

Appendix 1: Substrates for fixed assays (Euroimmun AG, Lübeck, Germany)

1. Hippocampus rat
2. Cerebellum rat
3. Cerebellum monkey
4. Nerve monkey
5. Intestine monkey
6. Pancreas monkey
7. GAD65
8. NMDA-NR1
9. GABAB
10. AQP4
11. LGI1
12. CASPR2
13. GRM5=mGluR5
14. AMPA 1+2
15. Amphiphysin
16. CARPVIII
17. CV2
18. DNER
19. GAD67
20. GRM1 = mGluR1
21. Homer 3

22. Hu
23. ITPR1
24. Ma2
25. pre-GLRA1b (induced mixed substrate)
26. pre-GLRA1b (uninduced mixed substrate) (as negative control)
27. Recoverin
28. Rho GTPase activating protein 26 (ARHGAP26)
29. Ri
30. untransfected cells acetone fixed (as negative control)
31. untransfected cells formalin fixed (as negative control)
32. Yo
33. ZIC4
34. DPPX
35. IgLon5

<i>Medical category</i> (data available on n subjects)	<i>Antibody positive</i> fixed CBA (n=10)	<i>Antibody</i> negative fixed CBA	<i>p</i>	<i>Antibody</i> positive live CBA (n=13)	<i>Antibody</i> negative live CBA	<i>p</i>
<i>Neurological</i>	0 (0.0)	15 (7.0)	1.000	1 (7.7)	14 (6.7)	0.606
<i>Autoimmune</i>	0 (0.0)	4 (1.9)	1.000	1 (7.7)	3 (1.4)	0.214
<i>Allergic/atopic</i>	0 (0.0)	5 (2.3)	1.000	0 (0.0)	5 (2.4)	1.000
<i>Cancer</i>	0 (0.0)	2 (0.9)	1.000	0 (0.0)	2 (1.0)	1.000
<i>Surgery</i>	6 (60.0)	80 (37.4)	0.188	8 (61.5)	78 (37.0)	0.086
<i>Serious infection</i>	1 (10.0)	17 (8.0)	0.579	1 (7.7)	17 (8.1)	1.000
<i>Brain infection</i>	0 (0.0)	1 (0.5)	1.000	1 (7.7)	0 (0.0)	0.059
<i>Head injury</i>	0 (0.0)	2 (0.9)	1.000	0 (0.0)	2 (1.0)	1.000

Supplementary table 1: self-reported medical history by NMDAR antibody serostatus. Diagnoses were self-reported by subjects following one of four open-ended questions, with prompts to specify the relevant problems if answered affirmatively: 'Have you seen your GP or a specialist in the last 2 years?', 'Have you had any operations?', 'Have you ever been seriously ill, or did you have to spend time in hospital?', 'Do you suffer from any physical problem? e.g asthma, heart disease, thyroid problems, diabetes, epilepsy, etc'.

	<i>CHR-NT (n=205)</i>	<i>CHR-T (n=49)</i>	<i>p</i>
<i>Age</i>	22.74 ± 4.99	22.53 ± 5.11	0.796
<i>Sex [M: n (%)]</i>	107 (52.2)	29 (59.2)	0.427
<i>Ethnicity [n (%)]</i>	White 147 (72.1), Black 14 (6.9), Other 43 (21.1)	White 31 (63.3), Black 8 (16.3), Other 10 (20.4)	0.105
<i>Smoker?* [n (%)]</i>	113 (55.9)	20 (42.6)	0.097
<i>BMI</i>	24.33	24.22	0.910
<i>S100B (ug/L)</i>	0.04 ± 0.05	0.04 ± 0.05	0.826
<i>C-reactive protein (CRP) (mg/L)</i>	1.25 ± 1.11	1.15 ± 0.99	0.996

Supplementary table 2: demographic and basic clinical information in CHR subjects who did (CHR-T) and did not (CHR-NT) transition to psychosis

*data available for 249 of 254 subjects

Abbreviations: CHR: clinical high risk, CHR-T: clinical high risk – transition, CHR-NT: clinical high risk – nontransition, S100B: S100 calcium-binding protein B, CRP: C-reactive protein

	<i>CHR-NT (n=205)</i>	<i>CHR-T (n=49)</i>	<i>p</i>	<i>CHR-R (n=187)</i>	<i>CHR-NR (n=67)</i>	<i>p</i>
<i>Any antibody fixed assay [n (%)]</i>	19 (9.3)	2 (4.1)	0.385	14 (7.5)	7 (10.4)	0.450
<i>NMDAR antibody fixed assay [n (%)]</i>	10 (4.9)	1 (2.0)	0.696	9 (4.8)	2 (3.0)	0.733
<i>NMDAR IgG fixed assay [n (%)]</i>	1 (0.5)	0 (0.0)	1.000	1 (0.5)	0 (0.0)	1.000
<i>NMDAR IgA fixed assay [n (%)]</i>	6 (2.9)	0 (0.0)	0.599	4 (2.1)	2 (3.0)	0.656
<i>NMDAR IgM fixed assay [n (%)]</i>	3 (1.5)	1 (2.0)	0.578	4 (2.1)	0 (0.0)	0.576
<i>NMDAR IgG live assay [n (%)]</i>	10 (4.9)	3 (6.1)	0.720	12 (6.4)	1 (1.5)	0.194

Supplementary table 3: NSAb serostatus in CHR subjects who did (CHR-T) and did not (CHR-NT) transition to psychosis and subjects who remitted (CHR-R) and did not remit (CHR-NR) from the CHR state

Abbreviations: CHR: clinical high risk, CHR-T: clinical high risk – transition, CHR-NT: clinical high risk – nontransition, CHR-R: clinical high risk – remission, CHR-NR: clinical high risk – nonremission, NMDAR: N-methyl-d-aspartate receptor.

	<i>B</i>	<i>S.E.</i>	<i>Wald</i>	<i>Sig.</i>	<i>Exp(B)</i>
<i>Age</i>	-0.005	0.035	0.021	0.884	0.995
<i>Gender</i>	0.388	0.347	1.254	0.263	1.475
<i>White ethnicity</i>	-0.108	0.422	0.065	0.798	0.898
<i>Black ethnicity</i>	0.956	0.591	2.619	0.106	2.600
<i>NMDAR antibody serostatus (fixed assay)</i>	1.220	1.098	1.236	0.266	3.388

Supplementary table 4: Logistic regression illustrating association between NMDAR antibody serostatus (fixed assay) and transition to psychosis.

Abbreviations: NMDAR: N-methyl-d-aspartate receptor.

	<i>B</i>	<i>S.E.</i>	<i>Wald</i>	<i>Sig.</i>	<i>Exp(B)</i>
<i>Age</i>	-0.005	0.035	0.025	0.875	0.995
<i>Gender</i>	0.348	0.345	1.017	0.313	1.416
<i>White ethnicity</i>	-0.147	0.420	0.122	0.727	0.864
<i>Black ethnicity</i>	0.924	0.586	2.490	0.115	2.520
<i>NMDAR IgG serostatus (live assay)</i>	-0.194	0.717	0.074	0.786	0.823

Supplementary table 5: Logistic regression illustrating association between NMDAR IgG serostatus (live assay) and transition to psychosis.

Abbreviations: NMDAR: N-methyl-d-aspartate receptor.

	<i>B</i>	<i>S.E.</i>	<i>Wald</i>	<i>Sig.</i>	<i>Exp(B)</i>
<i>Gender</i>	0.010	0.029	0.131	0.718	1.010
<i>Age</i>	-0.078	0.293	0.071	0.791	0.925
<i>White ethnicity</i>	0.352	0.372	0.894	0.344	1.422
<i>Black ethnicity</i>	0.003	0.609	0.000	0.996	1.003
<i>NMDAR antibody serostatus (fixed assay)</i>	0.581	0.804	0.522	0.470	1.788

Supplementary table 6: Logistic regression illustrating association between NMDAR antibody serostatus (fixed assay) and remission from the CHR state.

Abbreviations: NMDAR: N-methyl-d-aspartate receptor.

	<i>B</i>	<i>S.E.</i>	<i>Wald</i>	<i>Sig.</i>	<i>Exp(B)</i>
<i>Gender</i>	0.014	0.029	0.243	0.622	1.014
<i>Age</i>	-0.127	0.295	0.187	0.665	0.880
<i>White ethnicity</i>	0.342	0.374	0.835	0.361	1.407
<i>Black ethnicity</i>	0.038	0.613	0.004	0.951	1.039
<i>NMDAR IgG serostatus (live assay)</i>	1.541	1.058	2.123	0.145	4.669

Supplementary table 7: Logistic regression illustrating association between NMDAR IgG serostatus (live assay) and remission from the CHR state.

Abbreviations: NMDAR: N-methyl-d-aspartate receptor.

Antibody Antibody F (serostatus) p (serostatus)
 negative positive

NMDAR ANTIBODY (IgG, IgA, IgM; FIXED ASSAY)

<i>Change in GAF symptoms (136:15)</i>	4.96 ± 14.62	4.87 ± 11.90	0.000	0.990
<i>Change in GAF disability (145:15)</i>	6.49 ± 16.21	2.33 ± 9.85	1.191	0.277

NMDAR ANTIBODY (IgG; LIVE ASSAY)

<i>Change in GAF symptoms (141:10)</i>	5.43 ± 13.97	-1.70 ± 18.29	2.520	0.115
<i>Change in GAF disability (150:10)</i>	6.77 ± 14.94	-4.00 ± 23.75	4.234	0.041

Supplementary table 8: Change in GAF scores by NMDAR antibody serostatus (descriptive means shown with F and p values from ANOVA)

Abbreviations: NMDAR: N-methyl-d-aspartate receptor, GAF: global assessment of functioning.

<i>Diagnosis (data available on n subjects)</i>	<i>Antibody positive fixed CBA (n=11)</i>	<i>Antibody negative fixed CBA</i>	<i>p</i>	<i>Antibody positive live CBA (n=13)</i>	<i>Antibody negative live CBA</i>	<i>p</i>
<i>Current depressive episode (247)</i>	5 (45.5)	77 (32.6)	0.513	9 (69.2)	73 (31.2)	0.012
<i>Current manic episode (239)</i>	0 (0.0)	1 (0.4)	1.000	0 (0.0)	1 (0.4)	1.000
<i>Major depressive disorder (232)</i>	5 (50.0)	105 (47.3)	1.000	9 (75.0)	101 (45.9)	0.073
<i>Dysthymic disorder</i>	0 (0.0)	16 (7.1)	1.000	1 (9.1)	15 (6.6)	0.544
<i>Bipolar disorder I (235)</i>	1 (9.1)	8 (3.6)	0.355	0 (0.0)	9 (4.0)	1.000
<i>Bipolar disorder II (233)</i>	0 (0.0)	9 (4.0)	1.000	0 (0.0)	9 (4.1)	1.000
<i>Panic disorder (237)</i>	2 (18.2)	57 (25.2)	0.736	5 (41.7)	54 (24.0)	0.179
<i>Social phobia (238)</i>	1 (10.0)	47 (20.6)	0.692	2 (16.7)	46 (20.4)	1.000
<i>Specific phobia (239)</i>	2 (18.2)	28 (12.3)	0.633	1 (8.3)	29 (12.8)	1.000
<i>Generalized anxiety disorder (235)</i>	1 (9.1)	25 (11.2)	1.000	2 (16.7)	25 (10.8)	0.628
<i>Obsessive-compulsive disorder (221)</i>	2 (20.0)	20 (9.5)	0.261	2 (18.2)	20 (9.5)	0.301
<i>Body dysmorphic disorder</i>						

<i>Post-traumatic stress disorder (237)</i>	0 (0.0)	27 (11.9)	0.619	2 (16.7)	25 (11.1)	0.633
<i>Somatisation disorder (234)</i>	0 (0.0)	3 (1.3)	1.000	0 (0.0)	3 (1.3)	1.000
<i>Adjustment disorder (234)</i>	0 (0.0)	1 (0.4)	1.000	0 (0.0)	1 (0.5)	1.000

Supplementary table 9: frequency of DSM-IV diagnoses according to NMDAR antibody serostatus. Diagnoses made using the Structured Clinical Interview for DSM-IV (SCID). Frequencies are given, numbers in brackets are the proportion of that serostatus group who met DSM-IV criteria for the specified diagnosis.

Abbreviations: CBA: cell-based assay, NMDAR: N-methyl-d-aspartate receptor.

	<i>Antibody negative (fixed CBA)</i>	<i>Antibody positive (fixed CBA)</i>	<i>Antibody negative (live CBA)</i>	<i>Antibody positive (live CBA)</i>
<i>AVLT IR total</i>	Rho = .019 p = .815 n = 157	Rho = -.661 p = .106 n = 7	Rho = .000 p = .996 n = 155	Rho = -.166 p = .669 n = 9
<i>WAIS estimated total IQ</i>	Rho = .043 p = .526 n = 219	Rho = .189 p = .626 n = 9	Rho = .040 p = .559 n = 216	Rho = -.004 p = .991 n = 12
<i>BPRS total</i>	Rho = -.130 p = .054 n = 219	Rho = -.202 p = .576 n = 10	Rho = -.166 p = .014 n = 217	Rho = .590 p = .043 n = 12
<i>CAARMS total</i>	Rho = -.205 p = .004 n = 194	Rho = .062 p = .885 n = 8	Rho = -.226 p = .002 n = 190	Rho = .550 p = .064 n = 12
<i>BPRS positive sx</i>	Rho = -.150 p = .026 n = 220	Rho = -.168 p = .643 n = 10	Rho = -.158 p = .020 n = 218	Rho = .160 p = .620 n = 12
<i>SANS</i>	Rho = -.103 p = .139 n = 206	Rho = .012 p = .977 n = 8	Rho = -.123 p = .081 n = 202	Rho = .620 p = .031 n = 12
<i>YMRS</i>	Rho = -.154 p = .022 n = 222	Rho = -.055 p = .879 n = 10	Rho = -.144 p = .032 n = 221	Rho = -.072 p = .834 n = 11

<i>MADRS</i>	Rho = -.177 p = .008 n = 226	Rho = -.126 p = .728 n = 10	Rho = -.186 p = .005 n = 224	Rho = .570 p = .053 n = 12
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Supplementary table 10: Associations between cognitive/symptom scores and S100B levels by NMDAR antibody serostatus

Abbreviations: S100B: S100 calcium-binding protein B, NMDAR: N-methyl-d-aspartate receptor, AVLT: Rey Auditory Verbal Learning Task, IR: immediate recall, CAARMS: Comprehensive Assessment of At-Risk Mental States, WAIS: Wechsler Adult Intelligence Scale III, BPRS: Brief Psychiatric Rating Scale, SANS: Scale for the Assessment of Negative Symptoms, YMRS: Young Mania Rating Scale, MADRS: Montgomery-Asberg Depression Rating Scale

	<i>Antibody positive</i>	<i>Antibody negative</i>	<i>F (serostatus)</i>	<i>p (serostatus)</i>
<i>Neuronal surface antibody (any antigen; IgG, IgA, IgM; FIXED ASSAY)</i>				
<i>Amygdala bilateral (11:148)</i>	3708.15 ± 412.53	3528.79 ± 407.31	3.961	0.048
<i>Hippocampus bilateral (11:148)</i>	8417.65 ± 828.97	8405.90 ± 780.99	0.083	0.773

Supplementary table 11: Limbic volumes (voxels) by neuronal antibody serostatus. Numbers in brackets under variable names are the number of seropositive subjects and seronegative subjects for whom data were available for that variable.