LBA1

Non motor symptoms profiles between Indian patients with Parkinson's disease in West Bengal, India and White Caucasians in Europe

Anna Sauerbier[1,2], Hrishikesh Kumar[3], Rebecca Banerjee[3], Marium Umme Kulsum[3], Alexandra Rizos[4], Lauren Perkins[4], Theresa Chiwera[4], Dhaval Trivedi[4], Anne Martin[1], Miriam Parry[5], K Ray Chaudhuri[1,2,5]

[1] Neurology, King's College Hospital, London, UK

[2] Institute of Psychiatry, Psychology and Neuroscience, King's College Hospital, London UK

[3] Institute of Neurosciences, Kolkata, India

[4] Neurosciences, King´s College Hospital, London, UK

[5] Neurology, Lewisham and Greenwich NHS Trust, London, UK

Objective: The aim of this ongoing study is to have a holistic comparison between an European White Caucasian (WC) cohort with Parkinson's disease (PD) and resident Indian population from West Bengal as part of an international comparative survey.

Background: Previously, we reported that non motor and motor profiles might be different in WC people with Parkinson's disease (PwP) versus Indian PwP [1,2].

Methods: Indian PwP living in West Bengal, India and WC PwP living in London, UK were analysed. Cross sectional data is presented.

Results: Data from 46 Indian patients (80.4% male, mean age 64.2± 8.9 years, mean onset of disease 57.5±10.7 years, mean total scopa motor score 22.5±10.4) and 46 WC patients (65.2% male, mean age 67.3±12.3 years, mean onset of disease 60.3±12.9 years, mean total scopa motor score 16.5±9.2) are presented. The total non motor symptoms scale score was significantly higher in the Indian cohort compared to the WC cohort with the indian cohort reporting greater sleep, neuropsychiatric and autonomic symptoms.

Conclusions: These preliminary results suggest that NMS profiles might be different between WC versus Indian PwP. Further research investigating this is under way.

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References: [1] Sauerbier,A., [abstract]. Mov Disord 2014;29 Suppl 1:1060 [2] Ray Chaudhuri et al., Mov Disord 2000; 15:18-23

LBA2

Stress precedes hemifacial spasm: A retrospective study in multi-ethnic Penang, Malaysia

Kenny Tan[1], Gaik Bee Eow[1], Han Bing Chow[1], Chun Fai Cheah[1], Yuen Kang Chia[1], Jyh Yung Hor[1], Ruban Kanesalingam[1], Md Hanip Rafia[2], P.E. Samuel Easaw[3], Azman Ali Raymond[4], Thien Thien Lim[5]

1 Department of Neurology, Penang Hospital, Penang, Malaysia;

2 Department of Neurology, Kuala Lumpur Hospital, Kuala Lumpur, Malaysia;

3 Department of Medicine, Penang Medical College, Penang, Malaysia.

4 Medical Faculty, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia;

5 Island Hospital, Penang, Malaysia.

Objective To study the demographics of hemifacial spasm patients in a Penang tertiary hospital and analyze the role of stress as a possible trigger of hemifacial spasm.

Background Physiological stress is a body's method of reacting to the challenge. Stress slows healing rates and is associated with diseases like anxiety and heart disease.

Methods Retrospective analysis of 40 patients with hemifacial spasm and 37 age-and-sex matched control (public individuals). Patients who presented as new onset or follow-up cases for hemifacial spasm were included. Interviewer administered questionnaires based on the Social Readjustment Rating Questionnaire (SRRQ) and the Perceived Stress Scale (PSS) were used to obtain demographic data and assess the patients' stress level. Subjects were required to answer the questionnaires based on recall of events prior to the onset of hemifacial spasm. Higher PSS score suggests a higher stress level and a higher SRRQ predicts a higher probability of disease manifestation.

Results Forty hemifacial spasm subjects (17.5% Malays, 75% Chinese, 7.5% Indians) and 37 controls were

included. The subjects age of onset ranged from 26 to 74 years. Mean age of onset for females was at 52.9 years and 51 years for males. Fifty-eight percent of the cohort were women and 50% of the cohort had right hemifacial spasm. Seventeen subjects (42.5%) received a combination of botulinum toxin injection and oral medication (Clonazepam, Baclofen or Carbamazepine). Another 42.5% subjects received exclusively botulinum toxin injection while 15% of the subjects were only on oral medication. MRI Brain was done for 42% (n=17) of the subjects whereas 58% (n=23) did not have an MRI done. Of the 17 patients who had a MRI Brain done, 59% (n=10) were reported as normal, 41% (n=7) were abnormal. Four out of the 7 abnormal MRI demonstrated vascular compression of the facial nerve by an ectatatic vertebral artery. The other 3 were reported as having microangiopathy and lacunar infarcts. Hemifacial spasm subjects had higher PSS mean scores (18.80) compared to the control group (11.36) ($p<0.0001$). Majority of the subjects (57 %) scored more than 150 points in The SRRQ

Conclusion Our study shows that patients with hemifacial spasm achieve symptom control with combination of botulinum toxin injection and oral medication. Our cohort also showed that hemifacial spasm subjects experience significantly more stress prior to the onset of illness. This is consistent with the study of Johnson et al who concluded that subjects with closely spaced stressful life events may be at increased risk of developing hemifacial spasm. The result of this study raises the awareness regarding the impact of psychological stress on the manifestation of physical illness. However, larger randomized studies are needed to confirm this finding.

LBA3

Genomic study and subsequent in silico drug discovery for Parkinson's disease

Wataru Satake[1], Takeshi Uenaka[1], Cha Pei Chieng[1], Yukinori Okada[2], Kenichi Kashihara[3], Shigeo Murayama[4], Kazuko Hasegawa[5], Hideki Mochizuki[6], Atsushi Takeda[7], Mitsutoshi Yamamoto[8], Miho Murata[9], Nobutaka Hattori[10], Tatsushi Toda[1].

[1]Neurol, Kobe Univ, Kobe, Japan; [2]Hum Genet Disease Diversity, Tokyo Med and Dent Univ, Tokyo, Japan; [3]Neurol, Okayama Kyokuto Hsp, Okayama, Japan; [4]Tokyo Metro Geriatr Hsp and Inst of Gerontol, Tokyo, Japan; [5]Neurol, Sagamihara Natl Hsp, Sagamihara, Japan; [6]Neurol, Osaka Univ, Suita, Japan; [7]Sendai Nishitaga Natl Hsp, Sendai, Japan; [8]Takamatsu Neurol Clinic, Takamatsu, Japan; [9]Natl Cen Hsp of Neurol and Psy, Kodaira, Japan; [10]Neurol, Juntendo Univ, Tokyo, Japan.

Objective: To identify genomic variants with disease-risk and discover neuroprotective drugs for sporadic Parkinson's disease (PD).

Background: Sporadic PD is a complex disorder caused by multiple genetic variants. We previously reported a SNP-GWAS (Genome-Wide Association Study) which detected 4 sporadic PD-risk loci; *PARK16*, *BST1*, *α-synuclein*, and *LRRK2* (Satake et al, *Nature Genet* 2009). For further identification of PD-genes, we are intensively performing two large scale genomic studies; exome association study and expanded SNP-GWAS in Japan. Caucasian teams reported meta-GWAS which detected twenty four PD-risk loci. In order to link these PD-genes to drug-discovery directly, we applied *in silico* drug-discovery method to PD.

Methods: From information of two drug databases, we obtained 871 drug target genes. Using a protein-protein interaction (PPI) database, we listed genes which show PPI with PD-risk genes reported by GWAS.

Results: We detected 761 genes as PD-risk genes and those PPI-genes. Among those, using drug databases, we found 77 genes which are targeted by 54 approved drugs for other diseases. In order to examine whether detected drugs in our scan have neuroprotective effects, we performed LDH assay and cell viability assay using SH-SY5Y cells with exposure of rotenone. We found that 2 drugs significantly improved LDH release ($p=0.01$) and cell viability ($p=0.01$) under condition of rotenone exposure, which suggests these 2 drugs have neuroprotective effect. Moreover, in our *in silico* drug screening, we could detect Modafinil and HDAC inhibitor as drugs which affect *α-synuclein* and *tau* respectively.

Conclusion: Gene-identification and subsequent *in silico* drug discovery are efficient for extract candidates of neuroprotective drugs for PD.

LBA4

The effect of expiratory muscle strength training in Cantonese speaking Parkinson's disease patients: A pilot

study

Tiksang Eric Tong, Manwa Lawrence Ng, Yan Nan
Speech Science Laboratory, Division of Speech and Hearing Sciences, The University of Hong Kong, Hong Kong, China
Key Laboratory of Human-Machine Intelligence-Synergy Systems, Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, Shenzhen, China

Objective: The current pioneering study aimed to evaluate the effect of expiratory muscle strength training (EMST) on speech production in Parkinson's disease (PD) patients in Hong Kong. Vocal loudness and maximum phonation time (MPT) associated with PD speakers were compared before and after the four-week EMST program.
Background: Upper airway obstruction (UAO) is commonly seen in PD patients. Speech production can be impaired that can further influence the social and daily activities of patients with PD. Hypokinetic dysarthria, characterized by reduced vocal loudness and imprecise consonant production, has been diagnosed in over 80% of patients with PD. Expiratory muscle strength training (EMST) was found effective to improve expiratory driving force for both ventilatory and non-ventilatory actions as a 4-week intensive program. Previous PD studies focused only on its effects on swallowing; few examined the effect of EMST on speech production among Hong Kong PD patients.
Methods: Ten individuals with PD (age = 64.4 ± 5.5 years) were recruited from the Hong Kong Parkinson's Disease Association. Speech disorder severity was assessed and matched by a specialized speech pathologist. Maximum expiratory pressure (MEP), vocal loudness (VL), and maximum phonation time (MPT) were obtained before and after EMST program. During the 4-week intensive training, participants were instructed to blow through the EMST device (EMST150, Aspire Products LLC, Florida, USA) (with loading set at 75% of MEP) as hard and fast as possible after a maximum inhalation for 25 times per day monitored by an experience speech pathologist. Baseline data on MEP, VL and MPT were then compared and analyzed statistically.
Results: All participants showed significant improvement in MEP, VL and MPT (increased by 60.5%, 114.5% and 18.9% respectively) after 4-week training of EMST. It suggests that EMST program can help improve the phonatory functions in patients with PD.
Conclusions: All participants with PD benefited from the EMST program in terms of vocal loudness and time of sustained phonation. Training in expiratory muscle strength can be considered as a new direction of speech training in PD.

LBA5

Design, synthesis and anticonvulsant activity of 1, 3, 5 -triazin-2-imine/one/thione incorporated pyridazines

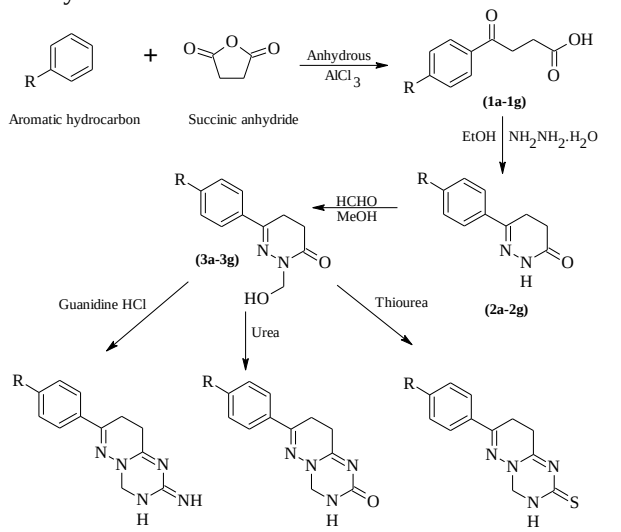
Ravinesh Mishra1,2, Anees A. Siddiqui2, Asif Husain2, Mohd Rashid2, Sweta Bhardwaj2*
1Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Jamia Hamdard (Hamdard University), Hamdard Nagar, New Delhi-110 062, India. 2School of Pharmacy & Emerging Sciences, Baddi University of Emerging Science & Technology, Baddi (Solan), Himachal Pradesh 173 205, India.

Objective: 1,3,5-Triazin-2-imine/one/thione incorporated pyridazines were synthesized and final compounds were structurally elucidated on the basis of IR, ^{1}H-NMR & mass spectral data and microanalyses. The final compounds were evaluated for anticonvulsant activity by maximal electroshock seizure (MES) method. The neurotoxicity was determined by rotorod toxicity test on male albino mice. The preliminary results showed that all of the tested compounds were protective against MES at 100-300 mg/kg dose levels. The compounds numbered **4d-4e, 4j-4k,** and **4m-4t** were most protective against MES even at 30 mg/kg dose levels.
Background: Pyridazines are an important class of five membered heterocyclic compounds and were found to have potential antimicrobial, anti-inflammatory, antipyretic, antidepressant, antibacterial, tranquillizing, anticancer, antiviral, antihypertensive, antiarrhythmic, antitubercular, psychoanaleptic and antidiabetic activity. However pyridazines are still least explored compounds for anticonvulsant profile even, their function is quite stable[14]. In view of this and our continued interest in the synthesis of bioactive heterocyclic compounds with stable fragment, it was thought of interest to synthesize some new pyridazines. In the initial step, β-aroyl propionic acids **(1a-g)** were synthesized by Friedel-Crafts acylation of appropriate hydrocarbons with succinic anhydride in the presence of anhydrous aluminum chloride. The β-aroyl propionic acid **1** was cyclized on hydrazinolysis to yield 6-(substituted-

phenyl)-4,5-dihydropyridazine-3(2*H*)-one **(2a-g).** Pyridazinone **2** was treated with formaldehyde to give the 2-hydroxymethyl derivative i.e. 2-(hydroxymethyl)-6-(substituted-phenyl)-4,5-dihydropyridazin-3(2*H*)-one **(3a-g)** which on cyclocondensation with guanidine hydrochloride/urea/thiourea yielded 7-phenyl-3,4,8,9-tetrahydro-2*H*-pyridazino[1,6-*a*][1,3,5]triazin-2-imine/one/thione **(4a-u)** (**Figure 1**).

Methods: General procedure for the synthesis of 7-substituted-phenyl-3,4,8,9-tetrahydro-2H-pyridazino[1,6-a][1,3,5]triazin-2-imine/one/thione derivatives **(4a-u).**

A mixture of 2-(hydroxymethyl)-6-(substituted-phenyl)-4,5-dihydropyridazin-3(2H)-one derivatives **3** (0.001 mole) and guanidine hydrochloride/urea/thiourea (0.001 mole) was heated in an oil bath for 3 hours, cooled and triturated with ethanol. The whole content was refluxed on water bath for 8 hours. After completion of the reaction ethanol was distilled off and the residue poured into crushed ice to separate out the title compound **(4a-u)**. The solid which separated out, was filtered and crystallized from ethanol.



4a	R= H	**4b**	R= H	**4c**	R= H
4d	R= CH_3	**4e**	R= CH_3	**4f**	R= CH_3
4g	R= CH_3O	**4h**	R= CH_3O	**4i**	R= CH_3O
4j	R= C_2H_5	**4k**	R= C_2H_5	**4l**	R= C_2H_5
4m	R= $CH_2CH(CH_3)_2$	**4n**	R= $CH_2CH(CH_3)_2$	**4o**	R= $CH_2CH(CH_3)_2$
4p	R= C_6H_5	**4q**	R= C_6H_5	**4r**	R= C_6H_5
4s	R= H	**4t**	R= H	**4u**	R= Cl

Figure 1. Synthesis protocol for various 7-substituted-phenyl-3,4,8,9-tetrahydro-2*H*-pyridazino[1,6-*a*][1,3,5]triazin-2-imine/one/thione derivatives.

Anticonvulsant activity Animal- Seven albino male mice (25-30 g) in our laboratory were used for each compound. They were kept under standard condition at an ambient temperature of 25 $\pm$ 2 °C. Food and water were withdrawn prior to the experiments.

Standard drug (Phenytoin): 5 mg/kg body weight

Test compounds (4a-t): equivalent to phenytoin/30 mg/kg body weight

Equipments- Electroconvulsometer [Stimulator (Grass S88, Astro-Med. Inc.), constant current unit (Grass CCU1A, Grass Medical Instruments), and corneal electrode, rotarod used in the neurotoxicity test]. An apparatus with ear electrodes (Woodbury and Davenport 1952) was used to deliver the stimuli.

The compounds were screened for their anticonvulsant activity by MES method. Supra maximal electroshock of alternating current intensity of 50mA, 60Hz (five to seven times that necessary to elicit minimal seizures) for 0.2 sec. duration was given to mice via ear electrodes. All compounds were solubilized or suspended in 30% aqueous polyethylene glycol 400 (PEG 400), administered with test compounds in a volume of 0.01 ml/g body weight. Control animals received 30% aqueous PEG 400. Mice were tested at 30 minutes and 4 hours following doses of 30, 100 and 300 mg/kg of test compound. The animals were observed closely for 2 min. The abolition of the hind limb tonic extensor spasm indicated the test compound's ability to inhibit MES-induced seizure spread/

discharge through neural tissue and was recorded as an increase of anticonvulsant activity. Percent of inhibition of seizures relative to controls was calculated.
In MES Test: Values represent number of mice protected divided by number of mice tested.

Neurotoxicity test: Toxicity induced by a compound was detected in mice using the standardized Rotorod test. All mice were trained to stay on rotating rotorod. Untreated control mice, when placed on a six rpm rotation rod (one inch diameter knurled plastic rod) can maintain their equilibrium for a prolonged period of time. Neurological impairment like ataxia, sedation and hyper excitability can be demonstrated by the inability of a mouse to maintain equilibrium for one minute in each of three successive trials.
The animal was placed on a one inch diameter knurled wooden rod rotating at six rpm. Normal mice remain on a rod rotating at this speed indefinitely. Neurologic toxicity was defined as the failure of the animal to remain on the rod for one min.
In Rotorod Test (NT): Values represent number of mice toxic divided by number of mice tested.

Data from screen **I** (anticonvulsant & Neurotoxicity identification) was described in Table 2.

Table 2: Screening data of synthesized compounds

				MES (30 min) % Protection							MES (30 min) % Protection		
Compd.	R^1	R^2	R^3	30	100	300 (mg/kg)	Compd.	R^1	R^2	R^3	30	100	300 (mg/kg)
4a	H	H	H	50*	100	100	**4k**	CH_3	H	H	75**	100	100
4b	H	H	OCH_3	50*	100	100	**4l**	CH_3	H	OCH_3	50*	100	100
4c	H	H	Cl	50*	100	100	**4m**	CH_3	H	Cl	75*	100	100
4d	H	Cl	H	75 **	100	100	**4n**	CH_3	Cl	H	75**	100	100
4e	H	H	F	100***	100	100	**4o**	CH_3	H	F	100***	100	100
4f	OCH_3	H	H	50*	100	100	**4p**	Br	H	H	75**	100	100
4g	OCH_3	H	OCH_3	25	100	100	**4q**	Br	H	OCH_3	75**	100	100
4h	OCH_3	H	Cl	50*	100	100	**4r**	Br	H	Cl	75**	100	100
4i	OCH_3	Cl	H	50*	100	100	**4s**	Br	Cl	H	100***	100	100
4j	OCH_3	H	F	100***	100	100	**4t**	Br	H	F	100***	100	100
Phenytoin	-	-	-	100***	100***	100***							

*p < 0.05, **p < 0.01, ***p < 0.001

Statistical analysis: Results were expressed as Mean±SEM (Standard Error Mean). Data obtained from pharmacological experiments were analyzed by one way analysis of variance (ANOVA) followed by Dunnett's post

hoc test and used to evaluate the results, employing Pharmacologic Calculation System Version 4.1. (Microcomputer Specialists). A p-value of less than 0.05 was considered statistically significant.
Results: The compounds numbered **4d-4e, 4j-4k,** and **4m-4t** were most protective against MES even at 30 mg/kg dose levels. Neurotoxicity was observed in almost none of the compounds in the dose range of 30-100 mg/kg as shown in Table 1. All of the tested compounds were found protective against MES-induced seizures at 100-300 mg/kg dose levels. The compounds numbered **4d-4e, 4j-4k,** and **4m-4t** were most protective against MES even at 30 mg/kg dose levels. Neurotoxicity was observed in almost none of the compounds in the dose range of 30-100 mg/kg. The minimal behavioral toxic dose was found to be >30 mg/kg but <100 mg/kg. The test substances also appear to have a relatively rapid onset and short duration of action because both the anticonvulsant and toxic effects are greater at 30 min than at 4 hours. The compounds with electron withdrawing groups were found to be the most active as an anticonvulsant than those with electron releasing groups. The compounds with weaker releasing groups were found to be more active as an anticonvulsant than those with strong releasing groups. The anticonvulsant activity is more affected by the electron withdrawing substituent on the benzene 'attached to pyrazoline ring at *5*-position' than those 'attached to pyrazoline ring at *3*-position'. Any substituent on the benzene 'attached to pyrazoline ring at *3*-position' was found to have little effect on the anticonvulsant activity. The 4-fluoro derivatives were found to be most active as an anticonvulsant than the others, because of fluorine (an electron withdrawing group on *p*- position). The 3-chloro derivatives were found to be more active as an anticonvulsant than the 4-chloro derivatives. The compound with both fluorine and bromine substituent at the 'benzenes attached to pyrazoline ring at 5- and 3-positions respectively' was found to be the most active anticonvulsant among all the synthesized compounds.
Conclusion: The 7-substituted-phenyl-3,4,8,9-tetrahydro-2*H*-pyridazino[1,6-*a*][1,3,5]triazin-2-imine/one/thione derivatives **(4a-4u)** can be further modified to exhibit better potency than the standard drugs. Despite the usefulness of pyridazines, simple methods for the introduction of a range of substituents into this six membered heterocycle have not yet been extensively developed and for this reason, new advances in this area continue to be of interest. Further studies to acquire more information about Quantitative Structure Activity Relationships (QSAR) are in progress in our laboratory. The pyridazine derivatives discovered in this study may provide valuable therapeutic intervention for the treatment of Parkinson's disorder because it is one of the most serious health problems of the modern world with a continuous rise in the number of patients. The final compounds were evaluated for anticonvulsant activity by maximal electroshock seizure (MES) method. The neurotoxicity was determined by rotorod toxicity test on male albino mice. The preliminary results showed that all of the tested compounds were protective against MES at 100-300 mg/kg dose levels. The compounds numbered **4d-4e, 4j-4k,** and **4m-4t** were most protective against MES even at 30 mg/kg dose levels.

LBA6
JPDA (Japan Parkinson's disease Association)
Yoshiji Matsumoto
Abstract: Japanese total population are close to flat or almost slightly going down, and the peak ages of patients with PD in the demographic is increasing. Peak ages of PD age distribution are about 40~60 years old, so that, Parkinson Disease patient ratio (Total patient number/total population) will be increasing JPDA Organization has been initiated in year of 1973 by only 3 Persons (they are all PD patients). Oct 1976 JPDA started overed whole Japan but patients joined were 110 persons. JPDA funded at Feb 1977 by publishing bulletin No.1 More detail historical issues will be discussed JPDA Organization has been grown up from initial stage 110 membership to 8400, membership who will be able to various activities. General patients' assembly was held to discuss each other Study for Parkinson Disease inviting Doctors who will be medical doctor, government staff sometime. Negotiation with governmental organization to get more medical fund money. Have been succeeding. Lastly, JPC (Japan Parkinson Congress) constructed last year (2015) and first meeting was good results. This JPC meeting will be held by every two years.

LBA7
Slower deterioration of non-motor symptoms and quality of life in LRRK2 protective variant carriers with

Parkinson disease

*Xiao Deng [1,2], Bin Xiao [1,2], Hui-Hua Li [3], Kumar M. Prakash [1,4], Yu-Lin Ng[1], Yew-Long Lo [1,4], Eng-King Tan [1,4]**
[1]Department of Neurology, National Neuroscience Institute, Singapore General Hospital, Singapore, 169608, Singapore.
[2]Department of Neurology,The First Affiliated Hospital, Guangxi Medical University, Nanning, 530021, China.
[3]Department of Clinical Research, Singapore General Hospital, Singapore, 169608, Singapore.
[4] Duke-NUS Graduate Medical School, Singapore, 169857, Singapore
**corresponding to Dr. Tan E K: gnrtek@sgh.com.sg*
+these authors contributed equally to this work

Objectives: To assess the impact of LRRK2 R1398H and N551K variants on the clinical features and its progression in patients with Parkinson disease (PD).
Methods: In this prospective study, 31 LRRK2 protective variant carriers and 69 non-carriers were assessed and followed up to monitor disease severity, motor conditions, non-motor burden, quality of life, depression and daily living ability using Modified Hoehn and Yahr (H&Y) staging scale, Unified Parkinson's Disease Rating Scale (UPDRS) part III, Non-Motor Symptom Scale (NMSS), Parkinson's Disease Questionnaire-39 item version (PDQ-39), Hamilton Depression Rating Scale (HAMD), Schwab and England activities of daily living scale (ADL scale). The differences from baseline in LRRK2 protective variant carriers were compared to non-carriers by means of generalized estimating equation (GEE) model.
Results: LRRK2 R1398H and N551K variants decrease risk of developing young-onset PD (P=0.0326). A protective effect of the variants against depression (P=0.0217), disturbance in attention and/or memory (P=0.0347) and overall non-motor symptoms (P=0.0379) was found in the carriers at baseline. The longitudinal evaluation disclosed that R1398H and N551K carriers experienced little deterioration in most of the aspects of non-motor symptoms in the 4-year follow-up. Our study failed to find any effect of the variants on motor symptoms.
Conclusions: LRRK2 R1398H and N551K variants significantly halt the deterioration of non-motor symptoms and quality of life in PD and may represent a potential new target for PD treatment.

LBA8

Profile of Japanese encephalitis and autoimmune encephalitis patients in an 18-month period admitted in a tertiary hospital setting

Philippine Children's Medical Center, Philippines
Madelyn P. Pascual, Lillian V. Lee, Marilyn H. Ortiz

Objective: This report aims to present the clinical profile and similar signs and symptoms among proven cases of Japanese Encephalitis and Autoimmune Encephalitis admitted in an 18-month period in a tertiary hospital setting.
Background: Similar signs and symptoms are reported on both autoimmune and infectious causes of encephalitis, in particular, Japanese Encephalitis and N-methyl-D-aspartate receptor antibody encephalitis. Recent data reported co-existence between H1N1 influenza and Herpes Simplex Virus causing encephalitis and autoimmune antibody which suggests possible autoimmune mediation of these viruses in patients unresponsive to recommended treatment with prolonged neurologic or psychiatric symptoms.
Method: We reviewed the medical records of proven cases of Japanese Encephalitis and Autoimmune Encephalitis admitted from January 2014 to June 2015.
Results: There were four proven cases of Japanese Encephalitis and four proven Autoimmune Encephalitis cases. Mean age was 7 to 9.5 years old with a female predominance of 3:1 ratio for both diseases. Prodromal symptoms with fever were commonly seen in Japanese Encephalitis patients. The most common presenting symptoms for both diseases were seizures, aphasia, sleep-wake cycle abnormalities and movement disorders. Psychiatric symptoms were mostly seen in patients with autoimmune encephalitis. Neuroimaging and electroencephalogram abnormalities were seen in both conditions.
Conclusion: Similar symptoms such as seizures, movement disorders, aphasia and sleep-wake cycle abnormalities were manifested by both Japanese Encephalitis and Autoimmune Encephalitis patients. Viral causes of encephalitis may co-exist in patients tested to be positive for autoimmune antibodies. Antibody-testing to detect autoimmune-mediated encephalitis co-existing with Japanese Encephalitis Virus infection is recommended because of a possible improvement in outcome if immunotherapy is offered for this untreatable viral encephalitis.

LBA9

Assessment of sleep spindle density among genetically positive spinocerebellar ataxias type 1, 2 and 3

patients: A comparative study

Ragasudha Botta[a], Seshagiri Doniparthi [b], Arun Sasidharan[c], Ravi Yadav[b], Pramod Pal[b] ,Sanjeev Jain[d] , Bindu M. Kutty[c]

[a]Department of Clinical Neurosciences, [b]Department of Neurology, [c]Department of Neurophysiology, [d]Department of Psychiatry, National Institute of Mental Health and Neuro Sciences (NIMHANS), Bengaluru, India

Introduction: Sleep problems are frequently observed in Spinocerebellar ataxia (SCA) patients. Thalamic degeneration is reported in SCA2 and SCA3. Sleep spindles are distinctive electroencephalogram (EEG) oscillations (11-16 Hertz) generated by thalamo-cortical interplay during stage 2 sleep.

Objectives: To study and compare the sleep spindle densities (SSDs) of genetically proven autosomal dominant SCA1, SCA2 and SCA3 patients with controls.

Methodology. Prospectively genetically confirmed cases of SCA and controls were recruited from Neurology outpatient and inpatient services at NIMHANS, Bangalore. Ethical clearance was obtained from Institutional ethical board. Sleep quality was assessed using various rating scales. Overnight polysomnography was performed. SSDs were analyzed using neuroloop gain plugin of Polyman v1.15 software, and averaged across the NREM sleep using custom scripts written in MATLAB-2013a.

Results: Eighteen patients of SCA1 (n=6), SCA2 (n=5), SCA3 (n=7) and six controls were recruited in our study. Mean age of SCA1 patients was 39.17±5.42, SCA2 patients was 30.80±9.45, and SCA3 patients was 35.43±6.35 years. Mean duration of illness in SCA1 was 4.67±1.63 years, SCA2 was 4.28±4.4 years, and SCA3 was 5±2.3 years. Disease severity as measured by ICARS was 39.33±17.85 in SCA1, 29.4±14.32 in SCA2 and 45.57±19.77 in SCA3 patients. The median sleep spindle density values (percentage loop gain) during stage 2 of non-rapid eye movement sleep were 16.91% in SCA1, 0.0% in SCA2, 1.2% in SCA3 and 59.48% in controls. There was a significant difference in sleep spindle density values between SCA2 (p=0.04), SCA3 (p=0.02) patients and controls. There was no significant difference in SSD values between SCA1, SCA2 and SCA3 patients.

Conclusion: This study shows "thalamic switch" disruption, observed as reduced SSDs in SCA2 and SCA3. Sleep spindle deficits could act as one of the biomarkers of ongoing neurodegeneration in the thalamic circuitry of SCA patients. This novel finding needs to be confirmed in larger cohort.

LBA10

Neural underpinnings for the freezing of gait in PD: Diffusion tensor and resting state functional MRI study

Masahito Mihara MD PhD[1], Hiroaki Fujimoto MD PhD[1,2], Hironori Otomune MD PhD[1], Yoshiyuki Watanabe MD PhD[3], Noriaki Hattori MD PhD[2], Hideki Mochizuki MD PhD[1].

1: Department of Neurology, Osaka University Graduate School of Medicine

2: Neurorehabilitation Research Institute, Morinomiya Hospital

3: Department of Radiology, Osaka University Graduate School of Medicine

Objective: To investigate the neural mechanisms and pathophysiology of freezing of gait in PD.

Background: The Freezing of gait (FOG) in PD is famous phenomenon, but FOG does not affect all PD patients. Although previous findings suggests that the supraspinal gait-related neural network may contribute the FOG in PD, the primary lesion site for FOG in PD is still unclear.

Methods: In total, 23 PD patients with FOG and 13 age-matched healthy subjects participated this study. After clinical evaluation, diffusion tensor and resting state functional MR imaging were performed. Firstly, we performed group comparison using fractional anisotropy (FA) map of the both PD and healthy subjects. After determining the brain areas where FA value reduced significantly in PD, we evaluated the voxel-based regression analysis to determine the brain area where FA value reduction significantly correlated with freezing severity. Using significant cluster associated with FOG severity, we performed the tractography analysis and functional connectivity analysis to compare the anatomical and functional connectivity from the significant clusters between healthy and PD patients.

Results: Our findings revealed that the dorsal tegmentum area in the midbrain showed the significant correlation between freezing severity and FA values. Tractography analysis showed that the dorsal tegmentum cluster has anatomical connectivity with gait-related functional network, but there was right dominant reduction in the PD with FOG. In addition, the functional connectivity analysis revealed that functional connectivity with the dorsal

tegmentum area reduced in the bilateral cerebellar cortex, bilateral temporal cortex, precuneus, right premotor cortex, left sensorimotor cortex, and supplementary motor area in PD with FOG.
Conclusions: Our finding suggested the deteriorated gait related network function contributes to the FOG in PD, and dorsal tegmental area would be a possible "key structure" for FOG in PD.

LBA11

Chronic cerebral hypoperfusion accelerates cognitive dysfunction and microvascular impairment in the PTP mouse model of Parkinson's disease

*Hongmei Tang, Ruiming Zhu, Liang Gao, Kun Nie, Shujun Feng, Zhenpeng Duan, Youwen Zhang, Xin Zhao, Linmin Wang, Jiehao Zhao, Zhiheng Huang, Yuhu Zhang, Lijuan Wang **
Department of Neurology, Guangdong Neuroscience Institute, Guangdong General Hospital and Guangdong Academy of Medical Sciences, Guangzhou 510080, China

Background: Vascular pathology and Parkinson's disease (PD) pathology have been shown to coexist in the brains of dementia patients. However, the mechanisms underlying microvascular impairment and cognitive dysfunction remain poorly understood. In this study we aim to investigate how cognitive impairment could be exacerbated in a C57BL/6 mouse model of combined injury through the interaction of chronic cerebral hypoperfusion and MPTP toxicity.
Methods: PD mouse model was established by intraperitoneal injection of MPTP combined with probenecid. All the mice were divided into control group, PDCN (Cognitively normal Parkinson's disease) group and PDCI (mild cognitive impairment in Parkinson's disease) group according to their cognitive function via Morris water maze test. Further, chronic cerebral hypoperfusion was modeled by bilateral common carotid atrery stenesis (BCCAs) with piano wire. The experimental animals were divided into 7 groups, including the control group, the sham group, the BCCAs group, the PDCN group, the PDMCI group, the PDCN+BCCAs group, and the PDMCI+BCCAs group. A Morris water maze task, Open field test, and histological investigation, including tyrosinehydroxylase (TH) staining, Nissl staining were performed. Microvascular-related pathology including Evans blue (EB) permeability test, Fluorescein isothiocyanate-Dextran (FITC-Dextran) staining, CD34 staining and transmission electron microscope were also performed. Last but not least, Western blot was used to investigate the underlying mechanisms of cerebral microvascular injury.
Results: Spatial memory impairment was synergistically exacerbated in the PDMCI +BCCAs group as compared to the BCCAs group or PDCN+BCCAs group ($P<0.01$). Either single MPTP treatment or BCCAs operation might induce increased vascular permeability, broken tight junctions of the vascular endothelial cells, decreased vasoganglion density and neovascularization, Moreover, when combined MPTP treatment with cerebral hypoperfusion, these observed injuries became worse, and we observed the most prominent microvascular structural damage in the PDMCI+BCCAs group then PDCN+BCCAs group ($P<0.01$). We further demonstrated that the mentioned microvascular injuries were related to the activation of AKT/MAPK signal pathways and subsequent reduced expression levels of tight junction protein ZO-1 and Occludin.
Conclusion: Our experimental results support a clinical hypothesis of the deleterious interaction between chronic cerebral hypoperfusion and MPTP injection. Chronic cerebral hypoperfusion-induced perturbation in the equilibrium of PD-related pathology may exacerbate cognitive impairment in a mouse model of combined injury.

LBA12

Effect of single task training and dual task training on balance in individuals with Idiopathic Parkinson's disease

Vaithiamanithi Perumal, Specialist OT, King Saud University, Riyadh, KSA

Background: Individual with Parkinson's disease have increased risk of falling. Balance difficulties are common characteristics of idiopathic PD.
Objective: To evaluate the effect of single task training and dual task training on balance in individuals with Parkinson's disease.
Methodology: A total of 36 individuals diagnosed with PD were selected for this study. They were randomly allotted to three groups who received single task training (n=12), dual task training with fixed priority instruction (n=12) and dual task training with variable priority instruction (n=12). Every training session lasted for 45 minutes and subjects underwent this training for three times a week for eight weeks. Participants were evaluated before and after the training using Berg Balance Scale (BBS), Dynamic Gait Index (DGI) and Geriatric Depression Scale (GDS).

Results: Post treatment data analysis show that significant improvement was observed in all the three groups however, groups underwent dual task training showed more improvement than single task training group. Further analysis showed that participants who underwent dual task training with variable priority instruction showed significantly more improvement. No significant changes were observed in scores GDS.
Conclusion: Dual task training with variable priority is more effective in improving the balance performance of individuals with Idiopathic Parkinson's disease.
Key Term: Balance, BBS, DGI, Dual task training, GDS, Parkinsonism, Single task training

LBA13

Asymmetric and upper body parkinsonism in patients with idiopathic normal-pressure hydrocephalus

Jinsung Park[1], MD, Pan-Woo Ko[1], MD, Kyunghun Kang[1,2], MD, Ho-Won Lee[1,2], MD
Department of Neurology, Kyungpook National University School of Medicine, Daegu, Korea
Brain Science & Engineering Institute, Kyungpook National University, Daegu, Korea

Objective: Our aims were to analyze the characteristics of parkinsonian features, to explore whether a relationship exists between gait function and parkinsonism severity, and to characterize changes in parkinsonian motor symptoms before and after the cerebrospinal fluid tap test (CSFTT) in idiopathic normal-pressure hydrocephalus (INPH) patients with a positive CSFTT response.
Background: Diagnosis of INPH can be ambiguous because of varying combinations or degrees of each of the classic clinical elements and overlap with symptoms of other common disorders such as Parkinson's disease. However, the detailed features of parkinsonian signs in INPH have been rarely described.
Methods: INPH subjects were selected in consecutive order from a prospectively enrolled INPH registry. Fifty-five INPH patients constituted the final sample for analysis.
Results: The pre-tap mean Unified Parkinson's Disease Rating Scale motor (UPDRS-III) score was 24.5±10.2. There was no significant difference between the upper and lower body UPDRS-III scores. Higher lower body scores correlated significantly with higher upper body scores. The parkinsonian signs were asymmetrical in 32 of 55 patients (58.2%). The Timed Up and Go Test and 10-meter walking test scores were positively correlated with the total motor score, global bradykinesia score, global rigidity score, upper body score, lower body score, and postural instability/gait difficulties (PIGD) score of UPDRS-III. After the CSFTT, the total motor score, global bradykinesia score, upper body score, lower body score, and PIGD score of UPDRS-III improved significantly. There was a significant decrease in the number of patients with asymmetric parkinsonism.
Conclusion: In the differential diagnosis of elderly patients presenting with asymmetric and upper body parkinsonism, we need to consider a diagnosis of INPH. The association between gait function and parkinsonism severity suggests the involvement of similar circuits producing gait and parkinsonian symptoms in INPH.
Key Words: normal pressure hydrocephalus, parkinsonism, Parkinson's disease.

LBA14

Evaluation of TENM4 association with essential tremor in Singapore Chinese population

Yin Xia Chao[1, 6,7], Ebonne Yu Lin Ng[1, 6], Fiona Setiawan[1,6], Kandiah Nagaendran[6] , Yuen Yih[3], Mei Sian Chong[5], Prakash Kumar[1, 6], Louis Chew Seng Tan[6], Wing Lok Au[6], Yi Zhao[2], Zhi Dong Zhou[1,6], Murni Tio[1, 6], Ratnagopal Pavanni[1, 6], Eng King Tan[1, 2, 6, 7]
Departments of Neurology[1] and Clinical Research[2], Health Assessment Centre[3], Health Services Research[4], Singapore General Hospital Institute of Geriatrics and Active Ageing, Tan Tock-Seng Hospital[5], National Neuroscience Institute[6], Duke-NUS Graduate Medical School[7]

Objectives: To evaluate the relationship of TENM4 variant c.4324 G>A (p. A1442T) with essential tremor (ET) in Singapore Chinese population.
Background: ET is one of the most common forms of movement disorder, characterized by involuntary movements of part(s) of a body - arm, hand, head or face - which typically intensify during voluntary motion. No exact cause has been found for the condition. There are known risk factors, which include old age and family history. Nevertheless, genetic studies have yet to found any conclusive genetic cause for this disorder.

Methods: Genomic DNA was extracted from venous blood of consented individuals. Taqman-based platform was subsequently used to detect the SNP of interest, namely TENM4 variant c.4324 G>A (p. A1442T).
Results: A total of 777 Chinese subjects (421 males and 356 females) were recruited from both National Neuroscience Institute and Singapore General Hospital campuses. This includes 379 subjects diagnosed with ET (211 males and 168 females) and 398 controls (210 males and 188 females). All controls had no history of ET. The mean age and median of the ET cases are 51 years old and 55 years old respectively. The mean age and median of the controls are 53 years old and 52 years old. The polymorphic variant c.4324 G>A (p. A1442T) was not observed in the ET population. However, 2 positive individuals were detected in the control group.
Conclusions: In this study, TENM4 variant c.4324 G>A (p. A1442T) does not seem to have any relationship with ET in Singapore Chinese population. The incidental finding of 2 positive TENM4 individuals in the control group will need to be further investigated.

LBA15

Rapid eye movement sleep behavior disorder symptoms correlate with domains of cognitive impairment in Parkinson's disease

Jin-Ru Zhang[a], Jing Chen[a], Zi-Jiao Yang[a], Hui-Jun Zhang[a], Yun-Ting Fu[a], Yun Shen[a], Pei-Cheng He[a], Cheng-jie Mao[a], Chun-Feng Liu[a,b,c,]*

[a] Department of Neurology and Sleep Center, the Second Affiliated Hospital of Soochow University, Suzhou 215004, China

[b] Institutes of Neuroscience, Soochow University, Suzhou 2151123, China

[c] Beijing Key Laboratory for Parkinson's Disease, Beijing 100053, China

Objectives: To investigate the domains of cognitive impairment in patients with Parkinson's disease (PD) and rapid eye movement sleep behavior disorder (RBD). To explore risk factors for PD-mild cognitive impairment (PD-MCI) and relationship between RBD severity and impairment in different cognitive domains in PD.
Background: PD with RBD patients tend to have the akinetic-rigid dominant subtype of PD and exhibit severe non-motor symptoms. However, no study has investigated the relation between the severity of RBD and the different domains of cognitive impairment.
Methods: The participants were grouped as follows: PD without RBD (PD-RBD; n=42), PD with RBD (PD+RBD; n=32), idiopathic RBD (iRBD; n=15), and healthy controls (HC; n=36). Demographics, clinical characteristics, neuropsychological assessment, and RBD severity data were obtained from all participants. 35 PD and all iRBD patients completed an overnight video-polysomnography study.
Results: Compared to PD-RBD subjects, PD+RBD patients were more likely to have olfactory dysfunction and their Epworth Sleepiness Scale scores were higher (P<0.05). During neuropsychological testing, PD+RBD patients performed worse than PD-RBD patients, including delayed memory function, especially. The MCI rates were 33.3%, 62.5%, 33.3%, and 8.3% for PD-RBD, PD+RBD, iRBD, and HC groups, respectively. RBD was an important factor for explaining the PD-MCI variance (odds ratio=5.204, P=0.018). During correlation analysis, higher RBD Screening Questionnaire and RBD Questionnaire-Hong Kong (RBD-HK) scores were significantly associated with poorer performance on the Trail Making Test-B (errors) and Auditory Verbal Learning Test (delayed recall), and higher RBD-HK scores were also associated with Rey-Osterrieth complex figure (copy) results. However, no correlation between tonic/phasic densities with cognitive tests was found.
Conclusions: When PD-RBD and PD+RBD patients have equivalent motor symptoms, PD+RBD patients still have more olfactory dysfunction and worse daytime somnolence. RBD is an important risk factor for MCI, including delayed memory. Deficits in executive function, verbal delayed memory, and visuospatial function were consistently associated with more severe RBD symptoms.