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BRAINCHILD

The Official Publication of HKCNDP
Special Issue on Paediatric Neuro-Surgery

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香港兒童腦科及體智發展學會
The Hong Kong Society of Child Neurology and Developmental Paediatrics

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SPECIAL ISSUE ON PAEDIATRIC NEURO-SURGERY

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The Hong Kong Society of Child Neurology & Developmental Paediatrics

BRAINCHILD October 2010 - Editor's Note

Paediatric Neuro-Surgery

Chok-wan CHAN

The current issue of Brainchild is devoted to Paediatric Neuro-Surgery. Thanks to the Guest Editorship of Dr. Dawson Fong, Consultant Neuro-surgeon of Hong Kong Hospital Authority, we have an excellent collection of six outstanding papers on *"Neurocognitive assessment for a 7-year old girl with left medial temporal sclerosis – A single case"*, *"Diffusion Tensor Imaging and its Clinical Application in Epilepsy"*, *"Ictal and Interictal Brain SPECT Imaging"*, *"Pre-surgical Psychiatric Assessment Protocol for Medically Refractory Paediatric Epilepsy Patients"*, *"The Role of Paediatric Neurologist in Pre-surgical evaluation of Epilepsy Surgery - the Current Evidence and the Experience in the past 10 years"* and *"Epilepsy Surgery"*. These represent a comprehensive spectrum of subjects contributed by a transdisciplinary team of experts from the domain of neurosciences consisting of neurologists, radiologists, neurosurgeon, psychologists and others exemplifying close collaboration between professionals within the area of neurosciences in Hong Kong. I would also like to take this opportunity to thank Dr. Catherine Lam, Dr. Eric Yau and Dr. Chak Wai Kwong for editing these excellent papers for our readers. I wish you enjoyable reading pleasure.

Good team approach for professionals within the neurosciences in Hong Kong has been a good template for colleagues elsewhere well illustrated by the effective interfacing between clinical practices between public and private practice via clinical meetings and scientific seminars over the years notably in areas of neurosurgery and epilepsy surgery. Our current mission for planning the Centre of Excellence for Paediatrics (CEP) serves as a good example for close collaboration between professionals within the medical specialties and paediatric subspecialties. Paediatric Neuro-Surgery is specially included within CEP by virtue of its close relationship with other subspecialties within paediatrics and child health. We look forward to witnessing this innovative planning bearing fruitful result by 2016!

At the Continuing Medical Education (CME) and Continuous Professional Development levels, Hong Kong professionals in the neurosciences are most privileged to have world experts patronizing the Pearl of the Orient in the past three months sharing their expert knowledge and experiences with local professionals. We have Professor Simon Harvey from Australia talking to us on Childhood Epilepsy in September 2010, Professor Peter Wong from Vancouver providing us with an EEG Course in October 2010 and Professor Joe Watt from Canada delivering a commissioned series of lectures on physiatry in November 2010. We also actively participate at the international and region congresses on neurosciences and our members contributed significantly to medical literature in these areas. Hong Kong professionals should therefore be proud of our professional collaboration and outcome deliverables for the good and welfare of the children we serve.

While we are preparing this issue of Brainchild, we are pleased to report an important event occurring in Hong Kong earlier this year. On 27 June 2010, Mr. Anthony Wu (Chairman of the Hospital Authority of Hong Kong -"HA") announced the adoption of a new Chinese

name for epilepsy for use under its governance. The HA is an official health organization in Hong Kong that provides services to more than 95% of its population. Mr. Wu officially mandated the use of (腦癇症) in all public hospitals under HA. Henceforth, this becomes an official Chinese term for epilepsy in the HA. This announcement started a new era and the decision is made to encourage equal opportunity with no discrimination. This announcement has been published in all major local newspapers. Professionals strongly believe this change will have a significant impact among the Chinese speaking population. On a wider front, 27 June 2010 will be remembered as an important day in the history of epilepsy. In Hong Kong, there are between 35,000 and 70,000 individuals with epilepsy. Apart from physical suffering and psychological stress, individuals with epilepsy suffer from inequalities as a result of the old Chinese name of epilepsy (癲癇症). Epilepsy has long been so described in ancient Chinese literature. The clinical entity was mentioned in one of the oldest medicine textbooks in China which was firstly published more than 2000 years ago as *"Huang Di Nei Jing"*《黃帝內經》. This clearly described epileptic semiology under two terms: *dianji* (癲疾) and xian (癇) which eventually joined together as *dianxian* (癲癇). Unfortunately after many years, the meaning of the prefix word dian (癲) became corrupted and was wrongly interpreted and associated with the word madness by mistake. Furthermore, the Chinese name became transformed into having close proximity to animals with subsequent names describing the disease as the *bizarre movements of goats* (羊癲風) or *pigs* (豬婆風). The names of animals suggested disease etiologies linking to animals and the word *dian* (癲) carried the strong implication of psychiatric illnesses. The Hong Kong Epilepsy Association (香港協癇會) has long been trying to rectify the inequality and stress caused by such naming. In 1997, Ms Marion Fang Sum Suk, Dr Ko Wing Man, Dr Patrick Li, Professor Virginia Wong, and groups of relatives of epilepsy patients first brought this issue into the public. This continued to be raised. In 2008 when Dr Ko and Ms Shelly Lai Kuen Lee (the then Deputy Secretary for Health and Welfare) jointly wrote letters to Prof Peter Wolf (President of International League Against Epilepsy), Susanne Lund (President of International Bureau for Epilepsy) and Lee Sai Cheuk (President of China Association Against Epilepsy) endeavouring to initiate review of the Chinese name for epilepsy. They suggested to use a name called (腦癇症) which literally means *epilepsy due to the brain*. From 2008 to 2010, many meetings were held and preparations were made in an attempt to promote this change. The various patient and neurological groups in Hong Kong all then agreed to adopt this new name which is accurate and orthodox with clear definition and truth clinical semantics. We are most pleased to witness good solidarity between all sectors in our community and the official Name Ceremony on 27th June 2010 exemplifying the success of our collective effort for the mission.

Finally do accept our deepest appreciation for the good work of all responsible professionals and key players for child health services in Hong Kong in providing quality management and for striving the best welfare and rights for our children with problems in the neurosciences. Together we should be able to achieve the noble goal of Healthy Children for a Healthy World!

I wish you all reading pleasure and best of health!

Dr. Chok-wan CHAN
Editor-in-Chief, The Brainchild
President, The HK Society of Child Neurology & Developmental Paediatrics
23rd October 2010

Epilepsy Surgery

Dr. Dawson Fong

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Patients with epilepsy who bear a definable focus or a discernable epileptic zone are potential candidates for epilepsy surgery.

Every seizure potentially incurs damage to a growing and maturing brain leading to irreparable consequences. The longer it is not well controlled with anti-epileptic drugs (AEDs), the worse we would expect the eventual cognitive development to be. The simple aim for every kind of epilepsy surgical procedures is to excise the epileptic zone without causing undue morbidity. When complete excision is not possible, disconnecting fibre tracts within the brain helps to limit the spread of attacks and thus its damages. Generally epilepsy surgery can be classified as in Table 1.

Table 1. Common Surgical Procedures in Epilepsy

Nature	Procedures
Diagnostic	Intracranial recording with ❇ Subdural strip/grid electrodes ❇ Depth electrodes
Therapeutic	With a defined focus ❇ Temporal resection ❇ Selective amygdalo-hippocampectomy ❇ Extratemporal corticectomy ❇ Multiple subpial transection over eloquent areas
	Diffuse epileptogenic zone or with multiple foci - Interruption of spread ❇ Corpus callosotomy ❇ Functional hemispherotomy/hemispherectomy ❇ Multiple subpial transaction
	Miscellaneous ❇ Vagus Nerve Stimulation

Pre-surgical Evaluation

When medication is not good enough to control the epilepsy and a surgical option is contemplated, a series of evaluation is to be conducted to assess its suitability. The semiology itself says a lot about the origin of the abnormal discharge. With the advent of neuroimaging, we now have a large array of imaging modalities to confirm the abnormality both anatomically as well as metabolically. Examples include MR, Ictal SPECT, Interictal PET and functional MRI. If we have a concordance, we are generally ready to propose a treatment strategy.

Long history of intractable epilepsy takes a serious toll on the child's education, behaviour and psychosocial development. Thorough neuropsychological and psychiatric assessments are important not only as an integral part of pre-surgical evaluation but also to set the baseline

for post-operative follow up. Special test like WADA Test - selective intracarotid injection of amobarbital - serves as a functional test to determine the dominance of the hemispheres and 'rehearse' the effect of a temporal lobectomy on the patient's memory.

Intracranial Recording

Intracranial recording involves surgical placement of electrodes on the brain surface and serves to further delineate the area of onset and early propagation of a seizure that is suspected but not proven by extracranial EEG. (Figure 1) The strategy of electrodes placement is derived from a plausible hypothesis built on the findings of earlier presurgical evaluation.

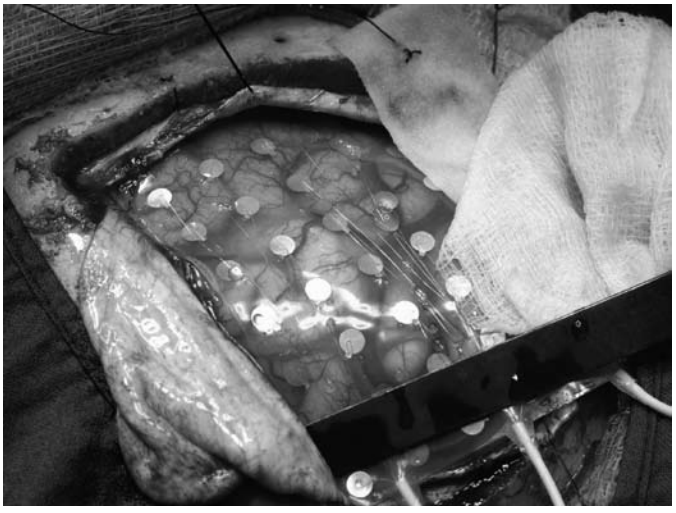


Figure 1. Subdural grid electrode placement – a form of intracranial monitoring

It is usually indicated for the determination of lateralisation in 'bitemporal syndrome' which is characterised by the presence of bilateral and equal amounts of interictal anomalies arising in both temporal lobes. In extratemporal epilepsy, a lead of seizure spread could be traced across various lobes because of the direct and clearer pick up on the cerebral surface.

With the electrodes in-situ over functional areas, electrical stimulation of the desired leads can help clinicians to define functional areas with high accuracy and the extent of excision of the epileptogenic zone tailored carefully. Since it is a surgical procedure in itself the decision for an intracranial recording should be made with discretion and taken as a prelude to the actual epilepsy surgery.

Temporal Lobectomy

Temporal lobe epilepsies (TLEs) are the single most common type of seizure disorder, accounting for about 25% of all epilepsies and approximately 70% of patients referred for surgical consideration.[1-3] The same is true for the paediatric population. Mesial temporal sclerosis (MTS) remains the commonest cause of complex partial seizures of temporal lobe origin in children who eventually undergo temporal lobectomy.[4]

TLEs could further be classified into limbic and lateral TLEs according to the origin of the epileptogenic origin.[5] However such a classification does not give surgeons a definite indication of how extensive the lobectomy should be performed. Since the circuitry of the limbic system might be a common pathway for complex partial seizures, sparing the mesial temporal structures in a lobectomy leads to inferior outcome in seizure control.[3]

Therefore, in practice, temporal lobectomy varies within the extremes of a selective amygdalo-hippocampectomy for MTS and a classical temporal lobectomy for lesion in the lateral cortex. How far back should the lateral temporal cortex be removed often depends on the findings on ECoG. (Figure 2)

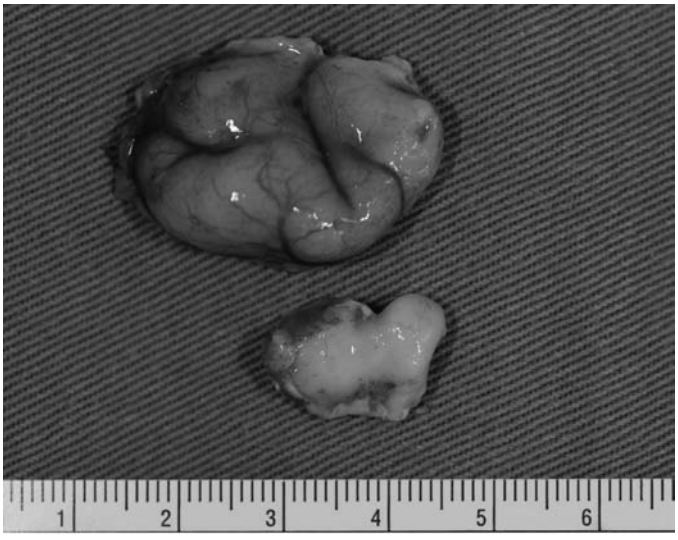


Figure 2. Specimen after an anterior temporal lobectomy. The bigger piece is the anterior pole of the temporal lobe and the smaller one the sclerotic hippocampus.

The main worry concerning the removal of the temporal lobe is the effect on memory – verbal on the dominant and visuo-spatial on the non-dominant hemisphere. But in general, these candidates with medically intractable epilepsy would, by the time of surgery, be compromised to some extent in these faculties. If not, plasticity must have shifted these functional areas. Thus, anatomically excising these sclerotic tissues would generally impart no further damages as shown by serial follow up of patients, local as well as abroad.[7]

Visual field deficit in the form of a quardrantic field defect is often taken as an unavoidable but acceptable side effect because of the damage on the optic radiation, the Meyer's Loop, situated around the superior and lateral aspects of the temporal horn. With the advent of diffusion tensor imaging (DTI), we can now locate the trajectory of the Meyer's Loop and fuse these images onto our neuro-navigation to give us the opportunity of actually avoiding damaging these fibres at operation. From the preliminary study of the author's personal series, we could significantly decrease the probability of a postoperative field defect down to around 11%. (Figure 3)

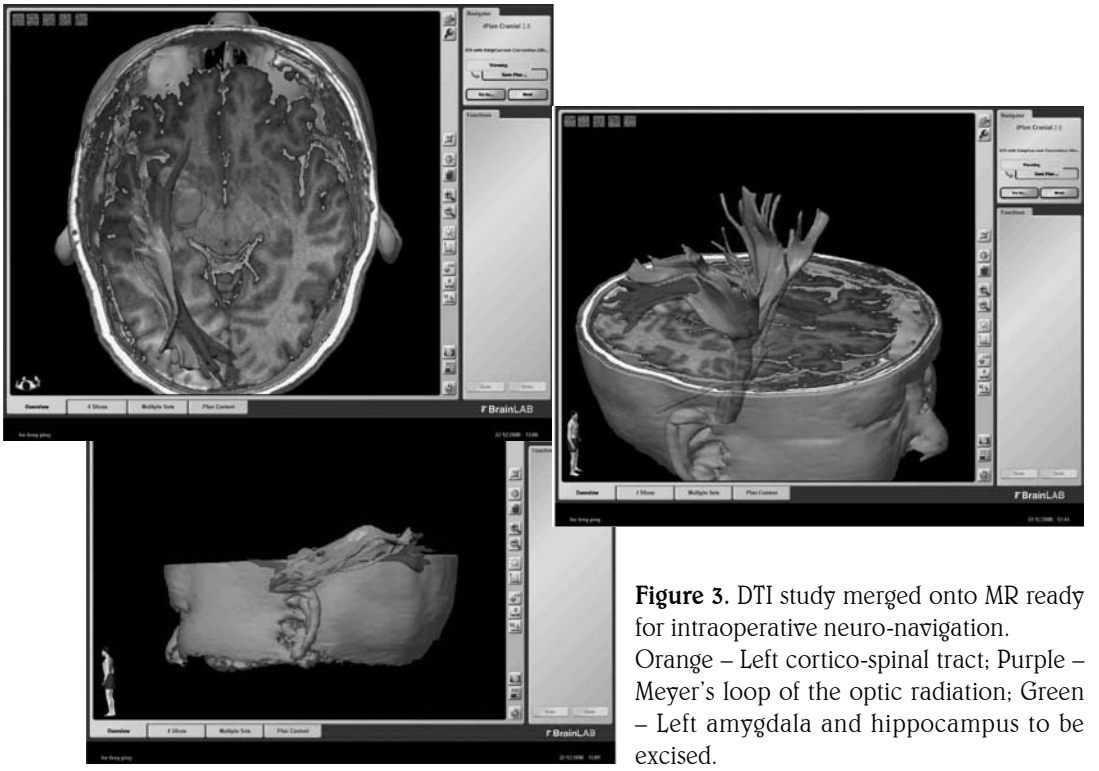


Figure 3. DTI study merged onto MR ready for intraoperative neuro-navigation.
Orange – Left cortico-spinal tract; Purple – Meyer's loop of the optic radiation; Green – Left amygdala and hippocampus to be excised.

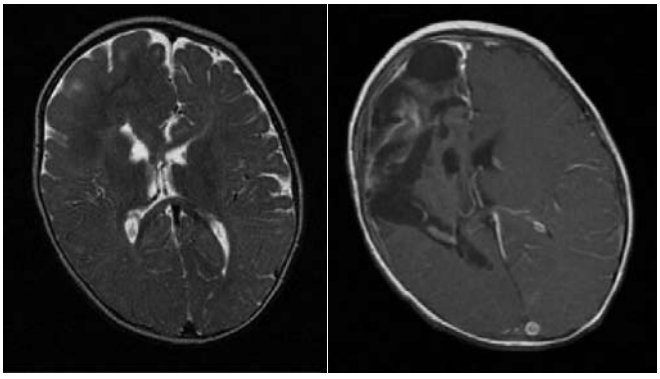
Extratemporal Excision

Unlike temporal epilepsy that can usually be managed in a standardised manner, once the epileptogenic zone falls outside the temporal lobe, it calls for careful studies not only to identify its exact location but also a safe strategy to take, lest the functional deficit be unacceptable. A common cause for these epilepsies is cortical dysplasia which is grossly normal to naked eyes and could not be differentiated from normal brain. It is therefore equally important to identify the focus and the functional areas in the vicinity. Functional MR helps a great deal for the localisation of these functional areas but for the speech areas in particular, invasive monitoring still serves an important role. With the expertise in neuro-anaesthesiology, neurosurgeons can now operate with patients fully awake. This gives us the best opportunity to map out accurately the functional areas, motor, speech or even sensory, and allow us to come to the best option of excising as much as possible the lesion leaving the functions intact.

Disconnection Surgery

When the epileptogenic zones are ill-defined or multiple and to excise them all becomes not practicable, disconnecting fibres within the cortex helps to interrupt the spread of discharges and alleviate the effect of an attack.

Rasmussen encephalitis is a condition in which the afflicted develops intractable epilepsy, gradual intellectual deterioration, progressive hemiplegia and atrophy of the cerebral hemisphere. When it was first reported in the 1950's, extensive excision of the affected hemisphere – hemispherectomy was the surgery offered. But such an extensive surgery carries too much morbidity. Instead we know now it is much safer just to do a peri-insular 'incision' along the lateral ventricle disconnecting the ipsilateral frontal, temporal, parietal and occipital lobes from the diencephalon - functional hemispherotomy.[6] (Figure 4)



A B

Figure 4. 10-month old boy with tuberous sclerosis and intractable epilepsy A – before surgery B after a right frontal lobectomy and functional hemispherotomy of the right side

For secondary generalized seizures spreading to the contralateral hemisphere or drop attacks as in Lennox Gastaut Syndrome, callosotomy is an effective treatment option. Up to two-third of the corpus callosum can be safely severed without undue side effects. (Figure 5)

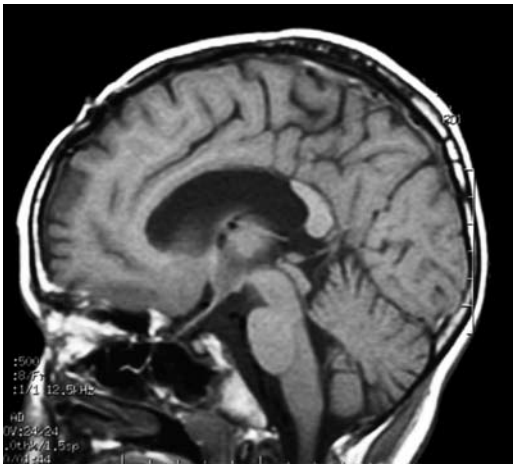


Figure 5. 7-year old girl with Lennox-Gastaut Syndrome after corpus callostomy

When the seizures arise from the eloquent cortex that could not be excised, multiple subpial transection can limit cortical neuronal synchronisation and seizure spread while preserving cortical function.[7]

Vagus Nerve Stimulation

For patients with medically refractory epilepsy who are not suitable candidates for surgery hitherto mentioned, vagus nerve stimulation (VNS) might still be considered.

Vagus nerve is well known to have extensive cortical projections and from animal experiments since the 1930s, it does have an effect on EEG pattern. With different frequency and intensity, cortical EEG can be synchronised or desynchronised. Exact mechanism on its effect on epilepsy is still controversial but apart from its effect on electrical discharges, chronic VNS can have a myriad of physiological changes from an increase of neuronal nos; activation of CN structure; increase of regional cerebral blood flow etc.[8-10]

VNS is effective in reducing epilepsy frequency in more than 50% of cases.[11] However, for young and small children the sizeable stimulator renders it not practicable.

Result

Due to the diversity of epilepsy syndromes and the variable surgical strategies, it is not easy to state exactly the general effectiveness of surgery in the management of intractable epilepsy. TLE, as the most prevalent type of epilepsy that could be treated surgically, is also the one that has the best response from anterior temporal lobectomy. Engel reported from a multi-centre series of 3579 patients, 2429 (68%) were seizure free and 860 (24%) improved after surgery.[12] Extratemporal epilepsy usually has a lesser success than this. Overall, with the advent of neuroimaging and elaborate pre-surgical evaluations, the outcome from surgery has considerably improved, in adult and paediatric patients alike. It is important to note that the control of epilepsy is not the only yardstick for success. Crippling psychological and social consequences of the intractable seizures of earlier years, in many instances leave these patients in a disabled state and their ordeals are far from over.[14]

Conclusion

For the carefully selected group of patients, epilepsy surgery provides a fair chance of cure by eradicating the cause of the seizure. Morbidity could in many instances be avoided by mapping out the functional and eloquent areas. Since epilepsy has a profound effect on the cognition and development of the individual, a holistic approach by a multi-disciplinary team is important not only in the pre-surgical evaluation but also after surgery when the patient ventures back into the community. In some instances, the 'burden of normality' – despite seizure-free – incurs new problems that have to be acknowledged early and managed accordingly.

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The Role of Paediatirc Neurologist in Pre-surgical Evaluation of Epilepsy Surgery - The Current Evidence and the Experience in the past 10 years

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To evaluate a child or an adolescent with epilepsy for feasibility of epilepsy surgery, it is usually a neurologist who needs to assess the patient first to see whether he or she is a suitable candidate or not. If the answer is yes, then the patient will be referred to an experienced neurosurgeon for further work-up.

The aim of pre-surgical evaluation has two roles: One is to find out where the epileptogenic focus is; the second is to find out where the eloquent cortex is, so that surgery can completely resect the epileptogenic focus and avoid the eloquent cortex to make the patient have seizure reduction or even seizure free and minimize any neurological deficits.

Who should be referred for pre-surgical evaluation and When?

Two third of people with epilepsy usually start to have the seizure in childhood or adolescent period. Generally speaking, most of childhood epilepsies (around two third) run a rather benign course and are responsive to medical treatment.[1] However, there is still a proportion (14% in NTWC) of children with epilepsy who run a malignant course and they are refractory to medical treatment even with the use of new anticonvulsants.[2] Although there are different definitions meeting criteria for medical intractable epilepsy, in principle they require the patient to have tried at least two or more different anticonvulsants with adequate dose for an adequate time period (2 years or more) and the patient still has frequent seizures (at least once a month). If the patient fulfills the above criteria, it is almost defines that further trial of other medications is very likely to be unsuccessful in terms of seizure control; the alternative non-medical treatment modalities should be considered e.g. epilepsy surgery or ketogenic diet.[3] More and more evidences are showing that the result of epilepsy surgery in children is as good as those in adults in term of seizure outcome.[4,5,6] Current evidence has even showed that paediatric patient who has undergone epilepsy surgery had even better cognitive outcome than those adult patients with similar etiology.[7] In the past, we usually waste our time by letting medical intractable epilepsy patients try all existing anticonvulsants before we consider referring them for epilepsy surgery. Base on the current evidence, once the patient's epilepsy become medically intractable, we should refer them for pre-surgical evaluation, so that the patient can benefit from epilepsy surgery much earlier.[3]

In children, not only medically intractability of seizure is considered, but also the disability caused by seizure (including medication side effects) is considered when choosing possible surgical candidates.[3] Poor developmental progress and cognitive dysfunction related to

intractable epilepsy are other important factors to consider referral for epilepsy surgery. Some studies show that earlier surgical intervention can result in better developmental outcome (DQ/IQ) especially in those who became seizure free after surgery;[8,9] the other study showed there is an improvement in verbral and perceptual intelligence quotients for children who underwent early temporal lobectomy.[7]

Apart from medical intractability, is there a particular group of epilepsy patients in which epilepsy surgery should be considered?

As we all know, paediatric epilepsy is a very heterogeneous disease. There are many different epilepsy syndromes. Each epilepsy syndrome has different natural course and prognosis. Many of them, especially those that are medical refractory, cannot be classified into specific epilepsy syndrome, but rather belong to a group of epilepsies called focal symptomatic epilepsy and focal cryptogenic epilepsy.[3,10]

Focal epilepsy belongs to a group of epilepsies with evidence of focal features e.g. semiology may reveal focal onset; EEG may show a focal abnormality such as slow wave or epileptiform discharge. Focal symptomatic epilepsy belongs to a group of focal epilepsies with underlying brain pathology. MRI brain may show a focal brain lesion e.g. tumour, cortical dysplasia. On the contrary, Focal cryptogenic epilepsy may show the above focal features in semiology or EEG, but the MRI brain may look normal.10 In this case, other functional imaging such as SPECT or PET may reveal the occult focal cortical abnormality. These two groups of patient could be potentially benefit from epilepsy surgery.

What else investigations should require? How to correlate the clinical seizure with underlying brain lesion? How to predict the possible cognitive dysfunction before and after surgery?

Before referring the patient to undergo resective surgery, the patient should have some more investigations done including: 1) video EEG to capture the patient's clinical seizure to document that the seizure onset is originated from the MRI brain lesion or due to other causes for example, psychogenic seizure or genetic cause etc. 2) patient should undergo neuropsychological assessment to assess baseline cognitive function. It is common that patient with focal unilateral (right or left) epilepsy will have corresponding (visuo-spatial or verbral) neuropsychological brain dysfunction. The result of neuropsychological assessment could also help us to predict the possible cognitive sequela after resective surgery.

A typical case scenario for epilepsy surgery

The common scenario is that a child with medically intractable complex partial seizure associated with epigastric aura and a sense of fear preceding seizure followed by eye staring, impaired consciousness and left arm dystonia. The interictal EEG shows slow wave and epileptiform discharge over right mid-temporal region. The MRI brain shows right mesial

temporal sclerosis. The patient undergoes video EEG monitoring with typical seizures captured, and all showed ictal recruiting theta rhythm over right temporal region. The neuropsychological assessment showed the patient has impaired visuo-spatial function with intact verbral function. In this case, all investigation results are concordant with right mesial temporal focus. Right temporal lobe resective surgery will be a good treatment option with 50-70% chance to make the patient seizure-free according to recent studies.[11]

What is surgical remedial epilepsy syndrome?

The surgical remedial epilepsy syndromes are specific etiologies of epilepsy which are medically unresponsive and could benefit from epilepsy surgery. They include: Malformation of Cortical Development; Mesial Temporal Sclerosis; Developmental benign brain tumour (DNET, Ganglioglioma); Unilateral cerebral vascular injury with or without infarction / porencephalic cyst; vascular malformation e.g. carvernous haemangioma; tuberous sclerosis; Sturge-Weber syndrome; Rasmussen's Encephalitis; Hemi-megalencephaly; hypothalamic hamartoma etc.[3]

What is epileptogenic zone and how to find it?

The epileptogenic zone is a theoretical brain region which causes epilepsy. By completely resecting or disconnecting it from the remaining brain, one can make patient seizure free. In clinical practice, the exact location of the epileptogenic zone could be estimated by knowing the following zone/region in brain includes:

1) Ictal onset zone – region of brain with ictal onset shown by intracranial EEG
2) Symptomatic zone –region of brain where seizures produce symptoms could reflect more to seizure propagation rather than the seizure onset
3) Lesional zone – a highly epileptogenic lesion usually is the culprit of the clinical seizure but not always; sometime it is the surrounding tissue of lesion causing seizure
4) Irritative zone – region showing abnormal interictal discharge
5) Functional deficit zone- region of brain showing hypo-function (hypo- metabolism in PET) which may or may not be related to epilepsy

The limitation of EEG in localization of epileptogenic focus

In order for EEG signals being detected by scalp EEG, it has to go through different layers of barriers in between, e.g. dura, skull bone, soft tissue and skin. This makes the high frequency EEG signal, especially, beta and gamma frequency EEG signal (which is the usual range of ictal EEG signal), impossible to get through. Due to the filtering effect, these make the high frequency EEG signal distorted and hence make the scalp EEG difficult to detect the ictal onset zone. This technical limitation could be resolved by intracranial EEG either performed intra-operatively or extra-operatively.

On the other hand, scalp EEG is good in localization of seizure which originates from the convexity of lateral frontal cortex with accuracy up to 68%.[12] But it has its limitation in

detecting EEG signal from deeper cerebral structure e.g. frontal and parietal mesial structure and orbital frontal, insular region etc.[13]

Moreover, localization by scalp EEG probably depends significantly on location of the epileptogenic zone; the following is the list of different regional epilepsy in order from the most reliable to least reliable localization by scalp EEG: Mesial temporal lobe epilepsy, Dorsolateral frontal lobe epilepsy, Parietal lobe epilepsy, Mesial frontal lobe epilepsy, Occipital lobe epilepsy.[5]

It is not uncommon that scalp EEG paradoxically localized the epileptogenic focus to the contralateral side in the mesial frontal, cingular epileptogenic focus due to unusual oblique dipole rather than the usual radial / vertical dipole from the gyrus on the convexity of the brain.

It is also not uncommon to have bilateral synchronous interictal EEG discharges in a patient who has a unilateral epileptogenic focus, especially in frontal lobe epilepsy

Because of the above reasons, the scalp EEG in certain situations may show misleading result. So it is important not to totally rely on scalp EEG to localize the epileptogenic focus and hence to select patient for epilepsy surgery or exclude patient from epilepsy surgery. The localization of epileptogenic zone requires other modalities of investigations including structural and functional brain imaging and neuropsychological assessment.

Why it is important to have a MRI lesion?

In a recent meta-analysis, the post-surgical seizure outcome was that 66% of seizure free patients with lesional, 34% of seizure free patients with non-lesional extra-temporal epilepsies. In children, 73% reached seizure-free status in the lesional group and 46% in the non-lesional group. Overall, the odds of being seizure-free were 2.5 times higher in those who had a lesion on MRI or histopathology.[14,15]

Because of significant better seizure outcome in lesional epilepsy surgery compared with nonlesional epilepsy surgery, we should try our best to detect any subtle epileptogenic MRI lesion either using higher resolution 3T-MRI or functional imaging.

The role of ictal SPECT scan in epilepsy surgery

In comparison with MRI, FDG-PET, MEG and scalp EEG, ictal SPECT is probably the most sensitive technique to localize the ictal onset in extratemporal lobe epilepsy, and to predict a seizure-free outcome after epilepsy surgery.16 The epileptogenic zone is often difficult to determine in MR-negative refractory extratemporal lobe epilepsy, and only around 40% of patients with MR-negative refractory extratemporal lobe epilepsy are rendered seizure-free after epilepsy surgery. 17Re-evaluation of the MRI guided by the ictal SPECT revealed a small focal dysplasic lesion in around 15% of MRI-negative patients.[18]

The role of PET in epilepsy surgery

Position emission tomography is a type of functional imaging technology which measures regional uptake of ligands in human body. FDG is the most widely used PET tracer for pre-surgical evaluation of patient with intractable focal epilepsy to measure glucose uptake by the different brain regions. In interictal state, PET shows hypo-metabolism in regions which are usually in the vicinity of the epileptogenic zone. PET is one of the tests that helps us to define the functional deficit zone.

Defining the location and extent of possible epileptogenic zone in the extratemporal lobe epilepsy is not easy, PET has a sensitivity of 50-68.4% in extratemporal paediatric epilepsy.[16] Especially, when MRI shows no clear lesion, PET may become the only tool to give us the clue where is the location of the epileptogenic zone. In children, FDG-PET has a sensitivity of around 43% in cases of non-lesional neocortical epilepsy. Study showed that hypometabolism on PET usually extends beyond the epileptogenic lesion.[19] Because of this, PET is not used to define the precise margin of epileptogenic zone, but is a good tool to guide placement of intracranial electrodes, particularly in nonlesonal epilepsies.

Who and how to decide which patient for epilepsy surgery? The experience from a tertiary level inter-disciplinary pre-surgical assessment program in NTWC

The modern management of epilepsy emphasizes not only on achieving seizure control, but also on a more comprehensive understanding of the underlying etiology; how patient is being affected by epilepsy; whether there is any cognitive or psychological dysfunction etc. and offer the patient a more comprehensive management.

Because of the complexity in paediatric medically intractable epilepsy which may be associated with profound developmental, behavioural and psychological effects, a tertiary level inter-disciplinary assessment is mandatory. A comprehensive paediatric pre-surgical evaluation team has been set up in Tuen Mun Hospital since 2006 which entails a multidisciplinary team of experts (paediatricians, nurses specialized in epilepsy, neurosurgeons, neuro-radiologists, nuclear medicine physicians, child psychiatrists and neuro-psychologists, occupational therapists and physiotherapists). Each patient with intractable epilepsy has undergone detailed pre-surgical evaluation including video EEG, high resolution MRI and neuropsychological assessment. In selected cases, PET and ictal SPECT were also performed to identify the epileptogenic focus. Epilepsy surgery was performed when the above investigation results were concordant.

In Tuen Mun Hospital , regular inter-disciplinary case conference is held to evaluate each case, each discipline will offer their professional advice and decide whether the patient would be benefit from surgery or not. Overseas expert advice will be sought in any difficult and challenging case to make sure the standard of case is up to international standard. If the patient is not a candidate for surgery, we will try to optimize their medical treatment or try

other treatment modalities including ketogenic diet. Each epilepsy patient will be followed up post-operatively to monitor the progress; this not only includes the seizure outcome, but more importantly the cognitive, psychological, psychiatric and quality of life outcome.

Fom1998 to 2009, 35 children underwent epilepsy surgery in Tuen Mun Hospital. Their age at operation ranged from 10 months to 19 years. 42% of them became seizure-free; 29% of them had seizure reduction; 29% had no change in their seizures. For temporal lobe surgery, 75% of patients became seizure-free and 6% had seizure frequency reduction after surgery.[21] The result is comparable to those in overseas epilepsy surgery centers.[4,11]

The direction of development and future challenging

The candidates of Paediatric Epilepsy Surgery came from a spectrum of disease with different degrees of difficulty. Some epilepsy patients have discrete brain lesion e.g. developmental brain tumour, type 2B cortical dysplasia; total surgical removal of lesion with clear margin will result in excellent outcome with chance of seizure-free being 60-80%. While some epilepsy patients have more diffuse and extensive pathology with unclear margin e.g. post-encephalitic epilepsy, post-traumatic brain injury, etc. and hence surgical resection will result in poorer seizure outcome and higher risk of neurological deficit or cognitive decline. Concerning the development of epilepsy surgery, this has started from temporal lobe surgery which showed satisfactory outcome with 65-80% of the patients being seizure-free.[4,11] Over the past years epilepsy surgery has progressively been targeting more extratemporal cases, especially in the paediatric age group, most likely because of better resolution of modern imaging technologies that can detect very subtle cortical lesions. In contrast to temporal lobe epilepsies, extratemopral epilepsies constitute a more heterogeneous group, encompassing different subgroups because of different location of epileptogenic zone required different surgical strategy and hence the possibility of neurological deficit and cognitive dysfunction will be different. Therefore the pre-surgical approach for these patients need to be individually tailored made.

Electro-clinical Anatomical Functional Correlation

The future direction of development of pre-surgical evaluation, especially in MRI-negative case involving co-registration of different investigation modalities including MRI, SPECT, PET, Functional MRI, EEG, MEG together to delineate the epileptogenic zone and functional cortex and also to guide the placement of intracranial electrodes, in order to increase the likelihood to find the extent of epileptogenic zone and make complete resection possible and avoid involving the functional cortex.

Conclusion

For children with epilepsy not adequately controlled by medication, it is believed that early assessment and changing to a more appropriate treatment offers the best prognosis for seizure control, educational achievement and personal development.[22]

Epilepsy surgery is shown to be safe and an effective way of treatment in selected group of children and adolescents with intractable epilepsy and they should be considered for surgical evaluation at whatever age or IQ level they manifest with severe, intractable, disabling localization –related epilepsy.[5,6,22]

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Pre-surgical Psychiatric Assessment Protocol for Medically Refractory Paediatric Epilepsy Patients

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Epilepsy is the most common neurological disorder in children with a prevalence of 0.05 to 1%. It is a disease of the central nervous system but is also a chronic medical illness. It carries risk of developing emotional, behavioral or mental problems. Studies showed that there is an increased risk of having psychiatric symptoms in patients with epilepsy compared with normal controls. More than 20% of the young population with uncomplicated epilepsy may have some form of psychiatric problem compared with 10% in those who suffer from chronic medical illness. However, more than 50% of children and adolescents with complicated epilepsy may have psychiatric involvement. Among all types of psychiatric illness, anxiety and depression are the most commonly reported psychiatric problem followed by attention deficit hyperactivity disorder, obsessive compulsive disorder and tics disorder. Patients with epilepsy have higher risk of suicide and deliberate self-harm than general population.

Despite the high prevalence of psychiatric illness among epileptic patients, only a small proportion of them received formal psychiatric assessment or treatment due to various reasons including the social stigma on psychiatric illness and epilepsy. Study showed that only one third of child and adolescent epileptic patients presented with mood symptoms received psychiatric services. This unrecognized and under-estimated situation can lead to adverse psychiatric consequences and outcomes in epileptic patients. Early intervention to this group of patient will greatly reduce the burden of the health care system, family and the patient.

The Goal of Pre-surgical Psychiatric Assessment

The goal of the pre-surgical psychiatric assessment is to identify psychiatric and behavioral symptoms in epileptic patients before surgery. Study showed that pre-operative psychiatric status and psychosocial adjustment play an important role in post-surgical psychiatric outcome.

Pre-surgical Psychiatric Assessment Protocol

An assessment protocol was designed to look for their behavioral, psychiatric symptoms, self esteem profile and quality of life. The assessment was performed by a child and adolescent psychiatrist before the operation as baseline. Further assessment will be performed at 1, 3, 6, 12, 18, and 24 months after operation. Patients who are able to complete self-assessment questionnaire will be assessed by the Hospital Anxiety and Depression Rating Scale (HADRS), the Child Behavior Checklist (CBCL) parent report form, the Culture-Free Self Esteem Inventories (CFSEI), the Pediatric Quality of Life Inventory (PedsQL) and clinical interview. Those patients with HADRS score above the cutoff would further assess by another battery of assessment scales including the Hamilton Anxiety Rating Scale (HAMA), the Hamilton

Depression Rating Scale (HAMD), the Beck Depression Inventory (BDI), the Scale for Suicidal Ideation (SSI) and the Clinical Global Impression Scale (CGI). Only CBCL, PedsQL and clinical assessment were performed to patients who were mentally incapable to complete the self assessment questionnaire.

Protocol for pre-surgical assessment of epileptic patient (Intake assessment, 1, 3, 6, 12, 18 & 24 months post-operation)

- Patient with IQ >85

1. Hospital Anxiety and Depression Rating Scale (HADRS)
2. Child Behavioral CheckList (CBCL) Parent report form
3. Self Esteem Rating Scale (SERS)
4. Pediatric Quality of Life Inventory (PedsQL)
5. Clinical Assessment

- If HADRS show possible case of anxiety and/or depression, then for

1. Hamilton Anxiety Rating Scale (HAMA)
2. Hamilton Depression Rating Scale (HAMD)
3. Beck Depression Inventory (BDI)
4. Scale for Suicidal Ideation (SSI)
5. Clinical Global Impression (CGI)

- Patient with IQ <85

1. Child Behavioral CheckList (CBCL) Parent Report Form
2. Pediatric Quality of Life Inventory (PedsQL)
3. Clinical Assessment

- If patient present with psychiatric problem, then for

1. Clinical Global Impression (CGI)

The Hospital Anxiety and Depression Rating Scale (HADRS)

The Hospital Anxiety and Depression Rating Scale (HADRS) is a screening instrument that screen for the presence of a mood disorder in medically ill patients. It is appropriate for use in either community or hospital settings. It generates an anxiety and a depression score. It is a self-report scale with 14 items, rated on 4-point Likert-type scales. Score above 9 indicates the possibility of having the disorder.

The Child Behavior Checklist (CBCL)

Behavioral symptom was assessed by the Child Behavior Checklist (CBCL). It is a parent-rated dimensional measure of psychopathology over the previous 6 months designed to identify children at risk. It consists of 113 items of behavioral or emotional problems scored on a 3-point Likert scale. The resulting profile consists of eight subordinate problem scales (Anxiety/Depression, Withdrawal, Somatic Complaints, Aggression, Delinquent Behavior, Attention Problems, Thought Problems and Social Problems) that are grouped into superordinate scales: internalizing problems (withdrawal, somatic complaints, anxiety/depression), externalizing problems (delinquent behavior, aggression) and total problems. T-score of 70 was chosen as the cutoff score to discriminate best between referred and non-referred children and adolescents.

The Culture-Free Self Esteem Inventories (CFSEI)

The inventories are intended to measure an individual's perception of self. It is a self-rated scale with 30 items rated on a yes-no format. It generates 4 subscales (general, social/peer-related, academic/school-related, parental/home-related self-esteem). A lie subtest is also included.

The Pediatric Quality of Life Inventory (PedsQL)

Health-related quality of life was assessed by the Pediatric Quality of Life Inventory (PedsQL). It contains 23 questions about the child or adolescent's physical, emotional, social and school functioning in the past one month and is rated by the parent. Scores ranged from 0 to 100.

The Hamilton Anxiety Rating Scale (HAMA)

The Hamilton Anxiety Rating Scale (HAMA) is a clinician-rated scale that provide overall measure of global anxiety, including cognitive and somatic symptoms. It consists of 14 items, each scored 0 to 4. It assesses anxious mood, tension, fear, insomnia, intellectual symptoms, depressed mood, behavior at interview, somatic symptoms, cardiovascular symptoms, respiratory symptoms, gastrointestinal symptoms, genitourinary symptoms, autonomic symptoms and muscular symptoms. Score ranged from 0 to 56 with a cutoff above 14 indicates clinically significant anxiety.

The Hamilton Depression Rating Scale (HAMD)

The Hamilton Depression Rating Scale is a clinican-rated scale that measures the severity of depressive symptoms in patients with primary depressive illness. It can also monitor changes in depressive symptoms with treatment. It contains 17 items scored on a 4-point Likert scale.

The Beck Depression Inventory (BDI)

The Beck Depression Inventory (BDI) is a patient-rated scale assesses major symptom categories associated with depression. It is designed to standardize the assessment of depression severity in order to monitor change over time or to simply describe the illness. It covers 21 behavioral manifestations represented by four statements describing symptom severity from low to high. Patients were asked to identify the statement that best described their feeling. Scores ranged from 0 to 62.

The Beck Scale for Suicide Ideation (SSI)

The Scale for Suicidal Ideation is designated to measure the intensity, pervasiveness, and characteristics of suicidal ideation in patient. It is a clinician-rated scale contains 21 items scored on a 3-point Likert scale. There is no dichotomous cutoff score defining high risk, but increasing scores reflect increasing suicidal ideation and risk.

The Clinical Global Impression Scale (CGI)

The Clinical Global Impression Scale (CGI) consists of 2 subscales, the severity and the improvement scale. The CGI-Severity scale is a 7-point clinician-rated that measures the severity of a patient's symptoms. The CGI-Improvement scale is a 7-point clinician-rated scale that measures change in global patient condition from baseline.

Conclusion

Epilepsy is a common disorder of the central nervous system that carries a high risk of psychiatric comorbidity especially in medically refractory patient. The psychiatric need for this group of patient is highly under-estimated. Psychiatric assessment plays an important role in pre-surgical assessment for patient who plan to have operation. A protocol is designed to meet this purpose and for the monitoring of both psychiatric and behavioral outcome after operation.

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Ictal and Interictal Brain SPECT Imaging

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Nuclear Medicine is a branch of medical imaging that uses radiopharmaceuticals to diagnose or treat a variety of diseases. Radiopharmaceuticals are introduced into the body by intravenous injection (most common practice), swallowing or inhalation. A special camera (PET or gamma camera) is used to take images for analysis (Figure 1).

Figure 1. The latest gamma camera in Tuen Mun Hospital.

Brain SPECT (single photon emission computed tomography) images provides 3D information on the perfusion status of brain tissue. It is useful in various neurologic and psychiatric conditions like cerebrovascular disease, epilepsy, dementia, head injury, schizophrenia, drug abuse ...etc[1]. For patients having intractable focal epilepsy, finding out a definable epileptic focus or a discernable epileptic zone are potential candidates for epileptic surgery[2]. The epileptic focus can appear as structural lesion which can be detected by MRI up to 80% of the cases[3]. On the other hand, functional brain perfusion SPECT images may find out the epileptic focus in patients with normal or abnormal MRI findings[4].

In our department, ictal and interictal brain perfusion scans are performed by giving Tc-99m ECD (ethyl cysteinate dimer) intravenously during ictal and interictal condition respectively. After injection, the lipophilic radiopharmaceuticals will cross the normal blood brain barrier and enter into the brain cells. The radiopharmaceuticals will convert to hydrophilic compounds and remain inside the brain tissue soon after injection (first tens of seconds)[5]. Since the cerebral perfusion and metabolism are tightly coupled in most physiological and pathological conditions by autoregulation, brain perfusion SPECT images will reflect the metabolic status of brain tissue at/near the time of injection[6]. Epileptic focus is hypermetabolic during seizure and hypometabolic during interictal period. So the epileptic focus will appear “hot” in ictal and “cold” in interictal brain perfusion SPECT scan (Figure 2).

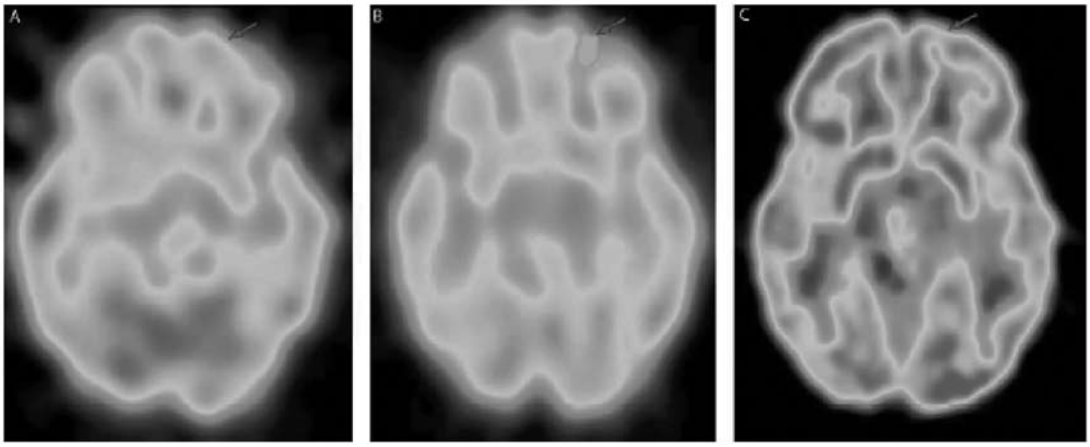

Figure 2. Patient with focal epilepsy in the left frontal lobe. (A) Ictal Tc-99m ECD SPECT. (B) Interictal Tc-99m ECD SPECT. (C) Interictal F-18 FDG PET.[6]

Concerning the sensitivity in detecting focal epileptic focus in temporal lobe, ictal brain SPECT scan (83.8%) is much better than interictal one (55.4%). The sensitivity of ictal brain SPECT scan is comparable to MRI (86.0%)[4]. Owning to the low sensitivity of interictal brain SPECT scan in localizing epileptic focus, its main role is to act as a baseline study that to compare with ictal SPECT images. To optimize the sensitivity of brain SPECT scan, we should pay attention to the technical details. In performing interictal SPECT scan, the patient should be monitored by EEG to make sure that there is no subclinical seizure attack. For ictal SPECT scan, the patient should be continuously monitored by video-EEG and the radiopharmaceutical must injected as soon as possible (<20s) after the onset of epileptic attack[7]. A simple dose delivery tubing system can assure rapid injection of tracer. It consists of three parts. Part 1 is permanently connected to the patient and the intravenous line is kept open by continuous infusion of normal saline. Part 2 is filled with radiopharmaceutical and put inside the lead container. Part 3 is a tube connected to a 20-ml syringe filled with normal saline. People can easily inject the tracer during onset of the aura by pushing the 20-ml volume into the system (Figure 3)

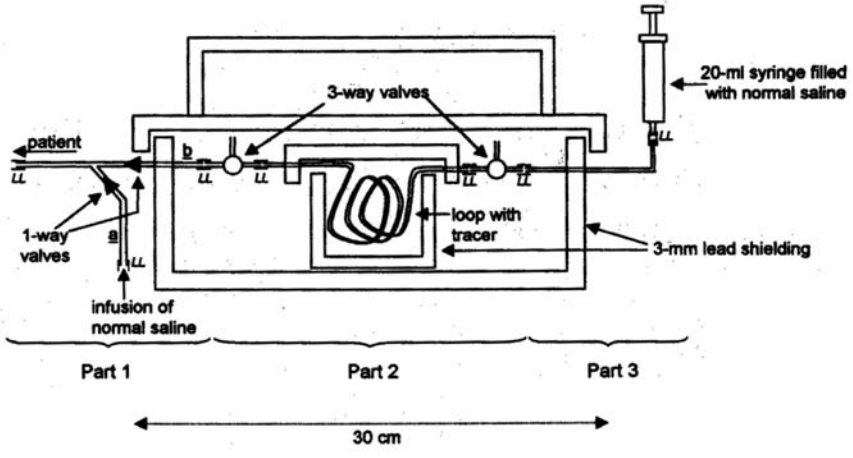

Figure 3. Schematic representation of the self-injection tubing system[8]

Traditionally, we compare the baseline interictal SPECT images with ictal SPECT images side by side visually. To further improve the sensitivity of the test, people develop many methods to meet the target. These methods include asymmetric index calculation (AIC), subtraction ictal SPECT co-registered to MRI (SISCOM) and statistical parametric mapping (SPM)[9]. Among these three methods, SISCOM is the most commonly used computer software that used to localize epileptic focus and study the propagation pattern (Figure 4). There are four basic steps in the SISCOM, namely SPECT to SPECT co-registration, SPECT normalization, SPECT subtraction & thresholding and subtraction SPECT to MRI co-registration.

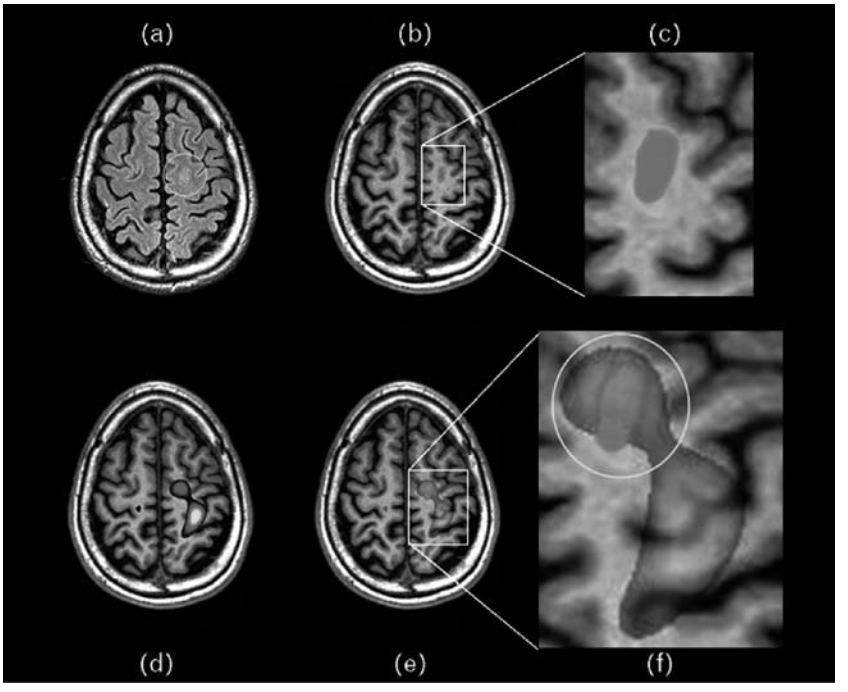

Figure 4. SISCOM can show the epileptic focus and propagation pathway.

(a) FLAIR: increased signal in the left superior frontal gyrus (white circle). (b) T1: blurring of the grey-white matter transition, consistent with a focal dysplastic lesion (FDL). (c) The FDL was manually outlined in green. (d) SISCOM, thresholded at z=+2. (e) Co-registration of the manual outline of the FDL and SISCOM. (f) The propagation pathway is "hotter" than the epileptic focus.[10]

In writing the final report of brain SPECT scan, besides looking at the images, we should know the patient's history, results of EEG/CT/MRI, patient's condition at the time of injection (ictal or interictal study, seizure semiology for ictal scan, relationship between onset of seizure and timing of injection), acquisition parameter used, post acquisition software enhancement ...etc[11].

Finally, we must stress that for successful management of patients having intractable focal epilepsy, a closely-related team involving physicians, neurosurgeons, radiologists, nuclear medicine physicians, nurses, EEG technologists and social workers are needed.

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Diffusion Tensor Imaging and its Clinical Application in Epilepsy

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Introduction

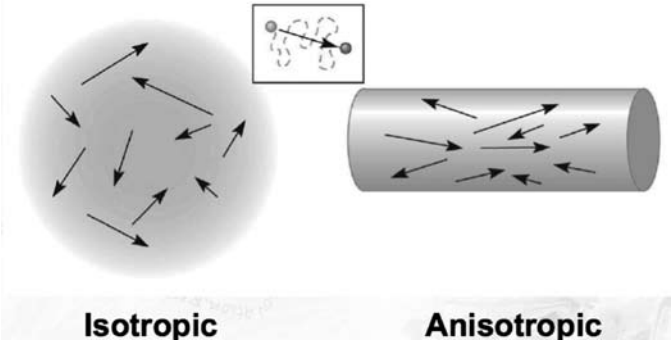
White matter tracts act as cables connecting different parts of the brain. Each tract has its own unique function. Studying white matter tract is important in managing epileptic patient and understanding the pathological process. In the past, fiber tracts can only be visualized in brain dissection or during operation. Even with conventional magnetic resonance imaging (MRI), fiber tracts cannot be identified individually. With the emergence of diffusion tensor imaging (DTI) of MRI, white matter tracts can now be visualized.

Diffusion Weighted Imaging and Diffusion Tensor Imaging

Diffusion is a random process resulting from thermal translation of motion molecules. The diffusion displacement distances are comparable with cellular dimensions, thus measurement of water diffusion might provide a means of exploring cellular integrity and pathology.

Diffusion weighted imaging (DWI) incorporates pulsed magnetic field gradient into standard MRI sequence resulting in images which are sensitive to small displacement of water molecules. The diffusion contrast is based on self-diffusion of water molecules in tissue. DWI has been used in daily clinical neuroimaging such as in acute stroke and cerebral abscess; these pathological processes resulted in restricted water diffusion that is detectable by DWI.

In cerebral tissues, cell membranes restricted diffusion. In tissue where diffusion is random in direction it is said to be isotropic; on the other hand tissue with more hindered diffusion in one direction than another is said to be anisotropic. White matter tracts are parallel-orientated structure in which diffusion of water molecules is along the fiber orientation due to restricted diffusion by fiber cell membrane. As a result white matter is anisotropic.



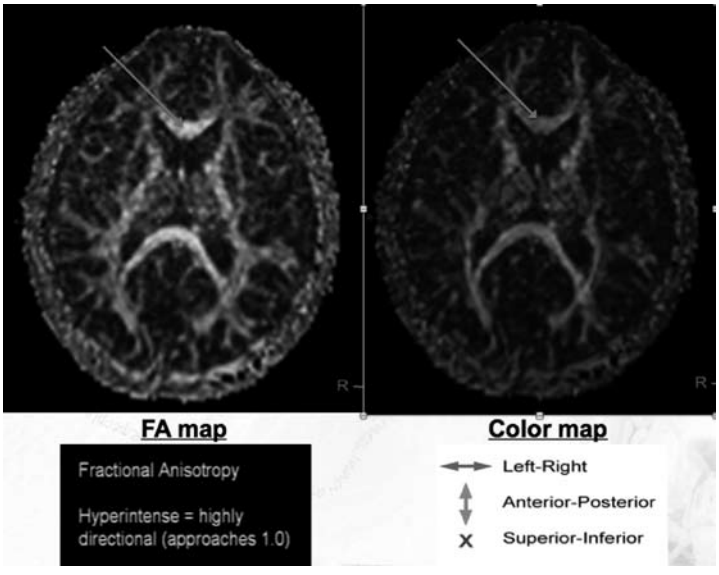
Diffusion tensor imaging (DTI) is a technique based on diffusion weighted imaging. It measures water diffusion from multiple directions instead of one in conventional DWI. Directional information is being incorporated into diffusion-weighted imaging. It measures both the direction and magnitude of water diffusion in tissues in vivo.

DTI measures two important parameters of water diffusion in each voxel of images:

1. Mean Diffusivity (MD) which represents the overall magnitude of water molecules.
2. Fractional anisotropy (FA) which represents the proportion of overall diffusion contributed by anisotropy.

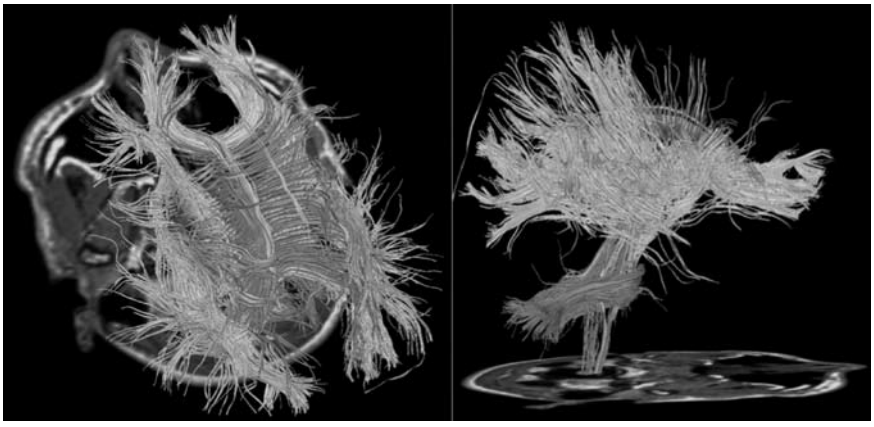
These calculated data in each voxel is fitted into a 3D diffusion ellipsoid model in which the shape and orientation of this ellipsoid carry the information on the diffusion characteristic (isotropic vs anisotropic) and principle direction of greatest water diffusion in each voxel. This fitting process involved mathematical calculation.

The calculated data is displayed on 2D images. 1) Fractional Anisotropy (FA) Map - Intensity of voxel correlates with anisotropy. 2) Colour Map - Three principle colour represent different direction of diffusion. For example, on FA map corpus collasum appears as hyperintense signal as it is anisotropic white matter fiber. On Colour Map it appears as red in colour since it runs in left to right direction or vice versa.



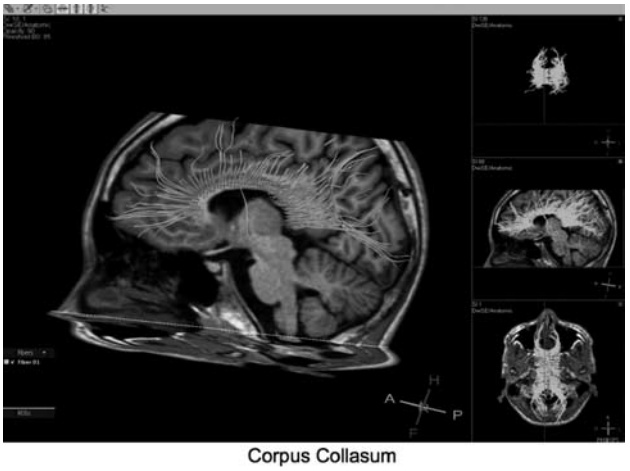
Diffusion Tensor Tractography (DTT)

Diffusion tensor Tractography (DTT) is an extension of DTI, which involves data post-processing. Tractography means tracking of white matter fiber. DTT uses directional information, i.e. anisotropy and orientation in each voxel to generate virtual 3D white matter map. It traces white matter fiber tract by demonstrating the pathway of least resistance to water diffusion with similar orientation.

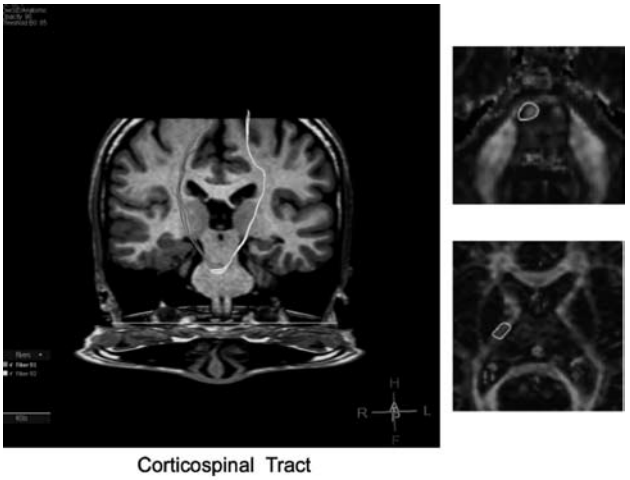


The most common fiber tracking technique is called **F**iber **A**ssignment by **C**ontinuous **T**racking: FACT. The operator starts fiber tracking by choosing a seed voxel. The operator is required to set the termination criteria for fiber tracking which included: 1) Fractional Anisotropy (FA) threshold; 2) Trajectory angle of fiber; 3) Minimum length of fiber. At the end of seed voxel, the computer will trace adjacent voxels with similar shape and orientation of ellipsoid, i.e. similar anisotropy and diffusion direction. Tracking pathway will continue until termination criteria appears such as isotropic diffusion or direction deviated from the principle pathway.

The seed voxel is based on the target white matter tract. The operator can choose single or multiple region of interest (ROI). For example by placing a ROI on corpus collasum, this midline crossing white matter tract can be traced and superimposed on the conventional MRI images. If ROIs are placed on posterior internal capsule and pons, the expected tract running across these regions that is the corticospinal tract can be isolated.



Corpus Collasum



Corticospinal Tract

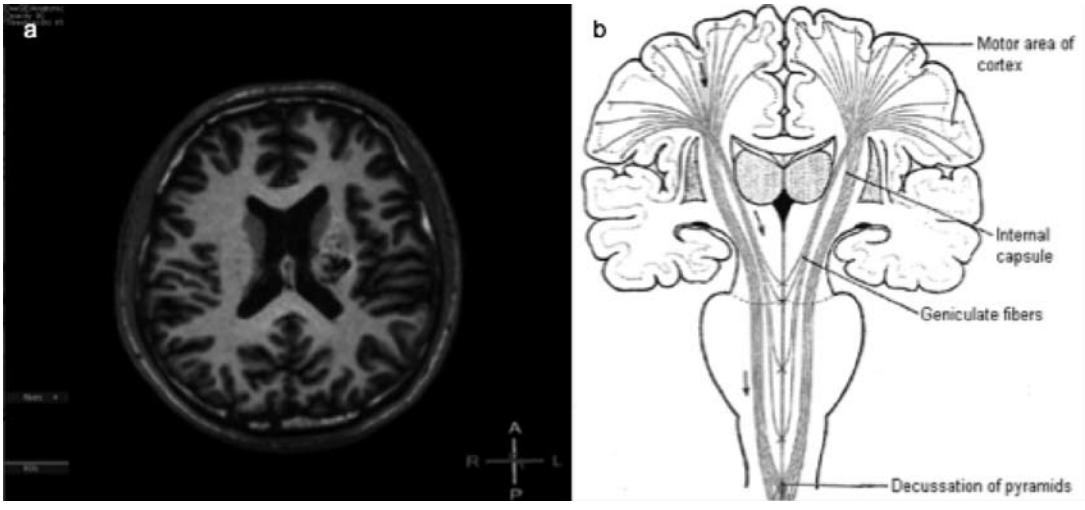
Clinical Application in Epilepsy

The most important clinical application in epilepsy is pre-operative planning. The goal is to preserve important fiber tract in epilepsy surgery. Frequently the involvement or modification of the tract by the epileptogenic foci can also be identified.

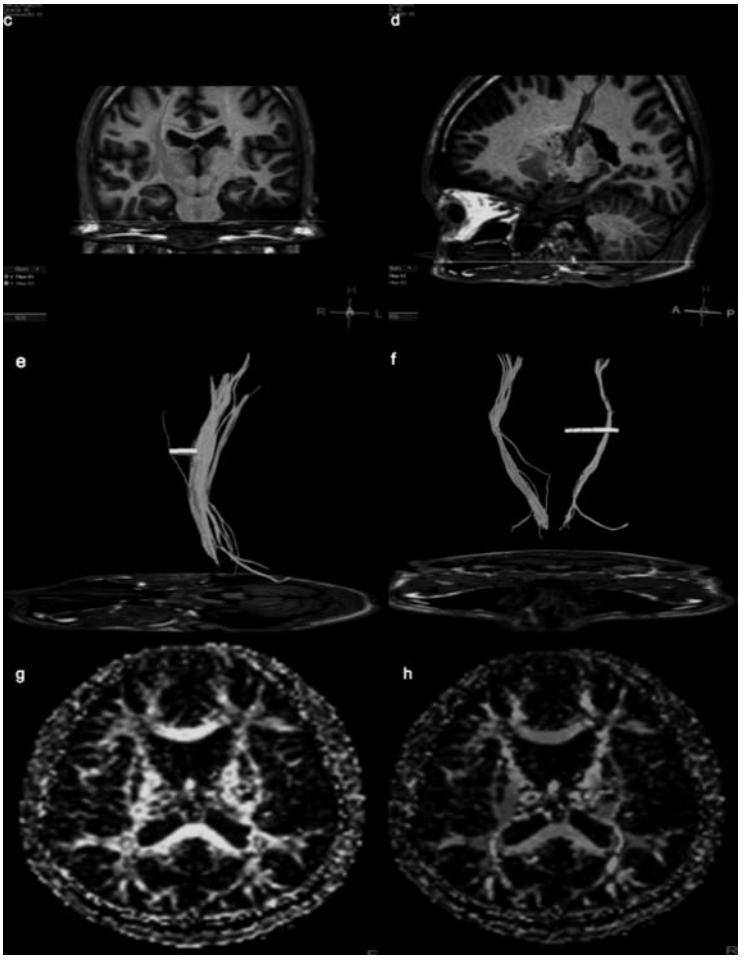
With the knowledge of white matter tract before operation:

1) Better surgical planning to prevent fiber tract damage
2) Predict the occurrence of post-operative deficits, which is important when obtaining consent from patients and their parents.
3) By incorporating tractography data into neuro-navigation devices, surgeon can monitor the procedure with imaging during operation to avoid damaging important white matter tract.

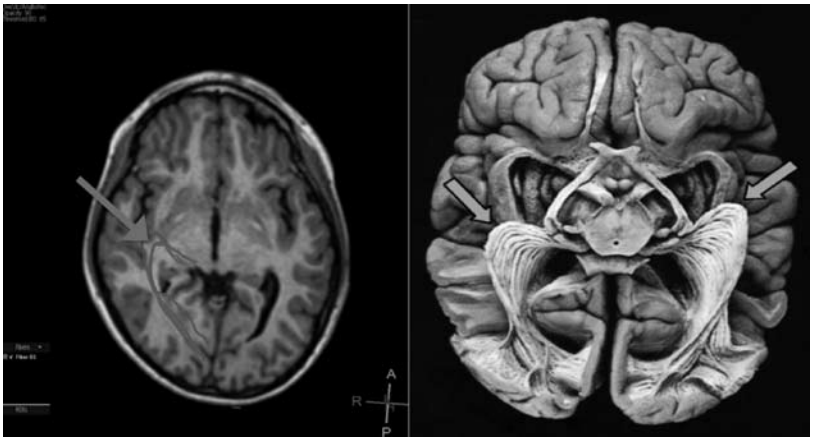
Example-



Teenager presented as convulsion with acute intracerebral hematoma in CT brain. Follow-up MRI was performed. Fig a-b: T1W image shows serpentine signal void at left corona radiata representing arteriovenous malformation (AVM). Corticospinal tract is the main fiber tract to preserve in surgery or radiosurgery. Fig c-d: By diffusion tensor tractography, corticospinal tract is isolated and superimposed on conventional images. Fig e-f: The tract on affected side (green) is displaced by the lesion (pink) posterolaterally compared to contralateral tract (orange). The tract is not disrupted nor terminated by the AVM. Fig g-h: The hyperintense signal on FA map and colour orientation on colour map of left corona radiata is preserved and comparable to contralateral side; again confirming the tract is intact. This is important information for neurosurgeon for planning of treatment.



Anterior temporal lobe resection (ATLR) is an effective procedure in treating mesial temporal sclerosis. ATLR can cause visual field defect in up to 10% of patients, typically visual defect at superior homonymous field contralateral to resection site. It is due to the resection of Meyer's loop, the most anterior extent of optic radiation which is in close proximity with temporal lobe. This Meyer's loop cannot be visualized on conventional MRI and varies from person to person. With diffusion tenor tractography, the extent of Meyer's loop can now be traced and displayed in multiple planes which is important information for neurosurgeon.



Other Potential A pplications

Apart from pre-operative planning, diffusion tensor imaging can also locate and assess the effects of chronic epilepsy on white matter tract. Many published papers already demonstrated loss of white matter fiber/ anisotropy adjacent to epileptogenic foci such as focal cortical dysplasia on diffusion tensor imaging. Loss of directional organization of subcortical white matter can be related to chronic seizure or focal cortical dysplasia, which may explain post-operative residual seizure. Tractography may also demonstrate the propagation pathway of seizure foci. Thus diffusion tensor imaging enable us to study the effect of epilepsy on white matter tract, to understand the pathological process which may guide treatment in the future.

Limitations

There are limitations in diffusion tensor tractography. It demonstrates the gross fiber architecture but not the true functional or synaptic connection. Tracking difficulty exists in areas of fiber crossing as most tracking technique assume single orientation in one voxel. Fiber tracking is also operator dependant, as placement of ROI location and termination criteria is not standardized; further development of quantification and standardization of these parameters is required. Tractography can only be visualized as macroscopic configuration of fiber tract and required cautious interpretation.

Conclusion

Nevertheless, diffusion tensor imaging (DTI) and tractography appear to be the only non-invasive method of obtaining information about fiber tracts and are able to show them three dimensionally. In the future by combing DTI with Functional MRI, we could precisely map the whole functional circuit. Understanding the anatomical reorganization of pathway and higher cognitive function related to epilepsy and post-operation is also possible. With intra-operative MRI and tractography, surgeon can have the best approach preserving important white matter tract during operation. Thus diffusion tensor imaging is a promising tool in managing epileptic patients at both clinical and research level.

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Neurocognitive Assessment for a 7-year-old Girl with Left Mesial Temporal Sclerosis

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Background

A 7-year-old girl, CK, was referred to the Tuen Mun Child Assessment Centre for neurocognitive assessment as part of the pre-surgical work up.

CK was born full term. No perinatal or neonatal complications were reported. Her birth and developmental history was reported as uneventful and unremarkable. She had no history of febrile convulsion. Gross motor and language developmental milestones were achieved at age appropriate times. Social development was normal.

CK suffered from the first afebrile seizure attack when she was 3 years 9 months old. She was put on Sodium valproate for three years and had been seizure free during that period. Medication was stopped in March 2008 and seizure recurred in June 2008. She was put back on sodium valporate and she had no more seizure afterwards. The seizure semiology included unresponsiveness, eye deviated to right, expressive dysphasia, right upper and lower limb stiffness, right facial twitching, head and neck turned to right with clonic turned to right. EEG showed interictal left mid-temporal sharp wave. MRI brain showed left mesiotemporal sclerosis with mild atrophy of left hemisphere when compared with contra-lateral hemisphere.

Test Behavior

CK was cheerful, alert, and oriented to time, place, and person. Age-appropriate social reciprocal interaction was noted. Her speech was coherent. She spoke with clear articulation though her verbal comprehension and expression was impressed to be fair. Her responses were somewhat tangential.

CK was very compliant and cooperative throughout the test session. However, on-seat behavior was fair to which she was squirmy and fidgety in seat. Attentional control was poor to which she showed poor vigilance to particularly mentally-taxing tasks. Attentional control was better in experimenter-paced than task-paced items. Frequents breaks were required to help her better sustain in vigilance and attentional control.

Results

General Intelligence

CK's cognitive ability, as measured by the Hong Kong Wechsler Intelligence Scale for Children (HK-WISC), indicated that her intellectual functioning fell within the low average range with Verbal Subscale IQ inferior to her Performance Subscale IQ. Her Verbal Subscale IQ fell between the range of Low Average to Limited Intelligence. Her Performance Subscale IQ fell between the range of Average to Low Average Intelligence.

CK exhibited a bit of scatter in her verbal subtest scores, with deficient performance on her fund of stored factual information, simple mental calculations, and working memory involving immediate recall of auditory stimuli. Among the non-verbal subtests, her performance was weak in a paper-pencil coding task which measured psychomotor speed.

Academic Achievement

On the Hong Kong Test of Specific Learning Difficulties in Reading and Writing For Primary School Students (HKT-P(II)), a test that assesses the ability in Chinese reading and dictation, CK's was significantly behind age cohort in all the literacy subtests involving Chinese Word Reading, One-minute Word Recall and Chinese Word Dictation. On the cognitive subtest of Digit Rapid Naming which gauged automaticity, her performance was significantly at a deficit level when compared with same-age peers.

The findings met the diagnostic criteria of grouping CK under the dyslexic classification though it was unsure whether the specific learning difficulties were of developmental nature or attributable to her medical condition.

Lateral Dominance

CK was right-handed to which she used solely her right hand in tasks such as writing, drawing, throwing, scissoring, and using chopsticks.

Language

Assessment conducted by the Speech Therapist in separate assessment indicated that CK suffered from language impairment.

Memory

Verbal Memory: On a verbal memory and rote learning test? the Hong Kong List Learning Test (HKLLT 2nd Edition), CK's overall learning ability, short and long retention, as well as recognition trial all fell within the mildly to moderately impaired range when compared with age cohort.

Visual Memory: On the Rey Complex Figure Test and Recognition Trial (RCFT), CK's performance on the immediate and delayed recall as well as on the recognition tests all fell between the mildly to severely impaired range.

Sustained attention

On the CPT-II which assessed sustained attention, there were indicators of inattentiveness and impulsivity. Overall the results indicated a high probability of the presence of a clinically significant attention problem.

Behavior and Mood

On the Child Behavior Checklist (CBCL) with the mother as the informant, all the scores were generally at a low level, indicating that CK was not considered as exhibiting any significant behavioral or emotional problem.

Discussion

Although this girl eventually has not undergone epilepsy surgery in view of satisfactory seizure control by medication alone, the pre-surgical evaluation can help us understand her epilepsy. Her clinical seizure semiology, the findings of EEG and brain imaging indicate that her seizure focus is from her left dominant hemisphere most likely from left temporal lobe. The left mesial temporal sclerosis and left hemispheric atrophy could be due to early antenatal or perinatal brain insult.

Children with idiopathic epilepsy usually have normal intelligence, though studies frequently report lower overall IQ scores, and left hemisphere seizure onset has been specifically associated with lower verbal IQ as well as decreased performance on other verbal intellectual measures (1). The present findings are in line with this conception that CK's overall intellectual functioning fell within the low average range, and her profile showed less developed verbal abilities than visual/constructional abilities. However, a mere global measure of intelligence provides little information regarding the specific nature of the cognitive deficits that a child with temporal lobe epilepsy (TLE) may display.

Findings from achievement testing indicated that CK suffered from significant reading and writing difficulties, to which learning difficulties of variable severity are reported to present in 5% to 50% of children with seizures (2), and children with left temporal discharges show lower reading performances than children with right TLE (3).

On the whole, CK performed poorly on a number of verbal, word learning, and sequential tasks typically thought to be dependent on left hemisphere functioning, whereas she exhibited relatively intact visual-spatial functioning. Such neurocognitive findings are compatible with the clinical seizure semiology, the brain imaging and EEG findings which suggest a lesion with left hemispheric involvement.

In terms of memory function, CK had significant difficulties with both verbal and visual/spatial memory. She exhibited deficient performance on the recall of immediate, delay and recognition of verbal and non-verbal information. These findings are in line with the consensus that epilepsy, and specifically TLE, is a risk factor for impaired new learning skills (4-7), and the severity of memory impairment is influenced by the extent to which mesial structures are involved (8). Mesial TLE was associated with poorer memory function than lateral TLE on tasks such as Rey Complex Figure Test (RCFT) (9). Findings from this single case lend support to the above notion, and TLE in childhood may not be associated with lateralized memory deficits. It may be difficult to delineate memory lateralization given the heterogeneous nature of the pathology, brain plasticity, plausible cortical reorganization as a response to early brain insult, and bilateral hippocampal involvement involving particularly material-specific memory.

Impairment of attention, automaticity and speed of information processing were indicated in CK which was compatible with the general observation that problem in sustained

attention, and psychomotor speed are frequently reported in those with TLE, and the detrimental effects of epilepsy-associated inattention on school success (10). CK had been faring very poorly in her academic studies and ranked amongst the last few in form.

Early seizure onset has been reported to be one of the predictors of academic failure (11) and causes greater disruption on cognitive development in children. CK's first seizure attack was reported when she was 3-year-9-month old. The early onset may constitute to be an additional risk factor to her neurocognitive functioning and prognostic outcome.

Conclusion

CK exhibited pervasive neurocognitive impairment pertaining to memory, language, word learning, attention, working memory and automaticity, which had adversely affected her academic functioning. Intensive remediation, accommodation to address her learning problems on the one hand and seizure control either through medication or non-drug treatment such as surgery on the other are essential to enhance her optimal development.

Longitudinal studies conducted with pediatric cases with temporal lobe epilepsy, investigating their responses to treatment, pattern and change of neurocognitive functioning overtime are necessary to gain a better understanding of the relationship of pediatric epilepsy and neurocognitive outcome.

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Appendix. Results of neuropsychological assessment of CK

Domain			
Intelligence	HK-WISC	Verbal IQ	Low Average to Limited
		Performance IQ	Average to Low Average
		Full Scale IQ	Low Average
Memory			
Verbal	HKLLT 2nd Edition	Immediate recall	3rd-6th centile
		Delayed recall	1st-2nd centile
		Recognition	1st-2nd centile
Visual	RCFT	Immediate recall	4th centile
		Delayed recall	2nd centile
		Recognition	Below 1st centile
Attention	CPT-II	Sustained attention	Clinical
Working Memory	HK-WISC	Digit span	Weak
Word Learning	HKT-P(II)	Chinese word reading	Deficit
		1-min word recall	Deficit
		Chinese word dictation	Deficit
Automaticity	HKT-P(II)	Digit Rapid Naming	Deficit

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