Young Onset Dementia, Huntington Disease & Brain Injury

GLOBAL NEUROPSYCHIATRY GROUP

RANZCP Section of Neuropsychiatry · 15th Annual Conference

13 November 2026 · Gold Coast · Summary and references

KEY MESSAGES

- **bvFTD is overdiagnosed.** About two thirds of 100 consecutive referrals did not have it; over-read imaging and neuropsychology drove most errors.
- **PCA hides in plain sight.** Patients in their 50s are misread as eye disease, FND or malingering. FDG PET settles it.
- **HD can start as a psychiatric illness.** Psychosis may precede chorea by years, and antipsychotics can mask motor signs.
- **AMT-130 shows the first gene therapy signal in HD.** About 75% slowing on cUHDRS and TFC at 36 months, sustained at 48.
- **Take a lifetime head impact history.** Repetitive subconcussive impact is the main CTE burden, in and beyond sport.
- **Post-concussion outcome is largely modifiable.** Early distress and poor coping predict delay; untreated depression doubles time off work.

Session 1 · Young onset neurodegeneration

1 YOUNG ONSET DEMENTIA: PCA AND BVFTD

Prof Peter Nestor · Mater Memory and Cognitive Disorders Clinic; Queensland Brain Institute

> The under-65 cut-off is a service construct. In younger referrals, psychiatric causes, other neurological disease and normal forgetting under stress outnumber neurodegeneration.

- **Epidemiology:** AD remains the commonest young onset dementia; FTD peaks at 55–65; Lewy body dementia is rare under 65.
- **PCA:** presents in the 50s with problems driving, reading and judging distance. Simultanagnosia can look like malingering. FDG PET is always severely abnormal; MRI atrophy is often overcalled.
- **bvFTD errors:** neuropsychology misdiagnosed 20 of 26 cases, none correct on scores alone; imaging errors came from reading statistical maps rather than the greyscale image.
- **True bvFTD:** frontal behaviour seen by the clinician, neurological signs (saccades for PSP, MND) and lack of insight.
- **Phenocopy red flags:** the patient seeking the diagnosis, informant overrating, and precise histories without objective signs, including forensic cases.
- **Tests:** FDG PET is best; NfL is helpful but non-specific; avoid SPECT where PET is available; low threshold for C9orf72.

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2 HUNTINGTON DISEASE PHENOTYPES

A/Prof Samantha Loi · Royal Melbourne Hospital

HD is a psychiatric, cognitive, behavioural and motor disorder; over 36 CAG repeats confers risk, 40+ near full penetrance.

- **Motor:** chorea, impersistence, delayed saccade initiation and dysarthria; easily mistaken for tardive dyskinesia.
- **Cognition:** subcortical slowing, inattention and executive dysfunction rather than amnesia.
- **Psychiatric:** depression, anxiety, suicide risk and substance use; psychosis often needs high doses or clozapine.
- **Course:** about 20% of at-risk people take up predictive testing; median survival is about 18.8 years from onset.
- **Treatment:** risperidone for chorea; tetrabenazine with caution; orexin antagonists for insomnia.

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—	UHDRS motor examination video 1 (shown on slide).	YouTube
—	UHDRS motor examination video 2 (shown on slide).	YouTube

3 AMT-130 AND THE FUTURE OF GENE THERAPY IN HD

Prof Anne Rosser · Cardiff University; site investigator, no financial conflicts

AMT-130 is an AAV5 microRNA that lowers huntingtin, delivered to the striatum by MRI-guided surgery. High dose met primary and secondary endpoints at 36 months.

- **Results:** about 75% slowing on cUHDRS and TFC against an Enroll-HD external control, CSF NfL below baseline, and effects sustained at 48 months.
- **Safety:** good; high-dose inflammatory events responded to perioperative steroids.
- **Caveats:** external control, 11–18 hour surgery, scalability and manufacturing. Conditional approval is being sought.
- **Next:** targeting somatic CAG expansion (MSH3, FAN1, PMS1); the goal is combination management rather than a single cure.

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Session 2 · Case-based session

4 CASES IN YOUNG ONSET DEMENTIA AND HD

Prof Dennis Velakoulis (neuropsychiatrist) and Wendy Kelso (neuropsychologist), Royal Melbourne Hospital; with Prof Nestor and A/Prof Loi

Logopenic PPA due to Alzheimer disease in a young adult

- Language decline first attributed to grief; family history of early-onset dementia. Biopsy initially read as autoimmune encephalitis, later revised to AD.
- **Lessons:** smell testing as a marker of organic disease; vertical saccades for PSP; screening is insensitive in high premorbid ability; consider autosomal dominant AD.

Gene-positive HD with superimposed FND

- Falls, stuttering and fatigue after bereavement, with low UHDRS, normal saccades and intact ward function.
- **Lessons:** mild HD can carry predominant functional symptoms, and later cognitive decline can worsen them. Watch carer burden and polypharmacy.

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Session 3 · Traumatic brain injury

5 TRAUMATIC BRAIN INJURY: A LONG-TERM TRAJECTORY

Prof Karen Barlow · University of Queensland

> TBI is a psychiatric as well as a physical condition, with a long-term course at every level of severity.

- **Athletes:** objective processing speed deficits usually resolve within about 10 days despite reported "fog"; fMRI shows equal performance with different activation.
- **Attribution:** anxiety contributes to symptoms, and newly diagnosed attention problems usually predate the injury.
- **Services:** mild TBI rarely qualifies for NDIS.
- **Research gap:** physical and chemical restraint of moderate to severe TBI inpatients is an unmeasured confounder.
- **Precision treatment:** similar initial GCS can lead to very different outcomes; treatment matched to a measured biomarker (DAT SPECT, CRP, connectivity-guided TMS) outperforms one-size-fits-all treatment.

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6 CHRONIC TRAUMATIC ENCEPHALOPATHY

Prof Rowena Mobbs · neurologist, Sydney

> TBI accounts for about 3% of dementia and is one of 14 modifiable risk factors. CTE is best seen as a traumatic neurodegenerative tauopathy.

- **Exposure:** repetitive subconcussive impacts (10,000 to over 200,000 in a football career) carry the main burden, alongside blast and diffuse axonal injury.
- **Pathology:** perivascular p-tau at the sulcal depths, spreading frontally and top-down, the opposite of AD.
- **Clinical picture:** explosivity, impulsivity, paranoia, depression, substance use and motor signs after a latency.
- **Evidence:** at least 1 in 4 of 338 brains from former NFL players had CTE. Diagnosis uses the 2021 NINDS TES criteria.
- **Practice:** ask about sport, military, police and family violence exposure. Rule changes in sport cut concussions.

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7 LIVED EXPERIENCE: A CARER'S PERSPECTIVE

Carer of a family member with FTD and probable CTE

> The family member spent years labelled with personality disorder, addiction and drug-induced psychosis before a non-psychiatric cause was recognised.

- Listen to carers, and do not assume violence reflects character.
- Take a head impact history, including in forensic and violent populations.
- Misdiagnosis carries heavy costs for families and services.

RESOURCE

— Connecters Australia: health promotion charity supporting people and families affected by CTE, and advocating for research and support. connecters.org.au

8 MILD TBI INTERACTIVE WORKSHOP

> Mild TBI is 80–90% of TBI and is diagnosed clinically. 20–30% develop persisting symptoms, driven mainly by psychological and modifiable factors.

- **Predictors:** early distress and poor coping are the strongest modifiable factor; untreated depression doubles delay to work; litigation is associational.
- **Investigation:** MRI rather than CT for persisting symptoms. Performance validity failure is about 5% in research and 25% in clinical cohorts.
- **Good prognosis case:** graded activity (stop if symptoms rise 2–3 points), sleep and vestibular physiotherapy; contact sport at 21 days, with 14 symptom-free.
- **Complex case:** validate and educate; reduce codeine to prevent overuse headache; consider migraine therapy, occipital block or low-dose amitriptyline; reformulate when recovery stalls.
- **Resource:** new CPD-accredited GP concussion course (7 modules, about 2.5 hours) via RACGP and Connectivity TBI Australia.

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