Supplement 4. All included studies summarised

|  | Study | Country | Study design | Total sample size | Mean age (SD) | Male (%) | N catatonia and genetic abnormality (%) | Genetic abnormality |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 1 | Agabna et al., 2021 | UK | Prospective, single centre, case report | 1 | 14.0 | 0 (0) | 1 (100) | CACNA1D c.2305G>A, p.(Ala769Thr) variant |
| 2 | Alzahrani et al., 2023 | Saudi Arabia | Retrospective, single centre, case series | 3 | Not stated | 1 (33.3) | 1 (33.3) | SNV (CACNA1D NM\_001128840.3: c.2015C > T (p.Ser672Leu)) |
| 3 | Amott et al., 1972 | France | Retrospective, single centre, case series | 1 | 22.0 | 0 (0) | 1 (100) | Acute intermittent porphyria |
| 4 | Ayrolles et al., 2020 | France | Prospective, single centre, case report | 1 | 15.0 | 0 (0) | 1 (100) | c.529GNA nucleotide substitution, p. vAla177Thr, in RNASEH2B, |
| 5 | Barnardo et al., 2007 | UK | Retrospective, single centre, case report | 1 | 42 | 1 (100) | 1 (100) | Klinefelter syndrome |
| 6 | Bell et al., 2018 | UK | Prospective, single centre, cohort study | 102 | 26.1 (10.5) | 79 (77.5) | 15 (14.7) | Cornelia de Lange syndrome, Fragile X syndrome |
| 7 | Bengel et al., 1998 | Germany | Retrospective, multicentre, case-control study | 88 | 50.5 (15.7) | 20 (22.7) | Not stated | Group level association study of B33 CTG short tandem repeats |
| 8 | Boot et al., 2022 | Canada | Retrospective, single centre, cohort study | 92 | Not stated | Not stated | 16 (17.4) | DiGeorge syndrome |
| 9 | Breckpot et al., 2016 | Belgium | Retrospective, single centre, case series | 1 | 50.0 | 1 (100) | 1 (100) | 14q11.2dup |
| 10 | Brownstein et al., 2021 | USA | Prospective, single centre, case report | 1 | 18.0 | 1 (100) | 1 (100) | Stop-gain mutation in RCL1 (NM\_005772.4:c.370 C > T, p.Gln124Ter), |
| 11 | Butcher et al., 2018 | Canada | Retrospective, multicentre, case series | 18 | 27.4 (12.3) | 5 (27.8) | 18 (100) | DiGeorge syndrome |
| 12 | Cowan et al., 2022 | USA | Retrospective, single centre, case report | 1 | 58.0 | 0 (0) | 1 (100) | White-Sutton syndrome |
| 13 | Culleton et al., 2022 | USA | Retrospective, single centre, case report | 1 | 67.0 | 1 (100) | 1 (100) | C9orf72 repeat expansion |
| 14 | Deckert et al., 1992 | Germany | Retrospective, single centre, case report | 1 | 26.0 | 1 (100) | 1 (100) | 45X0/46XY mosaic |
| 15 | Diab et al., 2022 | France | Retrospective, single centre, case report | 1 | 18.0 | 1 (100) | 1 (100) | Baraitser- Winter Cerebrofrontofacial syndrome. Variant:c.224T>C; p.ILE75THR in the ACTB gene (Baraister-Winter cerebrofrontofacial syndrome) Karyotype : 46,XY |
| 16 | Diemer et al., 2018 | USA | Retrospective, single centre, case report | 1 | 17.0 | 1 (100) | 1 (100) | Down Syndrome / Trisomy 21 |
| 17 | Dille et al., 2023 | Belgium | Retrospective, single centre, case series | 24 | 25.5 (not stated) | 13 (54.2) | 4 (16.7) | Phelan-McDermid syndrome |
| 18 | Dormeuil et al., 2016 | France | Retrospective, single centre, case report | 1 | 37.0 | 0 (0) | 1 (100) | C9ORF72 - GGGGCC repeat expansion |
| 19 | Engel et al., 2023 | USA | Retrospective, single centre, case report | 1 | 15.0 | Not stated | 1 (100) | Pathogenic mutations in MMACHC gene |
| 20 | Faedda et al., 2015 | USA | Retrospective, single centre, case report | 1 | 15.0 | 0 (0) | 1 (100) | DiGeorge/22q11.2del  VCFS deletion of 22q11.2 spanning the typical approximately 3 megabase region that causes VCFS |
| 21 | Galosi et al., 2021 | Italy | Retrospective, single centre, case report | 1 | 19.0 | 0 (0) | 1 (100) | SHANK3 related disorder - not clearly Phelan-McDermid syndrome |
| 22 | Gawlik et al., 2016 | Germany | Prospective, single centre, case-control | 1653 | 41.0 (15.1) | 762 (46.1) | Not stated | SNP rs7292533 (C/T) at PANX2 |
| 23 | Ghaziuddin et al., 2015 | USA | Retrospective, multicentre, case series | 4 | 16.3 (1.1) | 2 (50) | 4 (100) | Down Syndrome / Trisomy 21 |
| 24 | Gobbi et al., 2008 | Italy | Retrospective, single centre, case report | 1 | 14.0 | 0 (0) | 1 (100) | Dravet's syndrome  Molecular analysis of the SCN1A gene - substitution of C to T at base posi- tion 1129 in the exon 8 codifying sequence, which caused the insertion of a stop codon at position 377 (R377X) |
| 25 | Grande et al., 2011 | Spain | Retrospective, single centre, case report | 1 | 80.0 | 0 (0) | 1 (100) | Creutzfeldt-Jakob Disease. Heterozygosity for methionine/valine at codon 129 PRNP gene. |
| 26 | Gross et al., 2001 | Germany | Retrospective, multicentre, case-control | 5 | Not stated | Not stated | 2 (40.0) | 22q13.33 loci variants examined in group level segregation analysis |
| 27 | Hauptman et al., 2021 | USA | Retrospective, single centre, case report | 1 | 16.0 | 0 (0) | 1 (100) | Down Syndrome Trisomy 21 |
| 28 | Hibbs et al., 2022 | USA | Retrospective, single centre, case report | 1 | 38.0 | 1 (100) | 1 (100) | Heterozygous de novo deletion of all five exons of the VAMP2 gene. |
| 29 | Holm et al., 2013 | USA | Retrospective, single centre, case report | 1 | 67.0 | 1 (100) | 1 (100) | C9ORF72 repeat expansion mutation |
| 30 | Jap et al., 2011 | USA | Retrospective, single centre, case series | 2 | 15.0 (2.0) | 0 (0) | 2 (100) | Down Syndrome / Trisomy 21 |
| 31 | Jungova et al., 2018 | Slovakia | Retrospective, single centre, case report | 1 | 30.0 | 0 (0) | 1 | Phelan-McDermid syndrome |
| 32 | Kaiser et al., 2000 | Germany | Prospective, multicentre, case-control | 1112 | 33.2 (10.3) | 738 (66.4) | Not stated | DRD4 48-bp variable number tandem repeats Catatonic patients (DSM-IV 295.2) more frequently carried the DRD4 D4.2 and D4.3 allele than did all other schizophrenic cases (P < 0.001; OR: 2.7; CI: 1.5-4.9) and controls (P < 0.004; OR: 2.3; CI: 1.3-4.2). |
| 33 | Katz et al., 2022 | USA | Retrospective, single centre, case report | 1 | 20.0 | 1 (100) | 1 (100) | Lafora disease |
| 34 | Kohlenberg et al., 2020 | USA | Retrospective, multicentre, cohort study | 38 | 24.7 (9.9) | 7 (18.4) | 20 (52.6) | Phelan-McDermid syndrome |
| 35 | Kury et al., 2003 | France | Retrospective, single centre, case-control | 6 | Not stated | Not stated | Not stated | Mutation screening for genetic variants of SLC30A4 in the coding region and putative promoter elements in chromosome 15q |
| 36 | Legrand et al., 2024 | France | Retrospective, single centre, case report | 1 | 17.0 | 1 (100) | 1 (100) | SNV\* (NM\_001371727.1: c.887 T > C) |
| 37 | Leroy et al., 2018 | France | Retrospective, single centre, case report | 1 | 4.0 | 1 (100) | 1 (100) | Mutation in the SCN2A gene, which encodes the voltage-gated sodium channel Nav1.2. |
| 38 | Lesch et al.,1994 | Germany | Retrospective, multicentre, cohort | 88 | 38.3 (10.9) | 37 (42.0) | 0 (0) | Group level association study of B37 CAG short tandem repeats |
| 39 | Loch et al., 2012 | Brazil | Retrospective, single centre, case series | 53 | Not stated | Not stated | Not stated | BDNF and HTR2C-rs6318 polymorphism associated with disorganised/catatonic factor |
| 40 | Maley et al., 2012 | USA | Retrospective, single centre, case report | 1 | 60.0 | 1 (100) | 1 (100) | Fahr’s disease |
| 41 | Manysheva et al., 2021 | Russia | Retrospective, single centre, case report | 1 | 72.0 | 0 (0) | 1 (100) | Heterozygous mutation in exon 8 of the WFS1 gene (chr4: 6303465G> A, rs150465110) |
| 42 | McKeane et al., 2004 | USA | Retrospective, single centre, case-control | 91 | Not stated | Not stated | Not stated | DLL4 polymorphism - The G/A SNP in exon 7 of DLL4 (nucleotide 69733 of GenBank file AC0200661.8) changes an arginine to a histadine., The C/T SNP in exon 8 of DLL4 (nucleotide 70091 of GenBank file AC0200661.8) does not change an amino acid.. |
| 43 | McKelvey et al., 2017 | USA | Retrospective, single centre, case report | 1 | 41.0 | 0 (0) | 1 (100) | Phelan-McDermid syndrome |
| 44 | McQuillin et al., 2002 | UK | Retrospective, single centre, case-control | 174 | Not stated | Not stated | Not stated | Association study of exon 11 of the WKL1 gene on chromosome 22 |
| 45 | Medjkane et al., 2021 | France | Retrospective, single centre, cohort study | 62 | Not stated | Not stated | 0 | Defined syndromes |
| 46 | Messias et al., 2013 | USA | Retrospective, single centre, case report | 1 | 38.0 | 0 (0) | 1 (100) | Phelan-McDermid syndrome |
| 47 | Meyer et al., 2002 | Germany | Retrospective, single centre, case-control | 32 | Not stated | Not stated | 9 (40.0) | Group level segregation analysis; Polymorphic markers around CHRNA7 on chromosome 15, Variants of the CX36 gene, Leu309Met mutation in WKL1, a positional candidate gene on chromosome 22q13.3 |
| 48 | Meyer et al., 2002 | Germany | Retrospective, multicentre, case-control | 5 | Not stated | Not stated | 2 | Group level segregation analysis; Variants of the CX36 gene. T to A 5'-regulatory region; nt 135853. TCC to TCT codon 196 (serine);nt588. GAG to GAA codon 296 (glutamic acid);nt888 |
| 49 | Meyer et al., 2001 | Germany | Retrospective, multicentre, case-control | Not stated | Not stated | Not stated | 7 | Group level segregation analysis; Leu309Met mutation in WKL1, a positional candidate gene on chromosome 22q13.3 |
| 50 | Miles et al., 2019 | USA | Prospective, single centre, case series | 7 | 23.7 (5.0) | 1 (14.3) | 7 (100) | Down’s syndrome/Trisomy 21 |
| 51 | Minamisawa et al., 2023 | Japan | Retrospective, single centre, case report | 1 | 12.0 | 0 (0) | 1 (100) | Mosaicism Down’s syndrome |
| 52 | Mizobuchi et al., 2023 | Japan | Retrospective, single centre, case report | 1 | 25.0 | 0 (0) | 1 (100) | Turner's syndrome |
| 53 | Montano et al., 2021 | Italy | Retrospective, single centre, case report | 1 | 41.0 | 0 (0) | 1 (100) | MELAS^ syndrome (m.3243A>G mtDNA) |
| 54 | Mormando et al., 2021 | USA | Retrospective, single centre, case report | 1 | 19.0 | 1 (100) | 1 (100) | Smith-Kingsmore Syndrome. Heterozygous mTOR variant of uncertain clinical significance [c.7628 (T>C); pIIe2543Thr (ATT>ACT) - exon 57. |
| 55 | Moyal et al., 2022 | France | Retrospective, multicentre, case series | 4 | 23.0 (6.5) | 2 (50) | 4 (100) | Pheland McDermid syndrome |
| 56 | Offenstadt., 1980 | France | Retrospective, single centre, case report | 1 | 34.0 | 1 (100) | 1 (100) | Hereditary coproporphyria |
| 57 | Ohmori et al., 2000 | Japan | Retrospective, single centre, case-control | 313 | 54.7 (9.5) | 152 (48.6) | Not stated | 2 x synapsin III gene polymorphisms (2631C/G and 2196G/A) - no association with catatonia |
| 58 | Oliveros et al., 2009 | Spain | Retrospective, single centre, case report | 1 | 43.0 | 1 (100) | 1 (100) | Fatal familial insomnia: D178N mutation coupled with MM homozygosis at codon 129. |
| 59 | Pan et al., 2019 | China | Prospective, single centre, cohort study | 132 | 29.0 (9.9) | 63 (47.7) | 1 (0.76) | Homozygous mutation of exon 4/5 c.18402 C>A |
| 60 | Pawar et al., 2013 | India | Retrospective, single centre, case report | 1 | 28.0 | 1 (100) | 1 (100) | Hallervorden-Spatz disease |
| 61 | Persico et al., 2022 | Italy | Retrospective, single centre, case report | 1 | 16.0 | 0 (0) | 1 (100) | Pheland McDermid syndrome chr. 22q13.33 microdeletion (51,123,520-51,218,980/hg19). Involving SHANK3, ACR, and RABL2B |
| 62 | Pollini et al., 2020 | Italy | Retrospective, single centre, case report | 1 | 17.0 | 1 (100) | 1 (100) | Rett syndrome MECP2 c.503G>A (p.Arg168Gln) |
| 63 | Poser et al., 2015 | USA | Retrospective, single centre, case report | 1 | 25.0 | 0 (0) | 1 (100) | Prader-Willi Syndrome |
| 64 | Raffin et al., 2018 | France | Retrospective, single centre, cohort stduy | 89 | Not stated | Not stated | 89 (100) | Various SNP† |
| 65 | Raj et al., 2014 | USA | Retrospective, single centre, case series | 2 | 27.0 (11.3) | 2 (100) | 2 (100) | Recessive G6PD deficiency |
| 66 | Rubie et al., 2003 | Germany | Prospective, multicentre, case-control | 410 | Not stated | 226 (55.1) | Not stated | Essentially run an association study screening cases and controls for genetic variants |
| 67 | Ryu et al., 2009 | South Korea | Retrospective, single centre, case report | 1 | 17.0 | 0 (0) | 1 (100) | MELAS  3243A>G mutation in mitochondrialDNA |
| 68 | Sachdev et al., 2002 | Australia | Retrospective, single centre, case report | 1 | 22.0 | 1 (100) | 1 (100) | Velo-cardio-facial syndrome 22q11 deletion |
| 69 | Sakhardande et al., 2021 | India | Retrospective, single centre, case series | 2 | 22.0 (1.0) | 1 (50) | 2 (100) | Homozygous pathogenic variant in the PLA2G6 (p.Arg741Gln) gene |
| 70 | Samanci et al., 2021 | Turkey | Retrospective, single centre, case series | 53 | 38.6 (8.7) | 32 (60.4) | 1 (1.9) | Wilson’s disease |
| 71 | Schanze et al., 2011 | Germany | Retrospective, multicentre, case-control | 510 | 41.0 (13.9) | 384 (75.3) | Not stated | Study looked for conserved and ultra-conserved non-genic sequence elements( CNGs, UCEs) ) at the Chromosome 15q15 Region (hypothesis driven) - no association found |
| 72 | Selch et al., 2007 | Germany | Retrospective, single centre, case-control | 602 | Not stated | Not stated | Not stated | Two single nucleotide polymorphisms (SNPs) located within the introns 6 (SNP1, rs2235349) and 7 (SNP2, rs2076137) of MLC1 |
| 73 | Serret et al., 2015 | France | Retrospective, multicentre, case series | 2 | 19.0 (2.0) | 1 (50) | 2 (100) | Phelan-McDermid syndrome |
| 74 | Sheikhi et al., 2015 | USA | Retrospective, single centre, case report | 1 | 61.0 | 0 (0) | 1 (100) | GGGGCC 9 open reading frame 72 (C9ORF72) alleles |
| 75 | Shetageriet al., 2011 | India | Retrospective, single centre, case report | 1 | 19.0 | 1 (100) | 1 (100) | Wilson’s disease |
| 76 | Shillington et al., 2021 | USA | Retrospective, single centre, case report | 1 | 21.0 | 1 (100) | 1 (100) | NLGN2-related neurodevelopmental disorder. Neuroligin 2: c.145G > A (NM\_020795.3), giving rise to a Gly49Arg (G49R) mutation |
| 77 | Silva et al., 2022 | Argentina | Retrospective, multicentre, case series | 2 | 55.9 (2.0) | 1 (50) | 1 (50) | Perry Syndrome |
| 78 | Slavnic et al., 2022 | USA | Retrospective, single centre, case report | 1 | 49.0 | 1 (100) | 1 (100) | Huntington/HD-like disorder. 52 repeats in the JPH3 gene (confirming Huntington disease-like type 2) |
| 79 | Stöber et al., 2000 | Germany | Retrospective, single centre, case serise | 135 | 51.1 (17.1) | 32 (23.7) | Not stated | Group level linkage study Looking for similar pedigrees between those with periodic catatonia at various chromosomal location (tested 6,11, 13, 15, 16, 20, 22) |
| 80 | Stöber et al., 2000 | Germany | Retrospective, single centre, case-control | 135 | 51.1 (17.1) | Not stated | Not stated | Group level linkage; CAG repeats on hKCNN3 gene |
| 81 | Stöber et al., 2002 | Germany | Retrospective, single centre, case-control | 48 | 48.4 (16.0) | 25 (52.1) | Not stated | Fine mapping of the chromosome 15q15-susceptibility region comprised 26 microsatellite markers between D15S165 (20.24 cM) and D15S117 (51.21 cM). |
| 82 | Stöber, 2013 | Germany | Retrospective, single centre, case-control | 929 | Not stated | Not stated | 344 (37.0) | Identification and validation of two new association loci for periodic catatonia on chromosomes 7 and 19 |
| 83 | Stöber et al., 2005 | Germany | Retrospective, multicentre, case-control | 225 | 44.6 (17.1) | 66 (29.3) | Not stated | Examined SNPs associated with genes KIAA0767 and KIAA1646 on chromosome 22 |
| 84 | Stowe et al., 2014 | Canada | Retrospective, single centre, case report | 1 | 21.0 | 1 (100) | 1 (100) | Duplication of chromosome 7q36.2 (193 kilobase duplicayion), overlapping the 5' end of DPP^ by 90 kilobases |
| 85 | Termini et al., 2023 | USA | Retrospective, single centre, case report | 1 | 14.0 | 0 (0) | 1 (100) | DiGeorge syndrome. 22q11 deletion |
| 86 | Torr and D’Abrera 2014 | Australia | Retrospective, single centre, case report | 1 | 23.0 | 0 (0) | 1 (100) | Down's syndrome (moasic type) |
| 87 | Toyoto et al., 2001 | Japan | Prospective, single centre, cohort study | 2 | 58.0 (17.0) | 0 (100) | 2 (100) | x chromosome mosaicism |
| 88 | Van Mierlo et al., 2023 | Netherlands | Retrospective, single centre, case report | 1 | 22.0 | 1 (100) | 1 (100) | Pathogenic frameshift variant of the HIVEP2 gene [HIVEP2 (NM\_006734.3): c.5863dup; p.(His1955fs) (GRCh37)] |
| 89 | Varshitha et al., 2019 | India | Retrospective, single centre, case report | 1 | 19.0 | 1 (100) | 1 | Wilson’s disease |
| 90 | Verhoeven et al., 2020 | Netherlands | Prospective, single centre, case series | 24 | 44.2 (19.4) | 2 (8.3) | 5 (20.8) | Phelan-McDermid syndrome |
| 91 | Vieira et al., 2021 | Brazil | Retrospective, single centre, case report | 1 | 23.0 | 0 (0) | 1 (100) | Pitt-Hopkins syndrome |
| 92 | Vithayathil et al., 2022 | USA | Retrospective, single centre, case report | 1 | Not stated | 1 (100) | 1 (100) | Heterozygote pathogenic CACNA1a variant (c.5126 T > C) (p.I1709T). |
| 93 | White et al., 2022 | Australia | Retrospective, single centre, case report | 1 | 26.0 | 1 (100) | 1 (100) | Fahr’s disease |
| 94 | Winarni et al., 2015 | USA | Retrospective, single centre, case report | 1 | 25.0 | 1 (100) | 1 (100) | Fragile X permutation. 72 CGG repeat in FMR1 |
| 95 | Yang et al., 2013 | China | Retrospective, single centre, case-control | 1025 | 27.3 (8.0) | 526 (51.3) | 18 (1.8) | SNP rs1344706 |
| 96 | Yang et al., 2023 | USA | Retrospective, single centre, case report | 1 | Not stated | 0 (0) | 1 (100) | SHINE syndrome |
| 97 | Ygland Rodstrom et al., 2021 | Sweden | Retrospective,  single centre, case report | 1 | 17.0 | 0 (0) | 1 (100) | Turner syndrome 46X, del (X)(p21) |
| 98 | Yokotsuka-Ishida., 2021 | Japan | Retrospective, single centre, case series | 241 | Not stated | Not stated | 2 | Marfan’s syndrome |
| 99 | Zinstok et al., 2020 | Netherlands | Retrospective, single centre, case report | 1 | 15.0 | 0 (0) | 1 (100) | DiGeorge syndrome |

\*Single nucleotide variant

^Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes

† Single nucleotide polymorphism