**Supplementary Table 1: Cognitive performances according to current tobacco smoking in a sample of n=1233 subjects with schizophrenia**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Current smoking** | | | | |  |  |
|  | **No** | **Yes** | **Univariate analysis** |  | **Multivariate analysis** | | |
|  | **(N=571, 46.3%)** | **(N=662, 53.7%)** | **Pvalue** |  | **Pvalue\*** | **Pvalue\*\*** | **Pvalue\*\*\*** |
| **Learning disorders, n (%)**  Do not know  No  Yes | 79 (41.9)  439 (36.5)  46 (31.3) | 81 (50.6)  503 (53.4)  69 (60.0) | 0.289 |  |  |  |  |
| **Current and premorbid intellectual ability** |  |  |  |  |  |  |  |
| **Premorbid Total IQ, Barona Index, mean (SD)** | **101.70 (9.4)** | **99.46 (8.3)** | **<0.001** |  | **<0.001** | **<0.001** | **<0.001** |
| **Full scale IQ (7 subtest short form)** | **85.85 (15.9)** | **83.99 (14.7)** | 0.084 |  | **0.018** | **0.028** | **0.027** |
| **Working memory** |  |  |  |  |  |  |  |
| Digit span (Standard score), mean (SD) | 8.43 (2.8) | 8.28 (2.7) | 0.347 |  |  |  |  |
| Arithmetic (Standard score), mean (SD) | 7.50(3.3) | 7.47 (3.0) | 0.871 |  |  |  |  |
| Working memory index (WMI), mean (SD) | 87.84 (15.5) | 87.02 (14.3) | 0.442 |  |  |  |  |
| **Learning abilities, episodic and semantic memory** |  |  |  |  |  |  |  |
| CVLT short delay free recall, mean (SD) | 9.40 (3.5) | 9.12 (3.3) | 0.182 |  | 0.355 | 0.347 | 0.335 |
| CVLT short delay cued recall, mean (SD) | 9.99 (3.3) | 9.88 (3.1) | 0.550 |  |  |  |  |
| CVLT long delay free recall, mean (SD) | 9.75 (3.5) | 9.65 (3.3) | 0.630 |  |  |  |  |
| CVLT long delay cued recall, mean (SD) | 10.02 (3.4) | 9.97 (3.2) | 0.817 |  |  |  |  |
| CVLT recognition, mean (SD) | 14.39 (2.8) | 14.34 (1.9) | 0.119 |  | 0.418 | 0.395 | 0.413 |
| CVLT perseverations | 5.66 (6.0) | 5.99 (5.9) | 0.316 |  |  |  |  |
| CVLT intrusions | 5.15 (6.0) | 5.49 (6.2) | 0.310 |  |  |  |  |
| CVLT word discrimination | 92.36 (10.3) | 91.99 (10.5) | 0.107 |  | 0.367 | 0.339 | 0.337 |
| **Information (Standard score), mean (SD)** | **9.35(3.2)** | **8.66 (3.0)** | **0.001** |  | **0.001** | **0.002** | **0.002** |
| **Executive functions and problem solving** |  |  |  |  |  |  |  |
| Trail making test B (errors), mean (SD) | 0.72 (1.5) | 0.68 (1.2) | 0.885 |  |  |  |  |
| Trail making test B, perseverations | 0.18 (0.6) | 0.17 (0.5) | 0.727 |  |  |  |  |
| B - A (Time), mean (SD) | 63.26 (50.1) | 62.39 (46.6) | 0.806 |  |  |  |  |
| B- A (errors), mean (SD) | 0.53 (1.6) | 0.51 (1.3) | 0.519 |  |  |  |  |
| **Matrix reasoning (Standard score), mean (SD)** | **8.50 (3.2)** | **8.07 (3.2)** | **0.024** |  | **0.019** | **0.027** | **0.027** |
| Similarities (standard score), mean (SD) | 9.90 (3.5) | 9.68 (3.5) | 0.297 |  |  |  |  |
| **Visual attention and speed of processing** |  |  |  |  |  |  |  |
| **TMT A (time), mean (SD)** | **42.74 (20.9)** | **39.52 (16.7)** | **0.003** |  | 0.188 | 0.233 | 0.233 |
| TMT A (errors), mean (SD) | 0.20 (0.5) | 0.19 (0.5) | 0.594 |  |  |  |  |
| **Digit symbol coding (Standard score), mean (SD)** | **6.40 (3.1)** | **5.89 (2.9)** | **0.011** |  | 0.224 | 0.244 | 0.235 |
| Picture completion test (standard score), mean (SD) | 7.49 (3.3) | 7.57 (3.1) | 0.713 |  |  |  |  |

**Note: Statistically significant in bold (P< .05). All cognitive tests are expressed with mean scores and standard deviation (SD); fNART= French National Adult Reading Test; IQ= Intellectual Quotient; CVLT= California Verbal Learning Test; CPT-IP= Continuous Performance Test-Identical Pairs; SSTICS= Subjective Scale to Investigate Cognition in Schizophrenia.**

**\*Chi square test for categorical variable and student test or Wilcox test for continuous variables.**

**\*Logistic regression was compute to assess the relation between cognitive performance and current tobacco consumption.**

\*For standard score of neuropsychological variables, we adjusted on chlorpromazine equivalents (CPZeqtot), Lifetime alcohol and cannabis abuse.

\*\*For standard score of neuropsychological variables, we adjusted on chlorpromazine equivalents (CPZeqtot), Lifetime alcohol and cannabis abuse, and benzodiazepine, and anticholinergic.

\*\*\*For standard score of neuropsychological variables, we adjusted on chlorpromazine equivalents (CPZeqtot), Lifetime alcohol and cannabis abuse, benzodiazepine, anticholinergic, and antidepressant.

\*For others scores of neuropsychological variables, we adjusted on chlorpromazine equivalents (CPZeqtot), alcohol, cannabis abuse, sex, age, mean years of education.

\*\*For others scores of neuropsychological variables, we adjusted on chlorpromazine equivalents (CPZeqtot), alcohol, cannabis abuse, sex, age, mean years of education, benzodiazepine and anticholinergic.

\*\*\*For others scores of neuropsychological variables, we adjusted on chlorpromazine equivalents (CPZeqtot), alcohol, cannabis abuse, sex, age, mean years of education, benzodiazepine, anticholinergic, and antidepressant.

**Supplementary Table 2: Sociodemographic and clinical two by two comparisons, according to smoking status in a sample of 1233 schizophrenia patients.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Smoking status** | | |  |  |  |  |
|  | **Never** | **Ex** | **Yes** |  |  | **P-value\*** |  |
|  | **N=454, 36.8%** | **N=117, 9.5%** | **N=662, 53.7%** |  | **N vs S** | **N vs E** | **E vs S** |
| **Sociodemographic characteristics** |  |  |  |  |  |  |  |
| **Sex, n (%)**  ***Female***  ***Male*** | **154 (33.9)**  **300 (66.1)** | **27 (23.1)**  **90 (76.9)** | **144 (21.8)**  **518 (78.2)** |  | **<0.001** | 0.065 | 0.843 |
| **Mean age (SD)** | **30.54 (10.3)** | **34.57 (8.9)** | **31.37 (8.8)** |  | 0.144 | **<0.001** | **0.003** |
| **Mean years of education (SD)** | **12.65 (2.6)** | **13.24 (2.5)** | **11.94 (2.3)** |  | **<0.001** | **0.020** | **<0.001** |
| **Income (>1000 euros)*,* n (%)** |  |  |  |  |  |  |  |
| ***No*** | **287 (80.4)** | **60 (61.9)** | **448 (82.8)** |  | 0.405 | **0.001** | **<0.001** |
| ***Yes*** | **70 (19.6)** | **37 (38.1)** | **93 (17.2)** |  |  |  |  |
| **Clinical Variables** |  |  |  |  |  |  |  |
| Age at onset, mean (SD) | 21.07 (7.0) | 22.14 (5.5) | 21.41 (5.7) |  | 1.000 | 1.000 | 1.000 |
| Age at first antipsychotic treatment, mean (SD) | **22.12 (6.6)** | **23.84 (6.7)** | **22.66 (6.0)** |  | 0.293 | 0.108 | 0.293 |
| Illness duration (y), mean (SD) | **9.46 (8.3)** | **12.38 (8.4)** | **9.86 (7.1)** |  | 0.417 | **0.004** | **0.007** |
| Diagnosis, n (%)  *Schizophrenia*  *Schizoaffective and schizophreniform disorder* | 361 (79.5)  93 (20.5) | 88 (75.2)  29 (24.8) | 492 (74.3)  170 (25.7) |  | 0.160 | 0.750 | 0.93 |
| Duration of untreated psychosis (y), mean (SD) | 1.35 (2.9) | 1.47 3.7 | 1.44 (3.0) |  | 1.000 | 1.000 | 1.000 |
| Global assessment of functioning (GAF) score, mean (SD) | 49.50 (13.8) | 51.79 (13.3) | 50.06 (12.9) |  | 0.946 | 0.946 | 0.946 |
| Psychotic symptomatology (PANSS total score), mean, (SD) | **70.51 (18.1)** | **63.95 (17.0)** | **68.37 (19.3)** |  | 0.082 | **0.008** | 0.082 |
| Positive symptoms (PANSS positive score), means (SD) | 14.47 (5.4) | 13.40 (5.3) | 14.69 (5.8) |  | 0.529 | 0.285 | 0.221 |
| Negative symptoms (PANSS negative score), mean (SD) | **20.78 (7.2)** | **18.23 (6.6)** | **19.28 (7.1)** |  | **0.006** | **0.006** | 0.148 |
| General psychopathology (PANSS general score), mean (SD) | **35.28 (9.9)** | **32.32 (8.9)** | **34.39 (10.0)** |  | 0.158 | **0.040** | 0.159 |
| Depressive symptoms (CDSS score), mean (SD) | 3.92 (4.1) | 3.29 (3.8) | 4.17 (4.2) |  | 0.584 | 0.584 | 0.321 |
| Manic symptoms (YMRS score), mean (SD) | 2.16 (3.6) | 1.85 (3.5) | 2.35 (4.1) |  | 1.000 | 1.000 | 1.000 |
| **Current alcohol use disorder, n (%)**  ***No***  ***Yes*** | **271 (92.5)**  **22 (7.5)** | **53 (69.7)**  **23 (30.3)** | **175 (47.2)**  **196 (52.8)** |  | **<0.001** | **<0.001** | **0.001** |
| **Lifetime alcohol use disorder, n (%)** |  |  |  |  |  |  |  |
| **No** | **116 (46.8)** | **17 (20.5)** | **48 (12.9)** |  | **<0.001** | **<0.001** | 0.110 |
| **Yes** | **132 (53.2)** | **66 (79.5)** | **325 (87.1)** |  |  |  |  |
| **Current substance use disorder, n (%)**  ***No***  ***Yes*** | **263 (88.9)**  **33 (11.1)** | **38 (46.9)**  **43 (53.1)** | **122 (27.3)**  **325 (72.7)** |  | **<0.001** | **<0.001** | **0.0006** |
| **Current cannabis use disorder, n (%)**  ***No***  ***Yes*** | **341 (97.7)**  **8 (2.3)** | **64 (64.0)**  **36 (36.0)** | **220 (44.0)**  **280 (56.0)** |  | **<0.001** | **<0.001** | **0.002** |
| **Lifetime cannabis use disorder*,* n (%)** |  |  |  |  |  |  |  |
| **No** | **230 (94.3)** | **30 (36.1)** | **76 (20.2)** |  | **<0.001** | **<0.001** | **0.003** |
| **Yes** | **14 (5.7)** | **53 (63.9)** | **301 (79.8)** |  |  |  |  |
| Number packs years), mean (SD) | - | 9.29 (8.9) | 13.35 (13.2) |  |  |  |  |
| Fagerstrom score), mean (SD) | - | - | 5.34 (2.3) |  |  |  |  |
| Severity dependence of nicotine, n (%)  *Fagerstrom score <7*  *Fagerstrom score >=7* | -  - | -  - | 400 (66.0)  206 (34.0)) |  |  |  |  |
| **Treatment** |  |  |  |  |  |  |  |
| CPZ equivalents, mean (SD) | **445.09 (403.3)** | **535.24 (560.5)** | **605.76 (654.0)** |  | **<0.001** | 0.804 | 0.804 |
| Adherence (MARS score), mean (SD) | **6.49 (2.2)** | **6.72 (2.1)** | **5.98 (2.2)** |  | **0.002** | 0.331 | **0.005** |
| Antidepressant, n (%)  *No*  *Yes* | 283 (79.1)  75 (20.9) | 71 (75.5)  23 (24.5) | 432 (79.9)  109 (20.1) |  | 1.000 | 1.000 | 1.000 |
| Benzodiazepine*,* n (%) |  |  |  |  |  |  |  |
| *No* | **287 (77.4)** | **69 (71.1)** | **374 (68.2)** |  | **0.009** | 0.503 | 0.655 |
| *Yes* | **84 (22.6)** | **28 (28.9)** | **174 (31.8)** |  |  |  |  |
| Anticholinergic corrector, n (%)  *No*  *Yes* | 297 (83.0)  61 (17.0) | 80 (85.1)  14 (14.9) | 462 (85.4)  79 (14.6) |  | 1.000 | 1.000 | 1.000 |

**Note:** Statistically significant in bold (P< .05). N= never smokers; E= Ex-smokers; S=Current smokers. SD=standard deviation; DUP= duration of untreated psychosis; GAF= Global assessment of Functioning; PANSS= Positive and Negative Syndrome Scale; CDSS= Calgary Depression rating Scale for Schizophrenia; YMRS= Young Mania rating Scale; CPZeq= chlorpromazine equivalent doses (CPZ100eq), calculated according to the minimum effective dose method (Leucht et al., 2015); MARS = Medication Adherence Rating Scale

**\* Multiple comparisons with correction of p-value by Holm method.**

**Supplementary Table 3: Socio-demographic and clinical factors associated to smoking status (according to 3 groups: never-smokers, ex-smokers, smokers)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Current smoking** | | |  |  |  |
|  | **No** | **Ex** | **Yes** | **Univariate analysis** |  | **Multivariate analysis** |
|  | **N=454, 36.8%** | **N=117, 9.5%** | **N=662, 53.7%** | **P-value** |  | **P-value\*** |
| **Sociodemographic characteristics** |  |  |  |  |  |  |
| **Sex, n (%)**  ***Female***  ***Male*** | **154 (47.7)**  **300 (33.0)** | **27 (8.3)**  **90 (9.9)** | **144 (44.3)**  **518 (57.0)** | **< 0.001** |  | 0.014 |
| **Mean age (SD)** | **30.54 (10.3)** | **34.57 (8.9)** | **31.37 (8.8)** | **<0.001** |  | 0.149 |
| **Mean years of education (SD)** | **12.65 (2.6)** | **13.24 (2.5)** | **11.94 (2.3)** | **<0.001** |  | 0.054 |
| **Income (>1000 euros)*,* n (%)** |  |  |  |  |  |  |
| ***No*** | **287 (36.1)** | **60 (7.5)** | **448 (56.4)** | **<0.001** |  | 0.142 |
| ***Yes*** | **70 (35.0)** | **37 (18.5)** | **93 (46.5)** |  |  |  |
| **Clinical Variables** |  |  |  |  |  |  |
| Age at onset, mean (SD) | 21.07 (7.0) | 22.14 (5.5) | 21.41 (5.7) | 0.269 |  |  |
| **Age at first antipsychotic treatment, mean (SD)** | **22.12 (6.6)** | **23.84 (6.7)** | **22.66 (6.0)** | **0.038** |  | 0.219 |
| **Illness duration (y), mean (SD)** | **9.46 (8.3)** | **12.38 (8.4)** | **9.86 (7.1)** | **<0.001** |  | 0.488 |
| Diagnosis, n (%)  *Schizophrenia*  *Schizoaffective and schizophreniform disorder* | 361 (79.5)  93 (20.5) | 88 (75.2)  29 (24.8) | 492 (74.3)  170 (25.7) | 0.128 |  | 0.318 |
| Duration of untreated psychosis (y), mean (SD) | 1.35 (2.9) | 1.47 3.7 | 1.44 (3.0) | 0.535 |  |  |
| Global assessment of functioning (GAF score), mean (SD) | 49.50 (13.8) | 51.79 (13.3) | 50.06 (12.9) | 0.266 |  |  |
| **Psychotic symptomatology (PANSS total score), mean, (SD)** | **70.51 (18.1)** | **63.95 (17.0)** | **68.37 (19.3)** | **0.003** |  | 0.654 |
| Positive symptoms (PANSS positive score), means (SD) | 14.47 (5.4) | 13.40 (5.3) | 14.69 (5.8) | 0.067 |  |  |
| Negative symptoms (PANSS negative score), mean (SD) | **20.78 (7.2)** | **18.23 (6.6)** | **19.28 (7.1)** | **<0.001** |  |  |
| General psychopathology (PANSS general score), mean (SD) | **35.28 (9.9)** | **32.32 (8.9)** | **34.39 (10.0)** | **0.015** |  |  |
| Depressive symptoms (CDSS score), mean (SD) | 3.92 (4.1) | 3.29 (3.8) | 4.17 (4.2) | 0.141 |  | 0.461 |
| Manic symptoms (YMRS score), mean (SD) | 2.16 (3.6) | 1.85 (3.5) | 2.35 (4.1) | 0.307 |  |  |
| **Current alcohol use disorder, n (%)**  ***No***  ***Yes*** | **271 (92.5)**  **22 (7.5)** | **53 (69.7)**  **23 (30.3)** | **175 (47.2)**  **196 (52.8)** | **< 0.001** |  |  |
| **Lifetime alcohol use disorder, n (%)** |  |  |  |  |  |  |
| **No** | **116 (46.8)** | **17 (20.5)** | **48 (12.9)** | **< 0.001** |  | **0.021** |
| **Yes** | **132 (53.2)** | **66 (79.5)** | **325 (87.1)** |  |  |  |
| **Current substance use disorder, n (%)**  ***No***  ***Yes*** | **263 (88.9)**  **33 (11.1)** | **38 (46.9)**  **43 (53.1)** | **122 (27.3)**  **325 (72.7)** | **< 0.001** |  |  |
| **Current cannabis use disorder, n (%)**  ***No***  ***Yes*** | **341 (97.7)**  **8 (2.3)** | **64 (64.0)**  **36 (36.0)** | **220 (44.0)**  **280 (56.0)** | **< 0.001** |  |  |
| **Lifetime cannabis use disorder*,* n (%)** |  |  |  |  |  |  |
| **No** | **230 (94.3)** | **30 (36.1)** | **76 (20.2)** | **< 0.001** |  | **<0.001** |
| **Yes** | **14 (5.7)** | **53 (63.9)** | **301 (79.8)** |  |  |  |
| **Age of first cigarette** | **-** | **16.43 (4.1)** | **15.50 (4.1)** | **0.015** |  |  |
| Age at onset of daily tobacco consumption | - | 18.19 (5.2) | 17.46 (4.5) | 0.195 |  |  |
| **Number packs years** | **-** | **9.29 (8.9)** | **13.35 (13.2)** | **<0.001** |  |  |
| Fagerstrom score | - | - | 5.34 (2.3) |  |  |  |
| Severity of the nicotine dependence  Fagerstrom score <7  Fagerstrom score >=7 | -  - | -  - | 400 (66.0)  206 (34.0) |  |  |  |
| **Treatment** |  |  |  |  |  |  |
| **CPZ equivalents, mg (SD)** | **445.09 (403.3)** | **535.24 (560.5)** | **605.76 (654.0)** | **<0.001** |  | **0.003** |
| **Adherence (MARS score), mean (SD)** | **6.49 (2.2)** | **6.72 (2.1)** | **5.98 (2.2)** | **<0.001** |  | 0.134 |
| Antidepressant, n (%)  *No*  *Yes* | 283 (79.1)  75 (20.9) | 71 (75.5)  23 (24.5) | 432 (79.9)  109 (20.1) | 0.634 |  |  |
| **Benzodiazepine*,* n (%)** |  |  |  |  |  |  |
| ***No*** | **287 (77.4)** | **69 (71.1)** | **374 (68.2)** | **0.011** |  | 0.269 |
| ***Yes*** | **84 (22.6)** | **28 (28.9)** | **174 (31.8)** |  |  |  |
| Presence at time of evaluation of an anticholinergic corrector  *No*  *Yes* | 297 (83.0)  61 (17.0) | 80 (85.1)  14 (14.9) | 462 (85.4)  79 (14.6) | 0.604 |  |  |

**Note:** Statistically significant in bold (P< .05). SD, standard deviation; DUP= duration of untreated psychosis; GAF, Global assessment of Functioning; PANSS, Positive and Negative Syndrome Scale; CDSS, Calgary Depression rating Scale for Schizophrenia; YMRS, Young Mania rating Scale; CPZeq: chlorpromazine equivalent doses (CPZ100eq), calculated according to the minimum effective dose method (Leucht et al., 2015); MARS: Medication Adherence Rating Scale.

**\*Test chi2 or fisher test for categorical variables, and Anova or Kruskal Wallis test for the continuous variables.**

**\*Multinomial regression analysis adjusted on Sex, Age, Mean years of education, income, Age at first antipsychotic treatment, Illness duration, Diagnosis, Positive and Negative Syndrome Scale, Calgary depression rating scale, Lifetime alcohol consumption disorder, Lifetime cannabis consumption disorder, Chlorpromazine equivalent, Adherence rating scale, and Benzodiazepine.**