Case Series and Literature Review on Cingulate Epilepsy

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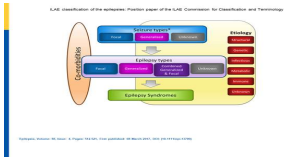
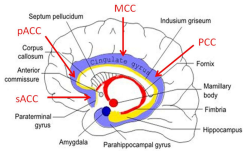
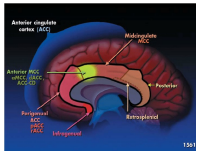
Introduction

Epilepsy is a common Neurological disorder that affects over 70 million worldwide. (Singh & Trevick, 2016).

The international league against Epilepsy classification in 2017 as shown in the diagram below classifies seizure types into 3 namely focal, generalised and unknown.







Aim

Cingulate gyrus epilepsy is a rare and diagnostically challenging form of epilepsy, with a wide range of clinical manifestations.

This poster highlights 2 case reports and a literature review of the topic.

Clinical symptoms

Auras (fear and laughter) hyperkinetic behaviour, ictal vocalization.

Behavioral changes with aggression, poor judgment

Gelastic Seizures- The seizures usually start with laughter. The laughter is often described as being 'hollow' or 'empty' and not very pleasant. The laughter occurs suddenly y lasts less than 30 to 45 seconds and stops suddenly. It may then be followed by signs that are more usually seen in focal seizures. These signs can include eye and head moving to one or the other side, automatisms (such as lip-smacking, mumbling or fidgeting of the hands) and altered awareness. These signs may last for seconds to many minutes and then stop.

Background

The Cingulate Gyrus is a deep structure in the brain and is a component of the limbic system, it is involved in processing emotions and behaviour regulation. It also helps to regulate autonomic motor function.

Although previously viewed as a mysterious territory of the brain, evidence from cognitive and fMRI studies have established a better understanding of the cingulate cortex.

The anterior cingulate cortex lies in a unique position in the brain, with connections to both the emotional and limbic system as well as the cognitive domain of the prefrontal cortex.

The location of the Cingulate within the brain and its complex neural networks have often resulted in seizures arising from this area to be masqueraded as Frontal lobe seizures or Temporal lobe seizures.

The limbic system-subcallosal area, cingulate gyrus, Para hippocampal gyrus, uncus, hippocampal formation with several subcortical nuclei receive input from and project to wide and diverse areas of the brain. The complex connections of the limbic system is known to influence behaviour, memory, and pain perception. The Papez circuit in which the cingulate gyrus has a crucial role was the first description of an anatomical and physiological mechanism for emotion.(Willis & Haines, 2017)

The cingulum comprises a series of short fibres that connect the cingulate cortex and, second, long fibres that project extensively, including to the hippocampus and amygdala, as well as to the premotor, prefrontal and orbitofrontal areas, insula and parietal lobe.

These reciprocal connections reflect the key role played by cingulate as an interface between brain regions involved in cognitive, motor, sensory and emotional processing, and further explains the widely diverse semiology in seizures that arise from the cingulate cortex.(Powell, Elwes, Hamandi, & Mullatti, 2018a)

6 Cortical Zones

1. **Symptomatogenic zone-** area in the brain that produces the ictal symptoms and is often identified from the seizure description or from the EEG
2. **Irritative zone-** area of cortical tissue that generates interictal electrographic spikes
3. Ictal onset zone- ictal epileptiform discharges.
4. Functional deficit zone- area of cortex that is functionally noted to be abnormal in the interictal period. This can be measured by Neurological examination, neuropsychological testing, EEG, PET and interictal SPECT scanning
5. Epileptogenic Zone- area where the seizure is generated
6. Eloquent cortex.- area of the cortex that must be spared during surgery in order to avoid any new deficits for the patient.

Literature review

Authors	Seizure localisation	Seizure features and summary
Bancaud J , Talairach J . Clinical semiology of frontal lobe seizures. Adv Neurol 1992;57:3–58.	Anterior cingulate	Intense fright or dread, screaming, shouting, aggressive verbalisation, complex gestural automatisms and poorly formed visual hallucinations
Correlation between extreme fear and focal cortical dysplasia in anterior cingulate gyrus: Evidence from a surgical case of refractory epilepsy(Qiao et al., 2017)	Anterior Cingulate Gyrus	aura of extreme fear and hypermotor seizures
Structural abnormalities in benign childhood epilepsy with centrotemporal spikes (BCECTS)(Kim et al., 2015)	Posterior Cingulate	Children with ADHD and benign childhood epilepsy had a thicker left cingulate cortex and large left pars opercularis volume.
Mirth, laughter and gelastic seizures. (S. et al., 1993)	Anterior Cingulate	bursts of laughter accompanied by a feeling of mirth
Cingulate gyrus epilepsy(Powell et al., 2018a)	Cingulate Gyrus	worsened emotional dysregulation and obsessive–compulsive features
Report of 3 Electroclinical Subtypes With Surgical Outcomes Alkawadri (Alkawadri, So, Van Ness, & Alexopoulos, 2013)	Anterior cingulate 'typical' group Anterior cingulate 'atypical' group Posterior cingulate	fear, laughter, hypermotor features Simple partial motor seizures with frequent generalisation and less favourable surgical outcome (all had infiltrating astrocytomas) Clinical features of temporal lobe seizures also present (abdominal and gustatory auras, déjà vu and jamais vu)
Pathological Hyperfamiliarity for Others From a Left Anterior Cingulate Lesion(Nente, Carrillo-Mezo, Mendez, & Ramirez-Bermudez, 2014)	Anterior Cingulate	Hyperfamiliarity syndrome with initial akinetic muteness
Souirti et al (Souirti, Landré, Mellerio, Devaux, & Chassoux, 2014) Neural network underlying ictal pouting ("chapeau de gendarme") in frontal lobe epilepsy. Epilepsy & Behavior 2014;37:249–57	Anterior cingulate	Downturned mouth or 'chapeau de gendarme' expression. Ictal semiology allows differentiating rostroventral and dorsal ACC involvement.
Posterior cingulate epilepsy: clinical and neurophysiological analysis (Enatsu et al., 2014)	Posterior cingulate cortex spreading to frontal areas Posterior cingulate cortex spreading to temporal areas	Prominent motor manifestations, including bilateral asymmetric tonic seizures and hypermotor seizures Clinical features more typical of complex partial 'dyscognitive' seizures
A case of unusual sensations (Whitney et al., 2017)	Middle cingulate	Unpleasant unilateral painful sensory phenomena, including sensations of spiders crawling on his forehead, ladybirds causing right ear pain and bees stinging his head. Ictal bradycardia, mood change, fear, hypermotor activity.
Gelastic seizures in a child with focal cortical dysplasia of the cingulate gyrus.(McConachie & King, 1997)	Anterior Cingulate	Bursts of laughter and mirth
Childhood obsessive-compulsive disorder and cingulate epilepsy(Levin & Duchowny, 1991)	Anterior Cingulate Gyrus	Humming, lip smacking, Bruxism, Handwashing, OCD symptomatology

Case Report 1

A 44-year-old right-handed man. movement of the shoulders, irregular, jerking movements of the limbs, giggling or muffled laughing. Video EEG telemetry showed 10 seizures characterised by brief hyper motor movements with left and covering his face and an EEG correlate of semi rhythmic movements slowing over the left frontocentral region. MR brain scan showed possible cortical dysplasia in the left anterior cingulate gyrus. FDG PET brain scan showed bilateral hypometabolism in the inferior temporal lobes with slightly more pronounced hypometabolism in the lateral left temporal lobe compared to the right. The impression was that he had frontal lobe seizures which was further supported by the clinical semiology picture which implicated the anterior cingulate region, EEG showed electro decrement at seizure onset and neuroimaging which shows anterior cingulate Dysplasia on MRI.

Case Report 2

A 24-year-old right handed man with epilepsy who had a first seizure when he was 21 while riding a motorbike. He underwent assessment for epilepsy surgery. His MRI showed a left postero medial frontal left cingulate lesion, likely a low grade Glioma.

- Resective Epilepsy surgery is considered as a successful intervention as upto 80 % of patients will be seizure free.(Rosenow & Lüders, 2001)
- lesional cingulotomy
- In a meta analysis, Deep brain stimulation was noted to provide remarkable seizure reduction in Temporal lobe epilepsy(B. Chang & Xu, 2018)

Neuropsychiatric symptoms

The neuropsychiatric symptoms of epilepsy significantly impacts the person's quality of life. One in 3 persons with epilepsy are likely to experience mood or anxiety symptoms over their lifetime.(Korczyn et al., 2013). Some of the neuropsychiatric symptoms are emotional outbursts, aggressive outbursts, compulsive behaviours, organic mood instability, explosive screams including profanities and laughter. There is a higher prevalence of Depression in epilepsy and significant deficits in social integration. Individuals with epilepsy were more likely than individuals without epilepsy to report lifetime anxiety disorders or suicidal thoughts with higher prevalence of suicidal ideation.(Tellez-Zenteno, Patten, Jetté, Williams, & Wiebe, 2007).

The association of mood disorders with hippocampal volume loss is well-documented in the psychiatric literature, and such findings have been partially replicated in mesial temporal lobe epilepsy with hippocampal sclerosis. that the pathology underlying epilepsy-associated psychosis seems to be different from that of other psychoses. (Mula et al., 2014).

In people with epilepsy, death by suicide is more common than in the population as a whole (5% compared to 1.4%). Factors associated with increased risk have been reported to include: younger age (25–49 years) male patients, co-existing psychopathology including personality disorders, temporal lobe epilepsy, social stressors including social or work-related problems, prolonged duration of epilepsy, and inadequate control of seizures.

It is also well known that suicidal ideation has an increased incidence in Epilepsy as does completed suicide.. Forced normalization and postictal psychosis may also contribute to suicidal behaviour. Antiepileptic drugs have been implicated in causing psychiatric adverse effects and suicidal behaviour.(Bell & Sander, 2009). Obsessive Compulsive Disorder (OCD) has a long associated history with epilepsy. The link with temporal lobe epilepsy (TLE) is particularly well known