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# MJM

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#### Example references Journals:

##### Standard Journal Article

Rampal L and Liew BS. Coronavirus disease (COVID-19) pandemic. *Med J Malaysia* 2020; 75(2): 95-7.

Rampal L, Liew BS, Choolani M, Ganasegeran K, Pramanick A, Vallibhakara SA, et al.

Battling COVID-19 pandemic waves in six South-East Asian countries: A real-time consensus review. *Med J Malaysia* 2020; 75(6): 613-25.

NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. *Lancet* 2021; 11; 398(10304): 957-80.

#### Books and Other Monographs:

##### Personal Author(s)

Goodman NW, Edwards MB. 2014. *Medical Writing: A Prescription for Clarity*. 4 th Edition. Cambridge University Press.

##### Chapter in Book

McFarland D, Holland JC. Distress, adjustments, and anxiety disorders. In: Watson M, KISSANE D, Editors. *Management of clinical depression and anxiety*. Oxford University Press; 2017: 1-22.

##### Corporate Author

World Health Organization, Geneva. 2019. WHO Study Group on Tobacco Product Regulation. Report on the scientific basis of tobacco product regulation: seventh report of a WHO study group. WHO Technical Report Series, No. 1015.

NCD Risk Factor Collaboration (NCD-RisC). Rising rural body-mass index is the main driver of the global obesity epidemic in adults. *Nature* 2019; 569: 260-64.

World Health Organization. Novel Coronavirus (2019-nCoV) Situation Report 85, April 14, 2020. [cited April 2020] Accessed from: <https://www.who.int/docs/defaultsource/coronaviruse/situationreports/20200414-sitrep-85-covid-19>.

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Ministry of Health Malaysia. Press Release: Status of preparedness and response by the ministry of health in and event of outbreak of Ebola in Malaysia 2014 [cited Dec 2014]. Available from: [http://www.moh.gov.my/english.php/database\\_stores/store\\_view\\_page/21/437](http://www.moh.gov.my/english.php/database_stores/store_view_page/21/437).

#### Other Articles:

##### Newspaper Article

Panirchellvum V. 'No outdoor activities if weather too hot'. *the Sun*. 2016; March 18: 9(col. 1-3).

##### Magazine Article

Rampal L. World No Tobacco Day 2021 -Tobacco Control in Malaysia. *Berita MMA*. 2021; May: 21-22.

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# AI application in MRI & CT

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## **ABSTRACT**

Transformation in the realm of medical imaging, specifically within the domains of MRI and CT scans. This presentation serves as a comprehensive exploration into the multifaceted applications of AI technologies that have fundamentally reshaped the landscape of medical diagnosis. By harnessing the power of AI, healthcare professionals are witnessing a paradigm shift in the accuracy, speed, and efficiency of diagnosing a myriad of medical conditions through the lens of MRI and CT scans. With a laser focus on image recognition capabilities and the integration of automated diagnosis systems, AI is not just a promising tool but a transformative force that is revolutionizing healthcare outcomes. The seamless synergy between AI algorithms and medical imaging modalities has redefined the way medical professionals interpret and analyze results, enabling them to make more informed decisions with precision and confidence. As we delve deeper into the crux of this presentation, we invite you to embark on a journey with us to uncover the profound impact of AI in revolutionizing the analysis of MRI and CT scans. Through illuminating case studies, success stories, and cutting-edge research findings, we aim to showcase the immense potential of AI in augmenting diagnostic processes and ultimately improving patient outcomes. Join us in unraveling the intricate tapestry of AI's transformative influence on medical imaging practices and charting a path towards a future where innovation and technology converge to redefine the boundaries of healthcare excellence.

# Translating neuropathological marker of dementia syndromes into structural MRI

**Norzaini Rose Mohd Zain**<sup>1,2</sup>

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## **ABSTRACT**

Alzheimer's disease is the most common cause of dementia characterized by progressive neurodegeneration accompanied by cognitive impairments. With the rapid development of neuroimaging technology, it is possible to diagnose AD through neuroimaging. The images commonly used in the clinical detection of AD include MRI, which permits the anatomical imaging of neurodegenerative disease with improved resolution, and Positron Emission Tomography (PET). Development of PET ligands specific for pathological substances such as  $\beta$ -amyloid ( $A\beta$ ) and phosphorylated tau provides new perspectives on the diagnosis of dementia. Accumulation of amyloid plaques and neurofibrillary tangles in AD is contemplated to induce neural and synaptic loss that finally leads to cortical atrophy. Specific patterns of cortical atrophy distinguish typical AD from other neurodegenerative dementias such as frontotemporal dementia (FTD), corticobasal degeneration (CBD), progressive supranuclear palsy (PSP), and vascular dementia. Cortical atrophy patterns also potentially estimate preclinical or prognostic tissue damage in vulnerable regions such as the hippocampus and entorhinal cortex. Despite advancements made in structural MR imaging, radiologists are often reluctant to make specific diagnosis of clinical dementia based on subtle findings such as mild regional atrophy, which makes early diagnosis of AD often neglected or missed. Therefore, the introduction of a systematic and practical approach to the structural imaging diagnosis in AD is required as it remains the workhorse within the clinical practice. If done well, structural imaging plays a role in the identification and classification of dementia syndromes. Understanding the specific patterns of atrophy allows us to assess pathological progression over time and even physiological change in dementia syndromes.

# Functional MRI: An insight and pitfalls

**Norlisah Ramli**<sup>1,2</sup>

<sup>1</sup>Department of Biomedical Imaging, University of Malaya Medical Centre, Malaysia, <sup>2</sup>President, College of Radiology, Academy of Medicine Malaysia, Malaysia

## **ABSTRACT**

Functional MRI (fMRI) stands as a pivotal tool offering unparalleled insights into the functioning brain. However, its application is not without challenges and limitations. This lecture delves into the intricacies of fMRI, offering a comprehensive overview to both budding researchers and seasoned experts. From the underlying principles of fMRI to its applications in understanding neural processes, attendees will gain a nuanced understanding of this powerful technique. Moreover, the discussion will address the pitfalls and nuances inherent in fMRI data analysis, ensuring attendees are equipped to navigate the complexities of interpreting results accurately.

# MEG, TMS and AI in paediatric neuroimaging

**Noryati Mohammad**

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## **ABSTRACT**

Current medical advancement demands a highly accurate revelation of abnormalities and their sources. These prerequisites include the challenging conditions, hence new technologies are required to be established and incorporated in the management strategies. Magnetoencephalography (MEG) is a new dedicated development contributes substantially to the treatment of many neurological diseases while artificial intelligent (AI) is the groundbreaking new tool which calculates accurately the abnormalities via computerization to expedite the detection to assist the demanding radiology field. On the treatment perspective, Transcranial Magnetic Stimulation (TMS) provides a new light in management of difficult neurological disorders which in the past solely relied on the drugs and conventional rehabilitations.

# Introduction neuroscience and neuroimaging -bridging the gap between neurons and new technologies

**Subapriya Suppiah**<sup>1,2,3,4</sup>

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## **ABSTRACT**

The widespread adoption of artificial intelligence in medical imaging has become commonplace amidst the rapid progress of technology. In the realm of neuroscience and neuroimaging, advanced technologies like MRI, SPECT/CT, PET/CT, and EEG now leverage AI for enhanced data analysis, research, and streamlined clinical workflows. Neuroscience delves into the study of neurochemistry and experimental psychology, aiming to comprehend the functionality of neurons and other components of the brain and nervous system. Conversely, neuroimaging entails generating images that depict the structure or activity of the brain and nervous system using techniques such as MRI, CT, or EEG. This intersection allows for non-invasive exploration of the human brain's functions, employing cutting-edge technologies like computers, scanners, and software. In essence, NeuroCoB Society Malaysia serves as a collaborative platform, uniting radiologists, neuroscientists, nuclear medicine physicians, computer scientists, computer engineers, medical physicists, and imaging technologists. The emphasis is on fostering discoveries and innovations in brain imaging to map the unexplored terrain of the human brain and mind.



# Designing nuclear neurology imaging research -handy tips for clinicians

**Mahayuddin Abdul Manap<sup>1,2</sup>**

<sup>1</sup>Institut Perubatan dan Pergigian Termaju, Universiti Sains Malaysia, Kepala Batas, Pulau Pinang, Malaysia, <sup>2</sup>President, Malaysian Society of Nuclear Medicine and Molecular Imaging

## **ABSTRACT**

The 20th century was the century for the development of structural imaging of disease then it can say that the 21st century has the potential to be that of functional imaging. Significant advances especially in the molecular imaging technologies has driven up the utilization of this technologies in clinical imaging. In neurology, the molecular aspect of nuclear medicine imaging is playing an important role in the advancement of neuroimaging. It enables structural and functional data to be combined to provide a 'window' into the living brain. However, the human brain is known to be the most complicated organ for anyone to understand. This remains true even for the clinician, the group of people who were given the task of handling the organ medically. Despite all the clinical advancement, clinicians can still be at a loss and require assistance in guiding their clinical decision. Thus, good neurological research has to be formulated accordingly in order to answer the clinical questions at hand. It is hoped that this lecture will provide everyone, even more the clinician, with the necessary tips and tricks in designing outstanding nuclear neurology imaging research.

# PET/CT and molecular imaging in neurological disorders

**Kamalia Kamarulzaman**

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## **ABSTRACT**

In recent years, positron emission tomography-computed tomography (PET-CT) and molecular imaging techniques have revolutionized the diagnosis and management of neurological disorders. Molecular imaging offers two key advantages: first, it detects biological processes at the underlying molecular level, rather than simply at the tissue level; and second, compared with conventional anatomic imaging, it provides diagnostic information at an earlier time point during a disease onset or repair process. PET-CT enables the visualization and quantification of metabolic processes and receptor densities in the brain, offering valuable insights into the pathophysiology of neurological disorders. By utilizing radiotracers specific to neurotransmitter systems and metabolic pathways, PET CT and molecular imaging facilitate the identification of aberrant molecular signatures associated with conditions such as Alzheimer's disease, Parkinson's disease, epilepsy, and encephalitis. Molecular imaging techniques, including amyloid and tau PET imaging, have emerged as promising tools for early detection and differential diagnosis of neurodegenerative diseases. PET-CT and molecular imaging also play a pivotal role in the development and evaluation of novel therapeutic interventions for neurological disorders. One significant advancement for F18 FDG PET brain interpretation is the widespread use of statistical mapping for image interpretation and analysis. This approach not only improves overall diagnostic accuracy but also quantitative information on the significance level of detected abnormalities, helps to standardize interpretation, allows cross-institutional comparisons and helps support consistent scan interpretation by physicians with different levels of experience. By enabling the precise localization of disease pathology and monitoring treatment response, these imaging modalities facilitate personalized medicine approaches, leading to improved patient outcomes and therapeutic efficacy. In conclusion, PET-CT and molecular imaging represent invaluable tools in the diagnosis, management and research of neurological disorders. As technology continues to evolve and new radiotracers are developed, the potential of PET-CT and molecular imaging to transform our understanding and treatment of neurological conditions hold great promise for the future of neurology.

# Nuclear medicine application and innovation in neuroimaging

**Yeong Chai Hong**

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## **ABSTRACT**

The field of nuclear medicine has undergone transformative advancements in recent years, particularly in the realm of neuroimaging. Scintigraphy techniques such as single photon emission computed tomography (SPECT) and positron emission tomography (PET) provide qualitative and quantitative measurement of brain activity in both physiological and pathological states. This lecture delves into the cutting-edge technologies in nuclear medicine for the application of neurological studies. Emphasis will be placed on recent development in radiopharmaceutical, highlighting novel tracers designed for specific neuroreceptor imaging and molecular targeting. These innovations not only enhance diagnostic accuracy but also pave the way for personalized therapeutic interventions, marking a paradigm shift in the approach to neurological disorders. Furthermore, the integration of artificial intelligence (AI) in nuclear medicine for image analysis and interpretation will also be explored. This transformative synergy between nuclear medicine and AI promises to streamline diagnostics, improve quantitative assessments, and revolutionize the precision of treatment planning in neuroimaging.

# Human induced pluripotent stem cells-derived neural models for translational research in neurogenomic era

**Michael Ling King Hwa**

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## **ABSTRACT**

The advent of human induced pluripotent stem cells (hiPSCs) has revolutionized translational neuroscience, offering unprecedented opportunities to model neurodevelopmental and neurodegenerative disorders in vitro. Patient-derived hiPSCs for disease modelling allow the recapitulation of patient-specific genetic backgrounds and cellular phenotypes during disease onset and development. By reprogramming somatic cells into a pluripotent state, hiPSCs can be differentiated into various neural lineages, including neurons, astrocytes, and oligodendrocytes, faithfully representing the complexity of the human brain. HiPSC-derived 3D cerebral organoids or mini-brains in a dish have been proven beneficial to model more complex neurological disorders such as neurodegenerative and neuropsychiatric diseases in elucidating the pathogenic mechanisms underlying neurodevelopmental basis of Alzheimer's disease, bipolar disorder, and Down syndrome. These models recapitulate disease-specific phenotypes, such as protein aggregation, mitochondrial dysfunction, and synaptic loss, enabling screening potential disease-modifying therapies and personalized medicine approaches. Integrating hiPSC-derived neural models with cutting-edge genomic technologies, such as CRISPR/Cas9 genome editing and single-cell/bulk RNA sequencing, can unravel the genetic architecture of complex neurological traits and identify disease-associated genetic variants. In conclusion, hiPSC-derived neural models represent a powerful tool for translational research in the neurogenomic era, offering unprecedented opportunities to dissect the molecular and cellular mechanisms underlying neurological disorders and accelerate the development of precision therapies.

# MRI spectroscopy

**Azlan Che Ahmad**

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## **ABSTRACT**

Magnetic Resonance Spectroscopy (MRS) has emerged as a powerful biomedical imaging tool, offering unique insights into the molecular composition of tissues and organs. While magnetic resonance imaging (MRI) provides detailed anatomical images, MRS goes a step further by revealing biochemical information about tissues. Through spectral analysis, MRS generates valuable data about metabolite concentrations, chemical environments, and metabolic pathways. In this talk, I will explain the fundamental principles of MRS and explore its diverse applications in biomedicine.

# Technical development of artificial intelligence in magnetic resonance spectroscopy

**Hyeong Hun Lee**

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## **ABSTRACT**

This study investigates the application of Deep Learning (DL) techniques for enhancing Magnetic Resonance Spectroscopy (MRS) analysis of brain metabolites, with a focus on neurodegenerative diseases. MRS, a non-invasive tool capable of detecting around 20 metabolites in the human brain, faces challenges in clinical settings due to data quality variability and analysis software selection. By employing a fine-tuned Bayesian Convolutional Neural Network (BCNN) trained on an extensive in-silico MRS dataset, this study aims to improve the quantification of brain metabolites, thereby facilitating the diagnosis and study of degenerative brain diseases. The methodology involved multi-institutional MRS analyses on a cohort of healthy adults and examination of natural variations in brain metabolites in the posterior cingulate cortex among different ages. The study also includes a literature review on brain metabolites associated with neurodegenerative diseases. Results demonstrated that the proposed method significantly outperformed the traditional LCModel in quantification accuracy, reducing coefficients of variation and detecting metabolite changes associated with aging more effectively. Notably, the DL-aided analysis revealed statistically significant changes in nine brain metabolites, compared to only three identified by the LCModel. The findings highlight the DL approach's superior generalization performance and its potential for precise detection of metabolite changes. Furthermore, the literature review identified key metabolites such as N-acetylaspartate, myo-Inositol, gamma-aminobutyric acid, glutathione, glutamate, and glutamine, emphasizing their importance in diagnosing and understanding neurodegenerative diseases. In conclusion, DL-enhanced MRS analysis holds promise for medical research and clinical applications, particularly in identifying metabolite biomarker for neurodegenerative diseases.



# AI application in nuclear medicine

**Kenji Hirata**

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## **ABSTRACT**

In the realm of nuclear medicine, the integration of artificial intelligence (AI) has the potential to revolutionize diagnostic and therapeutic practices. My lecture will explore the synergistic relationship between the three fundamental components of nuclear medicine: the tracer, the scanner, and the software. Each component complements the others, forming a cohesive system that enhances the accuracy and efficiency of medical imaging. A focal point of the lecture will be the application of AI in diagnosing Alzheimer's disease (AD). While amyloid PET is a well-known diagnostic tool for AD, AI can also significantly enhance the diagnostic capabilities of FDG PET scans. AI's contributions to nuclear medicine are vast, encompassing lesion detection, characterization, and segmentation, as well as image generation and quality improvement. Notably, AI can generate images from different PET tracers and perform attenuation correction without the need for CT scans. In this lecture, I will introduce Metavol, a free software we developed to simplify the measurement of SUV, metabolic tumor volume (MTV), and total lesion glycolysis (TLG). Metavol aims to streamline the workflow for clinicians and researchers by providing easy-to-use tools for comprehensive image analysis. Additionally, I will present preliminary results from a statistical analysis conducted after anatomical normalization for whole-body PET scans. These findings underscore the potential of AI-enhanced nuclear medicine to provide more precise and individualized patient care. This lecture will provide an insightful overview of how AI is transforming nuclear medicine, offering practical examples and demonstrating the capabilities of innovative tools.

# Reproducible neuroimaging for everyone – how NeuroDesk uses software containers to make neuroimaging more accessible, portable, and reproducible

**Steffen Bollmann**

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## **ABSTRACT**

Neuroimaging data analysis requires a diverse collection of bespoke command-line and graphical tools. Installing and maintaining a neuroimaging software setup is challenging and often results in un-reproducible environments. We developed NeuroDesk, a platform built on container technology for processing and analysing neuroimaging data with the aim to lower the barrier of using various neuroimaging software in a reproducible environment. We developed a modular and open analysis environment consisting of a continuous integration system on Github to automatically build neuroimaging software containers based on community input. We also developed a toolset around software containers to make them easy to use. We provide all tools within a lightweight Linux desktop container accessible via a browser interface that runs on any operating system supporting Docker. Our open-source project (<https://www.neurodesk.org>) enables researchers and clinicians to use various neuroimaging software on any operating system. We developed a scalable and interoperable way of running scientific tools on any compute platform accessible to researchers and clinicians. The benefits of this setup are an easy-to-use and reproducible environment for neuroimaging data analysis. NeuroDesk enables to run a fully reproducible environment on cloud, on windows/mac or on a high-performance computing system and seamlessly transition between different hardware setups.

# Real time fMRI / Neurofeedback

**Epifanio Bagarinao**

Brain and Mind Research Centre of Nagoya University, Japan

## **ABSTRACT**

Current diagnostic procedures for neuropsychiatric disorders rely heavily on behavioral criteria. As a result, the diagnosis of these disorders can be influenced by several factors that can strongly affect diagnostic reliability including patient's psychological state, clinician training and experience, and inadequacy in disease nomenclature, among others. For the treatment to be effective, the correct identification of the disorder is crucial. Thus, it is imperative that patient assessments be based on more objective measures. Recent advances in brain imaging technology have enabled researchers to noninvasively identify changes occurring in the brains of patients with various neurological and psychiatric disorders. As such, several studies have investigated the feasibility of utilizing these changes as potential neuroimaging-based biomarkers of these disorders using machine learning algorithms, such as support vector machines, enabling the classification of patients from healthy controls. This talk will introduce techniques using magnetic resonance imaging to identify changes in brain structure and its functional organization in various brain disorders as well as present applications of machine learning algorithms in classifying patients from healthy controls based on these changes.

# Generative AI: Case studies in neuroimaging

**Eric Ho Tatt Wei**

Universiti Teknologi PETRONAS, Seri Iskandar, Perak, Malaysia

## **ABSTRACT**

Generative AI, a subset of artificial intelligence focused on creating new content from learned patterns, is revolutionizing various fields, including neuroimaging. This presentation explores groundbreaking case studies where generative AI has been applied to neuroimaging, demonstrating its potential to enhance diagnostic accuracy, streamline workflows, and uncover novel insights into brain function and structure. Key applications include the generation of synthetic brain images to augment training datasets, the reconstruction of high-resolution images from low-quality scans, and the identification of subtle patterns linked to neurological conditions. By showcasing these case studies, we aim to illustrate the transformative impact of generative AI on neuroimaging, highlighting both its current achievements and future possibilities. This presentation will be of interest to healthcare professionals, researchers, and technologists eager to understand how advanced AI techniques are shaping the future of neuroimaging.

# Preprocessing scalp-recorded EEG

**Makoto Miyakoshi**

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## **ABSTRACT**

EEG artifact removal and Artifact Subspace Reconstruction (ASR) is discussed in depth. In the conventional manual artifact rejection, we typically scroll multi-channel time-series data page by page to select a time window for rejection. Many researchers have considered this process as most basic and natural approach as long as human resource and their level of experience allow. However, this method fails to live up to expectations in the face of modern research requirements and standards, such as processing a large number ( $> 10^2$ - $10^4$ ) of datasets with complete reproducibility. Besides, I argue that this time-window rejection is actually unnatural because of the discontinuities introduced as a result of arbitrary splicing, which I visually confirm in the time-frequency domain plot. To address these issues, I introduce ASR. ASR is an automated sliding-window linear spatial filter method that targets high-frequency bursts, short or long, suitable for cleaning continuous data. ASR learns a clean part of the data as a reference and applies it after sliding-window component rejection, which distinguishes ASR from an adaptive sliding-window PCA methods. I demonstrate an extreme example using simulation in which 100% of data are rejected according to the conventional time-window rejection with amplitude threshold, while they are 100% salvaged with minimal change confirmed by pre-post ERP waveform comparison. It is concluded that ASR is one of the promising candidates for the dream solution for all EEG researchers about EEG signal preprocessing for artifact rejection.

# Precision with neuromodulation in neuropsychiatric disorder

**Sagarika Bhattacharje**

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## **ABSTRACT**

With the advancement of newer techniques of neuromodulation and neuroimaging, interindividual variability in the treatment response has surfaced as a major challenge. The present presentation will discuss how neuroimaging and mathematical modelling can help us solve such puzzles. For, complex problems like selective stimulation of dorsal and ventral network of cognitive behavior like reading that exist in close vicinity can be addressed by prior computational simulation. Structural T1 scans can be utilized to simulate the optimal electrode positions of brain stimulation technique like transcranial direct current stimulation (tDCS). This is published as a toolbox to be used by the scientific community named "SATA". Using the SATA customized montages in an experiment, it was found that network specific improvement in reading behavior is possible following brain stimulation. However, the improvement depends on an individual's baseline proficiency and there is significant inter-individual variability in the magnitude of improvement. Such variability could be result of interindividual variability in brain morphometry thereby causing variable current reaching the target region. Publicly available neuroimaging big data set was used to investigate this hypothesis. It was found that as the person ages, gender plays an important role in determining the spread of current at the desired brain region, and this is primarily mediated by degree of brain atrophy and shift in midline torque. So, the existing strategy of using same dosage for all individual or a "one size fits all" strategy of might not be adequate. To obtain an optimal benefit, there is an increasing demand for customizing brain stimulation parameters according to individual needs. So again, a toolbox was developed so that adequate dosage and electrode positions could be determined based on individual anatomy of an individual. Using neuroimaging, it was also shown that the location of CSF pockets in the brain relative to the placement of tDCS electrodes on the scalp influences the focality of tDCS current in the target region.-CSF pockets that are in the path between target and reference electrodes, and that are close to the target, tend to direct current into the target region, so individuals with greater amounts of CSF in those pockets show greater tDCS focality in the target region. In contrast, CSF pockets that are closer to the reference electrode and farther from the target will flux most of the current towards the distant reference electrode, so individuals with greater amounts of CSF in those pockets show reduced tDCS focality in the target region. Such findings are beneficial in designing any treatment protocol for patients using neuromodulation. Neuroimaging guided neuromodulation can be very helpful in not only identifying brain networks underlying the disease process but also the compensatory ways by which neuroplasticity could be leveraged to benefit cognitive impairment in patient. The stimulation of functionally intact network might fetch more results where there is room for improvement, rather than stimulating a damaged network. Inspired by this, a collaborative project shows that when the frontostriatal network is dissociated in OCD patients, a compensatory occipital-cerebellar network is developed that correlate with the disease severity score. Such networks could be the potential targets for brain stimulation and decreasing the disease severity. Such works with neuroimaging are especially important to direct the clinicians in exploring different neuromodulation sites and parameter so that the desired benefits could be achieved for the patient.



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# Applications of portable magnetic resonance imaging in neuroimaging of critically ill patients: A systematic review

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## ABSTRACT

**Introduction:** Magnetic resonance imaging (MRI) is one of the preferred imaging modalities in neuroimaging. However, the use of conventional MRI is often associated with the risk of adverse events during intrahospital transport (IHT) and MRI-related accidents for patients in the intensive care unit (ICU) or emergency department (ED). Portable MRI (pMRI) has been proposed to be a safer approach than conventional MRI for neuroimaging critically ill patients in the ICU or ED. **Materials and Methods:** This review identifies the type of brain abnormalities that can be diagnosed by pMRI for critically ill patients in the ICU or ED and evaluates its feasibility features. A systematic review was performed through a comprehensive literature search in PubMed, Scopus, and the Hyperfine website. Two reviewers independently reviewed relevant articles based on the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) guidelines. **Results:** Nine studies were included, comprising 410 adults and 14 neonates from ICU and ED. Of these numbers, 386 had brain abnormalities or were suspected of having them, and 38 were healthy controls. The types of brain abnormalities diagnosed using pMRI during neuroimaging of critically ill patients in ICU and ED were brain haemorrhage, stroke, infections, injury, neoplasms, and neonatal brain abnormalities. The feasibility features of pMRI include shorter scanning duration, patient and staff safety, mobility, and requirements in neuroimaging critically ill patients. **Conclusion:** Notably, pMRI can diagnose multiple brain abnormalities and is feasible for use on critically ill patients in ICU and ED. Nevertheless, more work is warranted to explore further the deployment of pMRI in emergency and neonatal examinations.

# Brain research agenda setting and its role in promoting advanced technologies in a developing country: The Philippine experience

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<sup>2</sup>Department of Science and Technology – Science and Technology Fellows Program, Metro Manila, Philippines

## ABSTRACT

**Introduction:** Cerebrovascular diseases are one of the leading morbidities and mortalities in the Philippines, a developing country known to have a triple burden of diseases (communicable, non-communicable, and injury). Despite this pressing health concern, the local advancements in neuroscience research, particularly innovations using advanced technologies, progress at a slow rate. One of the identified problems is the lack of a robust health research agenda encompassing neuroscience. Health research agenda setting is crucial for developing countries with limited resources as it ensures that: 1) actual needs and gaps in the selected area are addressed, 2) funds and efforts are properly allocated to maximize the efficiency and effectiveness of research investments, and 3) research priorities are harmonised across multiple stakeholders. Health research agenda also plays a role in steering the trajectory of science and technology in health research, such as in promoting the use of advanced technologies in research and development (R&D). To enhance neuroscience efforts in the Philippines, the Department of Science and Technology (DOST) – Philippine Council for Health Research and Development (PCHRD), as the national coordinating body for health research, initiated the development of the first Philippine Brain Research Agenda Setting that focuses on neuroscience research with the integration of advanced technologies. **Materials and Methods:** This study was conducted in two (2) parts. Part 1 involved the scoping of ongoing neuroscience research through landscape review and stakeholders' consultation with different government agencies, neuroscience centres, and higher education institutes that are involved in neuroscience R&D. Part 2 encompassed the actual research agenda setting which adhered to the Philippine National Health Research Systems (PNHRS) Agenda Setting Method. The methodology included an online survey across the 17 regions of the Philippines, and a face-to-face two-day round table discussion on prioritization, scoring, and ranking of research topics. The participants were neurologists, neuroscientists, psychiatrists, developmental paediatricians, molecular biologists, physicists, engineers, and advanced technology experts. **Results:** The online survey was deployed to 14 out of 17 regions of the country. A total of 86 respondents with diverse neuroscience expertise answered the survey, the majority (55.8%) of which are neurologists. A total of 170 priority topics were identified, which were discussed and ranked during the two-day face-to-face round table discussions. Figure 1 below shows the overview results of the agenda setting. **Conclusion:** Results from this agenda-setting activity highlighted the limited scope of neurosciences R&D in the Philippines and the limited application of emerging technology in the neurosciences. Despite this, the activity identified several experts who are willing to contribute to neuroscience research, given the appropriate support and resources. The Philippine Brain Research Agenda Setting is expected to increase the neuroscience research in the country which will not only contribute new knowledge to the field but also foster local and international collaboration. Most importantly, it will address the needs of the Filipino people in the different aspects of neurology.

# Brain responses to drug-related cues in former drug addicts: An fMRI study

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## ABSTRACT

**Introduction:** Despite the various treatments and rehabilitation services provided for managing drug addiction, drug relapse rates continue to skyrocket in Malaysia. One prominent factor that may have contributed to this increasing relapse rate is the exposure of former drug addicts (FDAs) to drug-related cues following their release into the community after serving time in rehabilitation centres. Emerging studies reported that exposure to drug-related cues may increase activations in the brain regions associated with drug cravings, and that heightened activations in these regions are linked to drug relapse. However, these studies focused mainly on active drug abusers, thus less is known about the FDAs. Therefore, this study investigates whether drug-related cues significantly evoke the brain regions associated with drug cravings in the FDAs. **Materials and Methods:** A total of 24 male FDAs were recruited from community-based rehabilitation centres operated by the National Anti-Drugs Agency (NADA) for this cross-sectional study. Four participants were excluded as they did not meet the eligibility criteria. The remaining 20 participants underwent a task-based functional MRI (fMRI) experiment. During the experiment, participants viewed a series of drug-related and neutral cues presented in a block-design manner. A total of 96 functional volumes were acquired during the 16-minute fMRI scan. The functional data underwent slice-timing correction, realignment, co-registration, segmentation, normalisation, and smoothing. Individual data were analysed using the fixed effect analysis (FFX). Individual brain activation maps were next generated for the following contrasts: i) drug > baseline, ii) neutral > baseline, and iii) drug > neutral. Within-group brain activation maps were then generated using the random fixed effect analysis (RFX). Data pre-processing and analyses were performed using Statistical Parametric Mapping 12 (SPM12) operating in MATLAB version 9.14 - R2023a. The statistical threshold was set at P<sub>FWE</sub> < 0.05. **Results:** When viewing drug-related cues, participants showed significant brain activations in the inferior occipital gyrus (IOG), inferior temporal gyrus (ITG), occipital fusiform gyrus (OFuG), middle occipital gyrus (MOG), occipital pole (OCP), left fusiform gyrus (FuG), and left calcarine cortex (Calc). On the other hand, when they viewed neutral cues, they showed significant brain activations in bilateral IOG, bilateral MOG, and bilateral OCP, left FuG, left OFuG, left Calc, right ITG, and right thalamus proper. However, the results did not reveal any significant brain activations when participants viewed drug-related cues compared to neutral cues. These findings indicate that the drug-related cues did not significantly evoke greater brain response in the brain regions associated with drug cravings. A plausible reason is that the FDAs may have recovered from drug addiction and were no longer enticed by drug-related cues. **Conclusion:** The study has provided evidence that the brains of the FDAs do not significantly respond to drug-related cues. This finding suggests that the treatment and rehabilitation services may have inhibited the activations in the brain regions associated with drug cravings of the FDAs. Future works are warranted to explore other factors that may have contributed to the high relapse rates in Malaysia.

# Investigating reward-related functional connectivity in late adolescents through an N-back task using functional MRI

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## ABSTRACT

**Introduction:** Rewards processing is a fundamental aspect of human behaviour, with implications for motivation, decision-making and social interactions. While previous studies have explored how the brain responds to rewards in general, few have investigated how the specific recipient of the reward (self-versus others) impacts the connections within the brain's reward network. This study investigates reward-related functional connectivity (FC) differences between individuals motivated to win rewards for themselves and those motivated to win rewards for their parents. **Materials and Methods:** Twenty-eight healthy Malaysian participants (mean age  $22.71 \pm 1.14$ ) underwent fMRI while performing an N-back task associated with different reward cues: self-reward, parental reward, certificate reward, and a neutral cue. Participants were divided into two groups (n=14 each) based on their highest performance on the N-back task: the "cash group" (motivated by self-reward) and the "filial group" (motivated by parental reward). FC analyses, utilizing the Conn Toolbox, focused on the nucleus accumbens (NAcc) as the seed region due to its central role in reward processing. A two-sample t-test with peak voxel and cluster size activation thresholds set at  $p < 0.001$  and  $p < 0.05$  respectively was conducted to identify significant differences in FC between the groups. **Results:** Filial motivation, compared to self-reward motivation, was associated with distinct patterns of functional connectivity during the N-back task. The filial group exhibited significantly increased functional connectivity (FC) between the left NAcc and the left precuneus when anticipating rewards for their parents (peak MNI coordinate: 8, -54, 18;  $t(185) = 5.34$ ,  $p < 0.05$ ), suggesting the engagement of brain regions involved in mentalizing and perspective-taking. Precuneus is a region previously found to be involved in self-referential processing and perspective-taking which is also related to empathy. Additionally, during the n-back task after the neutral cue (when no specific reward was anticipated) condition, there was a significant increase in FC between the left NAcc and left superior frontal gyrus in the filial group compared to the cash group (peak MNI coordinate -10 38 58,  $t[118] = 5.28$ ,  $p < 0.05$ ). This finding implicates enhanced integration of reward signals with cognitive control processes in the filial group, even in the absence of immediate external rewards. **Conclusion:** These findings provide novel insights into the neural mechanisms underlying reward processing in late adolescence, highlighting the influence of social factors, particularly the motivation to benefit family members, on the brain's reward system. The observed differences in FC may contribute to our understanding of how individuals weigh personal gain against the well-being of others, with potential implications for educational and clinical interventions targeting motivation and prosocial behaviour.

# Dopamine transporter imaging pet tracer [<sup>18</sup>F] FE-PE2I: From lab to clinic

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## ABSTRACT

**Introduction:** As one of the new dopamine transporters (DAT) positron emission tomography (PET) tracers, [<sup>18</sup>F] FE-PE2I is an option to be used for dopaminergic imaging in Parkinsonian syndromes (PS). This review focused on [<sup>18</sup>F] FE-PE2I within the PS scope, from the development of the tracer and its radiolabelling chemistry, to preclinical as well as clinical evaluation. **Materials and Methods:** [<sup>18</sup>F] FE-PE2I was developed as an improvement to the established PET DAT imaging agent [<sup>11</sup>C]PE2I as the latter has several drawbacks: slow kinetics and late peak equilibrium, which restrict the imaging duration to up to 40 minutes; and the presence of blood-brain barrier permeable radiometabolites, which potentially interferes with the quantification of the brain imaging. From a radioisotope standpoint, PET imaging in DAT using <sup>18</sup>F offers many benefits over <sup>11</sup>C: the longer half-life of <sup>18</sup>F enables for imaging at later time points and a longer imaging period for improved quantification; the lower energy and shorter positron range of <sup>18</sup>F provide better spatial resolution; and labelling with <sup>18</sup>F would also make it easier to produce and deliver the tracer to centres without a cyclotron, thereby enabling for a wider usage of the tracer, from research to clinical applications. The radiolabelling chemistry was established and optimised, from a two-step aliphatic nucleophilic radiofluorination method, to a simplified and more convenient one-step method. This method was subsequently adopted and further optimised, utilising automated Good Manufacturing Practice (GMP)-compliant radiosynthesis modules, resulting in higher radiochemical yield and molar activity, necessary for the increasing demand in clinical application. **Results:** The preclinical evaluation has demonstrated that FE-PE2I ligand is potent and selective for DAT. It has a better in vitro binding affinity than PE2I to DAT. The in vivo binding competition and displacement studies showed that [<sup>18</sup>F] FE-PE2I was reversible, highly selective and specific for DAT, and has high BPND values in caudate and putamen in vivo, which consistent with the established information on DAT-distribution pattern in the brain. With faster kinetics and relatively fast metabolism and elimination, it has more favourable pharmacokinetics and PET imaging advantages over [<sup>11</sup>C]PE2I. It also produced less abundant of more lipophilic radiometabolite, which helps in better DAT quantification in the brain, and showed quicker imaging time. Clinical evaluations in human subjects have shown that this radiotracer is safe, with effective dose in the range among doses for other DAT imaging tracers and for 18F-labelled tracer ([<sup>18</sup>F] FDG). [<sup>18</sup>F] FE-PE2I was also comparable to the established DAT imaging agent like [<sup>123</sup>I] FP-CIT in quantifying DAT availability, and cerebral perfusion standard imaging agent such as [<sup>15</sup>O] H<sub>2</sub>O in estimating relative cerebral blood flow (rCBF) for diagnosing PS and its differential diagnoses. Imaging DAT with [<sup>18</sup>F] FE-PE2I permits faster patient throughput due to its faster kinetics, therefore, allowing for a reduced time between injection and imaging, and a shorter imaging protocol. **Conclusion:** [<sup>18</sup>F] FE-PE2I has been validated to be a better option for DAT imaging and can be clinically used in diagnosing PS and its differential diagnoses. Recently, this tracer has been listed in the EANM practice guideline/SNMMI procedure standard for dopaminergic imaging in PS to be used in clinical settings.

# <sup>99m</sup>Tc-TRODAT-1 SPECT/CT molecular neuroimaging for dopamine metabolism: First clinical experience in Bandung

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## ABSTRACT

**Introduction:** <sup>99m</sup>Tc-TRODAT-1, a SPECT radiotracer that binds to the dopamine transporter (DaT), is a nuclear medicine imaging technique to provide objective data for establishing diagnosis and monitoring disease progression for Parkinson's Disease (PD) and other Parkinsonian syndromes such as multiple system atrophy (MSA) and progressive supranuclear palsy (PSP). We report our first clinical experience using <sup>99m</sup>Tc-TRODAT-1. **Materials and Methods:** <sup>99m</sup>Tc-TRODAT-1 brain SPECT/CT scans were performed on four subjects: two patients with motor disorders (A, B) and two healthy volunteers (C, D). Patients were asked to stop the anti-Parkinson drug for 12 hours before the brain scan. A brain SPECT/CT scan (NM/CT 860, GE) was performed 4 hours after injection of  $21 \pm 2$  mCi <sup>99m</sup>Tc-TRODAT-1 intravenously. Acquisition time per projection was 30 seconds, and attenuation corrections were performed using the Chang method. The images were reconstructed using the DATQuant program for visual analysis and grading. Radiopharmaceutical uptake in the basal ganglia was compared with the background (occipital region). Decreased uptake in the basal ganglia area was considered positive for Parkinson's disease. **Results:** Patient A (Female, age 68, normal MMSE), previously diagnosed with dementia and suspected of parkinsonism, showed markedly decreased uptake at bilateral putamen and caudate nucleus, consistent with grade IV PD. Patient B (Male, age 75), previously diagnosed with PD and presented with tremour and rigidity, showed slightly decreased uptake consistent with grade II PD. Patient C (Male, age 28) and D (Male, age 30) were cognitively-healthy and showed normal <sup>99m</sup>Tc-TRODAT-1 uptake in the basal ganglia area. **Conclusion:** Adjusting to the unique challenges presented in Indonesia for nuclear imaging services, we believe the <sup>99m</sup>Tc-TRODAT-1 brain SPECT/CT scan can serve as a good initial stepping stone to eventually offer full-fledged molecular neuroimaging services in the country.

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# Evaluation of cue-based protocol implementations in motor imagery - based brain-computer interface experiments

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## ABSTRACT

**Introduction:** Non-invasive Brain-Computer Interface (BCI) studies mostly centre on the motor imagery (MI) concept, where multi-channel Electroencephalogram (EEG) signals are collected and characterized by patterns for different imagined tasks. Previous studies put extensive efforts into data-driven techniques to improve classification performance on benchmark datasets; however, other aspects, such as experimental factors, still lack thorough investigation. This pilot study aims to evaluate the effect of different cue-based protocols on within-subject MI-BCI baseline performance to better guide the experimental instructions on a specific group of users. **Materials and Methods:** An Emotiv EEG headset kit integrated into the Lab-Streaming-Layer (LSL) was used for data acquisition. Three PsychoPy-based protocols were designed, namely, G1, G2, and G3, incorporating different visual instructions of image-cue, arrow-cue, and arrow-cue-feedback utilizing Event-Related (de)Synchronization (ERD/ERS) demonstration, respectively. Imagery data (left/right hand/foot) from 12 healthy college participants (age 20~22, five females) were collected (15 trials/task/run) and randomly allocated for each designated protocol. A processing framework was implemented using a conventional Lasso-based sparse Filter Bank Common Spatial Pattern (SFBCSP) for feature extraction/selection and Linear Discriminant Analysis (LDA) for classification to assess the baseline performance. Average ROC (5-fold cross-validation) was calculated for the upper-limb binary model of each run with different non-overlapping time segments. Statistical non-parametric tests were used for within-group and cross-group comparative analysis. **Results:** In within-group analysis, average performance between run1 & run2 is as follows: G1 (52.7% & 44.8%); G2 (62.0% & 57.8%); G3 (52.5% & 67.7%) where G3 group yielded significant improvement (run2 > run1,  $p < 0.05$ ), while no statistical difference had been found within the G1 or G2 group. In cross-group analysis, an average performance combining all runs of G1, G2 and G3 are 48.8%, 59.8%, and 60.1%, respectively, where it showed significant differences in G1&G2 ( $p < 0.05$ ) and G1&G3 ( $p < 0.05$ ) but not in G2&G3. In the after-run self-assessment analysis, while few elements strongly correlated with the overall performance, no significant difference was found between the image-cue and arrow-cue groups. **Conclusion:** The preliminary result highlights that different instructions (arrow/image cue & feedback) may affect the within-session performance between runs while reporting no evidence of changing the subject's psychological factors. The statistical analysis also suggests that verbal feedback with arrow-cue can enhance the model's efficacy, which can be further explained by orienting the alpha-band ERD/ERS response. Future studies may explore other human-based factors considering the motor response-ability within the larger target group of users, potentially advancing BCI application in a personalized paradigm.

# The conundrum of differentiating functional Parkinsonism and idiopathic Parkinson's disease: The pertinent role of DaTScan

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## ABSTRACT

**Introduction:** Functional Parkinsonism (FP) is infrequently reported within functional neurological disorders (FNDs) and can severely impact patients. FP represents 1.7%–25% of all FMDs. Symptoms resemble those of Idiopathic Parkinson's Disease (IPD), leading to misdiagnoses. Early, accurate diagnosis is essential, aided by advanced neuroimaging modalities, ensuring appropriate management. Clinical assessment remains the main diagnostic tool in diagnosing FP, while structural imaging like MRI helps exclude organic disorders. Recent advanced in functional neuroimaging technique namely presynaptic dopaminergic transporter scan (DaTScan) is emerging to aid physicians in managing the patients. Here, we report a case of FP with normal MRI brain and DaTScan which tremendously improved with intensive neurorehabilitation. **Materials and Methods:** A 36-year-old woman with diabetes mellitus and asthma presented with a right-hand tremour post-COVID-19 recovery. Her symptoms worsened in just few months, including walking and speech difficulties. Fluctuating symptoms included wrist stiffness and bradykinetic finger tapping, but resolved with reinforcement, which is the opposite to parkinsonian rigidity. Initial treatment with Mirtazapine, Lorazepam and Madopar availed no improvement. **Results:** In the context of normal MRI brain with no clinical improvement with Madopar, patient was referred for <sup>99m</sup>Tc-TRODAT-1 SPECT (DaTScan), which was interpreted as normal, making the diagnosis of Parkinson's disease unlikely. After the establishment of FP as a diagnosis by exclusion of other causes, Madopar was ceased, and she underwent 6 weeks of intensive neurorehabilitation. Significant improvement in her daily activities and independence were seen after initiation of neurorehabilitation. **Conclusion:** FP can frequently mimic PD, thus clinical differentiation is crucial. Apart from structural neuroimaging, functional neuroimaging namely DaTScan, helps differentiate FP from PD by assessing dopamine deficiency in the striatum. Recognizing FP from PD is vital, influencing therapy and quality of life. Treatment of FP poses challenges; however, intensive neurorehabilitation shows promise. Hence, diagnostic challenges and fluctuating nature of psychogenic Parkinsonism, emphasises the importance of comprehensive evaluation using nuclear scans and tailored management approaches.

# Structure learning associated bilateral DLPFC excitatory/inhibitory GLX / GABA+ modulation in healthy adults

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## ABSTRACT

**Introduction:** Homeostatic plasticity of neuronal circuits with regulated interplay of Glutamate and Gamma-aminobutyric acid (GABA) neurotransmitters has been associated with interaction of learning and cognition skills development, while its irregular disruption could lead to cognitive deficits. The underline neuro-cognitive model of these interactions is illusive, and we aim to investigate the impact of structure learning (SL) training on individual's cognitive flexibility (CF) and its transferability to other cognitive abilities, that pose significant implications in lifelong learning. **Materials and Methods:** 113 healthy volunteers (65-F, 48-M) aged between 18-55 years were pseudo-randomized to passive control (C) (55) and training (T) (58) groups [2], of which 106 (C: 53, T: 53) completed pre- and post-test sessions and only T-group underwent 2-week computerized SL training. Both the C- and T-groups were administered six CF tasks - Colour Shape Task (CST), Wisconsin Card Sorting Test (WCST), Trail Making Test (TMT), Task Set Switching (TSS), Intra-extradimensional Set Shifting (IED) and Probabilistic Reversal Learning (PRL), at post-SL training with only CST at both pre and post training sessions. Switch cost in reaction time and accuracy across trials were assessed for participant's performance. Consent to participate were obtained and the protocol was approved by NTU IRB. Participants were imaged in a 3T Siemens MAGNETOM Prisma MRI scanner with a 64-channel head coil. A 3D MPRAGE T1w MRI with  $1 \times 1 \times 1 \text{ mm}^3$  resolution was applied for MRS planning. GABA+ and Glx in bilateral left (L)- and right (R)-dorsolateral prefrontal cortex (DLPFC) were acquired at two different time points of pre- and post-SL training sessions of cognitive assessment using 1H MEGA-PRESS (voi:  $30 \times 15 \times 30 \text{ mm}^3$ , TE=68 ms, TR=2000 ms, ON=1.98 ppm, OFF=7.5ppm, TR=2000 ms; TE=68 ms; data points=2048; Navg=128) with one unsuppressed water spectra of Navg=4, all having linewidth $\leq 16$  Hz. Multi region and multi-session MRS data was structured in BIDS format and processed using Osprey software. MRS data was quality controlled for visual artefacts, head movements, broad Cr linewidth in the OFF-spectra, and poor fitting. **Results:** Tissue corrected GABA+ and Glx levels in both L- & R- DLPFC did not differ between groups at pre-training stage. Post-training R-DLPFC Glx significantly decreased in T-group ( $p=0.04$ ,  $5.74 \pm 0.922$ ), but not in C-group ( $p=0.119$ ). L-DLPFC GABA+, and Glx did not change across groups and sessions. Post-training R-DLPFC GABA showed significant positive correlation with both L-DLPFC GABA ( $r=0.36$ ;  $p=0.03$ ) and Glx ( $r=0.35$ ;  $p=0.03$ ) levels, but not in pre-training stage ( $r=0.07$ ) and ( $r=-0.11$ ) respectively. Post-training MRS measures was not correlated with SL test-scores. Post training L-DLPFC Glx in T-group (excluding participants following random strategies) showed a significant positive correlation ( $r=0.43$ ;  $p=0.0163$ ) with switch cost accuracy in CST task, but not with R-DLPFC Glx ( $r=-0.17$ ;  $p=0.3836$ ), indicating higher Glx level in L DLPFC, but not in R-DLPFC supports better CF in T-group as compared to C-group. **Conclusion:** Neuro-chemical modulations in bilateral DLPFC were found to be associated with better CF score after SL training. This suggests SL to impact cognitive flexibility on a neuro-basis, despite not observing significant differences in the SL test scores on the behavioural level.

# An analysis of motor area activation sequence during swallowing in a tasting task using functional MRI

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## ABSTRACT

**Introduction:** Previous research suggested that taste stimuli may increase neuromodulation in brain regions that controls swallowing, raising the possibility that specific taste stimuli may contribute to increase the primary motor cortex (M1) BOLD activity. Thus, we aimed to investigate the effects of concentration of saline on the brain activation of gustatory areas and motor areas by using time-resolved functional MRI. **Materials and Methods:** Ten neurologically normal subjects participated in this study. A sequence of 15 sec-tasting, 6 sec-rinse and 9 sec-rest periods in one trial was repeated for 20 times in a session. In the rinse period, subjects were instructed to swallow the intraoral liquid. At the beginning of the tasting period, NaCl solution of either a lower (0.9%, L-NaCl) or a higher concentration (9.0%, H-NaCl) was applied onto the subjects' tongue. Functional data were obtained using a T2\* weighted gradient echo EPI sequence on a 1.5T MRI scanner and statistical tests were performed using SPM12. The temporal analysis was performed using a set of onsets for event-related analysis for each sampling point at every 3 sec. **Results:** In H-NaCl, the activation in the M1 were observed from OS-5 (left Precentral Gyrus (PG), BA4) to OS-7 (right PG, BA4). The activations in the premotor motor cortex (PMA) were observed at OS- 6 (bilateral PG BA6). The activation in the supplementary motor cortex (SMA) were observed at OS-7 (bilateral Superior Frontal Gyrus (SFG), BA6) and OS-10 (left SFG, BA6). In L-NaCl, the M1 activation was observed from OS-6 (left PG, BA4) to OS-7 (right PG, BA4). The PMA activations were observed from OS-5 to OS-6 (bilateral PG, BA6). The SMA activation was observed from OS-6 (left SFG, BA6, right PG, and BA6) and OS-7 (bilateral medial frontal gyrus, BA6). **Conclusion:** It was suggested that motor performance for swallowing may be different between the H and L-NaCl conditions depending on their influences on the subjects' behaviour. In the L-NaCl, the activation peak sequence PMA - M1 is the usual order in motor execution. In H -NaCl, the reversed sequence M1 - PMA may suggest more attempt to remove the NaCl with higher concentration toward the end of rinse period. The activation peak of SMA later than that of PMA and M1 may suggest its independency from the motor generation to rinse. One possible explanation may be preparation to form still status in the rest period. Its activity at OS-10 in H-NaCl may also represent preparation and tension for the next strong stimuli.

# Interwoven realms: Exploring whole brain diffusion tensor imaging variations in Alzheimer's disease and healthy controls

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## ABSTRACT

**Introduction:** Alzheimer's disease (AD) is a neurological condition, and late onset AD (LOAD) is the most prevalent form of dementia. It is a neurodegenerative condition defined by a gradual decline in memory function. Diffusion tensor imaging (DTI) is a technique used to study the movement of water molecules in the white matter of the brain. It provides information about the direction of axonal fibres and the overall structural integrity of the brain. DTI is not used as an alone diagnostic tool, but it helps in comprehending the evolution of AD by identifying changes in the white matter of the brain that indicate cognitive impairment, especially in regions associated to memory. Within the context of AD, deterioration of the structural integrity of white matter visualized on DTI, can non-invasively demonstrate aberrations in the fractional anisotropy (FA) and mean diffusivity (MD) of the tracts. DTI can be used to identify and measure these changes. The objective of our study was to identify the disparities in whole brain diffusion tensor imaging between individuals with AD and healthy controls (HC). **Materials and Methods:** A cross-sectional case control study was performed to compare the brain white matter integrity between AD and HC subjects in Klang Valley. The experiment was conducted using DTI and structural MRI imaging in the period between 2020 to 2023. We utilized FSL DTI processing as a computational approach in neuroimaging to extract meaningful data about white matter integrity in the brain among our subjects. We quantified metrics like FA and MD, after converting DICOM images into nifti.gz format, employing Python scripts within the FMRIB Software Library (FSL) to execute various tools and pipelines, including the Brain Extraction Tool (BET) and DTI Toolbox, tailored to individual study requirements. Quantitative measures of FA and MD were recorded and correlated with structural information of grey matter volume (GMV) atrophy, for regions of interest (ROIs) based on a priori knowledge, such as the hippocampus and posterior cingulate cortex (PCC), along with subject coordinates, facilitating comprehensive analysis and understanding of AD-related alterations in brain structure. **Results:** Higher MD values were detected in AD in comparison to the HC group, with a particular emphasis on the right and left hippocampus and PCC. These results correlated the presence of GMV atrophy in the selected ROIs. In contrast, the FA levels exhibited variations, with elevated values observed in the right hippocampus and PCC, while decreased values were found in the left hippocampus among AD. **Conclusion:** DTI imaging reveals a notable decrease in fractional anisotropy and an increase in median diffusivity in the temporal areas, which showed a significant correlation with AD phenotype. This method sheds light on microstructural changes in white matter pathways implicated in AD progression, potentially serving as biomarkers for disease advancement.





  
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# Perspectives of radiographers towards artificial intelligence integration in medical imaging

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## **ABSTRACT**

**Introduction:** Artificial intelligence (AI) systems could replicate the intelligence of human brains are heavily being used in the medical industry and modalities as technology advanced and became increasingly valuable to people and the medical field. It undoubtedly aids with a variety of medical issues, including a cardiac event, fracture, neurological condition, or thoracic complications in which quick diagnosis and treatment options are possible with AI. **Materials and Methods:** A cross-sectional study design using questionnaires was used to survey 102 Malaysian radiographers working in various sectors of hospitals in the country, including research university hospitals, private hospitals, and public hospitals, that provided healthcare services with certain inclusive and exclusive criteria to gain their perspectives on an integration of AI in the medical imaging field. Data was processed using SPSS software version 27. Chi-Square Test was used to compare the expected outcomes in terms of percentages and p-value related to radiographers' perspectives. Correlation studies were utilized to investigate the relationships between the demographic backgrounds of the radiographers and their perspectives towards AI integration. **Results:** This current research has explored the potential uses of AI in Malaysian healthcare, such as improving the accuracy of medical imaging and predicting and preventing diseases, which can lead to better health outcomes for patients. The majority of radiographers in all sectors were in favour of AI in helping improve seamless workflow in diagnostic imaging. **Conclusion:** The findings of this research can be used to develop effective strategies for incorporating AI into radiology training programmes and workflows, which can enhance the efficiency and effectiveness of diagnostic medical imaging in Malaysia.

# Screening for atherosclerosis in Streptozotocin-induced type 2 diabetic rat models using trans-abdominal ultrasound evaluation of abdominal aortic tunica intima thickness

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## ABSTRACT

**Introduction:** Atherosclerosis is a common complication of Type 2 diabetes mellitus (T2DM) and is attributed to the development of cardiovascular diseases (CVD), such as ischaemic stroke and myocardial infarction. At present, most screening methods for CVD risks, such as the Framingham risk score, have their limitations, especially in predicting total future CVD events. In recent times, ultrasonography (USG) has shown promise to enable the detection of subclinical atherosclerosis through measurements of the tunica intima thickness in large arteries. Our study evaluates the potential of USG as a screening tool for the measurement of tunica intima thickness in the abdominal aorta in a Streptozotocin (STZ)-induced diabetic rat model and aimed to explore the association between T2DM and atherosclerosis. **Materials and Methods:** Our study used a pre-test and post-test-controlled group design, having 20 male Wistar rats (3-4 months old, weighing 200-300 grams), randomized into control and treatment groups (n=10 each). An intraperitoneal injection of STZ (45 mg/kg body weight) to induce T2DM was administered in the treatment group, while the control group did not receive any intervention. Blood glucose levels were measured on days 0 and 12 to confirm T2DM induction. Ultrasonographic measurements of tunica intima thickness in the abdominal aorta were taken on day 1 (baseline) and day 14, using an ultrasound scanner with a L12- 3 broadband linear array transducer. Statistical analysis was conducted with IBM® SPSS® Statistics 22.0 using non-parametric Wilcoxon tests due to non-normal data distribution. **Results:** The treatment group exhibited a significant rise in blood glucose levels from  $77.2 \pm 11.5$  mg/dL on day 1 to  $347.4 \pm 108.5$  mg/dL on day 12 ( $p = 0.005$ ), confirming T2DM induction. A significant increase in the tunica intima thickness of the abdominal aorta was noted, from  $4.1 \pm 0.8$  mm on day 1 to  $10.8 \pm 0.6$  mm on day 14 ( $p = 0.005$ ). In contrast, the control group showed no significant changes in tunica intima thickness ( $7.6 \pm 2.0$  mm on day 1 to  $4.0 \pm 0.9$  mm on day 14). This suggests that STZ-induced T2DM leads to significant thickening of the tunica intima in the abdominal aorta, an early marker of atherosclerosis. Ultrasound measurement of tunica intima thickness could serve as an effective screening tool for detecting early-stage atherosclerosis in diabetic models. **Conclusion:** Ultrasound-based assessment of tunica intima thickness in the abdominal aorta is a promising tool for early detection of atherosclerosis in T2DM. This method may aid in monitoring therapeutic interventions and guiding precision medicine to prevent cardiovascular complications in diabetic patients.



# Exploring the association between age-related bilateral hippocampal volume distribution in Alzheimer's disease and normal ageing using VBM and HippoDeep methods

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## ABSTRACT

**Introduction:** Alzheimer's Disease (AD) is a progressive neurological disorder that causes cognitive decline, memory loss, and behavioural changes. Hippocampus atrophy is strongly linked to AD pathogenesis. MRI is a useful tool for studying the hippocampus, and its volume can indicate neurodegenerative diseases like AD. A typical MRI analytic tool, Voxel-Based Morphometry (VBM), can detect very minor brain structural changes, making it beneficial for neurodegenerative disease research. HippoDeep, a deep learning-based device, can divide and measure the hippocampus, providing a precise insight of AD structural changes. Other studies have examined hippocampal volume changes in AD, but few have examined hippocampal volume distribution on both sides of the brain using advanced segmentation methods like HippoDeep and VBM. Due to age-related brain structure changes and the higher risk of Alzheimer's disease, age must be included as a covariate. This study will compare AD and HC bilateral hippocampus volume distributions using VBM and HippoDeep methods. We aim to improve our understanding of AD causes and create early diagnosis and intervention options. **Materials and Methods:** Comparison of bilateral hippocampus volume was done in a cross-sectional case control study. The study involved 15 AD and 15 HC subjects recruited from Hospital Kuala Lumpur and Hospital Sultan Abdul Aziz Shah, Universiti Putra Malaysia. Following the VBM methodology, segmentation produced a tissue class picture aligned with the original utilising the native space option. Normalising the tissue class image into a standard space and smoothing improved signal-to-noise ratio. For factorial design statistical analysis, images with identical dimensions, orientation, and voxel size were used. The Automated Anatomical Labelling toolset was overlaid on the Montreal Neurological Institute (MNI) template to obtain cluster-level volume. For HippoDeep, hippocampal volume segmentation methodology was used for automated segmentation. A sophisticated algorithm's output was used in transfer learning to train a model. The classifier was trained and tested using these simulated images. A Spearman rank correlation was calculated using VBM and HippoDeep Toolbox to examine hippocampus volume connection. Pearson correlation coefficient assessed the correlation of the two methods. Significance level set at <0.001. **Results:** By utilising HippoDeep, the disparity in volume was readily observed, since the linear discrepancy was far larger as compared to the VBM approach. The statistical significance was < 0.001 and provided 99.99% confidence level. This implied that HippoDeep has a higher level of sensitivity in detecting alterations in hippocampal volume in patients diagnosed with Alzheimer's disease when compared to VBM. **Conclusion:** Alzheimer's disease is a progressive neurodegenerative condition that calls for multimodal diagnostic instruments that are both accurate and efficient in characterising the disease. Through the utilisation of deep learning algorithms in the field of artificial intelligence automated measurements of hippocampal, a more accurate prediction of Alzheimer's disease can be achieved by combining various biomarkers.

# The correlation between the MRS brain metabolites value and neuropsychological tests among patients with Alzheimer's disease: A pilot study

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## ABSTRACT

**Introduction:** Alzheimer's disease (AD) is becoming one of the most concerning types of illness at the present time. This is because of the increase in the number of occurrences due to the increase in the number of elderly populations worldwide. Special attention is being given to manage the disease as it affects the quality of life of those affected. Increase in the number of deaths resulting from the disease has also been reported. Tremendous effort is being taken even from the past few decades to be able to diagnose the disease at an earlier stage for better management. Magnetic resonance spectroscopy (MRS) is a non-invasive in-vivo imaging method for measuring brain metabolites. Alterations in specific metabolite concentrations in the brain may serve as a surrogate marker for the diagnosis of AD. They can be applied to diagnosis, prognosis prediction and, or even monitoring treatment response. Despite having many advantages MRS is not being widely used clinically therefore, the effectiveness is not clear. Hence, this study aims to prove a standardized MRS technique and validation of the regional and temporal changes of the metabolites in the brain of those with AD compared to HC and to explore the relationship between brain metabolites and neuropsychological test scores. **Materials and Methods:** A cross-sectional study was conducted to compare the changes in the brain metabolites between AD and healthy control (HC) subjects in Klang Valley. The study was conducted using MRS and structural MRI imaging, for the duration of 2 years. The scans were performed using a 3.0 Tesla Siemens Magnetom PRISMA machine. The structural MRI images acquired is a T1-weighted magnetization-prepared rapid gradient-echo (MPRAGE) sequence and for the MRS single voxel spectroscopy technique, PRESS sequence were used. Both water-suppressed and water non-suppressed data were acquired. The placement of the <sup>1</sup>H-MRS voxel was done covering the right and left hemispheric posterior cingulate cortex (PCC). We utilized SPM Matlab Osprey software as a computational approach in neuroimaging to extract significant quantitative brain metabolites alterations among subjects from both groups. Besides, each of the subjects underwent neuropsychological tests which consisted of Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination prior to the MRI scan. **Results:** Decrease in N-Acetyl-Aspartate (NAA) and elevation in Myo-Inositol (mI) level were detected in AD in comparison with HC group. Significant difference is seen in gender and educational level of the subjects in both the groups. Lastly, metabolites such as Glutamate (Glu), Glutamine (Gln) and  $\gamma$ -Aminobutyric Acid and Glutathione (GABA) have positive correlations with neuropsychological test scores ( $p < 0.05$ ). **Conclusion:** MRS has the potential of being a biomarker for AD detection as it clearly shows alteration in brain metabolites in comparison to the healthy populations. Besides, it also supports the neuropsychological tests to further confirm the diagnosis.

# Contribution of structural and functional connectivity in brain tumour retention: A narrative review

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## ABSTRACT

**Introduction:** Brain tumours present significant challenges in neurosurgery due to their complex interactions with surrounding brain structures. Structural connectivity (SC) maps the physical pathways of the brain using techniques such as diffusion tensor imaging (DTI) and provides a detailed framework of neural pathways and white matter (WM) tracts. These maps are crucial for identifying critical brain regions to avoid during surgery, thus minimizing damage to essential neural circuits. Meanwhile, Functional connectivity (FC) examines the interactions between different brain regions during rest or task performance. This is often performed using functional magnetic resonance imaging (fMRI) and magnetoencephalography (MEG). Combining FC and SC data allows for a comprehensive understanding of individual patient neuroanatomy and network functionality. To date, the combined utility of DTI and resting state fMRI (rs-fMRI) has been established in mapping the networks in epilepsy, brain tumours, hydrocephalus, Alzheimer's disease, and Huntington's disease. The potential role of structural connectivity and functional connectivity analysis in neuro surgical planning (preoperative planning, intraoperative guidance, postoperative outcomes) has not been fully explored. **Materials and Methods:** A literature search was carried out to gather eligible studies from the following widely sourced electronic database, PubMed using the combination of the following keywords: structural connectivity, functional connectivity, and tumour. **Results:** There were only two research articles that investigated mapping of whole-brain FC and SC networks (preoperative planning) and only one study that further investigated the clinical applications the connectivity maps in post-operative monitoring. The findings of the studies suggest that brain tumours interfere with the network organization i.e., decrease in structural connectivity and tumour resection of related neural network could worsen the performance of brain networks. **Conclusion:** Combined use of SC and FC analyses in brain tumour surgery represents a transformative approach to neurosurgical practice. However longitudinal studies must be performed to evaluate the efficiency of connectivity-guided neurosurgery.

# The neuroprotective activity of phenolic compounds from Philippine oregano (*Coleus amboinicus*) against cognitive impairment in mice (*Mus musculus*)

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## ABSTRACT

**Introduction:** Cognitive impairment affects an individual's memory, comprehension, reasoning, judgment, and visual-spatial perception. A well-known and used medicinal plant in the Philippines, the Philippine oregano (*Coleus amboinicus*) is abundant in the phenolic compounds carvacrol, and thymol used in culinary and pharmaceutical applications. With the rising prevalence of cognitive impairment among the aging Filipino population, there is a greater need for better awareness, prevention, and treatment options. **Materials and Methods:** The mice underwent a habituation period, acquisition trial, and retention trial. The parameters measured were the latency to reach the target location and the number of errors made. Scopolamine-induced cognitive impairment was done in Groups 2, 3, 4, and 5 followed by the administration of treatments including the extract and donepezil as the standard drug for Group 2. These were all subjected to histopathological testing through H&E staining and microscopic examination. **Results:** The results showed the presence of phenolic contents of the *Coleus amboinicus* extract based on the Ferric chloride test and TLC. Total Phenolic Content and Total Flavonoid Content were determined ( $422.9 \pm 0.02108$  ppm GAE/ $\mu$ L and  $91.40 \pm 0.01127$  ppm QE/ $\mu$ L) that indicated the abundance of the compounds, respectively. Statistical analysis using Analysis of Variance (ANOVA) and Student's t-test were performed to summarize and compare the data collected. Results from the acquisition trial showed a significant difference ( $F > 2.32$ ), indicating mice could distinguish baited arms, while the retention trial ( $t = 4.77 > 3.182$ ) showed reduced movement with longer acquisition times. Histopathological testing revealed the presence of suspected amyloid- $\beta$  (A $\beta$ ) plaques in Group 2 (positive control), Group 3 (low concentration), Group 4 (medium concentration), and Group 5 (high concentration) wherein Group 3 exhibited fewer amyloid- $\beta$  (A $\beta$ ) plaques. **Conclusion:** The *Coleus amboinicus* extract showed no significant neuroprotective effects in scopolamine-induced cognitively impaired mice. However, low-concentration oregano extract showed potential benefits, with fewer Amyloid- $\beta$  (A $\beta$ ) plaques.

# Exploring neuronal activation during response to reward utilizing fMRI correlated with simultaneous EEG among undergraduates having problematic smartphone usage

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## ABSTRACT

**Introduction:** Smartphone usage among young Malaysian adults has increased dramatically in the past decade leading to smartphone addiction (SPA) particularly involving social networking applications such as Instagram. SPA prevalence has been noted to be as high as 47% among medical students in a Malaysian university. There is a need to objectively assess the cerebral mechanisms that respond to reward using electroencephalography (EEG)-informed functional magnetic resonance imaging (fMRI) also known as EEG-fMRI as a potential biomarker. **Materials and Methods:** An observational study using simple random sampling from a phase one cross sectional study, was conducted among 24 UPM students using the Smartphone Addiction Scale-Malay version (SAS-M) questionnaire, modified Instagram Addiction Scale (IAS) and EEG-fMRI. Subjects with SAS-M scores  $\geq 98$  and IAS  $\geq 37$  were considered as high scorers (HS) and deemed to be having SPA, whereas subjects with SAS-M scores  $< 98$  and IAS  $< 37$  were considered low scorers (LS) and deemed as healthy controls. A 64-channel EEG scalp electrode was placed on the participants (12 HS, 12 LS) and a task-based fMRI was performed with simultaneous EEG recordings. Evoked response potential (ERP) derivatives of EEG namely the P300 peak waves and contingent negativity variance (CNV) were analyzed using Brain-Vision EEG analyzer and fMRI dataset were analyzed using Statistical Parametric Mapping (SPM). **Results:** There was significant difference in the P300 wave amplitude between HS and LS, which corresponded well with cerebral activations regions related to response to reward. **Conclusion:** The combination of the high spatial resolution of fMRI with the high temporal resolution of EEG to correlate cerebral regional activation, in response to cue related reactivity during response to reward task among smartphone addicts, has the potential to be a surrogate biological marker for assessment of Instagram addiction.

# Correlation between inferior occipital gyrus and subjective drug craving in former drug addicts: An fMRI study

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## ABSTRACT

**Introduction:** While numerous attempts of treatment have been made to overcome drug addiction, the number of people abusing drugs and relapsing is still increasing in Malaysia. One of the contributing factors to substance addiction and relapse might be the feeling of craving, which is defined as a strong urge or need to consume a substance. Drug craving can be triggered by substance exposure or cues associated with the substance, and it has become a predictor for relapse and dropout from treatment. Several studies found a significant correlation between drug craving and brain region activation in the presence of drug-related cues. However, these studies are limited to active drug addicts, with little understanding of former drug addicts (FDAs) in Malaysia. **Materials and Methods:** Utilizing a cross-sectional study design, 24 former male drug addicts were selected from rehabilitation centres under National Anti-Drugs Agency (NADA). Out of the initial 24 participants, four were discarded for not meeting the inclusion criteria. The participants viewed drug-related cues displayed using a block-design task while undergoing functional magnetic resonance imaging (fMRI) for a duration of 16 minutes. After the fMRI procedure, subjects were required to rate their craving intensity to abuse drugs on scale of 0 to 100 using visual analogue scale (VAS). The fMRI data were pre-processed and analysed using fixed-effect analysis (FFX) and random-effect analysis (RFX) in Statistical Parametric Mapping 12 (SPM12). The significant brain region (PFWE < .05) with the highest t-value generated from the RFX was selected as the region of interest (ROI). The number of voxels (NOV) in the ROI were extracted from individual participants using WFU PickAtlas. A Spearman's rank-order correlation was conducted to assess the relationship between the NOV and VAS craving score. **Results:** The RFX results revealed significant activation in seven brain regions with the left inferior occipital gyrus (L\_I OG) showing the highest t-value. The activation in the L\_I OG may be due to its role in processing visual information that is linked to functional terms (object, task and visual). Correlation analysis indicated a non-significant, fair positive correlation between the NOV in the L\_I OG and the VAS scores ( $r = 0.372$ ,  $p = 0.106$ ). This finding suggests a trend where higher brain activity in L\_I OG is associated with higher drug craving. The insignificant correlation between brain activity and drug craving may be due to long-term drug abstinence. Additionally, FDAs might have developed desensitization, or they no longer feel cravings toward drugs. **Conclusion:** The study concludes that L\_I OG is activated by drug-related cues, however this activation is not correlated with drug craving. This finding suggests that the brains of FDAs who have undergone rehabilitation centre no longer show significant response to drug-related cues. Future research should compare brain response toward drug-related cues between FDAs with different genders.

# Effects of spatial smoothing on brain activity patterns in an auditory fMRI study

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## ABSTRACT

**Introduction:** Functional magnetic resonance imaging (fMRI) is a neuroimaging technique commonly used to investigate brain functions by measuring the blood oxygenation level dependent (BOLD) signal. However, the BOLD signal may consist of noises, such as head motions, thermal noise, respiratory rhythms, and cardiac cycles. Therefore, these noises must be filtered out from the BOLD signal through spatial smoothing — a pre-processing procedure to reduce the amount of noise in fMRI data. The degree of spatial smoothing is determined by adjusting the value of full width at half maximum (FWHM). Noteworthy, adjusting the FWHM value unnecessarily may affect the accuracy of the fMRI analysis. To date, researchers have not reached a consensus on the optimum FWHM value to eliminate noise while preserving the quality of the BOLD signal, especially when analysing auditory functional data. This study investigated the effects of different FWHM values on fMRI data acquired during an auditory working memory (AWM) task. **Materials and Methods:** The 20 original fMRI data (voxel size of 3 x 3 x 5 mm) have gone through four pre-processing steps, which are slice timing correction, realignment, spatial normalisation, and spatial smoothing. The data was smoothed using four FWHM values: (i) 3 x 3 x 5, (ii) 6 x 6 x 10, (iii) 9 x 9 x 15, (iv) 12 x 12 x 20 mm. The pre-processed data was analysed using first-level fixed-effect (FFX) for individual analysis and then further analysed using second-level random effect (RFX) analysis for group analysis. This procedure was performed using Statistical Parametric Mapping (SPM12). **Results:** The results revealed that using the FWHM value equivalent to or twice the original voxel size produced brain activity patterns that are relevant to the AWM brain areas. Interestingly, using the FWHM values of three to four times the original voxel size results in unprecise brain activity patterns, which are mostly irrelevant to the AWM brain regions. These findings suggest that excessive spatial smoothing may result in decreased quality of the BOLD signal. **Conclusion:** The outcome of this study underscores the importance of using the recommended FWHM when analysing fMRI data.



# Exploring the quiet mind of former drug addicts using fMRI

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## ABSTRACT

**Introduction:** Relapse refers to an act of taking drugs again which have previously been controlled or completely stopped. The issue related to drug relapse among former drug addicts (FDAs) is not new in Malaysia. Based on a previous study, this issue happens because of several factors including the activation of brain areas related to drug-craving behaviours when the FDAs are exposed to drug-related substances or images. However, it remains unclear whether these brain areas still show significant activation when the FDAs are not exposed to any drug-related substances or images. Thus, to address this issue, this study was performed using resting state functional magnetic resonance imaging (rs-fMRI) to identify whether the brain areas implicated with drug craving shows significant activation in FDAs at rest. **Materials and Methods:** A cross-sectional study involving 24 male FDAs recruited from community-based rehabilitation centres operated by National Anti-Drugs Agency (NADA) was conducted at the Universiti Kebangsaan Malaysia Children's Hospital. All participants were scanned using an MRI machine while they were at rest. The functional data then undergo pre-processing steps involving slice-timing correction, realignment, coregistration, segmentation, normalisation, and smoothing. Four out of 24 participants were excluded from this study as they did not meet the study's inclusion criteria. Fixed effect analysis (FFX) was used to analyse rs fMRI data for each participant. Random fixed effect analysis (RFX) was then used for within group brain activation maps. Data pre-processing and analyses were performed using Statistical Parametric Mapping 12 (SPM12) operating in MATLAB version 9.13 (R2022b). The significant level was set at  $P_{FWE} < .05$  and the number of voxels was thresholded at 10. **Results:** When FDAs are at rest, the right precentral gyrus (PrG), right superior parietal lobule (SPL), right middle cingulate gyrus (MCgG), left angular gyrus (AnG), left middle segment of the superior frontal gyrus (MSFG) and left supramarginal gyrus (SMG) showed significant activation. As supported by previous studies, only the right SPL and right MCgG are potentially related to drug craving. The right PrG which primarily associated with motor cortex, showed no direct link to drug craving. Meanwhile, the left AnG, left MSFG and left SMG are parts of the Default Mode Network (DMN) which usually show activation during resting state, also not associated to drug craving. However, these findings showed that the brain of FDAs at rest still exhibits significant activation in the areas involved in drug-craving. **Conclusion:** The rs-fMRI study showed that in the absence of drug related cues, the brain of FDAs still exhibits significant activation in the areas associated with drug-craving. Although the brain areas are not primarily involved in drug craving, their significant activation in brain of FDAs at rest suggests that the current treatment and rehabilitation programs are not fully effective to completely inhibiting the activations of brain areas involved in drug craving. However, further study is suggested to identify the correlation between the brain areas and the subjective craving scores of the FDAs to accurately determine whether the activated areas related to drug craving.



# Brain activities of healthy individuals are not significantly evoked by drug related cues

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## **ABSTRACT**

**Introduction:** Drug addiction is a chronic brain disorder marked by compulsive drug seeking and use. Healthy individuals may have tendency to use drugs while being aware of their harmful effects on their health. Studies show that drug-related cues increase brain activity linked to craving in active drug addicts. However, studies examining the effect of drug cues on the brain activity of healthy individuals have largely remained unexplored. This study shows whether brain areas that implicated in drug craving show significant activation when viewing the drug cues in healthy individuals. **Materials and Methods:** In this cross-sectional study, 24 healthy male participants in Malaysia were recruited. One participant was excluded as he did not pass the eligibility criteria and the remaining 23 participants were included in this study. During the experiment, participants were positioned inside the MRI and viewed 48 trials of drug and neutral cues in 16 minutes. After scanning, the functional data was collected and undergo slice-timing correction, realignment, co-registration, segmentation, normalization, and smoothing using Statistical Parametric Mapping 12 (SPM12) in MATLAB version 9.14 – R2023a. The individual data were analysed using fixed effect analysis (FFX) and the individual brain activation maps were generated for drug > baseline. The group brain activation maps were generated by using random fixed effect analysis (RFX). The statistical threshold was set at  $PFWE < 0.05$ . **Results:** When participants viewed the drug cues, five brain regions were significantly activated. The areas included left calcarine cortex (Calc), right occipital pole (OCP), right fusiform gyrus (FuG), right inferior occipital gyrus (IOG), and bilateral inferior temporal gyrus (ITG). These brain areas are related to visual processing in general, they are not particularly related to drug addiction. These findings suggest that the brain activity of healthy individual did not show any activation in brain area that control craving when exposed to the drug cues. A possible reason is that the healthy participants have not been previously exposed to addictive stimuli or are less prone to addictive behaviours. **Conclusion:** This study aimed to understand how healthy individuals' brain activity responds to drug cues. While significant activation occurred in five brain regions associated with visual processing, no activation was observed in areas linked to craving control. This suggests that healthy individuals may not show the same neural responses to drug cues as addicts, possibly due to their lack of prior exposure or susceptibility to addictive behaviours.

# Nonlinear time series analysis of simultaneous resting-state EEG and fMRI brain activity

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## ABSTRACT

**Introduction:** Traditional methods for analysing EEG and fMRI data often assume that the relationships between different brain regions are linear and can be captured using straightforward mathematical relationships like correlations. While linear methods are simple and computationally efficient, they might miss complex interactions in brain dynamics, such as the full extent of how brain regions influence each other through feedback loops or other nonlinear interactions. Moreover, we know little about the dynamic relationship between brain activity at the localized scale of EEG data versus the global scale of fMRI data. Because the brain operates through intricate, dynamic interactions that are inherently nonlinear, we sought to uncover hidden patterns and relationships by leveraging both linear and nonlinear time series analysis methods on a recently published open-access dataset of simultaneously recorded EEG and fMRI activity on a healthy 29-year-old male subject at rest. **Materials and Methods:** Pre-processed EEG and fMRI recordings of "Subject 4" at rest for one 600-s session were obtained from Telesford, QK, et al. *Scientific Data*, 10:554, 2023. All analyses were performed in MATLAB using a combination of algorithms from the Noolitia, EEGLAB, GIFT, and SPM toolboxes. Our analysis pipeline for both EEG and fMRI pre-processed data is as follows. Data were decomposed with Independent Component Analysis (ICA) to extract relevant brain activation components, which were either algorithmically (EEG) or visually (fMRI) selected. The time series of the six components chosen from each EEG and fMRI data were further analysed using nonlinear techniques: test for nonlinearity, phase-space reconstruction, and recurrence analysis. The captured source localizations (EEG) and spatial activations (fMRI) were then mapped to a standard atlas and the brain regions were compared. **Results:** Brain regions in the resting state of the healthy subject under investigation seemed to conform to canonical resting-state brain networks using our analysis method. More EEG source signals demonstrated significant nonlinearity compared to fMRI source signals. The patterns of observed EEG recurrence plots were more dynamic and rapid compared to the more spatially coherent patterns in fMRI recurrence plots. Evidence of a possible convergence in some recurrent patterns between the two modalities exists. **Conclusion:** Combining ICA for component extraction with nonlinear time series analysis for detailed dynamic analysis holds promise as a comprehensive approach to analysing brain function under non-invasive neuroimaging methodologies. It remains to be determined whether the patterns observed in one subject can be generalized to a group of healthy subjects in the resting state, and how the patterns may change on a task-based paradigm. This approach unlocks possibilities for better biomarkers for neurological conditions, more precise mapping of brain networks, and ultimately, a deeper understanding of the brain's complex dynamics.

# Potential targeted LAT1 focused on the management of glioblastoma in nuclear medicine perspective: A literature review

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## ABSTRACT

**Introduction:** Aggressive brain tumour glioblastoma multiforme (GBM) has few therapeutic choices and a dismal prognosis. Conventional treatments only marginally improve survival, which leads to the hunt for new targets like LAT1 (L-type amino acid transporter 1). From the standpoint of nuclear medicine, this literature review assesses the possibility of LAT1-targeted treatments in the treatment of glioblastoma. By examining preclinical and clinical research, we examine the role of LAT1 in glioblastoma metabolism, its utility for diagnosis, and the efficacy of radiopharmaceuticals targeting LAT1. Previous studies have established LAT1's overexpression in glioblastoma and its role in tumour metabolism but limited data appear, such as most studies are preclinical, with few clinical trials evaluating LAT1-targeted therapies in GBM patients, heterogeneous methodologies, diagnostic vs therapeutic focus, and long-term outcomes. **Materials and Methods:** A literature search was conducted using databases such as PubMed, Google Scholar, and ScienceDirect, covering publications from 2010 to 2024. Keywords included "glioblastoma," "LAT1," "nuclear medicine," "targeted therapy," and "radiopharmaceuticals." The inclusion criteria were studies looking at LAT1 expression in glioblastoma, evaluating LAT1-targeted therapies, and using LAT1 in diagnostic imaging. Outcomes LAT1 expression on Glioblastoma LAT1 and Tumour Metabolism, LAT1-Targeted Radiopharmaceuticals radiolabelled amino acids, showed good specificity and sensitivity in glioblastoma imaging, according to several important findings in the literature study. **Results:** Several key findings in literature review identified that LAT 1 expression on Glioblastoma LAT1 and Tumour Metabolism, LAT1-Targeted Radiopharmaceuticals radiolabelled amino acids, demonstrated high specificity and sensitivity in glioblastoma imaging and Therapeutic Potential Combined treatment approaches in preclinical models. **Conclusion:** The substantial promise of LAT1-targeted therapeutics in the therapy of glioblastoma is highlighted by the review, especially when viewed from the nuclear medicine perspective. Due to its crucial involvement in tumour metabolism and overexpression in glioblastoma, LAT1 is a desirable target for both therapeutic and diagnostic applications. LAT1 inhibitors have the potential to increase therapeutic efficacy, whereas LAT1-targeted radiopharmaceuticals provide better imaging accuracy.

# Sociodemographic influences on lumbar disc degeneration severity and the diagnostic potential of disc-CSF signal ratio: Insights from a Malaysian population study

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## ABSTRACT

**Introduction:** Lumbar disc degeneration involves structural changes and loss of water content in discs significantly impacts spinal health and quality of life. The Pfirrmann Grading System is a widely used method for assessing the severity of lumbar disc degeneration based on MRI findings. The primary objectives of this study are to investigate the relationship between sociodemographic factors (age, gender, and race) and the severity of lumbar disc degeneration based on the Pfirrmann Grading System and examine the correlation between the disc-CSF signal ratio and Pfirrmann grades to evaluate its potential as a diagnostic tool in a Malaysian population. **Material and Methods:** This retrospective cross-sectional study was conducted at Hospital Sultan Abdul Aziz Shah and included patients who underwent MRI lumbosacral spine scans between January 2022 and December 2022. Sociodemographic data and radiological images were collected, with ethical approval from the institutional review board. The Pfirrmann grading was applied to assess lumbar disc degeneration from L1/L2 to L5/S1 levels. The disc-CSF signal ratio was calculated by measuring the signal intensity of the nucleus pulposus and cerebrospinal fluid (CSF) on mid-sagittal T2-weighted images. Statistical analyses included Chi-square tests, Kruskal-Wallis, Mann-Whitney tests, and Spearman rank correlation to explore the relationships between sociodemographic factors, Pfirrmann grades, and disc-CSF signal ratios. **Results:** The study included 182 participants, with a female predominance (63.2%) and a majority of Malay ethnicity (84.1%). Age distribution showed the highest prevalence in the 60-69 age group (29.1%). The analysis revealed significant relationships between sociodemographic factors and lumbar disc degeneration. Females exhibited higher rates of moderate degeneration (Grade 3), while males showed more severe degeneration (Grades 4 and 5). Age-related trends indicated increased severity with advancing age, particularly in older age groups (60-69 and >70). Racial analysis highlighted significant differences, with Malays showing higher rates of moderate degeneration and Chinese and Indians exhibiting more severe degeneration. The disc-CSF signal ratio showed a significant inverse correlation with Pfirrmann grades ( $R^2 = 0.845$ ), indicating its potential as a reliable diagnostic measure. **Conclusion:** This study underscores the significant impact of sociodemographic factors on lumbar disc degeneration severity. The strong correlation between the disc-CSF signal ratio and Pfirrmann grades suggests that the disc-CSF signal ratio can serve as a valuable diagnostic tool particular in Malaysia clinical settings. Early detection and targeted interventions are crucial to mitigate the progression of lumbar disc degeneration, ultimately improving patient outcomes and quality of life.

# Reliability of spectral features for early ASD diagnosis in children using awake EEG

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## ABSTRACT

**Introduction:** Autism Spectrum Disorder (ASD) is a neurological condition that has been characterized with a wide variability of severity levels, subtypes and symptoms. Early diagnosis allows clinicians and caretakers to implement early and effective interventions that can help patients in their activities of daily living. Researchers have explored potential electroencephalography (EEG) neuromarkers to assist in the prognosis and diagnosis of ASD. However, inconsistent findings due to the heterogeneity of this disorder have led to poor generalization of these neuromarkers as a diagnostic tool for ASD. Hence, this study investigates the reliability of spectral feature extracted during awake conditions in ASD children and its potential or challenges in predicting the severity of this disorder. **Materials and Methods:** Data collection was conducted at the Hospital Pakar Kanak-Kanak (HPKK) where 18 ASD children between the ages 4-16 were recruited to record their brain activity whilst in awake condition. The experiment involved EEG recording during eyes closed and eyes open as the resting condition and watching three muted videos as the activated condition. In this work, the reliability of spectral features was compared between (1) minimal and Happilee automated pre-processing pipelines, and (2) five window lengths used to estimate Welch's power spectral density. Dispersion in the spectral features across 21 scalp regions was measured using coefficient of variation and analysed using the intraclass correlation coefficient (ICC) across four 30-second epochs for each resting and activated conditions. Surface Laplacian was conducted on the clean EEG signals to reduce the effects of volume-conduction. Finally, a regression analysis was conducted to observe whether the reliability of spectral features improves the prediction of restrictive and repetitive behavioural (RRB) symptoms in ASD children. **Results:** Reliability of the spectral features in the raw EEG signals during the first two sessions (eyes-closed and eyes-open) was low for all brainwaves ( $ICC < 0.5$ ) but not in the subsequent sessions (watching videos and eyes-open). This finding concurs with the remarks from lab technologists on the excessive movements exhibited by the subjects at the beginning of the EEG recording. Spectral features from the minimal pipeline had lower reliability after pre-processing ( $ICC < 0.75$ ), but this improved after conducting surface Laplacian ( $ICC > 0.75$ ). However, the opposite was observed from the Happilee pipeline where reliability of the spectral features extracted from surface Laplacian dropped between moderate to low ICC. Moreover, shorter window length was observed to have a slight increase in the ICC values, but still within the moderate to good reliability range. Lastly, spectral features extracted through minimal pre-processing with longer window length resulted in the strongest regression model ( $R^2 = 0.76$  and  $RMSE = 0.38$ ) in predicting RRB scores. **Conclusion:** Hence, this study concludes that reliability in spectral features of ASD children may not be a good benchmark to gauge potential neuromarkers. Due to the heterogeneity of the ASD, retaining the variability of EEG signals through minimal pre-processing and the use of longer window length to extract spectral features may improve the statistical and predictive power of ASD neuromarkers.

# Imaging samarium-153 on a small animal SPECT/CT system with pinhole collimators: A feasibility study

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## ABSTRACT

**Introduction:** Pre-clinical nuclear medicine research forms a valuable step in developing novel radiopharmaceuticals for diagnosis and therapy. Recently, dedicated animal imaging systems that feature single photon emission computed tomography (SPECT) technology have been developed. This study aims to demonstrate the feasibility of a small animal SPECT/CT system (Albira Si<sup>TM</sup>, Bruker, USA) for <sup>153</sup>Sm imaging in preclinical studies. **Materials and Methods:** The Albira Si<sup>TM</sup> SPECT/CT features a continuous CsI(Na) crystal detector with two pinhole collimators that can detect 30-400 keV gamma rays. To calibrate the system, a vial of 14.8 MBq/mL <sup>153</sup>Sm solution was imaged using 120-mm field-of-view (FOV), energy window of 103 keV  $\pm$  20%, and dual-energy scatter correction. The images were reconstructed using the OSEM algorithm and analyzed using PMOD software. The integral uniformity and sensitivity were assessed by drawing a cylindrical VOI at the centre of the image. As a pilot study, one liver tumor-bearing Sprague-Dawley rat injected with ~15 MBq <sup>153</sup>Sm microspheres was imaged at 24 h and 48 h post-injection to evaluate the biodistribution. **Results:** Phantom studies revealed that integral uniformity of the image is 20% with an 8% coefficient of variation. The sensitivity for a pinhole collimator configuration is 21.7 cps/MBq. The SPECT/CT images of the liver tumor-bearing rat treated with <sup>153</sup>Sm microspheres showed localized hotspots in the injected sites with no leakage to nearby normal tissues for both time points. The biodistribution study showed that 69% of the detected activity were localized in the tumour site. **Conclusion:** This feasibility study showed that the Albira Si<sup>TM</sup> micro-SPECT/CT system can be used to detect and quantify <sup>153</sup>Sm activity in phantoms and small animals. Characterization of the image quality and quantification accuracy will be conducted. The machine will be used for preclinical evaluation of <sup>153</sup>Sm for theranostic applications.

# Abnormal findings of interictal 18F-FDG PET-CT scan in children with refractory epilepsy: Case series and early institutional experience

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## ABSTRACT

**Introduction:** Refractory or intractable epilepsy could be challenging to manage with precise underlying disease mechanism is not completely understood. Literatures and prior studies have described that basal ganglia-thalamic metabolism can also be affected in epilepsy cases. Area of reduced tracer uptake or hypometabolism on interictal fluorodeoxyglucose positron emission tomography-computed tomography (FDG PET-CT) may suggest the possibility of epileptic focus. Our centre started to offer FDG PET-CT services in September 2020 including paediatric nuclear neurology. Thus, we aimed to primarily describe abnormal findings observed on interictal FDG PET-CT scan done among the initial cohort of paediatric refractory epilepsy cases and secondly investigate any altered basal ganglia-thalamic metabolism as reflected by reduction in maximum standardised uptake value (SUVmax). **Materials and Methods:** Case series and retrospective review done for intractable epilepsy patients aged below 18 years old who had abnormal FDG PET-CT scan (October 2020 – January 2021). Brain protocol with image acquisition performed from vertex to skull base in all cases. Consensus reporting done by nuclear medicine physicians and paediatric neurologist. Demographic, clinical parameters, prior brain EEG/MRI and FDG PET-CT scan findings including SUVmax readings of bilateral thalamus and basal ganglia (BG) were compiled. Descriptive and statistical analysis were applied accordingly. **Results:** Study sample consisted of 13 patients (6 males; 7 females). Mean age was 8.77 (4 – 17) years. Semiology and duration of seizure varies according to patients. Abnormal EEG observed in all patients while indeterminate or abnormal MRI findings were noted in only 9 patients. FDG PET-CT revealed hypometabolism involving unilateral cerebral hemisphere in 9 patients (69%) while bilateral cerebral involvement seen in 4 patients (31%). Most common region affected with hypometabolism was the temporal lobe in 8 cases (62%). Cerebellum diaschisis seen in 2 patients. Average SUVmax readings for right thalamus, left thalamus, right BG, and left BG for patients with epileptogenic foci in bilateral cerebral hemisphere were lower compared to those with unilateral cerebral involvement but not statistically significant (5.65, 5.43, 7.68 and 7.48 vs. 8.32, 8.37, 11.32 and 10.96 respectively,  $p > 0.05$ ). **Conclusion:** Among our early cohort of paediatric refractory epilepsy cases with abnormal interictal FDG PET-CT findings, majority had hypometabolism suggestive of epileptogenic foci involving unilateral cerebral hemisphere. Most common region affected was temporal lobe. Those with bilateral cerebral hemisphere involvement appeared to have altered basal ganglia-thalamic metabolism though not statistically significant. Future research recommended to validate these findings.