutiérrez, Lucio Díaz-Flores, María Rosa Arnau, Félix Machín, Julio Ávila, Alberto Lázaro and Pablo Martín-Vasallo

BMC Neuroscience 2024 25:44

Research | Published on: 15 September 2024

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The reliability and validity of rapid transcranial magnetic stimulation mapping for muscles under active contraction

Rapid mapping is a transcranial magnetic stimulation (TMS) mapping method which can significantly reduce data collection time compared to traditional approaches. However, its validity and reliability has only ...

Nahian S. Chowdhury, Wei-Ju Chang, Rocco Cavaleri, Alan K.I. Chiang and Siobhan M. Schabrun

BMC Neuroscience 2024 25:43

Research | Published on: 30 August 2024

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Neural acetylcholinesterase and monoamine oxidase deregulation during streptozotocin-induced behavioral, metabolic and redox modification in *Nauphoeta cinerea*

Genetic and environmental factors have been linked with neurodegeneration, especially in the elderly. Yet, efforts to impede neurodegenerative processes have at best addressed symptoms instead of underlying pa...

Opeyemi B. Ogunsuyi, Olawande C. Olagoke, Mayokun E. Famutimi, Damilola M. Olatunde, Diogo O. G. Souza, Ganiyu Oboh, Nilda V. Barbosa and João B.T. Rocha

BMC Neuroscience 2024 25:42

Research | Published on: 29 August 2024

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Neuroethics and AI ethics: a proposal for collaboration

The scientific relationship between neuroscience and artificial intelligence is generally acknowledged, and the role that their long history of collaboration has played in advancing both fields is often emphas...

Arleen Salles and Michele Farisco

BMC Neuroscience 2024 25:41

Review | Published on: 29 August 2024

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Modulation of audiovisual integration in the left and right sides: effects of side and spatial coherency

Using event-related potentials (ERPs), we aimed to investigate audiovisual integration neural mechanisms during a letter identification task in the left and right sides. Unimodal (A,V) and bimodal (AV) stimuli...

XiaoHui Wen, GuoQiang Li, XuHong Wang, XiaoLan Hu and HongJun Yang

BMC Neuroscience 2024 25:40

Research | Published on: 27 August 2024

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Comparative analysis of the effects of the computer-based and paper-based trail making tests on oxygenation in the prefrontal cortex

The trail making test (TMT) is a commonly used tool for evaluating executive functions, and the activation of cerebral oxygenation in the prefrontal cortex (PFC) during the test can reflect the participation o...

Li-Sha Xiang, Jia-Nan Zhang, Fan Xie, Xiao Fei, Ya Wang, Yue Shi and Yi Zhang

BMC Neuroscience 2024 25:39

Research | Published on: 26 August 2024

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Ectopically expressed rhodopsin is not sensitive to X-rays

Visual perception of X-radiation is a well-documented, but poorly understood phenomenon. Scotopic rod cells and rhodopsin have been implicated in visual responses to X-rays, however, some evidence suggests tha...

Kelli Cannon, Aundrea Bartley, Lynn Dobrunz and Mark Bolding

BMC Neuroscience 2024 25:38

Research | Published on: 23 August 2024

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Role of the sympathetic nervous system in cancer-associated cachexia and tumor progression in tumor-bearing BALB/c mice

Adipose and muscle tissue wasting outlines the cachectic process during tumor progression. The sympathetic nervous system (SNS) is known to promote tumor progression and research suggests that it might also co...

Isaias Gutierrez-Leal, Diana Caballero-Hernández, Alonso A. Orozco-Flores, Ricardo Gomez-Flores, Deyanira Quistián-Martínez, Patricia Tamez-Guerra, Reyes Tamez-Guerra and Cristina Rodríguez-Padilla

BMC Neuroscience 2024 25:37

Research | Published on: 22 August 2024

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Intracerebroventricular administration of the exercise hormone irisin or acute strenuous exercise alleviates epileptic seizure-induced neuroinflammation and improves memory dysfunction in rats

Status epilepticus is a common and potentially life-threatening neurological emergency with a high risk for cognitive and neurobiological impairment. Our aim was to evaluate the neuroprotective effects of cent...

Zarife Nigâr Ozdemir-Kumral, Tuğçe Akgün, Ceren Haşim, Ezgi Ulusoy, Mehmet Kaan Kalpakçioğlu, Muhammet Ferzan Yüksel, Tunahan Okumuş, Zeynep Us, Dilek Akakin, Meral Yüksel, Zafer Gören and Berrak Ç. Yeğen

BMC Neuroscience 2024 25:36

Research | Published on: 5 August 2024

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Establishment and evaluation of a clinical prediction model for cognitive impairment in patients with cerebral small vessel disease

There are currently no effective prediction methods for evaluating the occurrence of cognitive impairment in patients with cerebral small vessel disease (CSVD).

Fangfang Zhu, Jie Yao, Min Feng and Zhongwu Sun

BMC Neuroscience 2024 25:35

Research | Published on: 2 August 2024

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Efferent pathways from the suprachiasmatic nucleus to the horizontal limbs of diagonal band promote NREM sleep during the dark phase in mice

The regulation of circadian rhythms and the sleep–wake states involves in multiple neural circuits. The suprachiasmatic nucleus (SCN) is a circadian pacemaker that controls the rhythmic oscillation of mammalia...

Lei Chen, Changfeng Chen, Qiaoling Jin, Yue Liang, Jian Wu, Pingping Zhang, Juan Cheng and Liecheng Wang

BMC Neuroscience 2024 25:34

Research | Published on: 22 July 2024

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Cardiovascular history and risk of idiopathic Parkinson's disease: a cross-sectional observational study

Parkinson's disease (PD), while often associated with its distinctive motor symptoms, can also exert a notable impact on the cardiovascular system due to the development of severe autonomic dysfunction. One of...

Shubhra Acharya, Andrew I. Lumley and Yvan Devaux

BMC Neuroscience 2024 25:33

Research | Published on: 8 July 2024

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Simulated complexes formed from a set of postsynaptic proteins suggest a localised effect of a hypomorphic Shank mutation

The postsynaptic density is an elaborate protein network beneath the postsynaptic membrane involved in the molecular processes underlying learning and memory. The postsynaptic density is built up from the same...

Marcell Miski, Áron Weber, Krisztina Fekete-Molnár, Bence Márk Keömley-Horváth, Attila Csikász-Nagy and Zoltán Gáspári

BMC Neuroscience 2024 25:32

Research | Published on: 6 July 2024

 The [Correction to this article](#) has been published in *BMC Neuroscience* 2024 **25**:50

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Persistent vocal learning in an aging open-ended learner reflected in neural FoxP2 expression

Most vocal learning species exhibit an early critical period during which their vocal control neural circuitry facilitates the acquisition of new vocalizations. Some taxa, most notably humans and parrots, reta...

Bushra Moussaoui, Kennedy Ulmer, Marcelo Araya-Salas and Timothy F. Wright

BMC Neuroscience 2024 25:31

Research | Published on: 4 July 2024

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Changes of brain functional network in Alzheimer's disease and frontotemporal dementia: a graph-theoretic analysis

Alzheimer's disease (AD) and frontotemporal dementia (FTD) are the two most common neurodegenerative dementias, presenting with similar clinical features that challenge accurate diagnosis. Despite extensive re...

Shijing Wu, Ping Zhan, Guojing Wang, Xiaohua Yu, Hongyun Liu and Weidong Wang

BMC Neuroscience 2024 25:30

Research | Published on: 4 July 2024

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The angiotensin II receptors type 1 and 2 modulate astrocytes and their crosstalk with microglia and neurons in an in vitro model of ischemic stroke

Astrocytes are the most abundant cell type of the central nervous system and are fundamentally involved in homeostasis, neuroprotection, and synaptic plasticity. This regulatory function of astrocytes on their...

Daniel Navin Olschewski, Nilufar Nazarzadeh, Felix Lange, Anna Maria Koenig, Christina Kulka, Jella-Andrea Abraham, Stefan Johannes Blaschke, Rudolf Merkel, Bernd Hoffmann, Gereon Rudolf Fink, Michael Schroeter, Maria Adele Rueger and Sabine Ulrike Vay

BMC Neuroscience 2024 25:29

Research | Published on: 26 June 2024

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Diabetes mellitus and risk of incident dementia in APOE ε4 carriers: an updated meta-analysis

Diabetes raises the risk of dementia, mortality, and cognitive decline in the elderly, potentially because of hereditary variables such as APOE. In this study, we aim to evaluate Diabetes mellitus and the risk...

Ava Rashtchian, Mohammad Hossein Etemadi, Elham Asadi, Sara Binaei, Mina Abbasi, Maedeh Bayani, Erfan Izadi, Sayedeh-Fatemeh Sadat-Madani, Mahdyieh Naziri, Sahar khoshravesh, Mahsa shirani, Mahsa Asadi Anar and Niloofar Deravi

BMC Neuroscience 2024 25:28

Research | Published on: 25 June 2024

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Autism spectrum disorders detection based on multi-task transformer neural network

Autism Spectrum Disorders (ASD) are neurodevelopmental disorders that cause people difficulties in social interaction and communication. Identifying ASD patients based on resting-state functional magnetic reso...

Le Gao, Zhimin Wang, Yun Long, Xin Zhang, Hexing Su, Yong Yu and Jin Hong

BMC Neuroscience 2024 25:27

Research | Published on: 13 June 2024

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Automated glioblastoma patient classification using hypoxia levels measured through magnetic resonance images

The challenge of treating Glioblastoma (GBM) tumors is due to various mechanisms that make the tumor resistant to radiation therapy. One of these mechanisms is hypoxia, and therefore, determining the level of ...

Mohammad Amin Shahram, Hosein Azimian, Bita Abbasi, Zohreh Ganji, Zahra Khandan Khadem-Reza, Elham Khakshour and Hoda Zare

BMC Neuroscience 2024 25:26

Research | Published on: 25 May 2024

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Central nervous system anomalies in 41 Chinese children incontinentia pigmenti

Incontinentia pigmenti (IP) is a rare neuroectodermal dysplasia caused by a defect in the *IKBKG* gene. The pathogenesis of central nervous system injury is believed to be related to microvascular ischemia. Current...

Li Yin, Zhengyuan Li, Wenjuan Zhan, Yuanjie Kang, Qian Tian, Dan Li and Huifang Zhang

BMC Neuroscience 2024 25:25

Research | Published on: 21 May 2024

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Characterizing dysregulations via cell-cell communications in Alzheimer's brains using single-cell transcriptomes

Alzheimer's disease (AD) is a devastating neurodegenerative disorder affecting 44 million people worldwide, leading to cognitive decline, memory loss, and significant impairment in daily functioning. The recent...

Che Yu Lee, Dylan Riffle, Yifeng Xiong, Nadia Momtaz, Yutong Lei, Joseph M. Pariser, Diptanshu Sikdar, Ahyeon Hwang, Ziheng Duan and Jing Zhang

BMC Neuroscience 2024 25:24

Research | Published on: 13 May 2024

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A new era in cognitive neuroscience: the tidal wave of artificial intelligence (AI)

Translating artificial intelligence techniques into the realm of cognitive neuroscience holds promise for significant breakthroughs in our ability to probe the intrinsic mechanisms of the brain. The recent unp...

Zhiyi Chen and Ali Yadollahpour

BMC Neuroscience 2024 25:23

Editorial | Published on: 6 May 2024

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Computational modeling of light processing in the habenula and dorsal raphe based on laser ablation of functionally-defined cells

The habenula is a major regulator of serotonergic neurons in the dorsal raphe, and thus of brain state. The functional connectivity between these regions is incompletely

characterized. Here, we use the ability...

Ruey-Kuang Cheng, N. Suhas Jagannathan, Ahmad Ismat Kathrada, Suresh Jesuthasan and Lisa Tucker-Kellogg

BMC Neuroscience 2024 25(Suppl 1):22

Research | Published on: 16 April 2024

 This article is part of a Supplement: [Volume 25 Supplement 1](#)

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The effects of multi-colour light filtering glasses on human brain wave activity

The prevalence of electronic screens in modern society has significantly increased our exposure to high-energy blue and violet light wavelengths. Accumulating evidence links this exposure to adverse visual and...

Katherine Boere and Olave E. Krigolson

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Research | Published on: 12 April 2024

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The effect of early mobilisation (< 14 days) on pathophysiological and functional outcomes in animals with induced spinal cord injury: a systematic review with meta-analysis

The optimum time to mobilise (standing, walking) following spinal cord injury (SCI) is unknown but may have implications for patient outcomes. There are no high-quality experimental studies that examine this i...

Natalie Gray, Junaid Shaikh, Alison Cowley, Vicky Goosey-Tolfrey, Pip Logan, Nasir Quraishi and Vicky Booth

BMC Neuroscience 2024 25:20

Research | Published on: 25 March 2024

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Neuroscience of taste: unlocking the human taste code

Since antiquity human taste has been divided into 4–5 taste qualities. We realized in the early 1970s that taste qualities vary between species and that the sense of taste in species closer to humans such as p...

Göran Hellekant

BMC Neuroscience 2024 25:19

Review | Published on: 21 March 2024

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Auditory brainstem responses are resistant to pharmacological modulation in Sprague Dawley wild-type and Neurexin1 α knockout rats

Sensory processing in the auditory brainstem can be studied with auditory brainstem responses (ABRs) across species. There is, however, a limited understanding of ABRs as tools to assess the effect of pharmac...

Samuel Marashli, Philipp Janz and Roger L Redondo

BMC Neuroscience 2024 25:18

Research | Published on: 15 March 2024

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Serum interleukin-17 A and homocysteine levels in children with autism

Autism Spectrum Disorder (ASD) is a neurodevelopmental condition that typically emerges early in childhood. This study aimed to explore the potential link between serum levels of vitamin B12 and homocysteine (...)

Hui Li, Yunhao Dang and Ying Yan

BMC Neuroscience 2024 25:17

Research | Published on: 12 March 2024

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Administration methods and dosage of poly(lactic acid)-glycol intervention to myelin oligodendrocyte glycoprotein-induced experimental autoimmune encephalitis mice

Myelin oligodendrocyte glycoprotein-associated disorders (MOGAD) is an autoimmune central nervous system disease. Antigen-specific immune tolerance using nanoparticles such as Polylactic-co-glycolic acid (PLGA...

Amy E. Wright, Shuhei Nishiyama, Patrick Han, Philip Kong and Michael Levy

BMC Neuroscience 2024 25:16

Research | Published on: 11 March 2024

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Discrimination of the moving direction is improved depending on the pattern of the mechanical tactile stimulation intervention

The mechanical tactile stimulation, such as plastic pins and airflow-driven membrane, induces cortical activity. The cortical activity depends on the mechanical tactile stimulation pattern. Therefore, the stim...

Yuki Maruyama, Sho Kojima and Hideaki Onishi

BMC Neuroscience 2024 25:15

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State-transition dynamics of resting-state functional magnetic resonance imaging data: model comparison and test-to-retest analysis

Electroencephalogram (EEG) microstate analysis entails finding dynamics of quasi-stable and generally recurrent discrete states in multichannel EEG time series data and relating properties of the estimated sta...

Saiful Islam, Pitambar Khanra, Johan Nakuci, Sarah F. Muldoon, Takamitsu Watanabe and Naoki Masuda

BMC Neuroscience 2024 25:14

Research | Published on: 4 March 2024

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Resistance training modifies of serum levels of matrix metalloproteinase 2 and tissue inhibitor of matrix metalloproteinases in multiple sclerosis women - a randomized controlled trail

The objectives of the present study was to investigate the effects of resistance training (RT) on serum levels of controlling blood-brain barrier (BBB) permeability indices and cognitive performance in MS wome...

Nasrin Niazi Nezhad, Abdolhossein Parnow, Kianoosh Khamoushian, Rasoul Eslami and Julien S Baker

BMC Neuroscience 2024 25:13

Research | Published on: 4 March 2024

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Defined co-cultures of glutamatergic and GABAergic neurons with a mutation in *DISC1* reveal aberrant phenotypes in GABAergic neurons

Mutations in the gene *DISC1* are associated with increased risk for schizophrenia, bipolar disorder and major depression. The study of mutated DISC1 represents a well-known and comprehensively characterized appoa...

Johanna Heider, Aaron Stahl, Denise Sperlich, Sophia-Marie Hartmann, Sabrina Vogel, Ricarda Breitmeyer, Markus Templin and Hansjürgen Volkmer

BMC Neuroscience 2024 25:12

Research | Published on: 4 March 2024

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Prodromal Parkinson disease signs are predicted by a whole-blood inflammatory transcriptional signature in young *Pink1*^{-/-} rats

Parkinson disease (PD) is the fastest growing neurodegenerative disease. The molecular pathology of PD in the prodromal phase is poorly understood; as such, there are no specific prognostic or diagnostic tests...

Sarah A. Lechner, David G. S. Barnett, Stephen C. Gammie and Cynthia A. Kelm-Nelson

BMC Neuroscience 2024 25:11

Research | Published on: 4 March 2024

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Current state of neuroprotective therapy using antibiotics in human traumatic brain injury and animal models

TBI is a leading cause of death and disability in young people and older adults worldwide. There is no gold standard treatment for TBI besides surgical interventions and symptomatic relief. Post-injury infecti...

Katharina Ritter, Pawit Somnuk, Lingjiao Hu, Eva-Verena Griemert and Michael K.E. Schäfer

BMC Neuroscience 2024 25:10

Review | Published on: 29 February 2024

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RESEARCH

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Thymoquinone ameliorate oxidative stress, GABAergic neuronal depletion and memory impairment through Nrf2/ARE signaling pathway in the dentate gyrus following cypermethrin administration

Abubakar Lekan Imam¹, Akeem Ayodeji Okesina^{2*} , Fatimo Ajoke Sulaimon¹, Aminu Imam¹, Ruqayyah Yetunde Ibiyeye³, Lukuman Aboyegi Oyewole⁴, Sikiru Abayomi Biliaminu⁵, Monsur Shehu¹, Abdulhameed Oluwatomi Alli⁶, Oluwatosin Olasheun Omoola⁷ and Salihu Moyosore Ajao¹

Abstract

Background Exposure to chemical toxins, including insecticides, harms bodily organs like the brain. This study examined the neuroprotective of thymoquinone on the cypermethrin's harmful effects on the histoarchitecture of the dentate gyrus and motor deficit in the dentate gyrus.

Methods Forty adult male rats (180–200 g) were randomly divided into 5 groups ($n = 8$ per group). Groups I, II, III, IV, and V received oral administration of 0.5 ml of phosphate-buffered saline, cypermethrin (20 mg/kg), thymoquinone (10 mg/kg), cypermethrin (20 mg/kg) + thymoquinone (5 mg/kg), and cypermethrin (20 mg/kg) + thymoquinone (10 mg/kg) for 14 days respectively. The novel object recognition test that assesses intermediate-term memory was done on days 14 and 21 of the experiment. At the end of these treatments, the animals were euthanized and taken for cytoarchitectural (hematoxylin and eosin; Cresyl violet) and immunohistochemical studies (Nuclear factor erythroid 2-related factor 2 (Nrf2), Parvalbumin, and B-cell lymphoma 2 (Bcl2)).

Result The study shows that thymoquinone at 5 and 10 mg/kg improved Novelty preference and discrimination index. Thymoquinone enhanced Nissl body integrity, increased GABAergic interneuron expression, nuclear factor erythroid 2-derived factor 2, and enhanced Bcl-2 expression in the dentate gyrus. It also improved the concentration of nuclear factor erythroid 2-derived factor 2, increased the activities of superoxide dismutase and glutathione, and decreased the concentration of malondialdehyde level against cypermethrin-induced neurotoxicity.

Conclusion thymoquinone could be a therapeutic agent against cypermethrin poisoning.

Keywords Cypermethrin, Thymoquinone, Cresyl fast violet, GABAergic interneuron, Dentate gyrus

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Background

Oxidative stress arises from an imbalance between reactive oxygen species (ROS) and the antioxidant defense system. ROS can lead to covalent oxidative modifications, such as ribonucleic acid (RNA) oxidation, and induce mutations in mitochondrial DNA (mtDNA), thereby destabilizing nucleic acids [1, 2]. These modifications may result in cellular dysfunction and apoptosis. The mitochondrial-dependent caspase pathway is crucial in apoptosis [3]. Stimulation of this cascade releases pro-apoptotic factors, including cytochrome c (Cyc), activating caspase-9 and caspase-3, ultimately triggering cellular apoptosis [4, 5]. Hence, antioxidant pathways that mitigate oxidative damage may exhibit neuroprotective effects [6].

Persistent pesticide exposure, such as pyrethroids, adversely affects various physiological functions [7]. For example; long-term exposure can disrupt the functioning of different organs, posing serious health risks [8, 9]. Nigeria has witnessed numerous cases of food poisoning due to pesticides, resulting in significant fatalities and economic losses [10]. Pyrethroids, widely used in agriculture and household insect control, were detected in a large portion of the population [11]. Despite their broad application, pyrethroids exhibit adverse effects, including neurobehavioral and molecular target disruption in the nervous system [12, 13]. Cypermethrin, a common pyrethroid, crosses the blood-brain barrier, inducing oxidative stress and apoptotic cell death [14, 15].

Medicinal plants offer a sustainable therapeutic approach against chemical toxins; for example, thymoquinone (TQ), derived from *Nigella sativa* L., possesses antioxidant and anti-inflammatory properties [16, 17]. TQ has shown neuroprotective effects in various models of brain injury and neurodegenerative diseases by inhibiting lipid peroxidation and apoptosis [18, 19]. Its antioxidant effects are mediated through the nuclear factor erythroid 2-related factor 2 (NRF2) pathway, which regulates cellular defense mechanisms against oxidative stress [20, 21]. Activation of NRF2 induces the expression of antioxidative and detoxifying enzymes, crucial for cellular function [22]. Whereas, the Dysregulation of NRF2/ARE signaling has been implicated in neurodegenerative disorders [23].

Given the increasing incidence of pesticide-induced food poisoning, there is a need for effective antidotes with shared mechanisms of action. This study aims to evaluate the efficacy of thymoquinone against cypermethrin-induced neurotoxicity, focusing on GABAergic interneuron disruption, dentate gyrus cytoarchitectural disorganization, and oxidative stress-induced cell damage.

Methods

Experimental design

The experimental design involved 40 adult male Wistar rats (180–200 g). Thymoquinone was obtained from MedChemExpress (MCE) USA (Cat No: HY-d0803) Cypermethrin 10% EC product was sourced from Yubaili Agrotec (ACEC20L068) and NAFDAC No: A5-0108 was obtained from Ibukun Oluwa Agrochemical Distop. Ilorin, Nigeria. The rats were housed in the a Faculty of Basic Medical Sciences, College of Health Sciences, University of Ilorin's animal holding facility under natural day-night cycles, with a standard chow diet and water ad libitum. Informed consent was obtained from the owner(s) of the animals involved in this study. All procedures were conducted with the owners' approval and were reviewed and approved by the University of Ilorin Ethical Review Committee (Approval No. UERC\ASN\2021\2137).

The rats were randomly divided into 5 groups ($n=8$ per group). Groups I, II, III, and IV received oral administration of 0.5 ml of phosphate buffered saline, 20 mg/kg of cypermethrin, 10 mg/kg of thymoquinone, 20 mg/kg of cypermethrin plus 5 mg/kg of thymoquinone, and 20 mg/kg of cypermethrin plus 10 mg/kg of thymoquinone for 14 days respectively. Memory behavior was assessed on the 14th day of the experiment.

Behavioral evaluation

Intermediate memory recognition of the experimental rats following exposure to cypermethrin and thymoquinone was assessed using the novel object recognition (NOR) paradigm. The test apparatus is made from plywood measuring 100 cm by 100 cm with walls that are 50 cm high. Novelty preference and Discriminatory index were evaluated [24]. Twenty-four hours after the behavioral study, the animals were euthanized using 20 mg/kg bw ketamine intramuscularly, and brain tissue was excised and processed for histological, immunohistochemistry, and biochemical analysis.

Tissue collection

After the completion of perfusion (brain tissues for histology and immunohistochemistry), the whole brain tissues were excised and were post-fixed in 4% paraformaldehyde overnight. The whole hippocampal CA regions were excised and equilibrated in 30% sucrose solution, before histological and immunohistochemical analyses. The sections were taken at 2 μ m on paraffin wax-embedded tissue blocks and mounted on a glass slide [25].

Histological analysis and immunohistochemistry

The hematoxylin and eosin (H and E) staining technique was used to demonstrate the general histo-architecture of the cells; and to show the location of the normal or

abnormal nucleus of the hippocampal cells [26]. Cresyl violet: This technique was used to demonstrate Nissl bodies (endoplasmic reticulum and ribosomes) in the cells; and to show normal or abnormal protein synthesis in the cytoplasm of the hippocampus [27].

For immunohistochemistry: Nuclear factor erythroid 2-related factor 2 (Nrf2), Parvalbumin, and B-cell lymphoma 2 (Bcl2) (human monoclonal; Elisa and microarray) were used to understand their roles in oxidative stress response, neuronal survival, and apoptosis regulation within dentate gyrus. The avidin-biotin complex method was used. The antibody dilution factor used was 1:100 for all the antibody markers. The processed tissues were sectioned at two microns on the rotary microtome and placed on a hotplate at 90 °C for at least 40 min. Image J software cell counter was used for counting the immunopositive cells for Nrf2, Parvalbumin, and Bcl2 in the dentate gyrus [28].

Biochemical investigation

Following the end of the various treatments, some hippocampal tissues were homogenized. The homogenates were collected in a 5 ml plain bottle and centrifuged for 10 min at 5000 rpm using a centrifuge. The supernatant was carefully decanted and stored at -4 °C for enzymatic assays of superoxide dismutase (SOD) activity [29], glutathione (GSH) concentration [30], malondialdehyde (MDA) [29] concentration and nuclear factor erythroid 2-derived factor 2 (Nrf2) a product of Elabscience Biotechnology Inc.USA (E-EL-R0673) method and absorbance was read using microplate reader. A four-parameter logistic curve (4PL-curve) was plotted and values obtained from the samples were extrapolated using GraphPad Prism 8.0.

Statistical analysis

Data from the behavioral investigation, biochemical assays, and immunopositive cell count were analyzed using one-way analysis of variance (ANOVA) and subjected to post hoc Bonferroni's multiple comparison test. The results were expressed as mean $\pm$ SEM. Statistical analyses were performed using GraphPad Prism software (version 8.0.2). Values of $p \leq 0.05$ were considered statistically significant.

Results

Thymoquinone restore inter-mediate related behaviors following cypermethrin exposure

The novelty preference of Wistar rats in the CYM group for new objects in the novel object recognition test was significantly low (32.70 ± 3.93) compared to the PBS control group at $p < 0.05$, compared to the CYM group, the TQ group, and the CYM-LHQ group showed higher preference for new object which was significant at

$p < 0.05$. However, the CYM-10mgTHQ group showed a higher preference than the CYM group with no significance at $p < 0.05$ Fig. 1B. The discrimination index was significantly reduced in the CYM group (-0.34 ± 0.08) compared to the PBS group (0.47 ± 0.10) and THQ group (0.81 ± 0.11) at $p < 0.05$. Groups CYM-LTHQ and CYM-HHQ showed a higher discrimination index when compared to the CYM group but were not significant at $p < 0.05$ (Table 1).

Oxidative stress biomarker

The concentration of Nrf2 in the CYM group was significantly reduced $p < 0.05$ when compared to both the PBS control and the other experimental groups (Fig. 1A). Moreover, a significant reduction $p < 0.05$ in the SOD activity was observed in the CYM-exposed group, relative to the PBS control group, while all the other experimental groups showed a significant increase in the SOD activities $p < 0.05$ when compared to the CYM group (Fig. 1B). However, SOD activities in the TQ, CYM-LTQ and CYM-HTQ groups were not significantly lower compared to the PBS control (Fig. 1B). In addition, the GSH concentration was significantly reduced ($p < 0.05$) in the CYM group relative to the PBS group (Fig. 1C). Subsequent treatment with LTQ and HTQ led to a significant increase in the GSH levels ($p < 0.05$) when compared to the CYM-only group (Fig. 1C). Regarding the lipid peroxidation marker MDA, its level was notably higher ($p < 0.05$) in the CYM group compared to the PBS group (Fig. 1D). While MDA levels were lower in other experimental groups, significance ($p < 0.05$) was only observed in the CYM-LTQ group compared to the CYM group (Fig. 1D).

PBS=phosphate-buffered saline, CYM=cypermethrin, TQ=thymoquinone, CYM-LTQ=cypermethrin followed by low dose thymoquinone and CYM-HTQ=cypermethrin followed by High dose thymoquinone.

Histochemical examination of the dentate gyrus revealed chromatolytic-like alterations in rats exposed to CYM. This was characterized by the disrupted integrity of Nissl granules and distortions in the shape and organization of granule cells. Additionally, numerous pyknotic and vacuolated cells were observed due to CYM exposure. Thymoquinone demonstrated a mitigating effect against CYM-induced toxicity, this was observed as a result of a reduction in the extent of neurodegenerative-like changes. Specifically, there was an improvement in Nissl body integrity and better enhancements were observed in the cellular shape and arrangement in the rats exposed to thymoquinone following CYM neurotoxicity (Fig. 2).

The immunohistochemical assessment of the dentate gyrus utilizing anti-Nrf2, anti-Parvalbumin (Parv), and anti-Bcl2 antibodies revealed diminished expression of

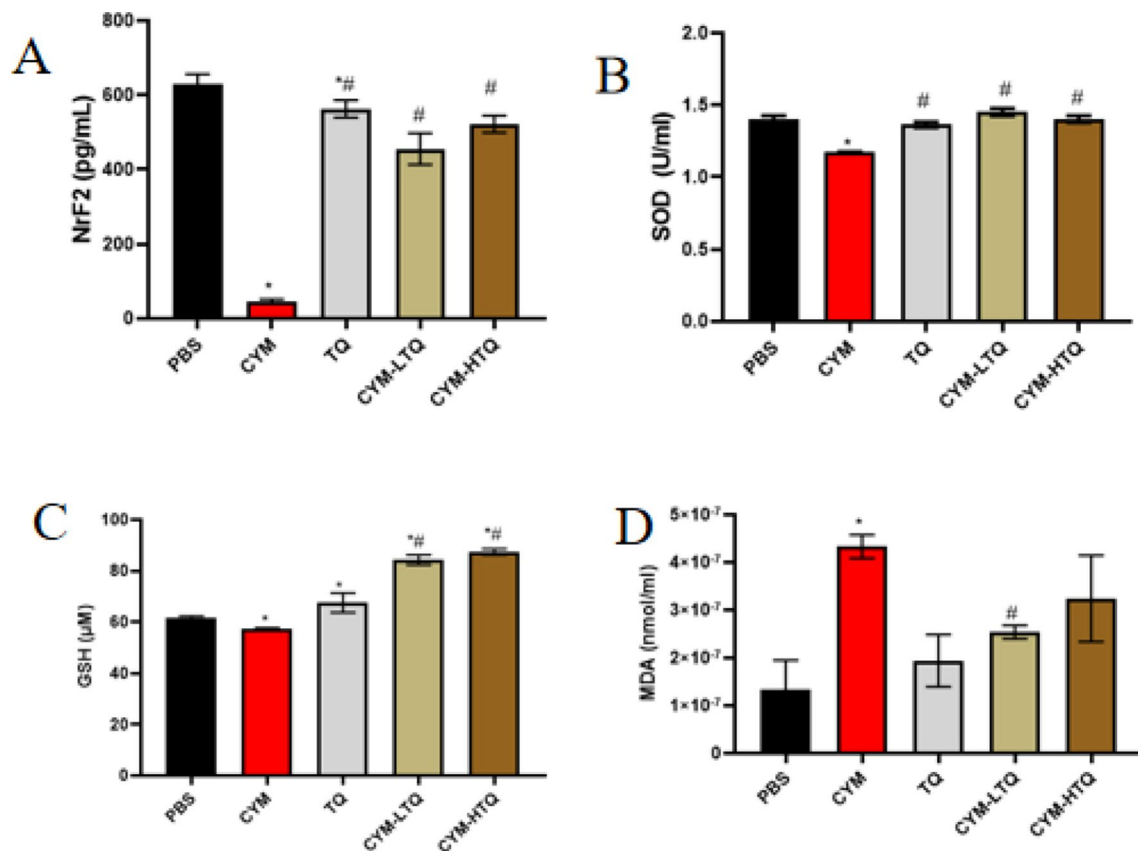


Fig. 1 Effects of thymoquinone post treatments on the cypermethrin-induced dentate gyrus oxidative stress. **(A)** Nrf2 **(B)** SOD **(C)** GSH **(D)** MDA. One-way ANOVA followed by Bonferroni's post hoc test multiple comparisons was used for analysis. Data is presented as mean $\pm$ SEM ($n=5$). * $p < 0.05$ compared to PBS group; # $p < 0.05$ compared to CYM group

Table 1 Novelty preference and discrimination index of rats following cypermethrin and thymoquinone exposure

Groups	Novelty preference (%)	Discrimination index
N=5		
PBS	77.60 $\pm$ 3.82	0.28 $\pm$ 0.24
CYM	39.30 $\pm$ 7.00*	-0.20 $\pm$ 0.15
TQ	90.30 $\pm$ 5.41#	0.81 $\pm$ 0.11#
CYM-LTQ	65.00 $\pm$ 11.20	0.44 $\pm$ 0.09
CYM-HTQ	46.00 $\pm$ 12.00	0.23 $\pm$ 0.06

PBS=phosphate-buffered saline, CYM=cypermethrin, TQ=thymoquinone, CYM-LTQ=cypermethrin followed by low dose thymoquinone and CYM-HTQ=cypermethrin followed by High dose thymoquinone. Single asterisk (*) indicates significant ($p < 0.05$) compared to PBS, Hash (#) indicates significant ($p < 0.05$) compared to CYM

Nrf2, Parv, and Bcl2 positive cells in the dentate gyrus of rats exposed to CYM. Conversely, post-treatment with thymoquinone exhibited a notable enhancement in the expression of Nrf2, Parv, and Bcl2 immunopositive cells in the dentate gyrus (Figs. 3, 4 and 5).

Quantification of immuno-positive cell counts using ImageJ software demonstrated a significantly higher ($p < 0.05$) Nrf2 cell count in the dentate gyrus of PBS control rats compared to those exposed to CYM (Fig. 3A & B). Thymoquinone administration led to a significant

increase ($p < 0.05$) in Nrf2 immunopositive cells in the CYM-LTQ and CYM-HTQ groups compared to CYM-exposed rats (Fig. 3A & B). Similarly, there was a significantly higher ($p < 0.05$) count of Parvalbumin-positive cells in the dentate gyrus of PBS control rats compared to CYM-exposed rats (Fig. 4A & B). Thymoquinone significantly ($p < 0.05$) increased the number of Parvalbumin cells in the CYM-LTQ and CYM-HTQ groups compared to CYM-exposed rats (Fig. 4A & B).

Moreover, the cell count of the anti-apoptotic protein Bcl2 was higher in the PBS control group than in CYM-exposed rats (Fig. 5A & B). Administration of thymoquinone resulted in a higher Bcl2 count in the CYM-LTQ and CYM-HTQ groups compared to CYM-exposed rats (Fig. 5A & B).

Discussion

Continuous application of pesticides and other agrochemicals, driven by the need to increase food production and prevent pest and insect-induced crop damages, has led to increased exposure to the harmful effects of these chemicals, including pyrethroid insecticides, due to their residual accumulation in crops, fruits, and

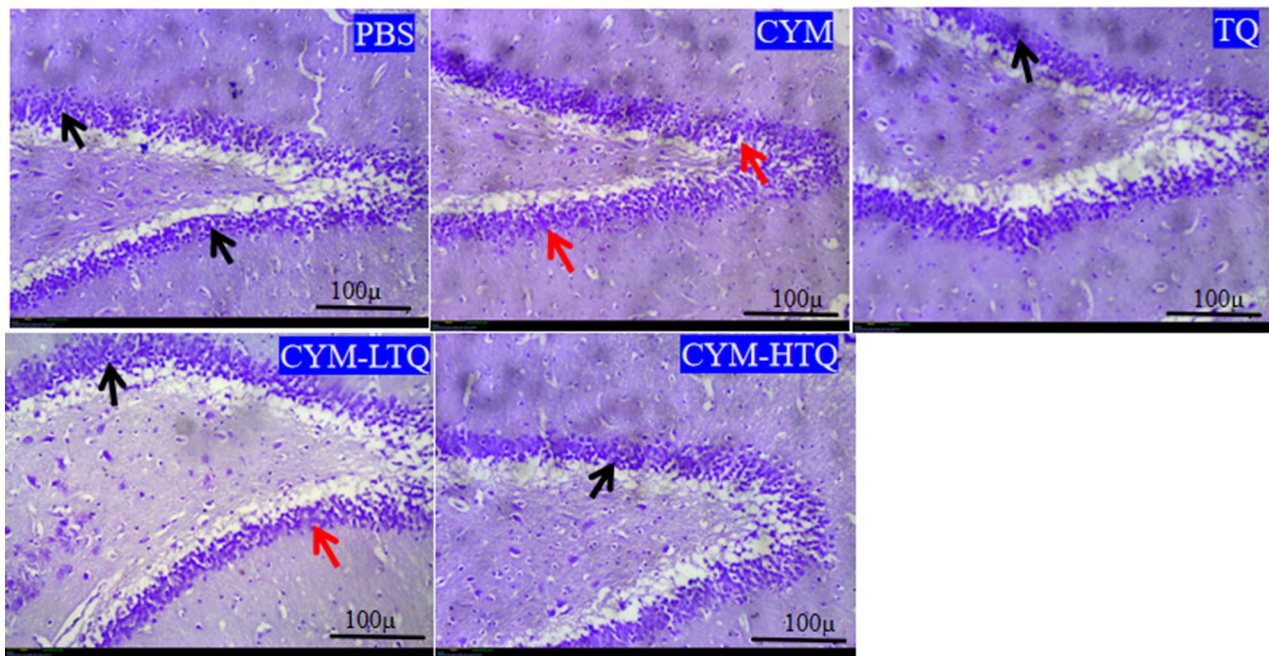


Fig. 2 Nissl substance of Dentate gyrus stained with cresyl fast violet (CFV). PBS group showed neurons with intact Nissl bodies (black arrows). the CYM group presented chromatolytic-like cytoplasm, indicating Nissl body loss with vacuolations (red arrow); TQ group displayed neurons with intact Nissl bodies (black arrows); CYM-LTQ group showed numerous neurons with well-stained cytoplasm indicating intact Nissl bodies (black arrows) and few pale neurons (red arrows); Also, CYM-HTQ group showed more neurons with well-stained cytoplasm indicating intact Nissl bodies (black arrows) and few pale neurons (red arrows). TQ=thymoquinone, CYM-LTQ=cypermethrin followed by low dose thymoquinone and CYM-HTQ=cypermethrin followed by High dose thymoquinone

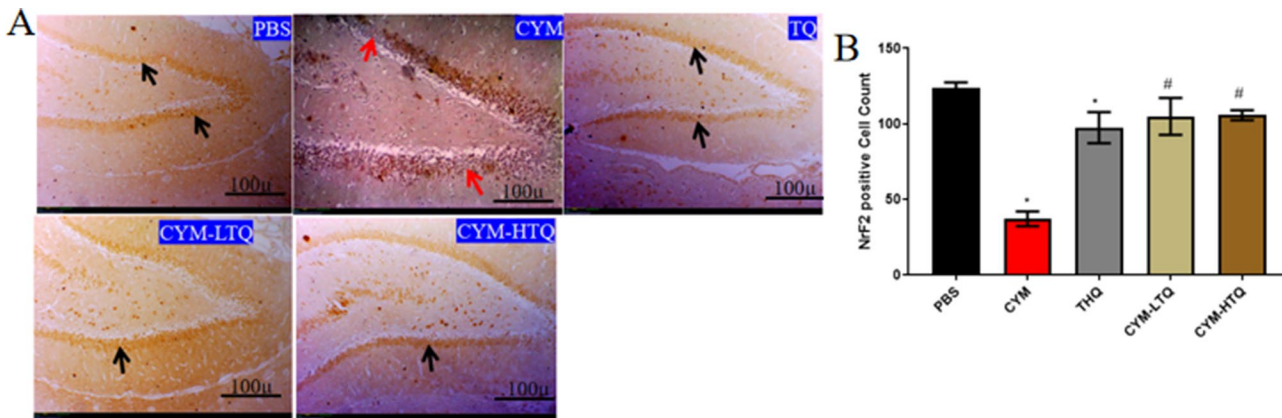


Fig. 3 (A) Immunostaining for Nrf2 in the dentate gyrus (scale bar = 100 μm), PBS group showed numerous Nrf2 expression (black arrows). CYM group displayed low Nrf2 expression indicating high Nrf2 inactivation (red arrows); TQ group showed high Nrf2 positive cells (black arrows); CYM-LTQ presented high Nrf2 positive cells (black arrows) compared to CYM group; CYM-HTQ group also displayed numerous Nrf2 positive cells (black arrow) compared to CYM group. (B). Nrf2 positive cell count. PBS group had significantly high Nrf2 positive cells (* $p < 0.05$) compared to CYM group. CYM group showed significant difference (# $p < 0.05$) compared to CYM-LTQ and CYM-HTQ groups $N = 6$. PBS = phosphate-buffered saline, CYM = cypermethrin, TQ = thymoquinone, CYM-LTQ = cypermethrin followed by low dose (5 mg/kg) thymoquinone and CYM-HTQ = cypermethrin followed by High dose (10 mg/kg) thymoquinone

vegetables. When humans and other animals are exposed to these chemicals, they can induce toxicity through mechanisms involving mitochondrial dysfunction, oxidative stress, and inflammation. This toxicity can manifest as movement disorders, loss of cognition, or a combination of both.

This study demonstrates that thymoquinone increases the activities of antioxidant enzymes, akin to its parent molecule *Nigella sativa* oil [31, 32], thereby preventing lipid peroxidation and preserving dentate gyrus architecture, ultimately enhancing memory function against CYM toxicity.

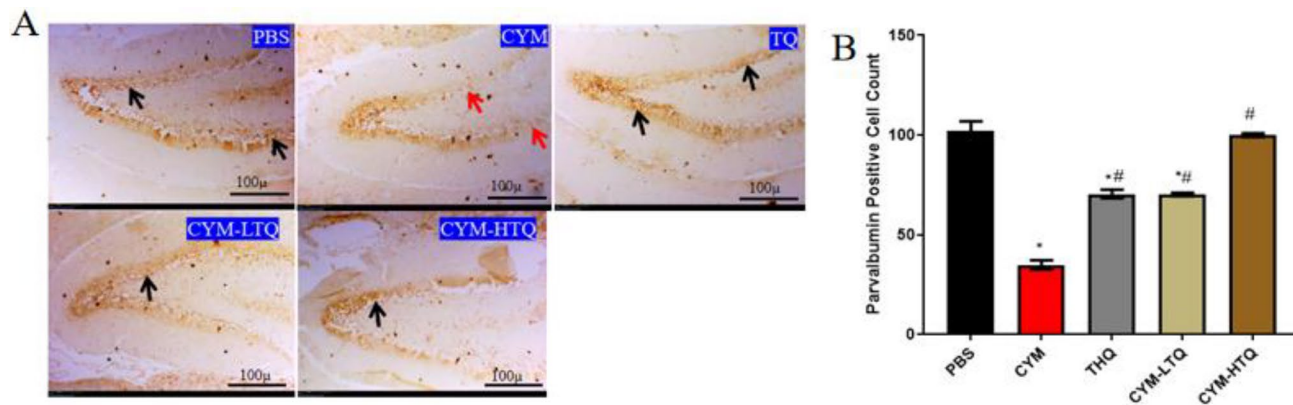


Fig. 4 GABAergic interneuron of the dentate gyrus. **(A)** immunostaining for Parvalbumin in the dentate gyrus (scale bar = 100 μm), PBS group showed numerous Parvalbumin positive cells (black arrows). CYM group displayed low parvalbumin positive cells indicating high inactivation of GABAergic interneuron (red arrows); TQ group showed high parvalbumin positive cells (black arrows); CYM-LTQ presented high parvalbumin positive cells (black arrows) compared to CYM group; CYM-HTQ group also displayed numerous parvalbumin positive cells (black arrow) compared to CYM group. **(B)**. Parvalbumin positive cell count. PBS group had significantly high parvalbumin positive cells (* $p < 0.05$) compared to CYM group. CYM group showed significant difference (# $p < 0.05$) compared to TQ, CYM-LTQ and CYM-HTQ groups ($N = 6$). PBS = phosphate-buffered saline, CYM = cypermethrin, TQ = thymoquinone, CYM-LTQ = cypermethrin followed by low dose (5 mg/kg) thymoquinone and CYM-HTQ = cypermethrin followed by High dose (10 mg/kg) thymoquinone

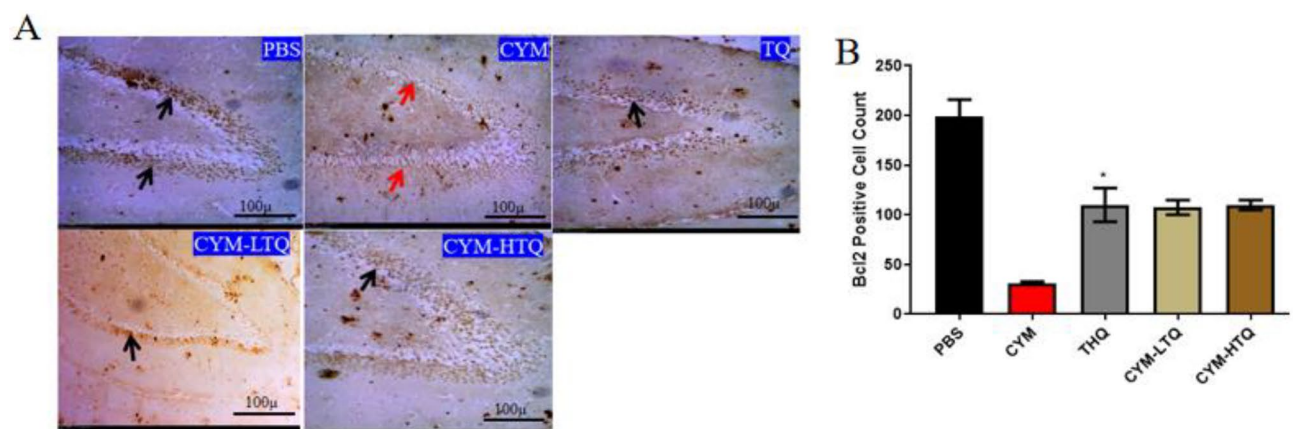


Fig. 5 Bcl2 expression in the dentate gyrus. **(A)** immunostaining for Bcl2 in the dentate gyrus (scale bar = 100 μm), PBS group showed high Bcl2 expression (black arrows). CYM group displayed low Bcl2 expression (red arrows); TQ group showed high Bcl2 expression (black arrows); CYM-LTQ presented high Bcl2 (black arrows) compared to CYM group; CYM-HTQ group also displayed numerous Bcl2 expression (black arrow) compared to CYM group. **(B)**. Bcl2 positive cell count. PBS group had significantly high Bcl2 positive cells (* $p < 0.05$) compared to CYM group. CYM group showed no significant difference (# $p < 0.05$) compared to TQ, CYM-LTQ and CYM-HTQ groups ($N = 6$). PBS = phosphate-buffered saline, CYM = cypermethrin, TQ = thymoquinone, CYM-LTQ = cypermethrin followed by low dose (5 mg/kg) thymoquinone and CYM-HTQ = cypermethrin followed by High dose (10 mg/kg) thymoquinone

In this study, cypermethrin caused a reduction in the expression of the Nuclear factor erythroid 2-related factor 2 (Nrf2), a regulatory protein responsible for initiating and expressing the antioxidant system. The reduced concentration and low expression of Nrf2 cells in the dentate gyrus of CYM-exposed rats are undoubtedly responsible for the reduction in the activities of the antioxidant enzymes SOD and GSH, leading to oxidative stress as indicated by the high level of MDA in CYM-exposed rats. Due to high unsaturated fatty acids, the brain is especially susceptible to oxidative stress, which causes membrane lipid peroxidation and disrupts the normal organizational structure of brain cells, as observed in

the dentate gyrus of CYM-exposed rats. Cypermethrin exposure caused neuronal damage, impaired Nissl body integrity, and induced chromatolytic-like changes in the dentate gyrus due to oxidative stress. It was observed that continuous CYM exposure not only disrupted neuronal shapes in the dentate gyrus but also induced Nrf2 expression. Since appropriate activation of Nrf2 and its nuclear translocation establishes the Nrf2/ARE complex and subsequently boosts the expression and synthesis of antioxidant enzymes, the decreased level of Nrf2 observed contributes to the lower activity of antioxidant enzymes SOD and GSH, which encourages further oxidative stress damage and raises the level of MDA. Cypermethrin

decreased the level and activity of antioxidant enzymes like SOD, GSH, and catalase (CAT) in cypermethrin-induced toxicity in the Wistar rat model of Parkinson's disease and peripheral blood. The findings of this study are indeed strengthened by earlier studies by [33–35], which reported an excessive increase in the level of MDA and reduced antioxidant capacity of SOD, CAT, GSH, and GPx, leading to increased lipid peroxidation in the peripheral blood and in the nigrostriatum of cypermethrin-exposed rats.

Intervention with thymoquinone was observed to reactivate Nrf2, as shown by the high expression of Nrf2 immunopositive cells. This increased nuclear availability of Nrf2 leads to the Nrf2/ARE complex, thereby stimulating the production and expression of antioxidant enzymes and resulting in high SOD and GSH activity, as reported in this study, and reduced MDA levels, indicating a low level of lipid peroxidation. This finding is consistent with an earlier study by [31], who found that the parent plant of thymoquinone, black seed oil, increased total antioxidant capacity and GSH while decreasing total ROS levels in rats exposed to Dichlorvos. The findings of this study are also strengthened by the study of Kanter, who reported enhancements in hepatic and pancreatic antioxidant capacities of catalase and GSH following *Nigella sativa* against STZ-induced diabetes in rats [36].

Apoptosis is characterized by morphological changes in cells such as nuclear pyknosis, DNA fragmentation, chromatin condensation, cytoskeleton destruction, membrane blebbing, formation of membrane apoptotic bodies phagocytosed by macrophages and so on [37]. Continuous exposure to environmental toxins frequently causes apoptosis in cells [38]. Anti-Bcl-2-stained dentate gyrus had a low expression of Bcl-2-positive cells due to cypermethrin exposure. Cypermethrin caused apoptosis in the rat brain by producing ROS and cytotoxins. Cypermethrin also induced apoptosis via mitochondrial damage, cytochrome c release, and activation of caspases 3 and 9, which are involved in both extrinsic and intrinsic apoptosis pathways [39–41]. When Bcl-2 and other anti-apoptotic proteins are cleaved by caspases following the initiation of apoptosis, their anti-apoptotic action is frequently converted to pro-apoptotic action [37]. The findings of this study are similar to the report of the previous study where a type 2 pyrethroid, deltamethrin, following its exposure in rats, induced apoptosis by increasing the level of Bax, caspase-3, cytochrome c, and decreasing the expression of Bcl-2 pro-survival proteins [42, 43]. Thymoquinone exhibits anti-apoptotic effects, as administration of thymoquinone brings about a marked increase in the expression of Bcl-2 immunopositive cells in the hippocampal dentate gyrus of the experimental rats. Bcl-2, as a pro-survival protein, has a hydrophilic carboxyl-terminal domain linked to mitochondria outer membrane

and helps preserve mitochondrial integrity, preventing unnecessary cytochrome c release and caspase activation [37]. Bcl-2 prevents Bax and other pro-apoptotic genes from oligomerizing, which stimulates the release of apoptogenic molecules from the mitochondria. Apart from inhibiting Bax oligomerization, Bcl-2 directly binds and inactivates B blocks cytochrome c release, and thus inhibits adaptor molecule APAF-1 and caspase-9 activation, thereby preventing caspase cascade activation [37, 44]. In accordance with the findings of this study [45], showed that thymoquinone, in concentrations of 10 M and 20 M, prevented arsenic-induced neurotoxicity, apoptosis, and cytotoxicity by either decreasing the levels of Bax or increasing the level of Bcl-2. Also, in agreement with the data of this study, a previous study revealed that thymoquinone administration decreased p53 and Bcl-2 gene expression but increased BAD gene expression in MCF-7 cells; however, it increased the expression of Bcl-2 gene and p53 gene but decreased Bax/BAD gene expression in non-cancer HEK293 cells [46].

In the dentate gyrus, basket cells constitute the GABAergic neurons in the granule layer with the receptors localized in the molecular layer. Reduced levels of parvalbumin-positive cells in the dentate gyrus of cypermethrin-exposed rats indicate that CYM inhibits GABAergic interneurons. GABAergic interneurons constitute the inhibitory neurons in the CNS that are vital for modulating various physiological activities [47]. Reduced GABAergic interneuron expression due to CYM exposure interferes with the activity of GABAergic interneurons and disrupts excitatory and inhibitory balance in the brain. Previous studies have shown that CYM hinders the opening of the voltage-gated chloride channels and inhibits the GABA-dependent uptake of chloride ions, resulting in hyper-excitation of neuronal cells and leading to changes in the delayed rectifier voltage-dependent potassium channel, which regulates neuronal excitability [15, 48, 49].

Thymoquinone enhances parvalbumin-positive cell expression against cypermethrin toxicity. The improvement in motor functions observed in this study, which is one of the crucial functions controlled by GABAergic interneurons, complements the increased expression of the Parvalbumin-positive cells [15]. As a result of thymoquinone's activation of GABA receptors, which results in hyperpolarization and inhibits neuronal activity, the N-methyl-D-aspartate NMDA receptor's enhanced glutamate functions produce prolonged neuronal stimulation [50]. According to earlier research by [51, 52], TQ increased GABA receptor activation after pentylenetetrazole-induced cardiotoxicity, epileptiform activity, and seizures in rats as well as seizures brought on by pentylenetetrazole.

Conclusion

Thymoquinone improves motor function by activating Nrf2, reducing the level of NF- κ B, increasing the activities of SOD and GSH, and decreasing the concentration of MDA against cypermethrin neurotoxicity. It also enhances the expression of parvalbumin-positive cells as well as Bcl-2-positive cells. Therefore, thymoquinone can be employed to manage pyrethroid and other insecticide poisoning.

Abbreviations

ROS	Reactive oxygen species
RNA	Ribonucleic acid
mtDNA	Mutations in mitochondrial DNA
Cyc	Cytochrome c
TQ	Thymoquinone
NRF2	Nuclear factor erythroid 2-related factor 2
NOR	Novel object recognition
Nrf2	Nuclear factor erythroid 2-related factor 2
Bcl2	B-cell lymphoma 2
MCE	MedChemExpress
NAFDAC	National authority for food and drugs administration control
SOD	Superoxide dismutase
GSH	Glutathione
MDA	Malondialdehyde
E	EL-Elabscience Biotechnology
4PL	Curve-four-parameter logistic curve
ANOVA	Analysis of variance
SEM	Standard error of mean
CYM	Cypermethrin
PBS	Phosphate-buffered saline
CYM	LTQ-cypermethrin followed by low-dose thymoquinone
CYM	HTQ-cypermethrin followed by High dose thymoquinone
H and E	Hematoxylin and eosin
CYM	LTQ-cypermethrin followed by low-dose thymoquinone
CYM	HTQ-cypermethrin followed by High dose thymoquinone
NMDA	N-methyl-D-aspartate *-singleasterisk
#	Hash

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12868-024-00896-7>.

Supplementary Material 1

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Author contributions

ALI: Conception, design, data collection data analysis, and interpretation, animal breeding, animal treatments, and writing of the manuscriptAAO: Conception, design, histochemical analysis and interpretation, critical revision and writing of the manuscriptFAS: Conception, design, histochemical analysis and interpretation, and critical revisionAI: Conception, design, histochemical analysis and interpretation, and critical revisionRYI: Conception, design, histochemical analysis and interpretation, and critical revisionLAO: Conception, design, data collection, biochemical analysis and interpretationSAB: Conception, design, data collection, biochemical analysis and interpretationSM: Conception, design, data collection, biochemical analysis and interpretationAOA: Conception, design, histochemical analysis and interpretation, and critical revisionOOO: Critical revision and referencing SMA: Conception, design, and project supervision.

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Data availability

Data submitted as supplementary file.

Declarations

Ethics approval and consent to participate

This study was approved by the University of Ilorin ethical review committee (UERC\ASN\2021\2137).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

- Angelova PR, Abramov AY. Role of mitochondrial ROS in the brain: from physiology to neurodegeneration. *FEBS Lett.* 2018;592:692–702. <https://doi.org/10.1002/1873-3468.12964>.
- Okesina A, Ajenikoko M, Mohammed A, Omoola O, Buhari M. Progesterone mitigates trimethyltin-induced hippocampal damage through oxidative stress biomarkers. *Trop J Health Sci.* 2022;29:27–31.
- Van Opendenbosch N, Lamkanfi M. Caspases in cell death, inflammation, and disease. *Immunity.* 2019;50:1352–64.
- Green DR, Lillambi F. Cell death signaling. *Cold Spring Harb Perspect Biol.* 2015;7:a006080. <https://doi.org/10.1101/cshperspect.a006080>.
- Okesina AA, Ajao MS, Buhari MO, Afodun AM, Okesina KB, Usman RY, et al. Activation of pro-apoptotic cells, reactive astrogliosis and hyperphosphorylation of tau protein in trimethyltin-induced hippocampal injury in rats. *Anat J Afr.* 2020;9:1782–8.
- Izumi Y, Kataoka H, Inose Y, Akaike A, Koyama Y, Kume T. Neuroprotective effect of an Nrf2-ARE activator identified from a chemical library on dopaminergic neurons. *Eur J Pharmacol.* 2018;818:470–9. <https://doi.org/10.1016/j.ejphar.2017.11.023>.
- Mohammadi H, Ghassemi-Barghi N, Malakshah O, Ashari S. Pyrethroid exposure and neurotoxicity: a mechanistic approach. *Archives Industrial Hygiene Toxicol.* 2019;70:74–89. <https://doi.org/10.2478/aiht-2019-70-3263>.
- Abdel-Daim M, El-Bialy BE, Rahman HGA, Radi AM, Hefny HA, Hassan AM. Antagonistic effects of *Spirulina platensis* against sub-acute deltamethrin toxicity in mice: biochemical and histopathological studies. *Biomed Pharmacother.* 2016;77:79–85. <https://doi.org/10.1016/j.biopha.2015.12.003>.
- Hamadache M, Benkortbi O, Hanini S, Amrane A, Khaouane L, Si Moussa C. A quantitative structure activity relationship for acute oral toxicity of pesticides on rats: validation, domain of application and prediction. *J Hazard Mater.* 2016;303:28–40. <https://doi.org/10.1016/j.jhazmat.2015.09.021>.

10. Afeez H. Food poisoning: How bacterial, chemical contamination, unsafe food handling cause children, adults' death - Punch Newspapers. Punchng. 2021. <https://punchng.com/food-poisoning-how-bacterial-chemical-contamination-unsafe-food-handling-cause-children-adults-death/> (accessed March 14, 2024).
11. Tang W, Wang D, Wang J, Wu Z, Li L, Huang M, et al. Pyrethroid pesticide residues in the global environment: an overview. *Chemosphere*. 2018;191:990–1007. <https://doi.org/10.1016/j.chemosphere.2017.10.115>.
12. Field LM, Emyr Davies TG, O'Reilly AO, Williamson MS, Wallace BA. Voltage-gated sodium channels as targets for pyrethroid insecticides. *Eur Biophys J*. 2017;46:675–9. <https://doi.org/10.1007/s00249-016-1195-1>.
13. Chen D, Yu SP, Wei L. Ion channels in regulation of neuronal regenerative activities. *Transl Stroke Res*. 2014;5:156–62. <https://doi.org/10.1007/s12975-013-0320-z>.
14. Hossain MM, Liu J, Richardson JR. Pyrethroid insecticides directly activate Microglia through Interaction with Voltage-gated Sodium channels. *Toxicol Sci*. 2017;155:112–23. <https://doi.org/10.1093/toxsci/kfw187>.
15. Kumar Singh A, Nath Tiwari M, Prakash O, Pratap Singh M. A current review of Cypermethrin-Induced neurotoxicity and Nigrostriatal Dopaminergic Neurodegeneration. *CN*. 2012;10:64–71. <https://doi.org/10.2174/157015912799362779>.
16. Shao Y, Li B, Huang Y, Luo Q, Xie Y, Chen Y. Thymoquinone attenuates brain injury via an antioxidative pathway in a status epilepticus rat model. *Translational Neurosci*. 2017;8. <https://doi.org/10.1515/tnsci-2017-0003>.
17. Dariani S, Baluchnejadmojarad T, Roghani M. Thymoquinone attenuates astrogliosis, neurodegeneration, Mossy Fiber sprouting, and oxidative stress in a model of temporal lobe Epilepsy. *J Mol Neurosci*. 2013;51:679–86. <https://doi.org/10.1007/s12031-013-0043-3>.
18. Isaev NK, Chetverikov NS, Stelmashook EV, Genrikhs EE, Khaspekov LG, Illarionov SN. Thymoquinone as a potential neuroprotector in Acute and Chronic forms of Cerebral Pathology. *Biochem Mosc*. 2020;85:167–76. <https://doi.org/10.1134/S0006297920020042>.
19. Ajenikoko MK, Ajagbe AO, Onigbinde OA, Okesina AA, Tijani AA. Review of Alzheimer's disease drugs and their relationship with neuron-glia interaction. *IBRO Neurosci Rep*. 2023;14:64–76. <https://doi.org/10.1016/j.ibneur.2022.11.005>.
20. He S, Zheng Y, Chen X. Assessing a new hip index as a risk predictor for diabetes mellitus. *J Diabetes Invest*. 2018;9:799–805. <https://doi.org/10.1111/jdi.12756>.
21. Jaramillo MC, Zhang DD. The emerging role of the Nrf2–Keap1 signaling pathway in cancer. *Genes Dev*. 2013;27:2179–91. <https://doi.org/10.1101/gad.225680.113>.
22. Alcantara-Martinez N, Guizar S, Rivera-Cabrera F, Anicacio-Acevedo BE, Buendia-Gonzalez L, Volke-Sepulveda T. Tolerance, arsenic uptake, and oxidative stress in *Acacia farnesiana* under arsenate-stress. *Int J Phytoremediation*. 2016;18:671–8.
23. Gureev AP, Popov VN. Nrf2/ARE pathway as a therapeutic target for the treatment of Parkinson diseases. *Neurochem Res*. 2019;44:2273–9. <https://doi.org/10.1007/s11064-018-02711-2>.
24. Miedel CJ, Patton JM, Miedel AN, Miedel ES, Levenson JM. Assessment of Spontaneous Alternation, Novel Object Recognition and Limb Claspings in Transgenic Mouse Models of Amyloid- β 946; and Tau Neuropathology. *JoVE*. 2017;55523. <https://doi.org/10.3791/55523>.
25. Gonzalez-Riano C, Tapia-González S, García A, Muñoz A, DeFelipe J, Barbas C. Metabolomics and neuroanatomical evaluation of post-mortem changes in the hippocampus. *Brain Struct Funct*. 2017;222:2831–53. <https://doi.org/10.1007/s00429-017-1375-5>.
26. Fischer AH, Jacobson KA, Rose J, Zeller R. Hematoxylin and eosin staining of tissue and cell sections. *Cold Spring Harb Protoc*. 2008;2008(pdbprot4986). <https://doi.org/10.1101/pdb.prot4986>.
27. Kádár A, Wittmann G, Liposits Z, Fekete C. Improved method for combination of immunocytochemistry and nissl staining. *J Neurosci Methods*. 2009;184:115–8. <https://doi.org/10.1016/j.jneumeth.2009.07.010>.
28. Kari E, Teppo H-R, Haapasaari K-M, Kuusisto MEL, Lemma A, Karihtala P, et al. Nuclear factor erythroid 2-related factors 1 and 2 are able to define the worst prognosis group among high-risk diffuse large B cell lymphomas treated with R-CHOP. *J Clin Pathol*. 2019;72:316–21. <https://doi.org/10.1136/jclinpath-2018-205584>.
29. Glick D, editor. *Methods of biochemical analysis*. Volume 1. New York: Interscience Publishers, Inc.; 1954.
30. Ellman GL. Tissue sulfhydryl groups. *Arch Biochem Biophys*. 1959;82:70–7. [https://doi.org/10.1016/0003-9861\(59\)90090-6](https://doi.org/10.1016/0003-9861(59)90090-6).
31. Imam A, Sulaiman NA, Oyewole AL, Chengetanai S, Williams V, Ajibola MI, et al. Chlorpyrifos- and Dichlorvos-Induced oxidative and neurogenic damage elicits neuro-cognitive deficits and increases anxiety-like Behavior in Wild-Type rats. *Toxics*. 2018;6:71. <https://doi.org/10.3390/toxics6040071>.
32. Aminu I, Moyosore Salu A, Abdulbasit A, Wahab Imam A, Abdulmumin I, Olajide, et al. Cannabis-induced Moto-cognitive dysfunction in Wistar rats: ameliorative efficacy of *Nigella Sativa*. *MJMS*. 2016;23:17–28. <https://doi.org/10.21315/mjms2016.23.5.3>.
33. Agrawal S, Dixit A, Singh A, Tripathi P, Singh D, Patel DK, et al. Cyclosporine A and MnTMPyP alleviate α -Synuclein expression and aggregation in Cypermethrin-Induced parkinsonism. *Mol Neurobiol*. 2015;52:1619–28. <https://doi.org/10.1007/s12035-014-8954-8>.
34. Tripathi P, Singh A, Agrawal S, Prakash O, Singh MP. Cypermethrin alters the status of oxidative stress in the peripheral blood: relevance to parkinsonism. *J Physiol Biochem*. 2014;70:915–24. <https://doi.org/10.1007/s13105-014-0359-7>.
35. Abdelhafidh K, Mhadhbi L, Mezni A, Badreddine S, Beyrem H, Mahmoudi E. Protective effect of *Zizyphus lotus* jujube fruits against cypermethrin-induced oxidative stress and neurotoxicity in mice. *Biomarkers*. 2018;23:167–73. <https://doi.org/10.1080/1354750X.2017.1390609>.
36. Kanter M, Coskun O, Korkmaz A, Oter S. Effects of *Nigella sativa* on oxidative stress and β -cell damage in Streptozotocin-induced diabetic rats. *Anat Rec*. 2004;279A:685–91. <https://doi.org/10.1002/ar.a.20056>.
37. Tzifi F, Economopoulou C, Gourgiotis D, Ardavanis A, Papageorgiou S, Scorilas A. The role of BCL2 family of apoptosis Regulator proteins in Acute and Chronic Leukemias. *Adv Hematol*. 2012;2012:1–15. <https://doi.org/10.1155/2012/524308>.
38. Redza-Dutordoir M, Averill-Bates DA. Activation of apoptosis signalling pathways by reactive oxygen species. *Biochimica et Biophysica Acta (BBA) - Mol Cell Res*. 2016;1863:2977–92. <https://doi.org/10.1016/j.bbamcr.2016.09.012>.
39. Martinez MM, Reif RD, Pappas D. Detection of apoptosis: a review of conventional and novel techniques. *Anal Methods*. 2010;2:996–1004. <https://doi.org/10.1039/C0AY00247J>.
40. Wong RS. Apoptosis in cancer: from pathogenesis to treatment. *J Exp Clin Cancer Res*. 2011;30:87. <https://doi.org/10.1186/1756-9966-30-87>.
41. Ko J, Park JH, Park YS, Koh HC. PPAR- γ activation attenuates deltamethrin-induced apoptosis by regulating cytosolic PINK1 and inhibiting mitochondrial dysfunction. *Toxicol Lett*. 2016;260:8–17. <https://doi.org/10.1016/j.toxlet.2016.08.016>.
42. Gasmi S, Rouabhi R, Kebieche M, Boussekine S, Salmi A, Toulbia N, et al. Effects of Deltamethrin on striatum and hippocampus mitochondrial integrity and the protective role of Quercetin in rats. *Environ Sci Pollut Res*. 2017;24:16440–57. <https://doi.org/10.1007/s11356-017-9218-8>.
43. Khalatbary AR, Ghaffari E, Mohammadnegad B. Protective role of oleuropein against Acute Deltamethrin-Induced neurotoxicity in rat brain. *Iran Biomed J*. 2015;19:247–53. <https://doi.org/10.7508/ibj.2015.04.009>.
44. Stewart CR, Stuart LM, Wilkinson K, Van Gils JM, Deng J, Halle A, et al. CD36 ligands promote sterile inflammation through assembly of a toll-like receptor 4 and 6 heterodimer. *Nat Immunol*. 2010;11:155–61.
45. Firdaus F, Zafeer MF, Anis E, Ahmad F, Hossain MM, Ali A, et al. Evaluation of phyto-medicinal efficacy of thymoquinone against Arsenic induced mitochondrial dysfunction and cytotoxicity in SH-SY5Y cells. *Phytomedicine*. 2019;54:224–30. <https://doi.org/10.1016/j.phymed.2018.09.197>.
46. Yildirim IH, Azzawri AA, Duran T. Thymoquinone induces apoptosis via targeting the Bax/BAD and Bcl-2 pathway in breast cancer cells. *Dicle Tip Dergisi*. 2019;41(17). <https://doi.org/10.5798/dicletip.620329>.
47. Xu M, Wong AHC. GABAergic inhibitory neurons as therapeutic targets for cognitive impairment in schizophrenia. *Acta Pharmacol Sin*. 2018;39:733–53. <https://doi.org/10.1038/aps.2017.172>.
48. Ullah R, Rehman A, Zafeer MF, Rehman L, Khan YA, Khan MAH, et al. Anthelmintic potential of Thymoquinone and Curcumin in *Fasciola gigantica*. *PLoS ONE*. 2017;12:e0171267. <https://doi.org/10.1371/journal.pone.0171267>.
49. Yu-Tao T, Zhao-Wei L, Yang Y, Zhuo Y, Tao Z. Effect of alpha-cypermethrin and theta-cypermethrin on delayed rectifier potassium currents in rat hippocampal neurons. *Neurotoxicology*. 2009;30:269–73. <https://doi.org/10.1016/j.neuro.2009.01.001>.
50. Pottot FH, Ibrahim AM, Alammam A, Alsinan R, Aleid M, Alshehhi A, et al. Thymoquinone: review of its potential in the treatment of neurological diseases. *Pharmaceuticals*. 2022;15:408. <https://doi.org/10.3390/ph15040408>.
51. Akgül B, Aycan İÖ, Hidişoğlu E, Afşar E, Yıldırım S, Tanrıöver G, et al. All-leviation of prilocaine-induced epileptiform activity and cardiotoxicity by

thymoquinone. *DARU J Pharm Sci.* 2021;29:85–99. <https://doi.org/10.1007/s40199-020-00385-2>.

52. Seghatoleslam M, Alipour F, Shafieian R, Hassanzadeh Z, Edalatmanesh MA, Sadeghnia HR, et al. The effects of *Nigella sativa* on neural damage after pentylenetetrazole induced seizures in rats. *J Traditional Complement Med.* 2016;6:262–8. <https://doi.org/10.1016/j.jtcme.2015.06.003>.

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