#### The Chinese University of Hong Kong Department of Psychiatry Schedule for April, 2025

<u>Date</u> Apr3	<u>Time</u> 14:30-15:30	Activity Research Seminar * Genetic and molecular association between inflammation related genes and mild cognitive impairment			Ms. I	Speaker(s) Ms. Ruonan GAO Supervisor: Dr. SL MA	
	15:30-16:15	Research Seminar * Leveraging artificial intelligence for detection of suicidal ideation through speech analysis				Ms. Phoebe CHAN  Supervisor: Dr. Tim LI	
	16:15-17:00	Research Seminar *  Smartphone-based digital phenotyping of motor and non-motor biomarkers across early stages of asynucleinopathies			Super Co-su	Maggie HE rvisor: Prof. YK WING upervisors: Dr. Joanne NNG, Dr. Tim LI	
		Registration link: <a href="https://bit.ly/4iY37US">https://bit.ly/4iY37US</a>					
Apr10	14:30-16:00		y Case Confer and Empathy	ence (MUL)*#	Dr. Irene KAM		
	16:00-17:00	0 Psychotherapy Supervision (MUL)*#					
Apr17	14:30-16:30	Quality Assurance Meeting (SH)# / (TPH)#					
Apr24	14:30-16:00	Academic Lecture (MUL)*  A social cognitive neuroscience perspective on Autism  Spectrum Disorder (ASD)  Registration link: <a href="https://bit.ly/4i08Zwi">https://bit.ly/4i08Zwi</a>			Resea Depa Facul The C	Dr. Ada WANG Research Assistant Professor Department of Psychiatry Faculty of Medicine The Chinese University of Hong Kong	
Venue: *Live	e video #Closed meeting	@Non-CME Event	MUL Seminar Room, Multi-centre, Tai Po Hospital Tai Po, N.T.	TPH Conference Room 1 G/F, Wing D Tai Po Hospital Tai Po, N.T.	Ward 7AB Dept. of Psychia	1AL Rm. 1005, Dining Room Ward 1AL, 1/F Tai Po Hospital spital Tai Po, N.T.	





# Research Seminar

Date: 3 APR 2025 (THU)
Time: 14:30-15:30
Venue: Zoom

**Register Now** 



Ms. Ruonan GAO
Supervisor: Dr. SL MA

Topic: Genetic and molecular association between inflammation related genes and mild cognitive impairment

#### **Abstract:**

Alzheimer's Disease (AD) is a neurodegenerative disease and it is the most common form of dementia. Mild cognitive impairment (MCI) is a state between normal aging and AD when memory starts to decline. The exact mechanism of AD has not been fully understood, however, several mechanisms have been suggested to participate in AD pathogenesis, including neuroinflammation. The NOD-like receptor pyrin domain-containing 3 (NLRP3) inflammasome is a multi-protein complex that regulates inflammation and plays an important role in the innate immune system. Recent studies have demonstrated the linkage between NLRP3 and AD. As AD was determined by both genetic and environmental factors, this study aims to evaluate the genetic relationship between NLRP3 and MCI in Chinese population, as well as the molecular relationship in microglia cell model.

In this project, the genetic association of NLRP3 single nucleotide polymorphisms (SNPs) with MCI was studied in 331 MCI patients and 235 healthy controls. 12 tag SNPs and 2 exon SNPs were selected and genotyped. The genotype distributions of rs7525979 and rs10754558 were significantly different between MCI patients and healthy controls. The expression level of ten inflammation-related genes were quantified in peripheral blood mononuclear cells (PBMC) by quantitative polymerase chain reaction (qPCR). The gene expression level of NLRP3 was positively correlated with the gene expression levels of IL-III, IL-18, IFN-III, AIM2, CASP1, CASP5, PYCARD, TNF-III and NEK7 in PBMC (p<0.001). The effects of NLRP3 SNPs on inflammation gene expression were also examined. rs12564791 was associated with the gene expression level of NLRP3, IL-18, PYCARD, CASP1 and rs10754557 was associated with the gene expression level of NEK7, indicating that NLRP3 SNPs may affect the expression level of inflammation related genes including NLRP3.

SNPs showing significant association with inflammation gene expression were selected and functional studies were performed. Luciferase assay with vectors containing the rs10754555 and rs10754558 G to C mutation showed significantly lower luciferase activity, suggesting G allele was associated to greater enhancer activity. The 3' untranslated region (UTR) SNP rs10754558 G to C mutation showed a potential suppressive effect on the interaction between NLRP3 and miR-425-3p.

181 subjects were followed up for 2 years, including 84 MCI patients and 97 healthy controls, to study the predictive value of NLRP3 SNPs on cognitive decline. rs7525979 and rs12564791 were associated with decrease in Mini-mental State Examination (MMSE) score. rs12143966, rs10754558 and rs12564791 were associated with Montreal Cognitive Assessment (MoCA) score decline. As miR-425-3p showed interaction with NLRP3, miR-425-3p expression in plasma were quantified by qPCR in a subset of MCI patients and age and gender matched healthy controls. The result showed miR-425-3p gene expression was negatively correlated to MMSE score and MoCA score.

The effect of miR-425-3p on modulating inflammation was further studied in vitro by using mouse microglia cell line BV2. Overexpression of miR-425-3p was found to inhibit inflammation induced by lipopolysaccharide (LPS). Gene expression of IL-1\(\text{IL}\), TNF-\(\text{IL}\), IL-6 and iNOS, secreted IL-1\(\text{IL}\) in cell supernatant and protein level of NLRP3, pro-IL-1\(\text{IL}\) and PYCARD were all decreased after miR-425-3p mimics transfection. LPS stimulation downregulated miR-425-3p expression in BV2. These results indicated that miR-425-3p inhibit inflammation induced by LPS in BV2. SUMO Specific Peptidase 6 (SENP6) was predicted to be the target gene of miR-425-3p and was confirmed by dual luciferase assay. SENP6 gene expression was decreased after miR-425-3p transfection. Knockdown of SENP6 by siRNA led to lower cell viability and significantly increased inflammation, as reflected by the upregulation of inflammation related genes and protein levels.

In conclusion, this project suggested that NLRP3 SNPs were associated with development of MCI and disease progression. NLRP3 SNPs might regulate inflammation gene expression through interactions with miRNA. miR-425-3p showed anti-inflammation effect in by inhibiting inflammation gene and protein expression in activated BV2 cells, probably through the interaction with SENP6. These results suggested that inflammation plays a pivotal role in the pathogenesis of AD.







### Research Seminar

Date: 3 APR 2025 (THU)
Time: 15:30-16:15
Venue: Zoom

**Register Now** 



Ms. Phoebe CHAN
Supervisor: Dr. Tim Ll

Topic: Leveraging artificial intelligence for detection of suicidal ideation through speech analysis

#### **Abstract:**

**Background:** Suicide is a leading cause of preventable death worldwide. Detecting suicidal ideation (SI) remains challenging due to stigma, patient reluctance, and resource constraints in healthcare systems. Speech analysis during routine clinical consultations offer a promising alternative. Artificial intelligence (AI) has shown potential in mental health research, particularly in analyzing language patterns to infer psychological states, while behavioral and neuroimaging studies have shown the close relationship between language use and social-emotional processing. Tools like the Linguistic Inquiry and Word Count (LIWC) translate words into linguistically and psychologically meaningful categories. Individuals with suicidal tendencies often exhibit distinct language patterns, such as increased use of first-person singular pronouns and negative emotion words.

**Objectivity:** This study aims to develop a speech-based SI detection system leveraging AI techniques, including natural language processing (NLP) and machine learning (ML). The model was trained on existing structured interview transcripts (n=299) of depressive patients and healthy controls, including clinician-rated SI. The model was further tested in a clinical setting to identify language features of SI with an aim to provide timely and accurate assessments to aid clinicians.

**Methodology:** The study involved 107 psychiatric outpatients recruited from a university-affiliated hospital in Hong Kong. Participants underwent a short screening interview, including an SI-related question, and their verbal responses during consultations were recorded. Participants also completed questionnaires after consultation. SI was evaluated based on the most severe outcome of clinician judgment, the Columbia Suicide Severity Rating Scale (self-report), and the SI screening question. Speech recordings were transcribed using Automatic Speech Recognition tools and manually refined, followed by language feature extraction. Ordinal logistic regression modeled the relationship between language features and suicide risk, adjusting for socio-demographic and emotional covariates. ML models were trained with these features to detect SI. Nine algorithms were used with various feature combinations (LIWC, part-of-speech [POS], and both), and performance was evaluated using Receiver Operating Characteristic (ROC) curve analysis. To account for multiple comparisons, Bonferroni correction was applied.

**Results:** Ordinal logistic regression revealed significant associations between SI and linguistic features during consultation, including time-related words (OR = 1.61, p = 0.01). The Support Vector Machine (SVM) achieved the best performance on 5-fold cross-validation with the clinical interview data (AUC = 0.998, F1 = 0.970, p < 0.01). However, performance on external validation using the consultation data was lower, with XGBoost using LIWC features performing best (AUC of 0.642, F1 = 0.354, p = 0.01). Retrained models on 5-fold cross-validation using consultation data improved results, with the SVM with LIWC and POS tagging performed the best (AUC = 0.878, F1 = 0.713, p < 0.01).

**Conclusion:** ML models incorporating linguistic features can effectively enhance SI detection in clinical settings, enabling early intervention with a possibility of reducing suicide risks through timely support. However, generalizing models across different conversational and clinical contexts remains a challenge. Future research should expand sample size and apply the model to other clinical settings to evaluate performance and applicability for early identification and support for at-risk individuals.







## Research Seminar

Date: 3 APR 2025 (THU)
Time: 16:15-17:00
Venue: Zoom

**Register Now** 



Ms. Maggie HE

Supervisor: Prof. YK WING

Co-supervisors: Dr. Joanne HUANG & Dr. Tim Ll

Topic: Smartphone-based digital phenotyping of motor and non-motor biomarkers across early stages of α-synucleinopathies

#### **Abstract:**

Neurodegenerative a-synucleinopathies, including Parkinson's disease (PD), are the second-most common neurodegenerative diseases characterised by an array of motor and non-motor symptoms. However, a long delay usually lies between the first noticeable symptom of PD and the formal diagnosis via conventional clinical evaluations. Currently, the identification of the disease features and signs at early stages is mostly based on conventional clinical assessments, sometimes with the aid of structured interview and rating scale such as the Unified Parkinson's Disease Rating Scale. However, when the PD patients would present with conspicuous motor dysfunction, it has usually reflected a substantial neuronal loss in the neuronal circuit. In addition, non-motor features usually predate motor manifestation in the development of PD for a long period. Moreover, conventional clinical assessments are subjected to other issues such as accessibility, training of assessors and inter-rater variability. Thus, it is crucial to develop a more sensitive and reliable tool to identify motor and non-motor symptoms/signs at its early stages.

In this regard, advancements in digital mobile technology have allowed unobtrusive, refined, and early assessment in the field of clinical medicine and research. Smartphone-based digital assessments, utilizing built-in sensors, offer objective and accurate data collection. Nevertheless, previous studies have only applied digital tools to assess a single or a specific group of functions in patients with full-blown asynucleinopathies. In other words, there have been only limited studies exploring digital measures in patients with isolated rapid eye movement sleep behaviour disorder (iRBD), a specific prodromal stage of a-synucleinopathies.

Therefore, we developed a custom application named 'SmartBrainApp' based on previous evidence that some early neurodegenerative features already appear in the prodromal stage of PD in motor (such as subtle motor, speech and facial expression signs) and non-motor functions (such as impaired colour vision, executive and visuospatial function, altered impulsivity features). 'SmartBrainApp' contains 5 domains of digitalized tests that assess psychomotor and cognitive, impulsivity, motor, voice and facial expression. We aimed to validate these comprehensive smartphone-based digital assessments in the measurement of  $\alpha$ -synucleinopathy by focusing on PD, including content, construct, criterion validity, and test-retest reliability. In addition, we will evaluate its acceptability and feasibility; and further validate the practicality of the 'SmartBrainApp' in capturing the subtle motor and non-motor features in the prodromal stage of  $\alpha$ -synucleinopathies (iRBD). The potential findings of this smartphone App-based digital study, with a better capture of the motor and non-motor features in the early and prodromal stages, will help better monitoring of neurodegeneration progress and pave the way to assist the future neuroprotection strategies for  $\alpha$ -synucleinopathies.







# ACADEMIC LECTURE



### **Dr. Ada WANG**

Research Assistant Professor
Department of Psychiatry
Faculty of Medicine
The Chinese University of Hong Kong

- **24 APR 2025 (THU)**
- <u>(4)</u> 14:30 16:00
- Seminar Room, Multicentre, Tai Po Hospital & Zoom



# Topic: A social cognitive neuroscience perspective on Autism Spectrum Disorder (ASD)

#### **Abstract:**

As social beings, humans do not rely solely on their own but also interact with others to enhance their chances for survival. This interdependence on social environment is fundamental to typical development, yet for individuals with Autism Spectrum Disorder (ASD), understanding and integrating into such environments can be exceptionally challenging. In this talk, three main topics will be covered. (1) How typically developing individuals process social information. (2) The atypical social information processing observed in individuals with ASD. (3) Recent advances in intervention protocols designed to improve social cognition in those with ASD. By drawing connections between basic research and clinical applications, this presentation aims to shed light on the challenges faced by individuals with ASD and to demonstrate emerging strategies that may enhance their social integration and overall quality of life.

#### **Biography:**

Dr. Yang Wang is a Research Assistant Professor in the Department of Psychiatry at the Chinese University of Hong Kong (CUHK). She earned her Ph.D. in Psychology from CUHK. Her research spans different research fields including cognitive, social, and clinical neuroscience, with a focus on understanding information processing in both typical and special populations (e.g., ASD, schizophrenia). She employs different methodologies including behavioural, brain imaging, and neuromodulation approaches – such as electroencephalography (EEG), event-related optical signal (EROS), and transcranial magnetic stimulation (TMS). Her current work focuses on understanding atypical social cognitive functions in individuals with ASD and developing personalized intervention protocols.



