HARDWIRED FOR FEAR: TREATMENT-RESISTANT DEPRESSION AND GAD IN THE PRESENCE OF AN AMYGDALA TUMOUR – A CASE REPORT

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INTRODUCTION

- Amygdala plays an important role in the pathogenesis of anxiety and fear processing.
- This includes integrating cortical and thalamic inputs to generate fear and anxiety-related behaviours via inhibitory neurons and synapses (Figure 1a; Babaev et al. Experimental and Modular Medicine 2018; 50:18), as well as its inhibitory activity over brainstem chemoreceptors during CO_2 build up (Figure 1b; Feinstein et al. Biological Psychology 2022; 170).

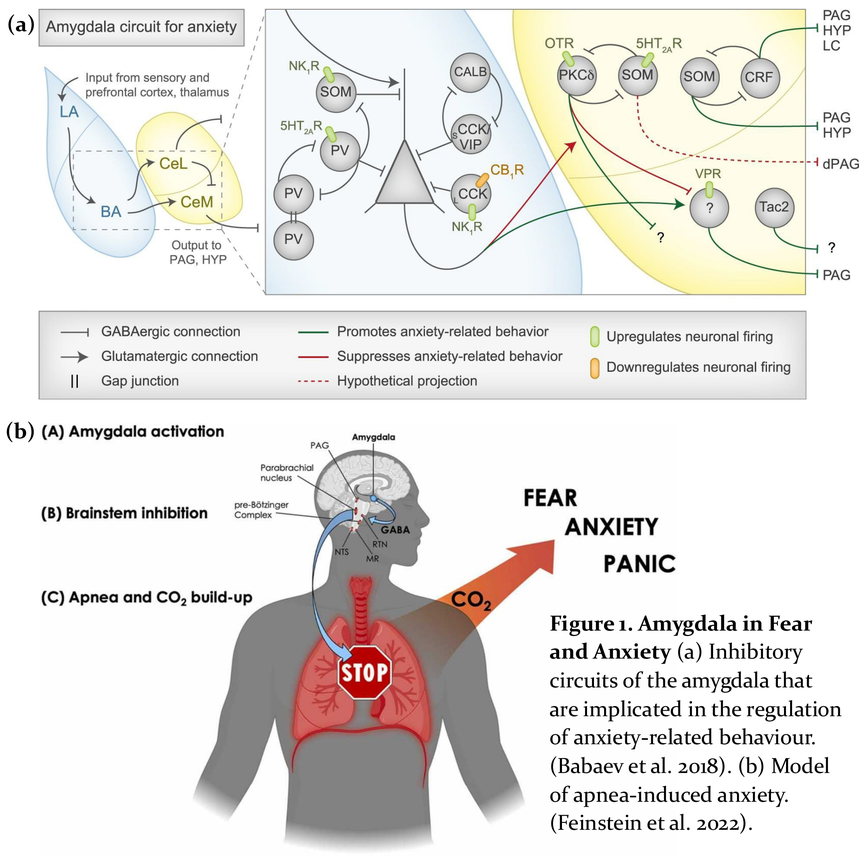

Figure 1. Amygdala in Fear and Anxiety (a) Inhibitory circuits of the amygdala that are implicated in the regulation of anxiety-related behaviour. (Babaev et al. 2018). (b) Model of apnea-induced anxiety. (Feinstein et al. 2022).

- Existing case reports suggest pharmacological resistance with antidepressants and supports neurointerventional approaches (Chen et al. Neurocase 2015; 21: 268-270).
- The aim of the current case report is to illustrate how underlying structural brain lesions can shift the management of mood disorders and anxiety from standard psychopharmacology to surgical or targeted neurological intervention.

CONCLUSION

- This is a complex neuropsychiatric case of generalised anxiety disorder and treatment resistant depression associated with an amygdala tumour.
- It emphasises the importance of inter-specialty collaborations with neurology and/or neurosurgical teams, and the need to consider other forms of neurointerventional approaches.
- Current research also suggests that non-pharmacological methods, to interrupt and prevent amygdala-driven apnea, may be useful for apnea-induced anxiety.

REFERENCES

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CLINICAL PRESENTATION AND INVESTIGATIONS

- This is a 71-year-old female who is first referred to psychiatry by outpatient services in July 2025 with 3-months of markedly lowered mood, excessive anxiety, lethargy, hopelessness and catastrophic thoughts of imminent death. She had recurrent <1-minute episodes of surging unexplainable fear that is accompanied with freezing and gasping. She also has somatic complaints of headaches, neck and backaches, dizziness.
- Her past medical history consists of CAD s/p PCI in 2008, transverse myelitis in 2008, left tibia fracture s/p fixation 2017-2018, HLD/HTN/pre-DM, fatty liver. She had no prior psychiatric history before her current presentation, and no family history of mental health illnesses. There is no prior alcohol nor substance use history.
- She has good social support and was previously working until her retirement in 2024. Her premorbid personality was described to be anxious and impatient. She otherwise enjoys exercising, walking and travelling.
- Her physical examination returned negative. Mental state examination revealed ongoing anxiety with reactive affect, reassurance-seeking behaviour with repetitive circumstantial and rambling speech.
- Brain magnetic resonance imaging revealed bilateral asymmetric mesiotemporal T2 hyperintensities (Figure 2a), with significantly increased cerebral perfusion on right more than left (Figure 2b). Brain spectroscopy suggested higher grade right mesiotemporal neoplasm (Figure 2c). Electroencephalography demonstrated subtle right temporal slowing. Serum and cerebral spinal fluid investigations including autoimmune screening were unremarkable. Other routine blood investigations were also unyielding.

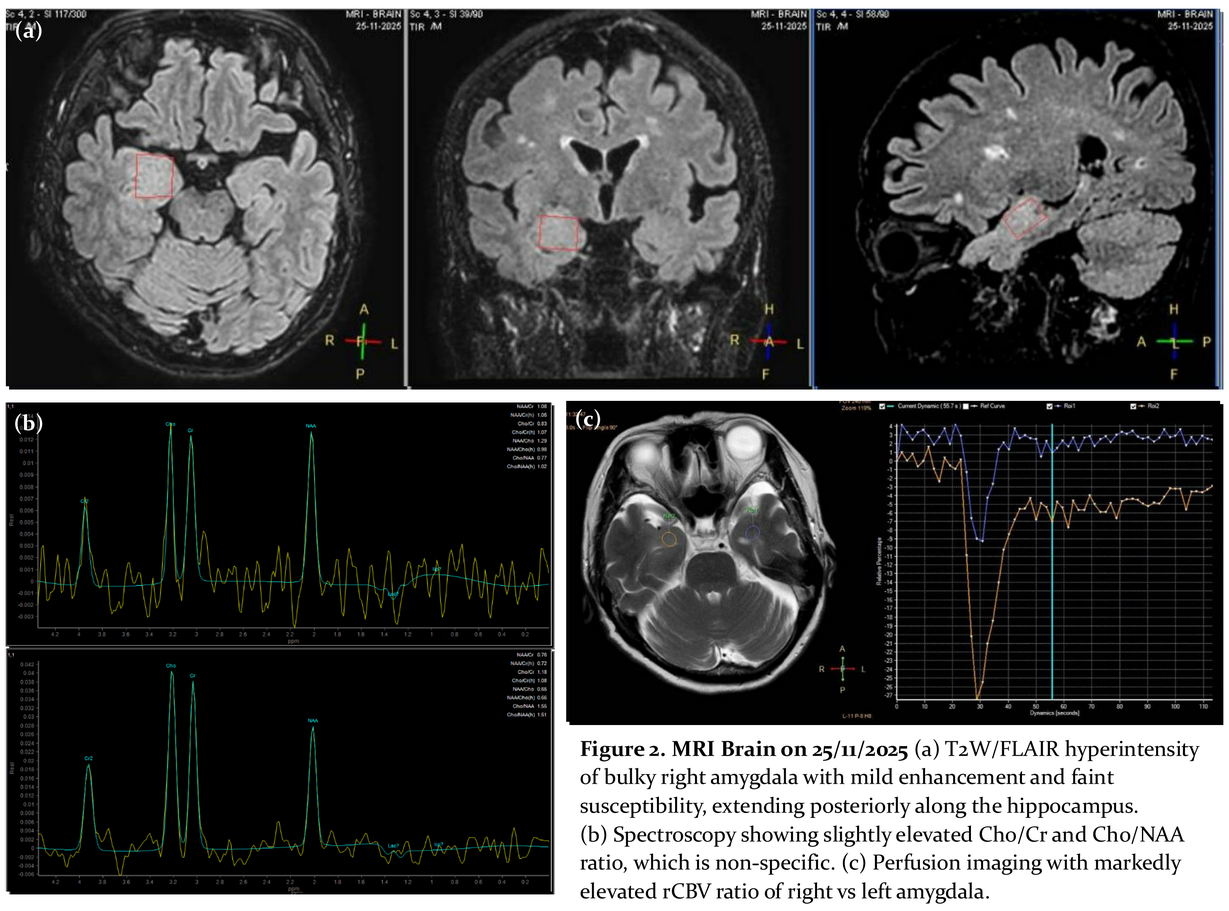

Figure 2. MRI Brain on 25/11/2025 (a) T2W/FLAIR hyperintensity of bulky right amygdala with mild enhancement and faint susceptibility, extending posteriorly along the hippocampus. (b) Spectroscopy showing slightly elevated Cho/Cr and Cho/NAA ratio, which is non-specific. (c) Perfusion imaging with markedly elevated rCBV ratio of right vs left amygdala.

Clinical Progress and Status

- Multiple antidepressants and cognitive behavioural therapy were ineffective.
  - Her psychotropic history with side effects are as follows: sertraline (nausea), escitalopram (shivering), mirtazapine up to 3.75mg ON (giddiness), fluoxetine up to 40mg (tremors), bupropion 150mg EOM (tremors), pregabalin up to 25mg TDS (leg swelling), gabapentin up to 100mg BD (tremors), sodium valproate up to 300mg BD (weight gain, hair loss), trazodone 25mg BT (postural hypotension, oversedation), vortioxetine up to 20mg OM (nausea, headache), agomelatine (not keen for blood tests).
- Intravenous methylprednisolone was trialled by neurology for a period of time, including under elective admission settings, with limited success.
- Levetiracetam was initiated for prophylactic seizure and mood control with partial effect for her fear episodes.
- She is currently on downtapering fluoxetine 10mg EOM, clonazepam 1mg ON and melatonin 2mg ON. In view of sensitivity to side effects, her main focus for management would be non-pharmacological. Her recent pharmacogenetics test revealed normal CYP2C19 enzyme activity and intermediate CYP2D6 enzyme activity.
- She is also referred to the psychologist for further brief interventions regarding deep breathing techniques. Daily walks have been observed to improve her mood and increased her tolerance for somatic distress. Patient also reports going to traditional Chinese medicine for acupuncture 2x/week for her head and gut.
- In terms of her medical/surgical management, she is on radiological surveillance with pending offers for surgical resection and biopsy.