**Association between cognitive phenotype in unaffected siblings and prospective three and six year clinical outcome in their proband affected by psychosis: supplementary tables**

**Supplementary table 1. Baseline characteristics of patients with PANSS administration at all three measurements (complete data) vs patients with missing data at 3-year and/or 6-year follow-up (dropout).**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Complete data (n=376) | Dropout (n=253) |  |  |
|  | Mean (SD) | Mean (SD) | t  | P |
| Age | 27.0 (7.1) | 26.6 (7.2) | -0.59  | 0.552 |
| Education | 4.3 (1.9) | 3.8 (2.0) | -3.21 | 0.0014 |
| IQ, estimated | 96.6 (15.2) | 91.7 (15.7) | -3.84 | 0.00014 |
| PANSS- positive symptoms- negative symptoms- disorganization- excitement- emotional distress | 13.4 (6.5)14.3 (6.1)15.8 (5.6)12.5 (4.3)15.6 (5.6) | 15.1 (6.9)16.2 (6.7)17.8 (6.7)11.7 (3.7)16.4 (5.8) | 3.043.423.812.461.81 | 0.00250.000670.000160.0140.072 |
| Duration of illness | 5.0 (4.1) | 4.6 (4.0) | -1.34 | 0.18 |
| GAF, level of functioning  - symptoms - disability | 57.6 (16.7)57.3 (16.0) | 53.6 (15.2)51.4 (15.9) | -3.01-4.49 | 0.0027<0.0001 |
|  | N (%) | N (%) | χ2 | P |
| Sex (male) | 292 (78) | 199 (79) | 0.039 | 0.84 |
| Remission (PANSS, yes) | 186 (50) | 75 (32) | 17.47 | <0.0001 |
| Sibling Cognitive Subtype- Normal- Mixed- Impaired | 112 (28.5)135 (34.4)129 (37.1) | 72 (29.8)87 (35.9)94 (34.3) | 0.53 | 0.77 |
| Cannabis positive | 46 (13.0) | 45 (19.2) | 3.34 | 0.068 |
| Antipsychotic drug use | 347 (92.3) | 223 (88.1) | 3.06 | 0.22 |
| Ethnicity (white) | 338 (90.9) | 206 (84,0) | 5.87 | 0.015 |

**Supplementary table 2. AIC and Likelihood-ratio tests regarding model fit of linear mixed models with covariates and time \* sibling cognitive subtype interaction subsequently added.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Outcome |  | AIC | Log likelihood | Chi-sqrd (df) | P |
| Symptomatic remission |  | 1685.088 | -827.54 |  |  |
|  | with SIBSC | 1669.37 | -817.69 | 19.72 | <0.0001 |
|  | with interaction | 1672.979 | -815.49 | 4.39 (4) | 0.35 |
| PANSS Positive symptoms |  | 8232.898 | -4098.5 |  |  |
|  | with SIBSC | 8232.949 | -4097.0 | 3.06 (2) | 0.22 |
|  | with interaction | 8231.502 | -4094.3 | 5.44 (4) | 0.25 |
| PANSS Negative symptoms |  | 8171.114 |  |  |  |
|  | with SIBSC | 8171.041 | -3905.8 | 5.17 (2) | 0.18 |
|  | with interaction | 8169.668 | -4063.4 | 3.37 (4) | 0.27 |
| PANSS Disorganization |  | 7853.779 | -3907.7 |  |  |
|  | with SIBSC | 7847.755 | -3902.8 | 9.83 (2) | 0.007 |
|  | with interaction | 7845.321 | -3899.1 | 7.39 (4) | 0.11 |
| PANSS Excitement |  | 6935.603 | -3445.0 |  |  |
|  | with SIBSC | 6938.308 | -3443.6 | 2.87 (2) | 0.24 |
|  | with interaction | 6938.308 | -3439.6 | 7.88 (4) | 0.09 |
| PANSS Emotional distress |  | 7965.668 | -3963.7 |  |  |
|  | with SIBSC | 7968.982 | -3963.4 | 0.46 (2) | 0.79 |
|  | with interaction | 7967.109 | -3960.1 | 6.76 (4) | 0.15 |

**Supplementary table 3. Estimated Marginal Means of (generalized) linear mixed models regarding longitudinal associations between sibling cognitive subtype and patient symptom severity\*.**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Effects | Baseline |  |  | 3-year follow-up |  |  | 6-year follow-up |  |  |
|  | EMMean | SE | 95% CI | EMMean | SE | 95% CI | EMMean | SE | 95% CI |
| PANSS, remission (yes/no) \*\* |
| Normal sibling cognitive profile | 0.50 | 0.049 | 0.40-0.59 | 0.80 | 0.047 | 0.68-0.87 | 0.73 | 0.058 | 0.60-0.83 |
| Mixed sibling cognitive profile | 0.42 | 0.044 | 0.34-0.51 | 0.70 | 0.044 | 0.59-0.79 | 0.72 | 0.052 | 0.61-0.81 |
| Impaired sibling cognitive profile | 0.32 | 0.063 | 0.25-0.41 | 0.46 | 0.041 | 0.34-0.58 | 0.46 | 0.062 | 0.34-0.58 |
| PANSS, positive symptoms  |
| Normal sibling cognitive profile | 13.64 | 0.51 | 12.63-14.65 | 11.06 | 0.63 | 10.52-12.98 | 11.75 | 0.62 | 10.52-12.98 |
| Mixed sibling cognitive profile | 13.98 | 0.47 | 13.05-14.91 | 11.73 | 0.57 | 11.37-13.61 | 12.49 | 0.57 | 11.37-13.61 |
| Impaired sibling cognitive profile | 14.08 | 0.48 | 13.14-15.02 | 12.15 | 0.58 | 12.87-15.14 | 14.01 | 0.58 | 12.87-15.14 |
| PANSS, negative symptoms  |
| Normal sibling cognitive profile | 14.84 | 0.52 | 13.81-15.86 | 12.29 | 0.47 | 11.37-13.21 | 11.86 | 0.58 | 10.71-13.01 |
| Mixed sibling cognitive profile | 14.85 | 0.48 | 13.92-15.79 | 12.93 | 0.43 | 12.07-13.79 | 12.41 | 0.52 | 11.37-13.43 |
| Impaired sibling cognitive profile | 15.09 | 0.48 | 14.15-16.03 | 13.22 | 0.44 | 12.34-14.10 | 13.86 | 0.53 | 12.81-14.90 |
| PANSS, disorganization  |
| Normal sibling cognitive profile | 15.82 | 0.48 | 14.86-16.77 | 13.53 | 0.38 | 12.87-14.27 | 13.84 | 0.55 | 12.76-14.92 |
| Mixed sibling cognitive profile | 16.24 | 0.45 | 15.37-17.11 | 13.97 | 0.35 | 13.28-14.66 | 14.73 | 0.50 | 13.75-15.71 |
| Impaired sibling cognitive profile | 16.92 | 0.45 | 16.04-17.80 | 14.90 | 0.36 | 14.18-15.60 | 16.72 | 0.50 | 15.73-17.71 |
| PANSS, excitement (8-56) |
| Normal sibling cognitive profile | 11.80 | 0.30 | 11.20-12.40 | 10.43 | 0.27 | 9.90-10.96 | 10.48 | 0.34 | 9.81-11.14 |
| Mixed sibling cognitive profile | 12.12 | 0.28 | 11.58-12.68 | 10.60 | 0.25 | 10.10-11.09 | 11.16 | 0.31 | 10.55-11.76 |
| Impaired sibling cognitive profile | 11.81 | 0.28 | 11.26-12.37 | 10.94 | 0.26 | 10.44-11.45 | 11.77 | 0.31 | 11.15-12.37 |
| PANSS, emotional distress  |
| Normal sibling cognitive profile | 15.82 | 0.44 | 14.95-16.67 | 13.50 | 0.42 | 12.66-14.32 | 13.05 | 0.52 | 12.03-14.09 |
| Mixed sibling cognitive profile | 15.93 | 0.40 | 15.14-16.73 | 13.00 | 0.39 | 12.23-13.77 | 13.95 | 0.47 | 13.03-14.88 |
| Impaired sibling cognitive profile | 15.81 | 0.41 | 15.01-16.61 | 13.48 | 0.40 | 12.70-14.28 | 14.45 | 0.48 | 13.51-15.38 |

Abbreviations: PANSS: Positive and Negative Syndrome Scale. n = number of cases included in analysis. EMMeans: estimated marginal mean. \*results are averaged over the levels of gender, cannabis use, antipsychotics use and ethnicity with proportional weights. \*\*values back-transformed to probabilities for PANSS remission from the logit scale.