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MEDICAL NEWS

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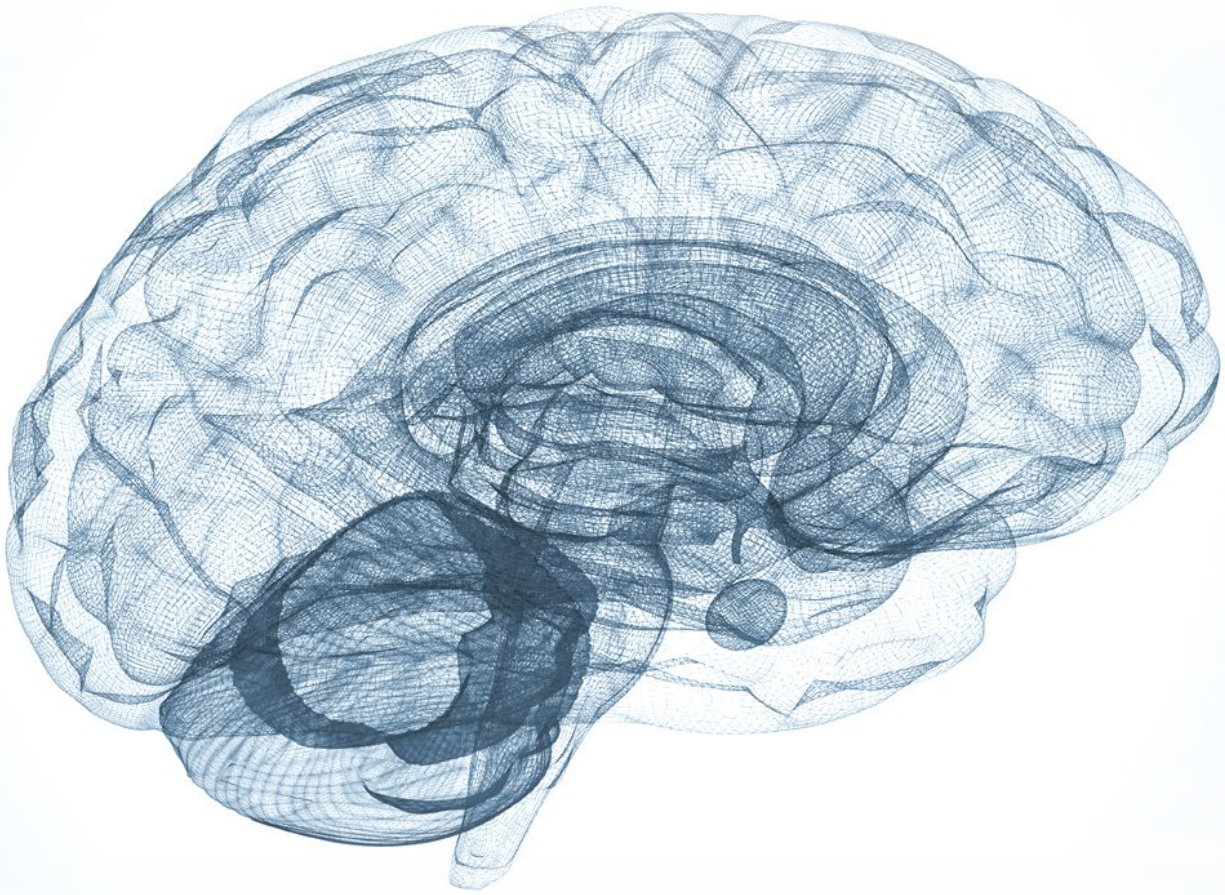

FOCUS : NEUROLOGY

- Innovations in Acute Ischaemic Stroke Intervention
- REM Sleep Behaviour Disorder
- Role of Amyloid PET Imaging in Young Onset Dementia
- Non-convulsive Status Epilepticus and Continuous Electroencephalogram Monitoring

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Innovations in Acute Ischaemic Stroke (AIS) Intervention

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Stroke is a significant global public health problem – 1 in 4 will get a stroke in their lifetime. The National Registry of Diseases Office reported that in 2016, there were more than 7,000 cases in Singapore, which approximates 20 cases per day. Cerebrovascular diseases, including stroke, ranks consistently among the top 5 causes of death in our country.

INTRODUCTION

A stroke occurs when a part of the brain gets damaged due to interruption of its blood supply.

Ischaemic stroke is the most common type of stroke and accounts for about 80% of strokes in Singapore. It occurs when a blood clot is lodged in an artery and cuts off blood supply to the brain.

Another type of stroke is haemorrhagic stroke, which occurs when there is a rupture of a blood vessel causing bleeding in the brain.

One of the factors affecting eventual outcome is how fast patients and their caregivers identify stroke symptoms, and present themselves at the nearest tertiary institution for treatment. Stroke symptoms using the acronym F.A.S.T was introduced through mass media and outreach programmes to educate the public in recognising early symptoms of stroke and calling an ambulance immediately for early diagnosis and treatment.

ADVANCEMENT OVER THE YEARS -MECHANICAL THROMBECTOMY

The emergent treatment of acute large vessel ischaemic stroke has advanced since 2015, after major clinical trials[1] proved the effectiveness of **mechanical thrombectomy** – a minimally-invasive endovascular procedure, where clots are extracted from larger brain vessels by a neurointerventional team - over non-intervention or conventional treatment methods using intravenous thrombolytics alone.

The innovative ideas behind the development of endovascular device-based methods have revolutionised the way clots lodged in larger brain vessels are extracted.

There are two main methods of clot extraction:
Aspiration (via large-bore catheters) - improvements in stent-retriever design have led to better clot-capturing efficacy.

Clot-capture (via stent-retrievers) - the increase in flexibility and calibre of the latest aspiration catheters have improved their reach and suction strength.

Used either alone or in synergy, these two methods can now result in recanalisation rates reaching as high as 80% to 90% of cases.

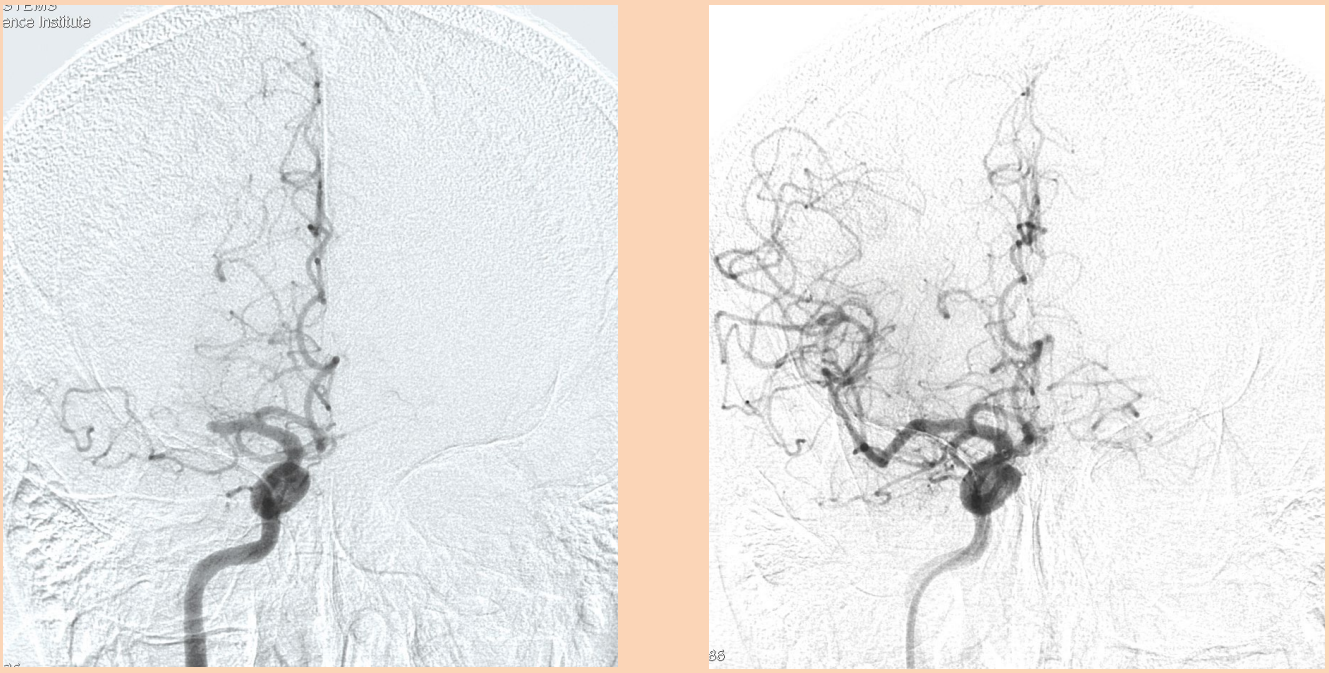
Recognise a stroke by thinking F.A.S.T

Face drooping
Is the person's smile uneven?

Speech difficulty
Does the person's speech sound slurred or unclear?

Arm weakness
Can the person raise both arms and keep them up?

Time to call 995
If the person shows any of these signs, they need to be rushed to the hospital immediately.



Cerebral angiogram before (left) and after (right) medical thrombectomy show recanalisation of occluded right middle cerebal artery.

TREATMENT

As mechanical thrombectomy can only be performed within a small therapeutic window, clinical assessment and imaging in the form of a CT scan or MRI should be performed urgently.

After confirming the blockage of a large vessel and presence of salvageable brain tissue, the patient is brought to the angiographic suite. A team comprising of a neurointerventionalist, anaesthetist, nurses and radiographers will perform the mechanical thrombectomy under X-ray guidance. Depending on the patient's condition, mechanical thrombectomy may be performed under moderate sedation or general anaesthesia.

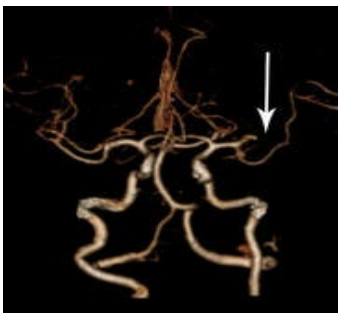


Figure 1

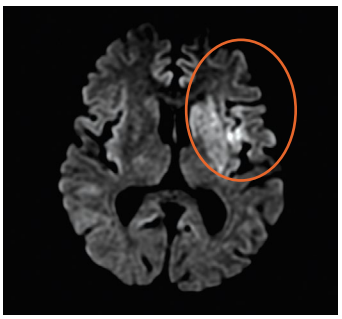


Figure 2

Through a femoral artery puncture, the guiding catheter is advanced close to the site of occlusion. The microcatheter is then navigated past the clot, followed by deployment of the clot-removal device of choice. Once deployed, the device is retrieved and checked for any clot removed.

A clot in the brain vessel at the white arrow on CT (Figure 1) leading to eventual tissue death, marked by the bright area in the orange circle on MRI (Figure 2).

Two main issues affecting the selection of clot-removal device are the site of obstruction, and how easily that site can be accessed by the delivery catheters.

Depending on the outcome, additional adjuvant intra-arterial thrombolytic therapy may be administered.

RISKS

As with any procedure, there are complications that can take place.

Mechanical manipulations can result in damage to the vessel wall, leading to bleeding. As a result, further artery blockage or clots may occur.

As X-rays are used, there will be exposure to radiation though steps are taken to minimise the exposure. An X-ray dye will also be introduced to better visualise the blood vessels and some patients may experience an allergic reaction.

These risks are weighed against the benefit of removing the clot, to improve clinical outcome and odds of functional independence.

Without mechanical thrombectomy, the chances of re-opening the blocked vessel are slim, leading to a loss of salvageable brain tissue, and subsequent large stroke territory with complications such as brain swelling and haemorrhagic transformation.

> "Mechanical thrombectomy benefits patients within 6 hours of symptom onset"

CONCLUSION

The 2015 clinical trials[1] proved that mechanical thrombectomy benefits patients who present within 6 hours of symptom onset.

More recent studies[2] show that in selected cases, patients may benefit from this procedure up to 16 hours of stroke onset.

However, the benefits remain greatest in patients who present to the hospital early. Brain tissue is sensitive to oxygen deprivation and cells start dying within minutes of a stroke onset. A core of damaged brain tissue forms, surrounded by salvageable "tissue-at-risk" which can be recruited into the core if blood flow is not restored.

Through improved devices and techniques for clot-retrieval, and stronger public awareness, more stroke patients can benefit from endovascular therapy, for improved clinical outcomes.

REFERENCES

1. Goyal M, Menon BK, van Zwam WH, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a metaanalysis of individual patient data from five randomised trials. Lancet 2016; 387: 1723-31.
2. Nogueira RG, Jadhav AP, Haussen DC, et al. Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct. N Engl J Med 2018; 378: 11-21.

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Role of Amyloid PET Imaging in Young Onset Dementia

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CASE STUDY

A 50-year-old male without any significant medical or psychiatric history presented to the memory clinic with progressive behavioural change and cognitive impairment over 18 months. His behavioural disturbance started with low mood, apathy, reduced appetite and fleeting suicidal thoughts. This gradually intensified to false beliefs that other people were out to harm his family. In addition, he had the constant thought that his father in-law was monitoring his movements. He also experienced auditory hallucinations telling him that he was "weak and useless", and commanding him to "run away from home".

Over time, he began to consider his wife as an imposter and he would always require a text message from her to prove that she was his wife. Only after confirming that the text message was sent from the same mobile number as belonging to his wife, would he be agreeable to speak to her.

At the same time, he became more forgetful and often repeated what he had said earlier. He was not able to cope at work and needed help to complete the tasks that he was previously familiar with. He also had difficulties managing his finances.

During physical examination, he was well-groomed and orientated. There were no focal neurological deficits, extrapyramidal signs or apraxia. However, he had anomia and difficulty in performing the Luria's three-step test and go-no-go test. He scored 15/30 for the mini-mental state examination, 9/30 for the Montreal Cognitive Assessment and 10/18 for the frontal assessment battery.

Laboratory testing revealed normal thyroid hormone profile, vitamin B12, folate, negative syphilis and HIV screen. Genetic testing revealed homozygosity for APOE e4 alleles. His brain MRI showed predominant parietal and medial temporal atrophy (*Figure 1*), [^{18}F]Fluorodeoxyglucose (FDG) PET scan showed frontal, parietal and posterior temporal hypometabolism and [^{18}F]Flutemetamol PET scan was positive for amyloid deposition (*Figure 2*), which is consistent with the diagnosis of Alzheimer's disease.

CASE DISCUSSION

Here, we describe an atypical presentation of a patient with young onset dementia (YOD) due to Alzheimer's disease (AD), who had prominent psychotic symptoms and Capgras syndrome. Capgras syndrome (CS) is a form of delusional misidentification syndrome characterised by a delusional belief that an identical or near-identical looking imposter has replaced the identity of a closely-related person. While CS was originally reported in schizophrenia and schizoaffective disorders, it is increasingly recognised in neurological conditions such as AD[1].

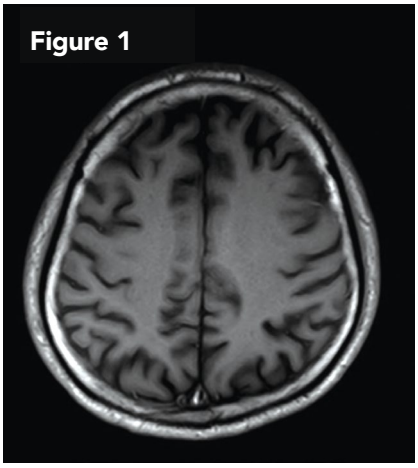

Figure 1 MRI Brain showing predominant bilateral parietal atrophy

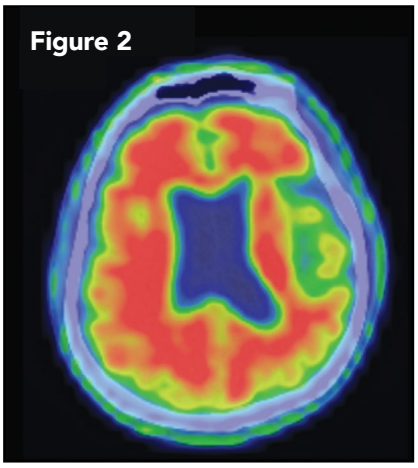

Figure 2 Amyloid PET showing amyloid deposition in bilateral frontal lobes, parietal lobes and striatum.

Although the patient's psychiatric symptoms at mid-life onset may be suggestive of late-onset schizophrenia, the presence of concurrent cognitive impairment typical of AD led to a detailed clinical evaluation using AD imaging biomarkers. Amyloid PET findings characteristic of AD led to a revision of the diagnosis to young onset dementia (YOD) due to AD.

This case discussion demonstrates the key role of AD neuroimaging biomarkers in the clinical evaluation of YOD patients with atypical presentation.

INCIDENCE OF YOUNG ONSET DEMENTIA IN SINGAPORE IS INCREASING

Dementia is a neurodegenerative disease that is characterised by a decline in at least one cognitive domain interfering with independence in everyday activities.

In 2018, dementia has affected 50 million people worldwide, and this number is expected to rise to 82 million by 2030 and 152 million by 2050[1]. In Singapore, one in 10 people aged 60 and above may have dementia, which translates to almost 82,000 people in 2018 and the number is expected to exceed 100,000 in a few years' time[3].

While dementia typically affects older adults aged 65 years and above, this condition is increasingly diagnosed in younger individuals in recent years. In this regard, the term young-onset dementia (YOD) is used to describe patients with onset of dementia before 65 years of age[4].

At the National Neuroscience Institute (NNI), the number of new patients with YOD (<65 years) has gradually increased from 180 in 2016 to 228 in 2018 and almost doubled from 2015. Hence, greater awareness of this condition among clinicians is paramount.

CLINICAL PRESENTATIONS OF YOUNG ONSET DEMENTIA DUE TO ALZHEIMER'S DISEASE

Alzheimer's disease (AD) is the most common cause of YOD, followed by vascular dementia and frontotemporal dementia[3].

1. In AD, amnestic syndrome is the most common presentation, including impairment in learning and recall of recently learned information[5].

2. In addition, there should also be evidence of cognitive impairment in at least one other cognitive domain, such as executive dysfunction, visuospatial impairment, language difficulties or changes in personality and/or behaviour.

3. Importantly, about a third of the patients with YOD may have an atypical presentation such as executive, behavioural, language dysfunction and posterior cortical atrophy which makes the diagnosis of AD in YOD challenging. This has been shown in a study where pathologically proven YOD patients with atypical presentations were often misdiagnosed[6].

NEUROPSYCHIATRIC SYMPTOMS - in Youth Onset Dementia due to Alzheimer's Disease

Neuropsychiatric symptoms (NPS) such as delusions are frequently observed in Alzheimer's disease (AD) and are associated with greater functional impairment, poorer quality of life and accelerated cognitive decline[7].

Common delusions observed in AD patients include delusions of persecution, abandonment and the belief that deceased relatives such as parents are still alive.

Misidentification delusions such as Capgras syndrome (CS) are also reported in AD patients[8]. This includes the belief that a family member is an imposter, and the home is not the patient's own home. The prevalence of CS among AD patients seen in memory clinics ranges from 10.1% to 14.8%[2,9]. The mean age of onset of CS among AD patients ranges from 72 to 82 years and AD patients with misidentification delusions are associated with increased cognitive impairment and advanced dementia[10].

In this case study, the presentation of prominent psychotic symptoms and CS at mid-life onset suggest the possibility of late-onset schizophrenia. However, unlike schizophrenia, delusions in AD are usually not bizarre and the first-rank symptoms of schizophrenia are not common. Furthermore, the patient has concurrent cognitive impairment such as amnesia and executive dysfunction which raises a differential diagnosis of AD. Hence, a further work up using AD imaging biomarkers is performed.

ROLE OF AD BIOMARKERS IN CLINICAL PRACTICE

Amyloid plaque is a core histopathological hallmark of AD and the amyloid cascade hypothesis suggests that AD begins with amyloid beta (Aß) deposition which results in neuronal dysfunction and neuronal cell death.

The advancement of amyloid biomarkers has enabled the identification of amyloid pathologies in vivo across the AD spectrum. The biomarkers of Aß deposition include low cerebrospinal (CSF) Aß42 and high uptake of amyloid PET tracers in the brain. There is a close correlation between in vivo amyloid biomarkers and brain amyloid plaques assessed in post-mortem studies.

Amyloid PET provides information regarding regional distribution and longitudinal changes of amyloid deposition in AD patients. However, 10–30% of cognitively normal people may have a positive amyloid PET scan[11] and pathological amyloid deposition in the brain is also shown in non-demented individuals[12]. Hence, its clinical utility in medical practice requires careful consideration. Prior to ordering of an amyloid PET scan, the physician should

consider the possibility of an incidental, age-related amyloid detection in a patient that may not be related to or relevant to the presenting symptoms.

A positive amyloid PET scan may also be seen in other neurodegenerative conditions such aas dementia with Lewy bodies (DLB). Hence, it is important to emphasise that a positive amyloid PET scan alone does not establish the diagnosis of AD or distinguish AD from other neurodegenerative conditions such as DLB.

The Alzheimer's Association and the Society of Nuclear Medicine and Molecular Imaging convened the Amyloid Imaging Taskforce (AIT) to define a set of specific appropriate indications and inappropriate use criteria as a guidance for the ordering of amyloid PET[13] (Table 1).

Table 1 **Appropriate use criteria for amyloid PET**

Preamble
(i) A cognitive complaint with objectively confirmed impairment
(ii) AD as a possible diagnosis, but when the diagnosis is uncertain after a comprehensive evaluation by a dementia expert
(iii) When knowledge of the presence or absence of amyloid pathology is expected to increase diagnostic certainty and alter management

Appropriate Indication
(i) Patients with persistent or progressive unexplained mild cognitive impairment
(ii) Patients satisfying core clinical criteria for possible AD because of unclear clinical presentation, either an atypical clinical course or an etiologically mixed presentation
(iii) Patients with progressive dementia and atypically early age of onset (usually defined as 65 years or less in age)

Inappropriate Indication
(i) Patients with core clinical criteria for probable AD with typical age of onset
(ii) To determine dementia severity
(iii) Based solely on a positive family history of dementia or presence of apolipoprotein E (APOE) ε4
(iv) Patients with a cognitive complaint that is unconfirmed on clinical examination
(v) In lieu of genotyping for suspected autosomal mutation carriers
(vi) In asymptomatic individuals
(vii) Nonmedical use (e.g. legal, insurance coverage, or employment screening)

K.A. Johnson et al. / Alzheimer's & Dementia 9 (2013) e1 – e16

The preamble restricts the group of patients for whom amyloid imaging would be appropriate.

Firstly, the patient must be evaluated by a dementia expert so as to determine that a cognitive complaint is supported with objectively confirmed impairment. This can be assessed through a detailed mental status examination or a neuropsychological assessment.

Secondly, the cause of the cognitive impairment should remain uncertain after a comprehensive evaluation and AD may be a possible differential diagnosis.

Thirdly, the physician must conclude that a determination of amyloid status would increase the level of diagnostic certainty and alter the plan for patient management.

CONCLUSION

This case study highlights YOD due to AD as a differential diagnosis in young patients who present with prominent neuropsychiatric symptoms and cognitive impairment. The availability of AD imaging biomarkers such as amyloid and FDG PET has enabled the identification of *in vivo* AD pathophysiology and play an important role in the accurate diagnosis of AD.

With the current advancement in the development of disease modifying drugs, early and accurate diagnosis will be essential. Furthermore, the ability to provide a definitive diagnosis and prognosis will enable patients and their families to plan for their future, including life, finances and advance directives.

REFERENCES

1. From Plan to Impact (Alzheimer's Disease International, 2017)
2. Josephs KA. Capgras syndrome and its relationship to neurodegenerative disease. Arch Neurol 2007;64:1762–6.
3. Subramaniam M, Chong SA, Vaingankar JA, Abdin E, Chua BY, Chua HC, et al. Prevalence of dementia in people aged 60 years and above: Results from the WiSE study. J Alzheimer's Dis 2015.
4. Rossor MN, Fox NC, Mummery CJ, Schott JM, Warren JD. The diagnosis of young-onset dementia. Lancet Neurol 2010;9:793–806.
5. McKhann GM, Knopman DS, Chertkow H, Hyman BT, Jack CR, Kawas CH, et al. The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimer's Dement 2011;7:263–9.
6. Balasa M, Gelpi E, Antonell A, Rey MJ, Sánchez-Valle R, Molinuevo JL, et al. Clinical features and APOE genotype of pathologically proven early-onset Alzheimer disease. Neurology 2011;76:1720–5.
7. Rosenberg PB, Mielke MM, Appleby BS, Oh ES, Geda YE, Lyketsos CG. The association of neuropsychiatric symptoms in MCI with incident dementia and Alzheimer disease. Am J Geriatr Psychiatry 2013;21:685–95.
8. Murray PS, Kumar S, Demichele-Sweet MAA, Sweet RA. Psychosis in Alzheimer's disease. Biol Psychiatry 2014.
9. Harwood DG, Barker WW, Ownby RL, Duara R. Prevalence and correlates of Capgras syndrome in Alzheimer's disease. Int J Geriatr Psychiatry 1999;14:415–20.
10. Ismail Z, Nguyen MQ, Fischer CE, Schweizer TA, Mulsant BH, Mamo D. Neurobiology of delusions in Alzheimer's disease. Curr Psychiatry Rep 2011;13:211–8.
11. Chételat G, La Joie R, Villain N, Perrotin A, de La Sayette V, Eustache F, et al. Amyloid imaging in cognitively normal individuals, at-risk populations and preclinical Alzheimer's disease. NeuroImage Clin 2013;2:356–65.
12. Price JL, Morris JC. Tangles and plaques in nondemented aging and "preclinical" Alzheimer's disease. Ann Neurol 1999;45:358–68.
13. Johnson KA, Minoshima S, Bohnen NI, Donohoe KJ, Foster NL, Herscovitch P, et al. Appropriate use criteria for amyloid PET: A report of the Amyloid Imaging Task Force, the Society of Nuclear Medicine and Molecular Imaging, and the Alzheimer's Association. Alzheimer's Dement 2013;9:E1–16.

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Dr Ng subspecialises in dementia and his research interest is PET imaging in neurocognitive diseases. He completed his 1-year clinical research fellowship at the McGill University Research Centre for Studies in Aging, Montreal, Canada in 2017.

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REM Sleep Behaviour Disorder (RBD)

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In normal rapid eye movement (REM) sleep, a descending, glutaminergic signal from the brainstem inhibits the motor neurons present in the spinal cord resulting in muscle atonia, which refers to the loss of muscle tone. In REM sleep behaviour disorder (RBD), progressive neurodegeneration of the inhibitory brainstem control results in the loss of normal REM atonia observed during REM sleep, resulting in dream enactment behavior alongside vivid and often violent dream content.

COMMONLY OBSERVED BEHAVIOURS

Behaviours commonly observed include shouting, kicking and punching, which reflect dream content. These events are typically violent, but a range of milder behaviours are also recognised[1]. RBD typically occurs in the second half of the night as the proportion of REM sleep increases with longer sleep duration.

This is in stark contrast to other sleep disorders such as restless legs syndrome and the non-REM (NREM) parasomnias, which tend to occur in the first half of the night when NREM sleep predominates.

Thus, enquiring about the approximate time the nocturnal behavioural events occur can help to narrow down the differential diagnoses of the events.

Up to 70% of patients will cause injury to themselves or their bed partner. It is common for patients to report falling out of the bed and sustaining fractures, or bed partners complaining of being bruised or hit by their unknowing partners at night. Bed partners may have also recognised RBD earlier, and have chosen to sleep in separate rooms but did not report these events to medical practitioners.

CAUSES OF RBD

The condition predominantly affects older men with a reported prevalence of at least 1% [2-3]. RBD was first described in 1986 from a small series of elderly men by Schenck[4]. However, RBD was in fact recognised much earlier in animals in 1967 as there were reports of selective brain stem lesions in cats causing oneiric or dreamlike behaviours[5].

RBD is traditionally classified into idiopathic or secondary forms.

Secondary RBD

Secondary RBD can be caused by a neurodegenerative disorder, particularly the synucleinopathies which include:

- Parkinson's Disease
- Dementia with Lewy Bodies
- Multiple System Atrophy

Idiopathic RBD

Other causes include :

- Structural lesion in the brain
- Antidepressants, in particular the selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs)
- Beta-blockers
- Alcohol withdrawal.

Highly serotonergic SSRIs such as mirtazapine can worsen existing RBD. Discontinuation of the antidepressant may result in clinical and polysomnographic resolution of RBD. However, in others, RBD has also been reported to persist and antidepressants may simply unmask individuals with a latent neurodegeneration.

There is increasing debate whether true idiopathic RBD exists with an increasing recognition of the strong association between RBD and the subsequent development of neurodegenerative disease, with 91% developing one of these conditions over 14 years of follow up[6]. As currently published longitudinal studies on RBD have been only of limited duration due to the relative recent discovery of RBD, it is anticipated that future published studies with even longer durations of follow up would show near 100% phenoconversion of RBD into another neurodegenerative disorder.

As such, long-term follow up of these patients is important to detect incipient development of neurodegenerative disease.

RBD is now commonly regarded as a prodromal phase of the alpha-synucleinopathies including Parkinson's Disease.

ASSESSMENT

The diagnosis of probable RBD can be made with a **positive history of dream enactment or complex motor behaviours** occurring from sleep. Patients are often unaware of these behaviours unless injury has occurred, so a complete history is essential for thorough understanding of the extent.

In RBD, sleep behaviours usually begin gradually and infrequently such as limb jerks and sleep talking, before progressing to become nightly or near nightly violent events.

A number of **validated screening questionnaires** are available to allow diagnosis of probable RBD. However, these questionnaires are unable to distinguish RBD from other NREM parasomnias, sleep apnoea and nocturnal confusion. Occasionally, severe obstructive sleep apnoea (OSA) can cause strikingly vivid dreams and agitated arousals termed as 'pseudo-RBD'.

Hence a **diagnostic polysomnography** should be performed in patients who have other features to suggest OSA. To make a definite diagnosis of RBD, polysomnography is required to identify the excessive electromyography (EMG) activity that occurs in REM sleep.

TREATMENT

There is debate as to how and when patients with idiopathic RBD should be counselled on their future risk of developing a neurodegenerative disorder.

Immediate treatment measures:

1. Behavioural interventions to ensure a safe sleeping environment should be implemented to prevent injury to the patient or their bed partner.

2. If comorbid OSA is present, treatment of OSA often improves RBD.

3. Medications known to worsen RBD should be discontinued where possible.

Clonazepam

There are no licensed therapies for RBD but clonazepam has been regarded as the first-line treatment for RBD. This drug should be used cautiously as common side effects like sedation, falls, confusion, cognitive impairment and respiratory depression often limit dose escalation. A lack of response to the drug should prompt the clinician to re-evaluate the diagnosis of RBD. Clonazepam should not be used in co-morbid OSA.

Melatonin

Melatonin has been used as a second-line therapy and was demonstrated to be effective when evaluated in one small randomised blinded cross-over trial[7]. Unlike clonazepam, melatonin is able to restore normal REM atonia. Melatonin also tends to be better tolerated with less adverse effects than clonazepam, with similar efficacy although there are no head-to-head trials[8].

The effective dose ranges between 2 and 12mg, with a recent large case series showing benefit at an average of 6mg[8]. It is common for patients not to achieve complete remission with melatonin, and supplementary clonazepam use is required to manage the symptoms.

In patients for whom RBD remains unmanageable, occasional case reports have described that rivastigmine and sodium oxybate may be effective[9-10].

Where To Seek Treatment at SingHealth

This condition is treated at the SingHealth Duke-NUS Sleep Centre. The Centre sees patients at six SingHealth institutions.

- Singapore General Hospital
- Changi General Hospital
- Sengkang General Hospital
- KK Women's and Children's Hospital
- National Dental Centre Singapore
- National Neuroscience Institute

It is staffed by a multidisciplinary team of specialists from ENT, Surgery, Respiratory Medicine, Neurology, Psychiatry, Psychology and Dentistry who have all undergone further specialised training in the field of Sleep Medicine locally and abroad.

REFERENCES

1. RODRIGUEZ, C. L., JAIMCHARIYATAM, N. & BUDUR, K. 2017. Rapid Eye Movement Sleep Behavior Disorder: A Review of the Literature and Update on Current Concepts. *Chest*, 152, 650-662.
2. CHIU, H. F., WING, Y. K., LAM, L. C., LI, S. W., LUM, C. M., LEUNG, T. & HO, C. K. 2000. Sleep-related injury in the elderly--an epidemiological study in Hong Kong. *Sleep*, 23, 513-7
3. KANG, S. H., YOON, I. Y., LEE, S. D., HAN, J. W., KIM, T. H. & KIM, K. W. 2013. REM sleep behavior disorder in the Korean elderly population: prevalence and clinical characteristics. *Sleep*, 36, 1147-52.
4. SCHENCK, C. H., BUNDLIE, S. R., ETTINGER, M. G. & MAHOWALD, M. W. 1986. Chronic behavioral disorders of human REM sleep: a new category of parasomnia. *Sleep*, 9, 293-308.
5. MOURET, J., DELORME, F. & JOUVET, M. 1967. [Lesions of the pontine tegmentum and sleep in rats]. *C R Seances Soc Biol Fil*, 161, 1603-6.
6. IRANZO, A., TOLOSA, E., GELPI, E., MOLINUEVO, J. L., VALLDEORIOLA, F., SERRADELL, M., SANCHEZ-VALLE, R., VILASECA, I., LOMENA, F., VILAS, D., LLADO, A., GAIG, C. & SANTAMARIA, J. 2013. Neurodegenerative disease status and post-mortem pathology in idiopathic rapid-eye-movement sleep behaviour disorder: an observational cohort study. *Lancet Neurol*, 12, 443-53.
7. KUNZ, D. & MAHLBERG, R. 2010. A two-part, double-blind, placebo-controlled trial of exogenous melatonin in REM sleep behaviour disorder. J *Sleep Res*, 19, 591-6.
8. MCCARTER, S. J., BOSWELL, C. L., ST LOUIS, E. K., DUEFFERT, L. G., SLOCUMB, N., BOEVE, B. F., SILBER, M. H., OLSON, E. J. & TIPPMANN-PEIKERT, M. 2013. Treatment outcomes in REM sleep behavior disorder. *Sleep Med*, 14, 237-42.
9. DI GIACOPO, R., FASANO, A., QUARANTA, D., DELLA MARCA, G., BOVE, F. & BENTIVOGLIO, A. R. 2012. Rivastigmine as alternative treatment for refractory REM behavior disorder in Parkinson's disease. *Mov Disord*, 27, 559-61.
10. MOGHADAM, K. K., PIZZA, F., PRIMAVERA, A., FERRI, R. & PLAZZI, G. 2017. Sodium oxybate for idiopathic REM sleep behavior disorder: a report on two patients. *Sleep Med*, 32, 16-21.

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Non-convulsive status epilepticus and continuous electroencephalogram monitoring

Dr Gosavi Tushar Divakar, *Consultant,*
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Non-convulsive status epilepticus (NCSE) is an under-recognised form of status epilepticus characterised by absence of motor manifestations of seizures in the presence of an ictal EEG rhythm (*Figure 1*). Thus, NCSE is essentially an electroencephalographic (EEG) diagnosis, and is characterised by lack of the classical clinical manifestations of convulsive seizures. It can be seen in a myriad of clinical situations, but the prototypical NCSE as discussed occurs in the setting of critically ill, comatose or stuporous patient in an intensive care unit.

The other situations where NCSE occurs include:
(a) after a convulsive seizure
(b) In a patient with chronic epilepsy (focal or generalised)

The diagnosis is often not straight forward and the most important variables contributing to the diagnostic dilemma are the clinical setting in which it occurs and the haziness in defining what EEG rhythm constitutes an ictal EEG.

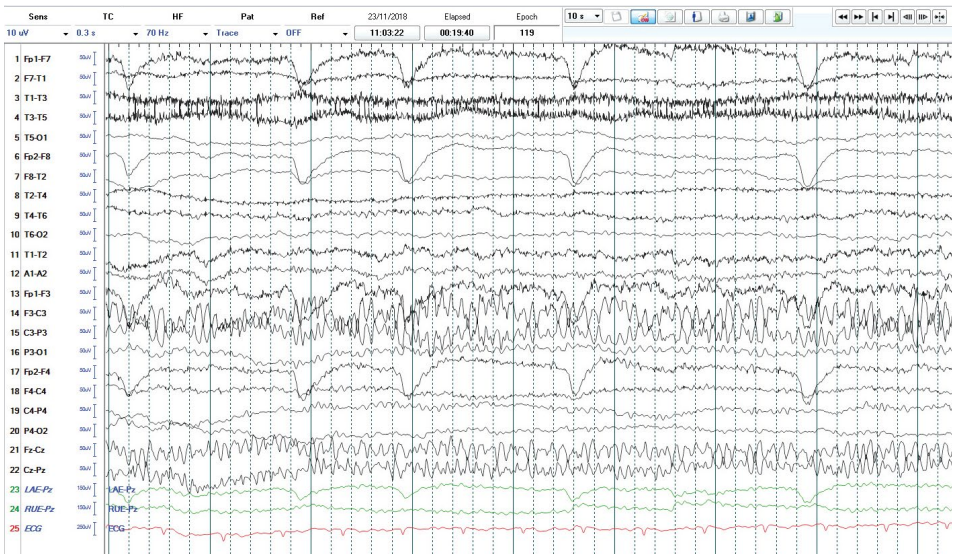

Figure 1 EEG seizure : An ictal EEG rhythm seen predominantly in the midline and left frontocentral elecrodes.

BACKGROUND

Back in the 19th century, before EEGs were developed, prolonged confusional states were thought to be seizures.

In the 1940s, the EEG was introduced. In 1956, Gastaut first described a case of psychomotor status – a type of status epilepticus associated with altered mental state which could be similar to NCSE.

NCSE is now gaining increasing attention. Diagnosis is based on ictal EEG pattern, together with altered mental state. Response to antiepileptic drugs (both clinical and EEG improvement) is often included in the criteria for its diagnosis.

HOW COMMON IS THE PROBLEM?

The incidence of NCSE differs in reported studies. This is particularly due to the differences in the baseline characteristics of the populations studied. In comatose or obtunded, critically ill patients, the incidence of NCSE ranges from about 8% to 27%. In 2000, Towne et al.[1], studied 236 comatose patients who underwent EEG for coma evaluation, and found that 8% of those patients had NCSE. In 2004, Claassen et al.[2] reported 570 critically ill patients with unexplained decreased level of consciousness. These patients underwent continuous EEG (CEEG) monitoring and 19% of them had seizures that were almost always non-convulsive in nature. Westover et al.[3] reported 27% seizure occurrence in a cohort of 625 acutely ill hospitalised adults. Thus, the problem of NCSE is real and significant in critically ill patients.

DECIDING BETWEEN ROUTINE EEG OR CONTINUOUS EEG FOR DIAGNOSIS

NCSE, particularly if prolonged, has potential to cause secondary neuronal injury. Hence it is important to recognise it in a timely manner. Since seizures are intermittent, an important question is whether a conventional half an hour duration EEG would be enough to confirm the diagnosis of NCSE.

It is known that CEEG monitoring is very likely to give a higher diagnostic yield as compared to routine EEGs. Sutter et al.[4] compared patients with suspected NCSE who underwent routine and continuous EEG monitoring and found

a significantly high NCSE detection rate with CEEG.

Therefore, despite the fact that continuous EEG is labour intensive and costly, it should be considered whenever it is feasible, when NCSE is in question. This is particularly true in high risk patients for NCSE, which include :

(a) patients who have had a generalised tonic-clonic seizure (GTCS) episode and continue to be obtunded beyond the expected postictal period

(b) patients with supratentorial brain injury with unexplained encephalopathy

(c) patients with sepsis and multi-organ failure with encephalopathy

(d) patients with refractory status epilepticus on weaning doses of anaesthetic agents, and

(e) patients who are found to have periodic lateralised epileptiform discharges (PLEDS) (*Figure 2*) or generalised periodic epileptiform discharges (GPEDS) (*Figure 3*) on routine EEG

LENGTH OF MONITORING

Once CEEG is initiated, the next step is to determine the duration of monitoring. There is evidence to suggest that seizure risk in acute neurologic illness reduces rapidly with time, and hence a substantial risk stratification is possible based on early EEG abnormalities.

About half of the seizures are recorded within the first hour itself, and by 24 hours, about 90% of seizures would be detected.

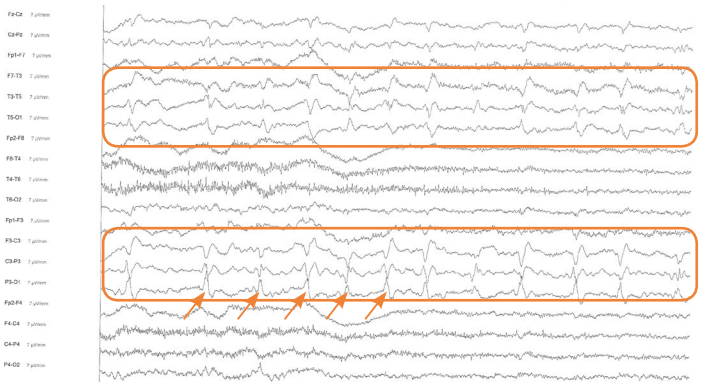

Figure 2
Example of periodic lateralised epileptiform discharges (PLEDS) in the left hemisphere.

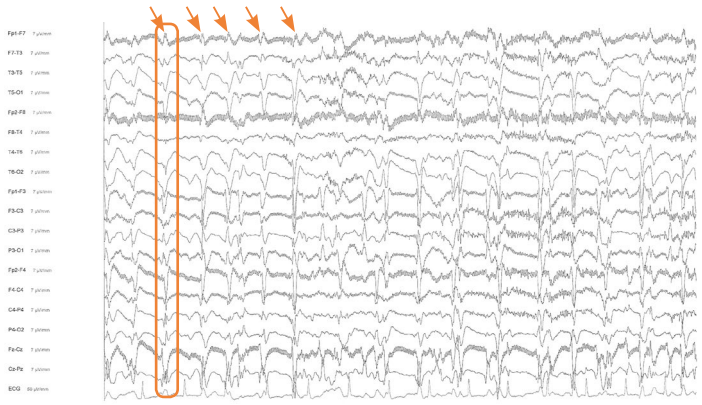

Figure 3
Generalised periodic epileptiform discharges.

Interestingly, the first four hours of CEEG gives a valuable clue.

In one study, when there was no epileptiform activity seen in first 4 hours, none of those patients went on to develop NCSE during further CEEG monitoring[5].

Based on this evidence, we often recommend 24 hours of CEEG monitoring for patients with confirmed non-convulsive seizures or NCSE after reasonable seizure control. This is to ensure that patients are no longer in NCSE. The duration can be modified based on clinician decision after consideration of holistic patient situation.

If there is a clinical suspicion of NCSE in a comatose intensive care unit (ICU) patient or altered mental status (AMS) after witnessed clinical seizure – there should be monitoring with CEEG for 4 hours. Any patient who, on conventional EEG, or during the first 4 hours of CEEG recording, has epileptiform discharges (EDs), the monitoring should be extended for 24 hours. If no seizure is recorded during this interval, CEEG monitoring can stop.

DIFFICULTIES OF CEEG MONITORING

Limitations of CEEG monitoring include:

- labour intensiveness
- high cost incurred
- ability to deal with technical issues out of office hours, e.g. leads dropping off
- ICU setting itself where a patient is connected to various monitoring equipment, and CEEG adding a big bulk to it. This not only adds to artefacts which make EEG reading difficult but also places limitations on patient handling due to fear of dislodging of electrodes.

There are pitfalls related to the diagnosis of NCSE as well. Firstly, there is an element of subjectivity and hence a high inter-rater variability as to what EEG pattern is ictal (equivalent to EEG seizure).

Also, there is a controversial border-zone in the ictal – interictal EEG spectrum, which may be interpreted as seizures by some neurophysiologists but not by others. Uniform consensus criteria are being developed with the most recent being the Salzburg criteria[6] for diagnosis of NCSE being widely used now.

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HOW TO MANAGE PATIENTS WITH NCSE

Two important issues should be borne in mind when considering treatment of NCSE in a critically ill patient. Firstly, though NCSE has the potential to cause neuronal injury, it is probably not as damaging as convulsive status epilepticus. Secondly, overzealous treatment with anaesthetic agents like propofol and thiopentone are associated with complications.

A balanced approach is recommended, with the aim to diagnose and treat NCSE as quickly as possible but with minimal use of sedatives and anaesthetics, so as to avoid prolonging the coma and intubation.

For critically ill patients with NCSE due to systemic causes, it is advisable to use boluses of benzodiazepines together with parenteral antiepileptic drugs (AEDs) like phenytoin, valproic acid or levetiracetam as first line agents. If continuous infusion of anaesthetic agent is needed, intravenous (IV) benzodiazepines like midazolam infusion will be administered with careful hemodynamic monitoring. NCSE following a convulsive SE may need more aggressive treatment.

The cause of NCSE may not often be clear, and there could be multiple etiologies. When known, treating the cause of NCSE is of utmost importance.

NNI'S EXPERIENCE WITH NCSE

According to NNI's figures on NCSE, a 3% incidence of NCSE amongst inpatient EEGs ordered was found.

Amongst the 81 NCSE episodes recorded, primary neurological cause was seen in 36%. 19% had purely systemic cause and 44% had combined neurologic and systemic cause. Poor outcome defined as death or significant functional decline, was seen in nearly half of the patients.

OTHER LONG-TERM EEG MONITORING

CEEG monitoring is a form of long-term EEG monitoring mostly used for inpatients with suspicion of non-convulsive seizures, or for monitoring after or during status epilepticus.

At NNI

Apart from CEEG for NCSE and status epilepticus, NNI currently has a video EEG monitoring room, where healthcare professionals conduct long-term diagnostic EEG studies for characterisation of episodes of uncertain etiology and also for pre-surgical work up for epilepsy patients.

When a patient with epilepsy reports of episodes which are different from usual historical seizures, if any patient presents with spells of uncertain nature, or suspected non-epileptic attack disorder, they can be referred to NNI's epilepsy clinic where specialists may consider long term video EEG monitoring for selected patients.

REFERENCES

1. Towne AR, Waterhouse EJ, Boggs JG, Garnett LK, Brown AJ, Smith JR, DeLorenzo RJ. Prevalence of non-convulsive status epilepticus in comatose patients. Neurology 2000;54(2):340-345.
2. Claassen J, Mayer SA, Kowalski RG, Emerson RG, Hirsch LJ. Detection of electrographic seizures with continuous EEG monitoring in critically ill patients. Neurology 2004;62:1743–1748
3. Westover MB, Shafi MM. Bianchi MT et al. The probability of seizures during EEG monitoring in critically ill adults. Clinical Neurophysiology 2015; 126: 463-471
4. Sutter R, Fuhr P, Grize L, Marsch S, Ruegg S. Continuous video-EEG monitoring increases detection rate of non convulsive status epilepticus in the ICU. Epilepsia 2011;52:453-457.
5. Shafi MM, Westover MB, Cole AJ, Kilbride RD, Hoch DB, Cash SS. Absence of early epileptiform abnormalities predicts lack of seizures on continuous EEG. Neurology 2012;79:1796-1801.
6. Lettinger M, Trinka E, Gardella E et al. Diagnostic accuracy of the Salzburg EEG criteria for non-convulsive status epilepticus: a retrospective study. Lancet Neurol. 2016;15:1054-1062.

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Stroke Memory Rehabilitation at National Neuroscience Institute

STROKE MEMORY REHABILITATION (SMART) PROGRAMME

The Temasek Foundation-National Neuroscience Institute Stroke Memory Rehabilitation (SMaRT) Programme is a three-year collaborative project which aims to provide a comprehensive preventive treatment regime for post-stroke patients to prevent cognitive decline.

SMaRT is a structured rehabilitation programme to help post-stroke patients improve aspects of cognition like memory, attention and executive function.

The programme caters to stroke patients (within the first year of suffering a stroke) with mild physical impairments but significant cognitive impairments.

Participants will take part in educational talks and hands-on activities. The programme covers commonly affected cognitive domains such as memory, attention and executive function (complex planning, higher thought process and execution of these tasks).

Cognitive decline may continue post stroke, though 16 to 20% of patients will improve in their cognition. While most improvements occur in the first three months, it is optimal for rehabilitation to continue for at least one year after the stroke.

Dementia in Stroke Patients

Stroke is currently the second largest cause of acquired cognitive decline globally. Singapore experiences one of the world's highest rates of stroke, with more than 7,000 new stroke patients each year. Currently, data from NNI demonstrates that 37.3% of patients develop post-stroke cognitive impairment (PSCI) within six months post stroke[1]. The global incidence of PSCI in stroke patients is reported to range from 20 to 40%.

PSCI patients being in the mild cognitive impairment stage, may present with a lesser degree of impairment in global cognition, mental flexibility, problem solving, attention, long-term memory, information processing speed, language, and navigation ability.

However, if left untreated or undiagnosed, these impairments can affect the quality of life, mental health and employability with deteriorating cognition. This is also likely to increase the chances of institutionalisation and contributes to a higher mortality rate.

As a growing public health burden, care options for PSCI are limited both in Singapore and worldwide as PSCI is under recognised and as a result undertreated. Current stroke rehabilitation programmes emphasise mainly on physical and functional rehabilitation but not cognition.

SMaRT programme participants taking part in cognitive exercises.

Studies have shown that effective cognitive rehabilitation approaches have been reported for neurological deficits such as neglect and aphasia, hence the SMaRT Programme seeks to improve cognitive outcomes for better management of PSCI.

ENROLMENT CRITERIA

To join the programme, participants should :

- Be between 18-80 years old
- Have had a stroke not more than 12 months ago
- Have been experiencing poor memory three to 12 months after their last stroke
- Not have prior memory complaints or diagnosis of dementia made by any doctor
- Not have any prior diagnosed psychiatric conditions
- Have made significant physical recovery with minimal physical disability or none

PROGRAMME STRUCTURE

Over 8 weeks, participants will be empowered and engaged with activities focusing on :

1. **Brain Essentials:** Staying healthy promotes both cognitive and general wellbeing. Participants will learn about eating well, activities to keep the body and mind fit, sleep and stress management to enhance emotional well-being.

2. **Exercise:** Low to medium impact exercises that can be done daily to keep fit.

3. **Core Cognitive Rehabilitation Component:** Memory, attention, executive function and visual spatial rehabilitation.

4. **Emotional Well-Being:** Stress management and relaxation techniques.

There will be an assessment before each run of the programme and on the last day of the programme to monitor progression. Upon completion of the programme, there will be a review of the patient again on the third and sixth month.

To find out more about the programme, contact the National Neuroscience Institute (NNI) at 6357 7153 or enquiry@nni.com.sg.

REFERENCES

1. Kandiah N, Chander R, Lin X, Ng A, Poh YY, Cheong CY, Cenina AR, Assam PN. Cognitive Impairment after Mild Stroke: Development and Validation of the SIGNAL2 Risk Score. Alzheimers Dis. 2016;49(4):1169-77

The Burns Centre at Singapore General Hospital

The Skin Bank Unit (SBU) is one of the tissue banks under Transplant Tissue Centre in SingHealth.

Located in the Singapore General Hospital's (SGH) Burns Centre, SBU began its operation in 1998 for the recovery, preparation, preservation and distribution of donated human skin. SBU maintains a ready supply of donor skin allografts to treat severe burn patients in Singapore during peacetime and in times of emergency.

The SGH Burns Centre is the only dedicated burns unit in Singapore and annually treats about 200 patients who suffer burn injuries due to industrial or domestic accidents. Typically, 10 – 15% of these patients require skin transplant.

Patients who suffer from major burns with a total body surface area (TBSA) in excess of 30% require human donated skin to cover the excised burn wounds (*Figure 1*). This is because there might not be sufficient donor sites to harvest their own skin for grafting.

The temporary skin allografts are life-saving as they help to prevent infection, reduce loss of critical fluids as well as relieve the patient's pain and discomfort during the critical phase of their injury. These allogeneic tissues help to improve the patient's morale and immunity until it is possible to graft autologous split thickness skin or cultured epithelial autograft (CEA) for definitive wound coverage.

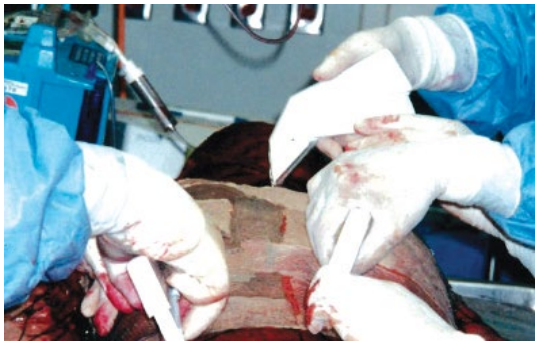

Figure 1
Meshed cadaveric skin grafting

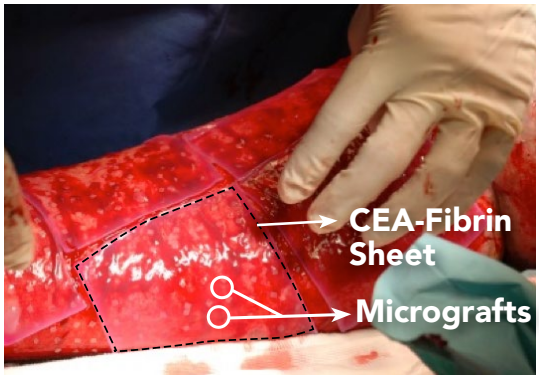

Figure 2
CEA-Fibrin sheets laid on micrografts (after removal of skin allograft) on full thickness burns

CULTURED EPITHELIAL AUTOGRAFT (CEA)

Cultured Epithelial Autograft (CEA) consists of fully-grown skin epithelial cells (keratinocytes) in a sheet cultured typically on specialised petri dishes. The autologous human keratinocytes are isolated from a small skin biopsy of up to 4cm^2 and then serially propagated in vitro with expansion ratio of up to 30 plates (total area 3,000cm^2) in about 3-4 weeks.

The use of CEA mitigates the disadvantage of limited donor site for harvesting of autologous split thickness skin in large surface burns. CEA is life-saving for TBSA >50% and reduces donor site morbidity.

ALLOGRAFT-MICROGRAFT SANDWICH METHOD

Currently the SGH Burns Centre employs a two-stage procedure which involves the onlay of micrografts covered with skin allograft on debrided wounds, followed by subsequent grafting of CEAs on granulating dermis.

The micrografts of size 3mm by 3mm each are cut from autograft sheets using a specialised device. They are then manually placed piece by piece on the dermis of the skin allografts in a grid-like pattern and sandwiched between the excised wound bed and the skin allografts in the grafting procedure.

After two to three weeks, the overlaid skin allografts are carefully removed to prevent the lifting of the micrograft islands and their surrounding epithelization. This is followed by the grafting of CEA sheets, typically on granulating and non-epithelized regions (*Figure 2*).

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Fax : 6844 9035
Email : transplant.tissue.centre@singhealth.com.sg
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Visit www.liveon.sg to find out more about legislation acts on organ and tissue donation in Singapore- Human Organ Transplant Act (HOTA) and Medical (Therapy, Education and Research) Act (MTERA)

REFERENCES

Chua, A., Khoo, Y., Thi Thu Ha, T., Woo, E., Tan, B., & Chong, S. (2018). From skin allograft coverage to allograft–micrograft sandwich method: A retrospective review of severe burn patients who received conjunctive application of cultured epithelial allografts. Elsevier Burns 44, 1032-1037.

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Division of Radiation Oncology

Dr Phua Li Gek Gillian
Associate Consultant
Division of Supportive & Palliative Care

Dr Zhuang Qingyuan
Associate Consultant
Division of Supportive & Palliative Care

NATIONAL DENTAL CENTRE SINGAPORE

Appointments: 6324 8798
Email: appointment@

PROMOTION – SENIOR CONSULTANT

Dr See Toh Yoong Liang
Senior Consultant
Dept
Restorative Dentistry
Sub-specialty
Prosthodontics

PROMOTION – CONSULTANT

Dr Ng Jing Hao
Consultant
Dept
Orthodontics

NATIONAL HEART CENTRE SINGAPORE

Appointments: 6704 2222
Email: central.appt@nhcs.com.sg

APPOINTMENTS

Dr Ignasius Aditya Jappar
Associate Consultant
Dept
Cardiology
Sub-specialty
Echocardiography

Dr Lee Shan Yin Audry
Associate Consultant
Dept
Cardiology
Sub-specialty
Echocardiography, Heart Failure

Dr Wong Ningyan
Associate Consultant
Dept
Cardiology
Sub-specialty
Interventional Cardiology

Dr Chia Ming Li Cynthia
Associate Consultant
Dept
Cardiothoracic Surgery

Dr Alicia Chia Xue Fen
Associate Consultant
Dept
Cardiothoracic Surgery
Sub-specialty
Cardiac Surgery (Adult)

Dr Sivaraj Pillai Govindasamy
Associate Consultant
Dept
Cardiothoracic Surgery

SINGAPORE NATIONAL EYE CENTRE

Appointments: 6322 9399
Email:appointments@snec.com.sg

PROMOTION – SENIOR CONSULTANT

Dr Chai Shu Ming Jean
Senior Consultant
Dept
Corneal & External Eye Disease
Sub-specialty
Ophthalmology

PROMOTIONS – CONSULTANTS

Dr Chong Guang Wei Wesley
Consultant
Dept
General Cataract & Comprehensive Ophthalmology
Sub-specialty
Ophthalmology

Dr Yap Zhu Li
Consultant
Dept
Glaucoma
Sub-specialty
Ophthalmology

Dr Shweta Singhal
Consultant
Dept
Neuro-Ophthalmology
Sub-specialty
Ophthalmology

DON'T LIMIT YOUR CHALLENGES. CHALLENGE YOUR LIMITS.

If you are a qualified doctor, a challenging career awaits you at SingHealth. We seek suitably qualified candidates to join us as:

- **SENIOR CONSULTANTS / CONSULTANTS/ ASSOCIATE CONSULTANTS**
- **RESIDENT PHYSICIANS**
- **STAFF REGISTRARS / SERVICE REGISTRARS**

Interested applicants are to email your CV with full personal particulars, educational and professional qualifications (including housemanship details), career history, present and expected salary, names of at least two professional references, contact numbers and e-mail address together with a non-returnable photograph.

Please email your CV to the respective institutions' email addresses/online career portals with the Reference Number MN1909.

SingHealth

www.singhealth.com.sg

The SingHealth Duke-NUS Academic Medical Centre draws on the collective strengths of SingHealth and Duke-NUS Medical School to drive the transformation of healthcare and provide affordable, accessible, quality healthcare.

With 42 clinical specialties, a network of 4 Hospitals, 5 National Specialty Centres, 9 Polyclinics and Bright Vision Community Hospital, it delivers comprehensive, multidisciplinary and integrated care.

To enhance community care, the new Outram Community Hospital on the SGH Campus will be completed by 2020.

Singapore General Hospital

Departments seeking:
Resident Physicians and Staff Registrars:

- Anaesthesiology
- Medical Departments (Various disciplines such as Geriatric Medicine & Psychiatry etc.)
- Surgical Departments (Various disciplines such as ENT & General Surgery etc.)
- Staff Clinic

Consultants:
- Acute Care Surgery/Trauma
- Anatomical Pathology
- Geriatric Medicine
- Psychiatrists

Website: www.sgh.com.sg
Career Portal: www.sgh.com.sg/subsites/sgh-careers/medical/pages/career-opportunites.aspx
Email: careers.medical@sgh.com.sg

KK Women's and Children's Hospital

Departments seeking:

Consultant/Associate Consultant (Haematologist, Microbiologist, Paediatric Pathologist):

- Pathology & Laboratory Medicine

Consultant/Associate Consultant:

- Diagnostic & Interventional Imaging

Resident Physicians:
- Emergency Medicine
- Obstetrics & Gynaecology

Staff Registrars:
- Diagnostic & Interventional Imaging
- Paediatric Surgery

Staff Physicians:
- Paediatric Surgery

Website: www.kkh.com.sg
Email: medical.hr@kkh.com.sg

National Heart Centre Singapore

Departments seeking Resident Physicians:
- Cardiology
- Cardiothoracic Surgery

Website: www.nhcs.com.sg
Email: joyce.soh.y.h@nhcs.com.sg

National Neuroscience Institute

Departments seeking Resident Physicians and Service Registrars:

- Neurology
- Neuroradiology
- Neurosurgery

Website: www.nni.com.sg
Email: nni_hr@nni.com.sg

Sengkang General Hospital

Departments seeking:
Resident Physicians and Staff Registrars:

- Anaesthesiology
- Cardiology
- Emergency Medicine
- Surgery
- General Medicine (with interest in Dermatology, Endocrinology, Gastroenterology, Geriatric Medicine, Rehabilitation Medicine, Renal Medicine and Respiratory Medicine)
- Intensive Care Medicine
- Neurology
- Orthopaedic Surgery (with interest in Hand Surgery and Orthopaedic Surgery)
- Otolaryngology
- Plastic, Reconstructive & Aesthetic Surgery Services
- Urology

Senior Consultants, Consultant, Associate Consultant:
- Radiology
- Pathology
- Urology

Website: www.skh.com.sg
Career Portal: www.skh.com.sg/careers/Pages/careers.aspx
Email: careers@skh.com.sg

Singapore National Eye Centre

Department seeking:
- Resident Physician,Opthalmology
- Resident Physician, Primary Eye Care
- Medical Officer

For more information, please visit the Career Opportunities section on the Singapore National Eye Centre website.

Website: www.snec.com.sg
Email: recruitment@snec.com.sg

SingHealth Community Hospitals

(Sengkang Community Hospital, Outram Community Hospital and Bright Vision Hospital)

Departments seeking:
Consultant, Associate Consultant, Staff Registrars, Resident Physician:

- Family Medicine

Website: http://www.singhealthch.com.sg/
Career Portal: www.singhealth.com.sg/SCH/careers/Pages/Careers.aspx
Email: schrecruitment@singhealthch.com.sg

10th KKH Scientific Meeting 2019

Patient-Centric Care: Precision Medicine and Personalised Care

11 and 12 October 2019 @ KKH Training Centre

Join us to gain insights on how medical advancements, precision medicine and personalised care are making an impact on patient experience and care.

Dates & Times	:	11 October 2019 (Friday) : 9.00 am to 6.00 pm 12 October 2019 (Saturday) : 8.30 am to 1.00 pm
Venue	:	KKH Training Centre, Women's Tower, Level 1
CME points	:	CME and CPE points will be awarded
Fees	:	11 October 2019 Launch of SingHealth Duke-NUS Genomic Medicine Centre and Main Conference Free admission for all Healthcare Professionals 12 October 2019 (Workshops) $250.00 per participant for Workshop 1 Free admission for all SingHealth Healthcare Professionals Free admission - Workshop 2 and 3

Registration for Workshops closes on 9 October 2019 (Wednesday)

For more details, please visit: www.kkh.com.sg/ScientificMeeting
For queries, please email: scientificmeeting@kkh.com.sg

16th Practice Update in Paediatrics (PUP)

Clinical Updates on Common Paediatrics Conditions

Join us to discuss topics deeply relevant to the children and parents who come to our clinical practice.

Topics include:

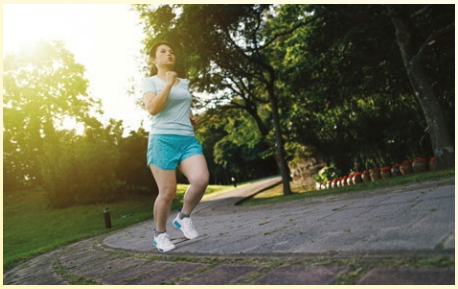
- Paediatric burns
- Common Otolaryngology scenarios, unhealthy eating habits and its link to mental health in adolescents
- Common skin infections

Date	:	9 November 2019, Saturday
Time	:	12.30 pm to 5.00 pm
Venue	:	KKH Auditorium (Training Centre), Women's Tower, Level 1
CME points	:	CME and SNB-CPE points will be awarded
Fees	:	$11 per participant (Includes lunch and tea refreshments)

Registration closes 6 November 2019, Wednesday

For more details, please visit: www.kkh.com.sg/events
For queries, please email: marcoms@kkh.com.sg

Pre-Diabetes Interventions and Continued Tracking to Ease-out Diabetes (Pre-DICTED) Programme



Pre-DICTED Programme

Individuals with pre-diabetes are at high risk of developing diabetes, which can lead to stroke, kidney disease and heart disease.

Pre-DICTED aims to evaluate the effectiveness of lifestyle intervention, with stepwise addition of metformin, if required, among those with pre-diabetes. The lifestyle interventions are designed to equip participants with the knowledge and skills to make lifestyle changes to reduce their risk of developing diabetes.

We are recruiting local participants with pre-diabetes for the programme.

Contact us if you have patients who:

- Are aged between 18 and 64 years-old (inclusive)
- Have a Body Mass Index (BMI) of 23.0 kg/m2 and above
- Are diagnosed with pre-diabetes based on:
- Fasting plasma glucose: 6.1 - 6.9 mmol/L (110-125 mg/dL) (Im paired Fasting Glucose; IFG) and/or
- 2-hr plasma glucose (OGTT): 7.8 - 11.0 mmol/L (140-199 mg/dL) (Impaired Glucose Tolerance; IGT)

Their blood sugar level will be monitored every 6 months for up to 3 years.

Study-related tests and evaluation will be provided at no cost. We will keep you informed on the status and test results of your patients if they are enrolled into the programme.

For more details, please visit **www.predicted.com.sg**

How to refer patients?

After seeking your patient's permission, please email **predicted@singhealth.com.sg** or text **9115 6276** with your patient's name and contact number. We will follow-up with them. You can also ask your patients to contact us directly.

Conducted by:

SingHealth DukeNUS ACADEMIC MEDICAL CENTRE
Diabetes Centre

SingHealth
www.singhealth.com.sg

GP FAST TRACK APPOINTMENT HOTLINES

Singapore General Hospital	6321 4402
Changi General Hospital	6788 3003
Sengkang General Hospital	6930 6000
KK Women's and Children's Hospital	6692 2984
National Cancer Centre Hospital	6436 8288
National Dental Centre Hospital	6324 8798
National Heart Centre Hospital	6704 2222
National Neuroscience Institute	6330 6363
Singapore National Eye Centre	6322 9399

DIRECT WARD REFERAL CONTACT NUMBERS

Singapore General Hospital	6321 4822
Changi General Hospital	6850 1648
KK Women's and Children's Hospital	6692 2984

SINGHEALTH DUKE-NUS ACADEMIC MEDICAL CENTRE

- Singapore General Hospital
- Changi General Hospital
- Sengkang General Hospital
- KK Women's and Children's Hospital
- National Cancer Centre Hospital
- National Dental Centre Hospital
- National Heart Centre Hospital
- National Neuroscience Institute
- Singapore National Eye Centre
- SingHealth Community Hospitals
- Polyclinics SingHealth

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