Neuropsychiatry & Intellectual and Developmental Disability

RANZCP Section of Neuropsychiatry · Joint session with the IDD psychiatry section

15 November 2026 · Gold Coast · Summary and references

GLOBAL NEUROPSYCHIATRY GROUP

KEY MESSAGES

- **Measure change against the person's own baseline.** Use records, family video and collateral rather than attributing decline to the disability.
- **Regression is a red flag.** Look for pain, constipation, dental disease, sleep apnoea, sensory loss, seizures, catatonia, dementia, psychiatric illness and trauma.
- **Catatonia is often missed in autism and IDD.** It may be hyperkinetic; treat with lorazepam and be cautious with antipsychotics.
- **Down syndrome is a genetic form of Alzheimer disease.** Baseline assessment at 30, screening from 40.
- **Genetic testing and biomarkers change management.** Microarray first; reanalyse older data; NfL helps separate neurodegeneration from psychiatric illness.
- **Epilepsy and autism mask each other.** Check seizure data and medication effects before antipsychotics or restrictive practices.

Genetics and dementia

1 MONOGENIC CAUSES OF DEVELOPMENTAL DELAY AND ID WITH PSYCHIATRIC FEATURES

Prof John Christodoulou · Murdoch Children's Research Institute; University of Melbourne

Look for red flags of a monogenic cause, start with microarray, and ask labs to reanalyse older exome or genome data.

- **Red flags:** dysmorphism, congenital anomalies, unusual growth, family history of ID or miscarriage, consanguinity, regression, multisystem disease, atypical course or poor treatment response.
- **Psychiatric phenotypes:** 22q11.2 deletion carries about 25% lifetime risk of schizophrenia; metachromatic leukodystrophy can present in adults as psychosis before regression.
- **Testing:** chromosomal microarray first (yield 15–20%, MBS-funded for any clinician); fragile X needs its own test; exome yields 30–40%; genome adds 5–10%.
- **MBS exome/genome:** children under 10 with at least moderate ID/developmental delay and/or multiple congenital anomalies (specialist-ordered).
- **ReNU syndrome (RNU4-2):** up to 0.5% of ID, seen only on genome sequencing; data analysed before 2024 missed it. Periodic reanalysis adds about 5% yield.
- **Fragile X:** full mutation (>200 CGG) silences FMR1; premutation (55–200) causes FXTAS in males and ovarian insufficiency in females. Long-read sequencing improves diagnosis.
- **Double hits:** about 5% have more than one genetic diagnosis; consider when the phenotype does not fit.
- **For psychiatrists:** order microarray and refer to clinical genetics if negative.
- **Targeted therapies:** everolimus (TSC), trofinetide (Rett; not TGA approved), fenfluramine (Dravet), antisense oligonucleotides (nusinersen, milasen, Angelman ASO in phase 3) and gene therapy (Zolgensma).

REFERENCES

1 Schneider M, Debbané M, Bassett AS, et al. Psychiatric disorders from childhood to adulthood in 22q11.2 deletion syndrome: results from the International Consortium on Brain and Behavior in 22q11.2 Deletion Syndrome. Am J Psychiatry. 2014;171(6):627-39. doi:10.1176/appi.ajp.2013.13070864

2 Vorstman JAS, Breetvelt EJ, Duijff SN, et al. Cognitive decline preceding the onset of psychosis in patients with 22q11.2 deletion syndrome. JAMA Psychiatry. 2015;72(4):377-85. doi:10.1001/jamapsychiatry.2014.2671

3	Wirrell EC, Hood V, Knupp KG, et al. International consensus on diagnosis and management of Dravet syndrome. Epilepsia. 2022;63(7):1761-77.	doi:10.1111/epi.17274
4	PanelApp Australia. Intellectual disability (panel 250). Melbourne: Australian Genomics.	panelapp-aus.org/panels/250
5	Slimani W, Ben Khelifa H, Dimassi S, et al. Clinical and molecular findings in nine new cases of tetrasomy 18p syndrome: FISH and array CGH characterization. Mol Cytogenet. 2019;12:5.	doi:10.1186/s13039-019-0414-8
6	Clark MM, Stark Z, Farnaes L, et al. Meta-analysis of the diagnostic and clinical utility of genome and exome sequencing and chromosomal microarray in children with suspected genetic diseases. NPJ Genom Med. 2018;3:16.	doi:10.1038/s41525-018-0053-8
7	McDonald-McGinn DM, Sullivan KE, Marino B, et al. 22q11.2 deletion syndrome. Nat Rev Dis Primers. 2015;1:15071.	doi:10.1038/nrdp.2015.71
8	Chen Y, Dawes R, Kim HC, et al. De novo variants in the RNU4-2 snRNA cause a frequent neurodevelopmental syndrome. Nature. 2024;632(8026):832-40.	doi:10.1038/s41586-024-07773-7
9	Greene D, Thys C, Berry IR, et al. Mutations in the U4 snRNA gene RNU4-2 cause one of the most prevalent monogenic neurodevelopmental disorders. Nat Med. 2024;30(8):2165-9.	doi:10.1038/s41591-024-03085-5
10	Tan WH, Bacino CA, Skinner SA, et al. Angelman syndrome: mutations influence features in early childhood. Am J Med Genet A. 2011;155A(1):81-90.	doi:10.1002/ajmg.a.33775
11	Angelman syndrome. In: StatPearls. Treasure Island (FL): StatPearls Publishing.	NBK560870
12	Tauber M, Hoybye C. Endocrine disorders in Prader-Willi syndrome: a model to understand and treat hypothalamic dysfunction. Lancet Diabetes Endocrinol. 2021;9(4):235-46.	doi:10.1016/S2213-8587(21)00002-4
13	Foundation for Angelman Syndrome Therapeutics. Traits and symptoms.	cureangelman.org/traits-and-symptoms
14	Fragile X syndrome. Wikipedia.	en.wikipedia.org/wiki/Fragile_X_syndrome
15	HudsonAlpha Institute for Biotechnology. HudsonAlpha researchers use highly accurate long-read sequencing technology to help diagnose rare disease.	hudsonalpha.org
16	Marx V. Method of the year: long-read sequencing. Nat Methods. 2023;20(1):6-11.	doi:10.1038/s41592-022-01730-w
17	Kim J, Hu C, Moufawad El Achkar C, et al. Patient-customized oligonucleotide therapy for a rare genetic disease. N Engl J Med. 2019;381(17):1644-52.	doi:10.1056/NEJMoa1813279
18	Finkel RS, Mercuri E, Darras BT, et al. Nusinersen versus sham control in infantile-onset spinal muscular atrophy. N Engl J Med. 2017;377(18):1723-32.	doi:10.1056/NEJMoa1702752
19	Neul JL, Percy AK, Benke TA, et al. Trofinetide for the treatment of Rett syndrome: a randomized phase 3 study. Nat Med. 2023;29(6):1468-75.	doi:10.1038/s41591-023-02398-1
20	Pestana Knight EM, Amin S, Bahi-Buisson N, et al. Safety and efficacy of ganaxolone in patients with CDKL5 deficiency disorder: results from the double-blind phase of a randomised, placebo-controlled, phase 3 trial. Lancet Neurol. 2022;21(5):417-27.	doi:10.1016/S1474-4422(22)00077-1
21	Lagae L, Sullivan J, Knupp K, et al. Fenfluramine hydrochloride for the treatment of seizures in Dravet syndrome: a randomised, double-blind, placebo-controlled trial. Lancet. 2019;394(10216):2243-54.	doi:10.1016/S0140-6736(19)32500-0
22	Franz DN, Belousova E, Sparagana S, et al. Efficacy and safety of everolimus for subependymal giant cell astrocytomas associated with tuberous sclerosis complex (EXIST-1): a multicentre, randomised, placebo-controlled phase 3 trial. Lancet. 2013;381(9861):125-32.	doi:10.1016/s0140-6736(12)61134-9
23	French JA, Lawson JA, Yapici Z, et al. Adjunctive everolimus therapy for treatment-resistant focal-onset seizures associated with tuberous sclerosis (EXIST-3): a phase 3, randomised, double-blind, placebo-controlled study. Lancet. 2016;388(10056):2153-63.	doi:10.1016/s0140-6736(16)31419-2
24	Berry-Kravis E, Des Portes V, Hagerman R, et al. Mavoglurant in fragile X syndrome: results of two randomized, double-blind, placebo-controlled trials. Sci Transl Med. 2016;8(321):321ra5.	doi:10.1126/scitranslmed.aab4109
25	Taysha Gene Therapies. FDA Breakthrough Therapy designation for TSHA-102 in Rett syndrome [press release]. 2 Oct 2025.	ir.tayshagtx.com
26	BioMarin Pharmaceutical; n-Lorem Foundation. Early research collaboration to develop potential first-in-disease medicine for ReNU syndrome [press release]. 27 Jul 2026.	nlorem.org
27	Ultragenyx Pharmaceutical. Ultragenyx announces Phase 3 Aspire results in Angelman syndrome [press release]. 2 Sep 2026.	ir.ultragenyx.com

28	Sutherland GR. Fragile sites on human chromosomes: demonstration of their dependence on the type of tissue culture medium. *Science*. 1977;197(4300):265–266.	doi:10.1126/science.877551

2 DEMENTIA IN INTELLECTUAL DISABILITY AND DOWN SYNDROME

Dr Madeleine Healy · Geriatrician, Monash Health; Dementia Support Australia

> Down syndrome is a genetic form of Alzheimer disease, with lifetime risk near 95%. Baseline at 30, screen from 40 and assess promptly at any age if concerned.

- **Burden:** dementia risk in ID is 5–7 times higher and about 10 years earlier. Dementia is now the leading cause of death in Down syndrome; median diagnosis at 54.
- **Biology:** APP triplication drives lifelong amyloid overproduction; cerebral amyloid angiopathy is common, raising ARIA risk with anti-amyloid antibodies.
- **Presentation:** amnestic change is typical early, not just behavioural or executive change. New seizures in an adult with Down syndrome should prompt assessment for AD.
- **Exclude contributors:** hearing and vision loss, sleep apnoea, hypothyroidism, mental illness, medications, relocation, life events and abuse. Overshadowing works both ways.
- **Tools:** DSQIID and NTG-EDSD (informant), CAMDEX-DS-II with CAMCOG-DS, and the Severe Impairment Battery for moderate–severe ID.
- **Biomarkers:** hippocampal atrophy from about 40; amyloid PET rises sharply after 40; plasma p-tau217 discriminates dementia (AUC about 0.96).
- **Treatment:** donepezil has some evidence; memantine has not shown cognitive benefit. Trials now include a donanemab study with modified titration.
- **Lifestyle:** exercise shows some cognitive benefit; evidence for diet, cognitive stimulation and social connection is inconclusive.

REFERENCES

29	Fortea J, Zaman SH, Hartley S, Rafii MS, Head E, Carmona-Iragui M. Alzheimer's disease associated with Down syndrome: a genetic form of dementia. Lancet Neurol. 2021;20(11):930-42.	doi:10.1016/S1474-4422(21)00245-3
30	Fortea J, Vilaplana E, Carmona-Iragui M, et al. Clinical and biomarker changes of Alzheimer's disease in adults with Down syndrome: a cross-sectional study. Lancet. 2020;395(10242):1988-97.	doi:10.1016/S0140-6736(20)30689-9
31	Jack CR Jr, Andrews JS, Beach TG, et al. Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup. Alzheimers Dement. 2024;20(8):5143-69.	doi:10.1002/alz.13859
32	Iulita MF, Garzón Chavez D, Klitgaard Christensen M, et al. Association of Alzheimer disease with life expectancy in people with Down syndrome. JAMA Netw Open. 2022;5(5):e2212910.	doi:10.1001/jamanetworkopen.2022.12910
33	McCarron M, McCallion P, Reilly E, Dunne P, Carroll R, Mulryan N. A prospective 20-year longitudinal follow-up of dementia in persons with Down syndrome. J Intellect Disabil Res. 2017;61(9):843-52.	doi:10.1111/jir.12390
34	Bittles AH, Petterson BA, Sullivan SG, Hussain R, Glasson EJ, Montgomery PD. The influence of intellectual disability on life expectancy. J Gerontol A Biol Sci Med Sci. 2002;57(7):M470-2.	doi:10.1093/gerona/57.7.M470
35	de Graaf G, Skladzien E, Buckley F, Skotko BG. Estimation of the number of people with Down syndrome in Australia and New Zealand. Genet Med. 2022.	doi:10.1016/j.gim.2022.08.029
36	British Psychological Society, Division of Clinical Psychology. Dementia and people with intellectual disabilities: guidance on the assessment, diagnosis, interventions and support of people with intellectual disabilities who develop dementia. Leicester: BPS; 20 May 2025.	doi:10.53841/bpsrep.2025.rep186
37	Rafii MS, Wishnek H, Brewer JB, et al. The Down syndrome biomarker initiative (DSBI) pilot: proof of concept for deep phenotyping of Alzheimer's disease biomarkers in Down syndrome. Front Behav Neurosci. 2015;9:239.	doi:10.3389/fnbeh.2015.00239
38	Carmona-Iragui M, Santos T, Videla S, et al. Feasibility of lumbar puncture in the study of cerebrospinal fluid biomarkers for Alzheimer's disease in subjects with Down syndrome. J Alzheimers Dis. 2017;55(4):1489-96.	doi:10.3233/JAD-160827
39	Deb S, Hare M, Prior L, Bhaumik S. Dementia Screening Questionnaire for Individuals with Intellectual Disabilities (DSQIID). Br J Psychiatry. 2007;190:440-4.	doi:10.1192/bjp.bp.106.024984

40	Deb S, Hare M, Prior L. Symptoms of dementia among adults with Down's syndrome: a qualitative study. J Intellect Disabil Res. 2007;51(9):726-39.	doi:10.1111/j.1365-2788.2007.00956.x
41	National Task Group on Intellectual Disabilities and Dementia Practices. NTG-Early Detection Screen for Dementia (NTG-EDSD).	the-ntg.org
42	Boyle R, Koops EA, Ances B, et al. Resistance and resilience to Alzheimer's disease in Down syndrome. Alzheimers Dement. 2025;21(4):e70151.	doi:10.1002/alz.70151
43	McGlinchey E, Pape S, Zaman SH, et al. Lifestyle intervention and cognitive outcomes in Down syndrome: a Horizon 21 European Down Syndrome Consortium scoping review. J Neurodev Disord. 2026;18:34.	doi:10.1186/s11689-026-09694-0
44	Krasny S, Yan C, Hartley SL, et al. Assessing amyloid PET positivity and cognitive function in Down syndrome to guide clinical trials targeting amyloid. Alzheimers Dement. 2024.	doi:10.1002/alz.14068
45	Zammit MD, Laymon CM, Koscik RL, et al. Predicting the time to tau onset in Down syndrome using amyloid chronicity [abstract]. Alzheimers Dement. 2020;16(Suppl).	doi:10.1002/alz.046060
46	Huber H, Arranz J, Arslan B, et al. Plasma p-tau217 as a biomarker of Alzheimer's disease pathology in individuals with Down syndrome. Nat Commun. 2025;16(1):9900.	doi:10.1038/s41467-025-65882-x
47	ALADDIN (donanemab in Down syndrome), ClinicalTrials.gov	NCT06911944
48	Costa ACS, Brandão AC, Boada R, et al. Safety, efficacy, and tolerability of memantine for cognitive and adaptive outcome measures in adolescents and young adults with Down syndrome: a randomised, double-blind, placebo-controlled phase 2 trial. Lancet Neurol. 2022;21(1):31-41.	doi:10.1016/S1474-4422(21)00369-0
49	Mohan M, Carpenter PK, Bennett C. Donepezil for dementia in people with Down syndrome. Cochrane Database Syst Rev. 2009;(1):CD007178.	doi:10.1002/14651858.CD007178.pub2
50	Livingstone N, Hanratty J, McShane R, Macdonald G. Pharmacological interventions for cognitive decline in people with Down syndrome. Cochrane Database Syst Rev. 2015;(10):CD011546.	doi:10.1002/14651858.CD011546.pub2
51	Healy ML, Brodtmann A, Foster AM, et al. Down syndrome and Alzheimer's disease: a qualitative study exploring understanding and perceptions of dementia and diagnostic pathways among people with Down syndrome and their families. *J Intellect Disabil Res*. 2026.	doi:10.1111/jir.70173
52	Livingston G, Huntley J, Liu KY, et al. Dementia prevention, intervention, and care: 2024 report of the Lancet standing Commission. *Lancet*. 2024;404(10452):572–628.	doi:10.1016/S0140-6736(24)01296-0

Regression and catatonia

3 REGRESSION AND CATATONIA IN NEURODEVELOPMENTAL DISABILITIES

A/Prof Aaron Hauptman · Kennedy Krieger Institute; Johns Hopkins University School of Medicine

> Confirm true loss of skills, then work through a broad differential. Catatonia in autism and IDD is often hyperkinetic and easily missed.

- **True regression?** Separate loss of skills from a plateau, and from typical early autistic regression (18–24 months).
- **Differential:** syndrome-specific regression (Rett, Kleefstra, Phelan-McDermid), psychiatric illness, trauma and transitions, autoimmune or metabolic disease, pain, seizures and neurodegeneration.
- **Common drivers:** dental pain and constipation are among the commonest causes of dramatic mental state change.
- **Hyperkinetic catatonia:** new or severe self-injury, aggression, purposeless movement, echophenomena, acrocyanosis, new incontinence and changed eating.
- **Caution:** antipsychotics can precipitate NMS or malignant catatonia when catatonia is unrecognised.
- **Baseline:** use records and family videos; score a premorbid Bush-Francis (often 4–9 in autism) and treat back to that, not to zero.
- **Treatment:** lorazepam first line, titrated to high doses if needed; a muted response does not exclude catatonia. Then NMDA antagonists or zolpidem; ECT is the gold standard for malignant or refractory cases.

REFERENCES

53	Verity C, Winstone AM, Stellitano L, Will R, Nicoll A. The epidemiology of progressive intellectual and neurological deterioration in childhood. Arch Dis Child. 2010;95(5):361-4.	doi:10.1136/adc.2009.173419

54	Verity C, Baker E, Maunder P, Pal S, Winstone AM. Differential diagnosis of progressive intellectual and neurological deterioration in children. Dev Med Child Neurol. 2021;63(3):287-94.	doi:10.1111/dmcn.14691
55	Kalb LG, Law JK, Landa R, Law PA. Onset patterns prior to 36 months in autism spectrum disorders. J Autism Dev Disord. 2010;40(11):1389-402.	doi:10.1007/s10803-010-0998-7
56	Shumway S, Thurm A, Swedo SE, et al. Brief report: symptom onset patterns and functional outcomes in young children with autism spectrum disorders. J Autism Dev Disord. 2011;41(12):1727-32.	doi:10.1007/s10803-011-1203-3
57	Vermeulen K, Staal WG, Janzing JG, et al. Sleep disturbance as a precursor of severe regression in Kleefstra syndrome suggests a need for firm and rapid pharmacological treatment. Clin Neuropharmacol. 2017;40(4):185-8.	doi:10.1097/WNF.0000000000000226
58	Bouman A, Gaasterland CMW, Sloof-Enthoven C, et al. International clinical evidence-based guideline for Kleefstra syndrome. Genet Med. 2026;28(6):102070.	doi:10.1016/j.gim.2026.102070
59	American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Arlington (VA): APA; 2013.	doi:10.1176/appi.books.9780890425596
60	Mahgoub Y, Hamlin D, Kindt H, Francis A. Catatonia and autism spectrum disorder: a common comorbid syndrome or a core feature? World J Psychiatry. 2025;15(5):103967.	doi:10.5498/wjp.v15.i5.103967
61	Dhossche DM. Autism as early expression of catatonia. Med Sci Monit. 2004;10(3):RA31-9.	medscimonit.com
62	Wing L, Shah A. A systematic examination of catatonia-like clinical pictures in autism spectrum disorders. Int Rev Neurobiol. 2006;72:21-39.	doi:10.1016/S0074-7742(05)72002-X
63	Wachtel LE. The multiple faces of catatonia in autism spectrum disorders: descriptive clinical experience of 22 patients over 12 years. Eur Child Adolesc Psychiatry. 2019;28(4):471-80.	doi:10.1007/s00787-018-1210-4
64	Vaquerizo-Serrano J, Salazar de Pablo G, Singh J, Santosh P. Catatonia in autism spectrum disorders: a systematic review and meta-analysis. Eur Psychiatry. 2022;65(1):e4.	doi:10.1192/j.eurpsy.2021.2259
65	Bush G, Fink M, Petrides G, Dowling F, Francis A. Catatonia. I. Rating scale and standardized examination. Acta Psychiatr Scand. 1996;93(2):129-36.	doi:10.1111/j.1600-0447.1996.tb09814.x
66	University of Rochester Medical Center. Bush-Francis Catatonia Rating Scale and video training.	urmc.rochester.edu
67	Carroll BT, Kirkhart R, Ahuja N, et al. Katatonia: a new conceptual understanding of catatonia and a new rating scale. Psychiatry (Edgmont). 2008;5(12):42-50.	PMC2729619
68	Hauptman AJ, Cohen D, Dhossche D, Raffin M, Wachtel L, Ferrafiat V. Catatonia in neurodevelopmental disorders: assessing catatonic deterioration from baseline. Lancet Psychiatry. 2023;10(3):228-34.	doi:10.1016/S2215-0366(22)00436-9
69	Benarous X, Consoli A, Raffin M, et al. Validation of the Pediatric Catatonia Rating Scale (PCRS). Schizophr Res. 2016;176(2-3):378-86.	doi:10.1016/j.schres.2016.06.020
70	Smith JR, Baldwin I, York T, et al. Alternative psychopharmacologic treatments for pediatric catatonia: a retrospective analysis. Front Child Adolesc Psychiatry. 2023;2:1208926.	doi:10.3389/frcha.2023.1208926
71	Withane N, Dhossche DM. Electroconvulsive treatment for catatonia in autism spectrum disorders. Child Adolesc Psychiatr Clin N Am. 2019;28(1):101-10.	doi:10.1016/j.chc.2018.07.006
72	Hauptman AJ, Salpekar JA, eds. *Pediatric Neuropsychiatry: A Case-Based Approach*. Cham: Springer; 2019.	doi:10.1007/978-3-319-94998-7

4 DOWN SYNDROME REGRESSION DISORDER (DSRD) AND THE FIRST RCT

Dr Cathy Franklin · QCIDAH, Mater Research Institute-UQ; Dr Jonathan Santoro · Children's Hospital Los Angeles

DSRD is a subacute loss of skills, often with hypokinetic catatonia. Treat catatonia without waiting for the full workup; immunotherapy gave the broadest gains in the first RCT.

- **Presentation:** loss of ADLs and communication over under 12 weeks, often with freezing, catalepsy, automatic obedience and staring.
- **Approach:** diagnosis of exclusion; confirm and treat catatonia, exclude treatable causes, look for neuroinflammation, consider early immunotherapy and use MDT rehabilitation.
- **Access:** IVIG is not listed for DSRD in Australia; some access it via seronegative autoimmune encephalitis indications.

- **Outpatient lorazepam:** start about 0.5 mg BD–TDS and increase over days; effect rarely below 2–3 mg/day; many settle on 6–8 mg/day. Bladder scan before IV lorazepam.
- **RCT design:** phase 2, open-label, ages 8–30, randomised to lorazepam, IVIG or tofacitinib for 12 weeks; 66 enrolled, none withdrew for adverse effects.
- **Results:** all three safe (over 94% of adverse events grade 1–2). Untreated run-in showed no improvement. IVIG and tofacitinib gave the broadest gains; lorazepam improved catatonia most, supporting it as an adjunct to immunotherapy.

REFERENCES

73	Santoro JD, Patel L, Kammeyer R, et al. Assessment and diagnosis of Down syndrome regression disorder: international expert consensus. Front Neurol. 2022;13:940175.	doi:10.3389/fneur.2022.940175
74	Rosso M, Fremion E, Santoro SL, et al. Down syndrome disintegrative disorder: a clinical regression syndrome of increasing importance. Pediatrics. 2020;145(6):e20192939.	doi:10.1542/peds.2019-2939
75	Ghaziuddin N, Nassiri A, Miles JH. Catatonia in Down syndrome; a treatable cause of regression. Neuropsychiatr Dis Treat. 2015;11:941-9.	doi:10.2147/NDT.S77307
76	Miles JH, Takahashi N, Muckerman J, Nowell KP, Ithman M. Catatonia in Down syndrome: systematic approach to diagnosis, treatment and outcome assessment based on a case series of seven patients. Neuropsychiatr Dis Treat. 2019;15:2723-41.	doi:10.2147/NDT.S210613
77	Cardinale KM, Bocharnikov A, Hart SJ, et al. Immunotherapy in selected patients with Down syndrome disintegrative disorder. Dev Med Child Neurol. 2019;61(7):847-51.	doi:10.1111/dmcn.14127
78	Down Syndrome Medical Interest Group–USA. Regression in persons with Down syndrome: information sheet.	dsmig-usa.org/dsmig-resources
79	National Down Syndrome Society, CARE-DS. Down syndrome regression disorder (DSRD) learning module.	careds.org
80	Rachubinski AL, Wallace E, Gurnee E, et al. JAK inhibition decreases the autoimmune burden in Down syndrome. *eLife*. 2024;13:RP99323.	doi:10.7554/eLife.99323
81	Santoro JD, Jafarpour S, et al. A comparative effectiveness study of lorazepam or IVIg versus no treatment for Down syndrome regression disorder. *Neurol Ther*. 2026;15:1099–1120.	doi:10.1007/s40120-026-00906-2

Autism and behaviour

5 AUTISM AND CO-OCCURRING MENTAL ILLNESS

Dr Solomon Shatananda · Queensland Children's Hospital; Griffith University · Dr Grace Min · Metro North Intellectual Disability Mental Health Service

> Ask what is usual for this person and what has changed. Keep formulations provisional during acute illness.

- **Masking:** camouflaging is effortful, linked with poorer mental health, and may break down under stress so autistic traits seem new.
- **Co-occurrence:** about 70% have at least one psychiatric condition: ADHD, anxiety, sleep disorders, depression, OCD, bipolar disorder, psychosis and trauma.
- **Anxiety and depression:** may present as shutdown, repetitive behaviour, aggression, irritability, changed special interests or loss of skills. Autistic burnout is common after Year 12.
- **Psychosis vs autism:** no single tool differentiates; use developmental history, videos, school reports and collateral. Do not diagnose on full-scale IQ alone.
- **Genotype:** indicates risk, not destiny (e.g. 22q11.2, maternal UPD Prader-Willi).
- **Trauma:** higher rates of bullying, abuse and ACEs; everyday sensory overload and misunderstanding can be traumatic.
- **Suicide:** up to 66% report suicidal thoughts; attempts and deaths 3–9 times higher. About 42% self-injure; do not dismiss self-harm as repetitive behaviour.
- **Prescribing:** start antipsychotics low and go slow, with opportunistic metabolic monitoring.

REFERENCES

82	American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed, text revision (DSM-5-TR). Washington (DC): APA; 2022.	doi:10.1176/appi.books.9780890425787
83	Australian Bureau of Statistics. Autism in Australia, 2022 (Survey of Disability, Ageing and Carers). Canberra: ABS; 2024.	abs.gov.au

84	Shaw KA, Williams S, Patrick ME, et al. Prevalence and early identification of autism spectrum disorder among children aged 4 and 8 years — Autism and Developmental Disabilities Monitoring Network, 16 sites, United States, 2022. MMWR Surveill Summ. 2025;74(2):1-22.	doi:10.15585/mmwr.ss7402a1
85	GBD 2021 Autism Spectrum Collaborators. The global epidemiology and health burden of the autism spectrum: findings from the Global Burden of Disease Study 2021. Lancet Psychiatry. 2025;12(2):111-21.	doi:10.1016/S2215-0366(24)00363-8
86	Hull L, Mandy W, Lai MC, et al. Development and validation of the Camouflaging Autistic Traits Questionnaire (CAT-Q). J Autism Dev Disord. 2019;49(3):819-33.	doi:10.1007/s10803-018-3792-6
87	Cook J, Hull L, Crane L, Mandy W. Camouflaging in autism: a systematic review. Clin Psychol Rev. 2021;89:102080.	doi:10.1016/j.cpr.2021.102080
88	Lai MC, Kassee C, Besney R, et al. Prevalence of co-occurring mental health diagnoses in the autism population: a systematic review and meta-analysis. Lancet Psychiatry. 2019;6(10):819-29.	doi:10.1016/S2215-0366(19)30289-5
89	Mazza MG, Rossetti A, Crespi G, Clerici M. Prevalence of co-occurring psychiatric disorders in adults and adolescents with intellectual disability: a systematic review and meta-analysis. J Appl Res Intellect Disabil. 2020;33(2):126-38.	doi:10.1111/jar.12654
90	Hirvikoski T, Mittendorfer-Rutz E, Boman M, et al. Premature mortality in autism spectrum disorder. Br J Psychiatry. 2016;208(3):232-8.	doi:10.1192/bjp.bp.114.160192
91	van Steensel FJA, Bögels SM, Perrin S. Anxiety disorders in children and adolescents with autistic spectrum disorders: a meta-analysis. Clin Child Fam Psychol Rev. 2011;14(3):302-17.	doi:10.1007/s10567-011-0097-0
92	Kent R, Simonoff E. Prevalence of anxiety in autism spectrum disorders. In: Kerns CM, et al, editors. Anxiety in children and adolescents with autism spectrum disorder. London: Academic Press; 2017. p. 5-32.	doi:10.1016/B978-0-12-805122-1.00002-8
93	Kerns CM, Kendall PC, Berry L, et al. Traditional and atypical presentations of anxiety in youth with autism spectrum disorder. J Autism Dev Disord. 2014;44(11):2851-61.	doi:10.1007/s10803-014-2141-7
94	Simonoff E, Pickles A, Charman T, et al. Psychiatric disorders in children with autism spectrum disorders: prevalence, comorbidity, and associated factors in a population-derived sample. J Am Acad Child Adolesc Psychiatry. 2008;47(8):921-9.	doi:10.1097/CHI.0b013e318179964f
95	Lau BY, Leong R, Uljarevic M, et al. Anxiety in young people with autism spectrum disorder: common and autism-related anxiety experiences and their associations with individual characteristics. Autism. 2020;24(5):1111-26.	doi:10.1177/1362361319886246
96	Hollocks MJ, Lerh JW, Magiati I, Meiser-Stedman R, Brugha TS. Anxiety and depression in adults with autism spectrum disorder: a systematic review and meta-analysis. Psychol Med. 2019;49(4):559-72.	doi:10.1017/S0033291718002283
97	Pezzimenti F, Han GT, Vasa RA, Gotham K. Depression in youth with autism spectrum disorder. Child Adolesc Psychiatr Clin N Am. 2019;28(3):397-409.	doi:10.1016/j.chc.2019.02.009
98	Kuo SS, Eack SM. Meta-analysis of cognitive performance in neurodevelopmental disorders during adulthood: comparisons between autism spectrum disorder and schizophrenia on the Wechsler Adult Intelligence Scales. Front Psychiatry. 2020;11:187.	doi:10.3389/fpsyt.2020.00187
99	Boer H, Holland A, Whittington J, et al. Psychotic illness in people with Prader Willi syndrome due to chromosome 15 maternal uniparental disomy. Lancet. 2002;359(9301):135-6.	doi:10.1016/S0140-6736(02)07340-3
100	Mulle JG, Dodd AF, McGrath JA, et al. Microdeletions of 3q29 confer high risk for schizophrenia. Am J Hum Genet. 2010;87(2):229-36.	doi:10.1016/j.ajhg.2010.07.013
101	McDonnell CG, Boan AD, Bradley CC, et al. Child maltreatment in autism spectrum disorder and intellectual disability: results from a population-based sample. J Child Psychol Psychiatry. 2019;60(5):576-84.	doi:10.1111/jcpp.12993
102	Rumball F, Happé F, Grey N. Experience of trauma and PTSD symptoms in autistic adults. Autism Res. 2020;13(12):2122-32.	doi:10.1002/aur.2306
103	Hedley D, Uljarević M. Systematic review of suicide in autism spectrum disorder: current trends and implications. Curr Dev Disord Rep. 2018;5(1):65-76.	doi:10.1007/s40474-018-0133-6
104	Kõlves K, Fitzgerald C, Nordentoft M, Wood SJ, Erlangsen A. Assessment of suicidal behaviors among individuals with autism spectrum disorder in Denmark. JAMA Netw Open. 2021;4(1):e2033565.	doi:10.1001/jamanetworkopen.2020.33565
105	Kirby AV, Bakian AV, Zhang Y, et al. A 20-year study of suicide death in a statewide autism population. Autism Res. 2019;12(4):658-66.	doi:10.1002/aur.2076

106	Cassidy S, Bradley L, Shaw R, Baron-Cohen S. Risk markers for suicidality in autistic adults. Mol Autism. 2018;9:42.	doi:10.1186/s13229-018-0226-4
107	Pelton MK, Cassidy SA. Are autistic traits associated with suicidality? A test of the interpersonal-psychological theory of suicide. Autism Res. 2017;10(11):1891-904.	doi:10.1002/aur.1828
108	Hannon G, Taylor EP. Suicidal behaviour in adolescents and young adults with ASD: findings from a systematic review. Clin Psychol Rev. 2013;33(8):1197-204.	doi:10.1016/j.cpr.2013.10.003
109	Hull L, Petrides KV, Allison C, et al. "Putting on my best normal": social camouflaging in adults with autism spectrum conditions. *J Autism Dev Disord*. 2017;47(8):2519–2534.	doi:10.1007/s10803-017-3166-5
110	Cassidy S, Bradley P, Robinson J, et al. Suicidal ideation and suicide plans or attempts in adults with Asperger's syndrome attending a specialist diagnostic clinic: a clinical cohort study. *Lancet Psychiatry*. 2014;1(2):142–147.	doi:10.1016/S2215-0366(14)70248-2

6 BEHAVIOURS OF CONCERN AND POSITIVE BEHAVIOUR SUPPORT

Tamara Smith · West Moreton Intellectual Disability Mental Health Team · Dr David Pryor · Intellectual Disability Psychiatrist

> Never assume a behaviour's function. Good PBS plans are multi-element, non-aversive living documents judged by quality of life.

- **Assessment:** describe behaviour objectively across settings from the person's perspective. A comprehensive functional analysis takes about 90 hours.
- **NDIS categories** are too crude; different behaviours may serve different functions.
- **Mediator analysis:** examine how each person in the support network responds, as responses can create or maintain behaviours.
- **Plan components:** ecological change, positive programming and skills teaching, focused supports, with reactive strategies only a small part.
- **Implementation:** step-by-step protocols, three-tier staff training (recall, role play, in vivo) and outcome data matched to the behaviour.
- **For psychiatrists:** ask whether a functional and mediator analysis has been done and updated after support team changes.

REFERENCES

111	LaVigna GW, Willis TJ. The efficacy of positive behavioural support with the most challenging behaviour: the evidence and its implications. *J Intellect Dev Disabil*. 2012;37(3):185–195.	doi:10.3109/13668250.2012.696597

EPILEPSY

7 DRUG-RESISTANT EPILEPSY: DIAGNOSIS AND SURGERY

Dr Stephen Malone · Paediatric Neurologist and Epileptologist, Queensland Children's Hospital; University of Queensland

> About one in three people have drug-resistant epilepsy. Refer early for surgical assessment, and remember psychiatric comorbidity affects outcomes.

- **Definitions:** epilepsy can be diagnosed after one seizure if recurrence risk is high; drug resistance is failure of two appropriate, tolerated medications.
- **Mimics:** 25–30% of tertiary referrals for refractory epilepsy have non-epileptic events; about 1 in 20 referred for functional seizures also have epilepsy.
- **Frontal seizures** can look bizarre; clues are brief, stereotyped events arising from sleep.
- **Psychiatric links:** up to half have psychiatric comorbidity; mood disorder raises epilepsy risk about 2.5-fold and psychosis up to 7-fold.
- **Classification:** the 2025 ILAE update describes seizure evolution; DEEs are often genetic, with emerging precision treatments.
- **Surgery:** up to about 70% seizure freedom in suitable candidates; cognition declines while waiting. Laser ablation is now first choice for hypothalamic hamartoma.
- **Forced normalisation:** psychiatric symptoms can emerge when seizures are suppressed, especially in temporal lobe epilepsy.

- **Policy:** the Senate inquiry made 27 recommendations; psychiatry is not referenced.

REFERENCES

112	Fisher RS, van Emde Boas W, Blume W, et al. Epileptic seizures and epilepsy: definitions proposed by the ILAE and IBE. Epilepsia. 2005;46(4):470-2.	doi:10.1111/j.0013-9580.2005.66104.x
113	Fisher RS, Acevedo C, Arzimanoglou A, et al. ILAE official report: a practical clinical definition of epilepsy. Epilepsia. 2014;55(4):475-82.	doi:10.1111/epi.12550
114	Berg AT, Berkovic SF, Brodie MJ, et al. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005–2009. Epilepsia. 2010;51(4):676-85.	doi:10.1111/j.1528-1167.2010.02522.x
115	Fisher RS, Cross JH, French JA, et al. Operational classification of seizure types by the International League Against Epilepsy. Epilepsia. 2017;58(4):522-30.	doi:10.1111/epi.13670
116	Beniczky S, Trinka E, Wirrell E, et al. Updated classification of epileptic seizures: a position paper of the International League Against Epilepsy. Epilepsia. 2025.	doi:10.1111/epi.18338
117	Mesraoua B, et al. Drug-resistant epilepsy: definition, pathophysiology, and management. J Neurol Sci. 2023;452:120766.	doi:10.1016/j.jns.2023.120766
118	Nurse E, et al. Seizure reporting in older patients with developmental and epileptic encephalopathies: a retrospective review of ambulatory video-EEG reports. Seizure. 2025;131:50-6.	doi:10.1016/j.seizure.2025.06.003
119	Dudley P, et al. Functional seizures and their mimics: a retrospective service review of cases from a tertiary video telemetry database. BMJ Neurol Open. 2024;6:e000738.	doi:10.1136/bmjno-2024-000738
120	Alva-Diaz C, et al. Peri-ictal psychiatric manifestations in people with epilepsy: an umbrella review. Epilepsia Open. 2024;9(4):1166-75.	doi:10.1002/epi4.12949
121	Calle-López Y, Ladino LD, Benjumea-Cuartas V, et al. Forced normalization: a systematic review. Epilepsia. 2019;60(8):1610-8.	doi:10.1111/epi.16276
122	Weisdorf S, et al. Ultra-long-term subcutaneous home monitoring of epilepsy. Epilepsia. 2019;60(11):2204-14.	doi:10.1111/epi.16360
123	Lagarde S, et al. Relationship between PET metabolism and SEEG epileptogenicity in focal lesional epilepsy. Eur J Nucl Med Mol Imaging. 2020;47(13):3130-42.	doi:10.1007/s00259-020-04791-1
124	Wiest R, et al. Widespread grey matter changes and hemodynamic correlates to interictal epileptiform discharges in pharmacoresistant mesial temporal epilepsy. J Neurol. 2013;260(6):1601-10.	doi:10.1007/s00415-013-6841-2
125	Bartolomei F, et al. Epileptogenicity of brain structures in human temporal lobe epilepsy: a quantified study from intracerebral EEG. Brain. 2008;131:1818-30.	doi:10.1093/brain/awn111
126	Bonini F, et al. Epileptogenic networks in seizures arising from motor systems. Epilepsy Res. 2013;106:92-102.	doi:10.1016/j.eplepsyres.2013.04.011
127	Spitzer H, Ripart M, Whitaker K, et al. Interpretable surface-based detection of focal cortical dysplasias: a Multi-centre Epilepsy Lesion Detection study. Brain. 2022;145(11):3859-71.	doi:10.1093/brain/awac224
128	Brodie MJ, Kwan P. Staged approach to epilepsy management. Neurology. 2002;58(8 Suppl 5):S2-8.	doi:10.1212/WNL.58.8_suppl_5.S2
129	Vining EP, Freeman JM, Ballaban-Gil K, et al. A multicenter study of the efficacy of the ketogenic diet. Arch Neurol. 1998;55:1433-7.	doi:10.1001/archneur.55.11.1433
130	Van Ness PC. Therapy for the epilepsies. Arch Neurol. 2002;59:732-5.	doi:10.1001/archneur.59.5.732
131	Morris GL III, Mueller WM. Long-term treatment with vagus nerve stimulation in patients with refractory epilepsy. Neurology. 1999;53:1731-5.	doi:10.1212/WNL.53.8.1731
132	Renfroe JB, Wheless JW. Earlier use of adjunctive vagus nerve stimulation therapy for refractory epilepsy. Neurology. 2002;59(Suppl 4):S26-30.	doi:10.1212/WNL.59.6_suppl_4.S26
133	Yates CF, Riney K, Malone S, et al. Vagus nerve stimulation: a 20-year Australian experience. Acta Neurochir (Wien). 2022;164:219-27.	doi:10.1007/s00701-021-05046-0
134	Ranpariya M, Kaur G, Shallwani H, et al. Long-term neuropsychiatric outcomes after neuromodulation in epilepsy patients: a systematic review and meta-analysis. Acta Neurol Belg. 2026.	doi:10.1007/s13760-026-03113-w
135	World Health Organization. Intersectoral global action plan on epilepsy and other neurological disorders 2022–2031. Geneva: WHO; 2023.	who.int

136	Kwan P, Arzimanoglou A, Berg AT, et al. Definition of drug resistant epilepsy: consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. *Epilepsia*. 2010;51(6):1069–1077.	doi:10.1111/j.1528-1167.2009.02397.x
137	Scheffer IE, Berkovic S, Capovilla G, et al. ILAE classification of the epilepsies: position paper of the ILAE Commission for Classification and Terminology. *Epilepsia*. 2017;58(4):512–521.	doi:10.1111/epi.13709
—	Senate Community Affairs References Committee. Inquiry into epilepsy in Australia.	aph.gov.au

8 EPILEPSY IN NEURODIVERGENT PEOPLE

Dr Melanie Johnston · Psychiatrist, QCIDAH, Mater Research Institute-UQ

Epilepsy and autism mask each other. Check seizure data before reaching for antipsychotics or restrictive practices.

- **Prevalence:** about 1 in 5 people with ID and 1 in 8 autistic people have epilepsy; about 1 in 11 people with epilepsy are autistic. Screen both ways.
- **Masking:** staring spells, automatisms and postictal agitation can be read as behaviour.
- **EEG access:** social stories with real photographs, OT desensitisation, event videos and seizure alert devices (e.g. bed mats).
- **Composite case:** overlaying PBS and seizure data showed aggression was postictal, worsened by levetiracetam and constipation. Switching to brivaracetam and a joint plan avoided antipsychotics.
- **Prescribing:** consider formulation, swallowing, monitoring and polypharmacy; avoid bias such as valproate without contraception.
- **SUDEP:** risk rises substantially with three or more tonic-clonic seizures a year; challenge therapeutic nihilism.
- **Mortality:** people with ID have twice the rate of preventable deaths and a 27-year gap in median age at death.

REFERENCES

138	Robertson J, Hatton C, Emerson E, Baines S. Prevalence of epilepsy among people with intellectual disabilities: a systematic review. Seizure. 2015;29:46-62.	doi:10.1016/j.seizure.2015.03.016
139	Lukmanji S, Manji SA, Kadhim S, et al. The co-occurrence of epilepsy and autism: a systematic review. Epilepsy Behav. 2019;98:238-48.	doi:10.1016/j.yebeh.2019.07.037
140	Liu X, Sun X, Sun C, et al. Prevalence of epilepsy in autism spectrum disorders: a systematic review and meta-analysis. Autism. 2022;26(1):33-50.	doi:10.1177/13623613211045029
141	Fiest KM, Sauro KM, Wiebe S, et al. Prevalence and incidence of epilepsy: a systematic review and meta-analysis of international studies. Neurology. 2017;88(3):296-303.	doi:10.1212/WNL.0000000000003509
142	Epilepsy Foundation. Seizure monitors & devices.	epilepsyfoundation.org.au
143	Akrout Brizard B, Limbu B, Baeza-Velasco C, Deb S. Association between epilepsy and psychiatric disorders in adults with intellectual disabilities: systematic review and meta-analysis. BJPsych Open. 2021;7.	doi:10.1192/bjo.2021.55
144	Deb S, Akrout Brizard B, Limbu B. Association between epilepsy and challenging behaviour in adults with intellectual disabilities: systematic review and meta-analysis. BJPsych Open. 2020;6.	doi:10.1192/bjo.2020.96
145	Harden C, Tomson T, Gloss D, et al. Practice guideline summary: sudden unexpected death in epilepsy incidence rates and risk factors. Neurology. 2017;88:1674-80.	doi:10.1212/WNL.0000000000003685
146	Young C, Shankar R, Palmer J, et al. Does intellectual disability increase sudden unexpected death in epilepsy (SUDEP) risk? Seizure. 2015;25:112-6.	doi:10.1016/j.seizure.2014.10.001
147	SUDEP Action. SUDEP and Seizure Safety Checklist.	sudep.org
148	Trollor J, Srasuebkul P, Xu H, Howlett S. Cause of death and potentially avoidable deaths in Australian adults with intellectual disability using retrospective linked data. BMJ Open. 2017;7:e013489.	doi:10.1136/bmjopen-2016-013489
149	Shankar R, et al. Epilepsy-related premature mortality in adults with intellectual disability in England: a population-based analysis. J Neurol Neurosurg Psychiatry. 2025.	doi:10.1136/jnnp-2025-337291

9 PSYCHIATRIC ASPECTS OF EPILEPSY AND ITS TREATMENT

Dr Emily Watson · Epileptologist, Mater Epilepsy Unit and Princess Alexandra Hospital, Brisbane

> 15–20% of people have psychiatric adverse effects from anti-seizure medications. Most psychotropics can be used safely with attention to interactions.

- **ASM effects:** levetiracetam and perampanel linked to irritability and aggression; topiramate and zonisamide to depression and cognitive effects; lamotrigine and carbamazepine more mood neutral.
- **Levetiracetam tips:** brivaracetam is often better tolerated; pyridoxine about 100 mg/day for a month may help (case series only).
- **Screening:** GAD-7 and NDDI-E; CBT has good evidence.
- **Antidepressants:** SSRIs first line with little seizure-threshold concern; avoid bupropion and high-dose tricyclics.
- **Antipsychotics:** clozapine clearly lowers seizure threshold (2–10%); valproate, lamotrigine or levetiracetam can keep patients on clozapine.
- **Interactions:** valproate raises lamotrigine levels; enzyme inducers lower many psychotropics; fenfluramine carries high serotonin syndrome risk.
- **Other points:** ADHD stimulants do not increase seizure risk overall; prophylactic ASMs after TBI do not prevent later epilepsy; high-THC cannabis may worsen control.
- **Remember:** psychosis evolving to seizures may be anti-NMDA receptor encephalitis.

REFERENCES

150	Pisani F, Pisani LR, Barbieri MA, de Leon J, Spina E. Optimization of therapy in patients with epilepsy and psychiatric comorbidities: key points. Curr Neuropharmacol. 2023;21(8):1755-66.	doi:10.2174/1570159X20666220526144314
151	Mula M, Trimble MR, Lhatoo SD, Sander JW. Topiramate and psychiatric adverse events in patients with epilepsy. Epilepsia. 2003;44(5):659-63.	doi:10.1046/j.1528-1157.2003.05402.x
152	Nguyen S, Varkey TC, Khan B, Cornelius MC. "Homicide and zonisamide": a review of the literature and illustrative case report on second and third generation antiseizure medications and psychiatric effects. Front Psychiatry. 2026;17:1805235.	doi:10.3389/fpsyt.2026.1805235
153	Wiggs KK, Chang Z, Quinn PD, et al. Attention-deficit/hyperactivity disorder medication and seizures. Neurology. 2018;90(13):e1104-10.	doi:10.1212/WNL.0000000000005213
154	Chen B, Choi H, Hirsch LJ, et al. Psychiatric and behavioral side effects of antiepileptic drugs in adults with epilepsy. *Epilepsy Behav*. 2017;76:24–31.	doi:10.1016/j.yebeh.2017.08.039
155	Chhabra N, Vanood A, Hoerth MT, et al. Can pyridoxine successfully reduce behavioral side effects from levetiracetam? *Neurologist*. 2023;28(5):349–352.	doi:10.1097/NRL.0000000000000496
156	Gilliam FG, Barry JJ, Hermann BP, et al. Rapid detection of major depression in epilepsy: a multicentre study. *Lancet Neurol*. 2006;5(5):399–405.	doi:10.1016/S1474-4422(06)70415-X
157	Alper K, Schwartz KA, Kolts RL, Khan A. Seizure incidence in psychopharmacological clinical trials: an analysis of Food and Drug Administration (FDA) summary basis of approval reports. *Biol Psychiatry*. 2007;62(4):345–354.	doi:10.1016/j.biopsych.2006.09.023

Biomarkers and Imaging

10 BLOOD AND CSF BIOMARKERS IN NEUROPSYCHIATRY: THE MIND STUDY

Dr Dhamidhu Eratne · Neuropsychiatry Centre, Royal Melbourne Hospital; MiND study

> Neurofilament light works like a "CRP for the brain": raised in neurodegeneration, low in primary psychiatric disorders.

- **Diagnostic odyssey:** young-onset dementia takes 3.5–4 years and 5–6 specialists to diagnose; up to 50% with bvFTD are first diagnosed with a psychiatric disorder.
- **NfL:** CSF and plasma NfL distinguish dementia from psychiatric disorders with high accuracy, especially in younger people; baseline NfL predicts bvFTD phenocopies.
- **p-tau217:** a specific marker of Alzheimer pathology.
- **Clinical value:** positive results uncovered HD, FTD-MND, C9orf72 bvFTD and NMDA receptor encephalitis; normal results supported FND.
- **Caveats:** early Parkinson disease can have normal NfL; acute or severe psychiatric illness can raise it slightly.
- **MiND:** over 1,000 participants with serial samples; open to collaboration.

REFERENCES

158	MiND study.	themindstudy.org
159	Eratne D, Loi SM, Walia N, et al. A pilot study of the utility of cerebrospinal fluid neurofilament light chain in differentiating neurodegenerative from psychiatric disorders: a 'C-reactive protein' for psychiatrists and neurologists? *Aust N Z J Psychiatry*. 2020;54(1):57–67.	doi:10.1177/0004867419857811
160	Eratne D, Keem M, Lewis C, et al. Cerebrospinal fluid neurofilament light chain differentiates behavioural variant frontotemporal dementia progressors from non-progressors. *J Neurol Sci*. 2022;442:120439.	doi:10.1016/j.jns.2022.120439
—	National Dementia Diagnostics Laboratory, The Florey: NfL and p-tau217 testing.	florey.edu.au

11 MOLECULAR AND FUNCTIONAL NEUROIMAGING IN DEMENTIA

Dr Zubair Ali Khan · I-MED Radiology Network, Brisbane

> Start with MRI. FDG-PET shows the topography of dysfunction before atrophy; amyloid and tau PET show the biology.

- **FDG-PET patterns:** AD temporoparietal and posterior cingulate; logopenic PPA left temporoparietal; bvFTD frontal; semantic variant anterior temporal; DLB occipital with the cingulate island sign.
- **Alternatives:** SPECT and ASL perfusion are inferior to FDG-PET.
- **Atypical AD** (posterior cortical, logopenic, dysexecutive, behavioural, corticobasal) can mimic other conditions.
- **Amyloid PET:** a negative scan effectively excludes AD; used for anti-amyloid eligibility and monitoring. Tau PET is a later marker for staging.
- **LATE (TDP-43):** medial temporal, amyloid and tau negative, often co-exists with AD.
- **Lewy body disease:** DaT SPECT is unavailable in Australia; F-DOPA PET is the local alternative.
- **Practice:** mixed pathology is common; MDT review with good clinical information on the request is the gold standard.

REFERENCES

161	Atri A, Dickerson BC, Clevenger C, et al. Alzheimer's Association clinical practice guideline for the Diagnostic Evaluation, Testing, Counseling, and Disclosure of Suspected Alzheimer's Disease and Related Disorders (DETeCD-ADRD): executive summary of recommendations for specialty care. Alzheimers Dement. 2025;21(1):e14337.	doi:10.1002/alz.14337
162	Jack CR Jr, Andrews JS, Beach TG, et al. Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup. Alzheimers Dement. 2024;20(8):5143-69.	doi:10.1002/alz.13859
163	Minoshima S, Cross D, Thientunyakit T, Foster NL, Drzezga A. 18F-FDG PET imaging in neurodegenerative dementing disorders: insights into subtype classification, emerging disease categories, and mixed dementia with copathologies. J Nucl Med. 2022;63(Suppl 1):2S-12S.	doi:10.2967/jnumed.121.263194
164	Peet BT, Spina S, Mundada N, La Joie R. Neuroimaging in frontotemporal dementia: heterogeneity and relationships with underlying neuropathology. Neurotherapeutics. 2021;18(2):728-52.	doi:10.1007/s13311-021-01101-x
165	Jones D, Pelak V, Rogalski E. Atypical presentations of Alzheimer disease. Continuum (Minneap Minn). 2024;30(6):1614-41.	doi:10.1212/CON.0000000000001504
166	McKeith IG, Boeve BF, Dickson DW, et al. Diagnosis and management of dementia with Lewy bodies: fourth consensus report of the DLB Consortium. Neurology. 2017;89(1):88-100.	doi:10.1212/WNL.0000000000004058
167	Outeiro TF, Koss DJ, Erskine D, et al. Dementia with Lewy bodies: an update and outlook. Mol Neurodegener. 2019;14:5.	doi:10.1186/s13024-019-0306-8
168	Chételat G, Arbizu J, Barthel H, et al. Amyloid-PET and 18F-FDG-PET in the diagnostic investigation of Alzheimer's disease and other dementias. Lancet Neurol. 2020;19(11):951-62.	doi:10.1016/S1474-4422(20)30314-8
169	Society of Nuclear Medicine and Molecular Imaging. Quantitative FDG PET and MRI framework detects emerging form of dementia — LATE [news release].	snmmi.org
170	Rabinovici GD, Knopman DS, Arbizu J, et al. Updated appropriate use criteria for amyloid and tau PET: a report from the Alzheimer's Association and Society for Nuclear Medicine and Molecular Imaging Workgroup. Alzheimers Dement. 2025;21(1):e14338.	doi:10.1002/alz.14338

171	Sims JR, Zimmer JA, Evans CD, et al. Donanemab in early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. JAMA. 2023;330(6):512-27.	doi:10.1001/jama.2023.13239
172	Nelson PT, Dickson DW, Trojanowski JQ, et al. Limbic-predominant age-related TDP-43 encephalopathy (LATE): consensus working group report. *Brain*. 2019;142(6):1503–1527.	doi:10.1093/brain/awz099

Global Neuropsychiatry Group (GNG)

An international virtual learning community bridging neurology and psychiatry, with over 1,500 members. Monthly virtual meetings on the last Thursday, 11:30 am – 1 pm GMT.

Website: www.globalneuropsychiatry.org · **Join:** globalneuropsychiatry.org/become-member

Email: globalneuropsychiatryg@gmail.com

Educational summary for professional learning, prepared from a recording of the sessions. Slide content belongs to the presenters. Check references against the published versions before reuse.