**SUPPLEMENTARY DATA**

**Supplementary Table 1.** Dose of psychopharmacological treatment received by patients included in the study sample (in monotherapy or combination therapy) and differences between study groups†.

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| --- | --- | --- | --- | --- |
| **Psychopharmacological treatment**‡ | **NON-RESISTANCE**  **(N=125)** | **MODERATE-SEVERE RESISTANCE**  **(N=104)** | **t-test (df)** | **p value** |
| Fluoxetine | 40 (14.77) | 60 (23.09) | -2.05 (14) | 0.060 |
| Paroxetine | 30 (14.14) | 30 (-) | 0.00 (1) | 1.000 |
| Sertraline | 142.86 (60.75) | 150 (70.71) | -0.14 (7) | 0.890 |
| Citalopram | 28.33 (7.53) | 25 (7.07) | 0.55 (6) | 0.604 |
| Escitalopram | 15 (5.00) | 22.50 (8.80) | -1.68 (9) | 0.127 |
| **Mirtazapine** | 24.75 (7.34) | 34.41 (18.20) | -2.18 (35) | **0.036** |
| Trazodone | 100 (27.39) | 129.41 (56.07) | -1.98 (36) | 0.060 |
| Mianserin | 12.50 (5.00) | 16.67 (11.55) | -0.66 (5) | 0.538 |
| **Venlafaxine** | 222.55 (78.42) | 263.89 (70.14) | -2.26 (71) | **0.027** |
| **Desvenlafaxine** | 95 (43.78) | 176.79 (76.25) | -3.32 (22) | **0.003** |
| **Duloxetine** | 93 (32.14) | 118.89 (36.73) | -2.52 (45) | **0.015** |
| Clomipramine | 103.12 (56.25) | 138.75 (58.76) | -1.11 (22) | 0.278 |
| Amitriptyline | 25 (-) | 50 (-) | - | - |
| Bupropion | 187.50 (75.00) | 257.14 (123.81) | -1.06 (16) | 0.306 |
| Agomelatine | - | 41.67 (14.43) | - | - |
| Vortioxetine | 11.67 (4.33) | 12.50 (4.63) | -0.383 (15) | 0.707 |
| Tranylcypromine | - | 60.00 | - | - |
| Tianeptine | - | 37.50 | - | - |
| Lithium | 800 (0.00) | 800.00 (200.00) | 0.00 (7) | 1.000 |
| Lamotrigine | 200 (0.00) | 240 (127.06) | -0.31 (14) | 0.765 |
| Quetiapine | 58.33 (34.16) | 122.83 (78.67) | -1.94 (27) | 0.063 |
| Olanzapine | 2.5 | 6.39 (4.53) | -0.82 (8) | 0.439 |
| Aripiprazole | 5 (0.00) | 8.33 (6.06) | -0.74 (6) | 0.488 |
| Risperidone | 2 (0.00) | 1 (0.71) | 1.15 (1) | 0.454 |
| Paliperidone | - | 4.50 (2.12) | - | - |
| Lorazepam | 2.53 (3.62) | 3.58 (3.52) | -0.86 (33) | 0.398 |
| Diazepam | 7.44 (4.75) | 14.10 (8.82) | -2.03 (18) | 0.058 |
| Lormetazepam | 1.70 (0.67) | 2.82 (2.52) | -1.36 (19) | 0.191 |
| Clonazepam | 1.36 (0.63) | 2.3 (1.53) | -1.75 (15) | 0.104 |
| **Clorazepate** | 5.00 (0.00) | 12.5 (3.54) | -4.03 (3) | **0.028** |
| **Alprazolam** | 0.97 (0.54) | 2.7 (1.96) | -1.94 (12) | **0.025** |

†7 patients in the non-resistance group and 1 patient in the resistance-group were not receiving pharmacological treatment during the study. One missing exists in each group for this variable. ‡doses reported as mean (SD), in mg/d.

**Supplementary Table 2.** Differences in objective cognition between resistant and non-resistant MDD groups after the exclusion of patients receiving antipsychotics, benzodiazepines, lithium, or anticonvulsants and covarying for the severity of depressive symptoms.

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| --- | --- | --- | --- | --- |
| **VARIABLES**† | **NON-RESISTANCE**  **(MSM = 3-6)** | **MODERATE-SEVERE RESISTANCE**  **(MSM = 7-15)** | **Statistic**  **F (df)** | **p-value**  **(2-tailed)** |
| *Final sample after exclusion of patients under* ***AP*** (110 NR/63 R) | | | | |
| **Verbal Memory** | -0.599 | -1.152 | 9.324 (1) | 0.003 |
| **Attention/Working Memory** | -0.629 | -0.790 | 0.375 (1) | 0.541 |
| **Executive functioning** | -0.592 | -0.863 | 1.362 (1) | 0.245 |
| **Processing speed** | -0.270 | -0.623 | 0.899 (1) | 0.345 |
| *Final sample after exclusion of patients under* ***BZD*** (72NR/39R) | | | | |
| **Verbal Memory** | -0.438 | -1.204 | 12.573 (1) | 0.001 |
| **Attention/Working Memory** | -0.502 | -0.980 | 6.842 (1) | 0.010 |
| **Executive functioning** | -0.474 | -1.004 | 7.057 (1) | 0.009 |
| **Processing speed** | -0.138 | -0.780 | 5.257 (1) | 0.024 |
| *Final sample after exclusion of patients under* ***lithium***(123NR/96R) | | | | |
| **Verbal Memory** | -0.619 | -1.154 | 14.052 (1) | <0.001 |
| **Attention/Working Memory** | -0.644 | -0.898 | 2.696 (1) | 0.102 |
| **Executive functioning** | -0.605 | -0.908 | 4.14 (1) | 0.043 |
| **Processing speed** | -0.328 | -0.702 | 2.976 (1) | 0.086 |
| *Final sample after exclusion of patients under* ***anticonvulsants*** (109NR/76R) | | | | |
| **Verbal Memory** | -0.607 | -1.228 | 18.330 (1) | <0.001 |
| **Attention/Working Memory** | -0.617 | -0.967 | 6.096 (1) | 0.014 |
| **Executive functioning** | -0.580 | -0.935 | 5.873 (1) | 0.016 |
| **Processing speed** | -0.282 | -0.663 | 3.382 (1) | 0.068 |

MDD: Major Depressive Disorder, MSM: Maudsley Staging Model, NR: non-resistant, R: resistant, AP: antipsychotics, BZD: benzodiazepines

†missing data exist for verbal memory, attention/working memory, processing speed and executive function in 8, 1, 2 and 2 subjects respectively.

**Supplementary Table 3.** Differences in subjective cognition between resistant and non-resistant MDD groups after the exclusion of patients receiving antipsychotics, benzodiazepines, lithium, or anticonvulsants and covarying for the severity of depressive symptoms.

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| --- | --- | --- | --- | --- |
| **VARIABLES** | **NON-RESISTANCE**  **(MSM = 3-6)** | **MODERATE-SEVERE RESISTANCE**  **(MSM = 7-15)** | **Statistic**  **F (df)** | **p-value**  **(2-tailed)** |
| *Final sample after exclusion of patients under* ***AP*** (110 NR/63 R) | | | | |
| **PDQ-20 attention** | 9.67 | 11.19 | 0.035 (1) | 0.852 |
| **PDQ-20 memory** | 13.71 | 16.51 | 0.030 (1) | 0.862 |
| **PDQ-20 executive functions** | 9.11 | 10.78 | 0.004 (1) | 0.951 |
| **PDQ-20 Total** | 32.49 | 38.48 | 0.004 (1) | 0.949 |
| *Final sample after exclusion of patients under* ***BZD*** (72NR/39R) | | | | |
| **PDQ-20 attention** | 9.24 | 11.26 | 0.293 (1) | 0.590 |
| **PDQ-20 memory** | 12.94 | 16.31 | 0.325 (1) | 0.570 |
| **PDQ-20 executive functions** | 8.65 | 10.44 | 0.029 (1) | 0.865 |
| **PDQ-20 Total** | 30.83 | 38.00 | 0.256 (1) | 0.614 |
| *Final sample after exclusion of patients under* ***lithium***(123NR/96R) | | | | |
| **PDQ-20 attention** | 10.11 | 11.07 | 0.444 (1) | 0.506 |
| **PDQ-20 memory** | 14.22 | 16.34 | 0.003 (1) | 0.955 |
| **PDQ-20 executive functions** | 9.48 | 10.47 | 0.284 (1) | 0.595 |
| **PDQ-20 Total** | 33.81 | 37.89 | 0.104 (1) | 0.748 |
| *Final sample after exclusion of patients under* ***anticonvulsants*** (109NR/76R) | | | | |
| **PDQ-20 attention** | 10.31 | 11.03 | 0.322 (1) | 0.571 |
| **PDQ-20 memory** | 14.39 | 15.66 | 0.123 (1) | 0.726 |
| **PDQ-20 executive functions** | 9.44 | 10.58 | 0.009 (1) | 0.925 |
| **PDQ-20 Total** | 34.15 | 37.26 | 0.102 (1) | 0.750 |

MDD: Major Depressive Disorder, MSM: Maudsley Staging Model, NR: non-resistant, R: resistant, AP: antipsychotics, BZD: benzodiazepines, PDQ: Perceived Deficit Questionnaire

**Supplementary Table 4.** Results of the logistic regression analysis after the exclusion of patients under antipsychotic and or anticonvulsant treatment.

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|  | **B** | **SE** | **Sig.** | **Exp (B)** | **95% C.I. for Exp (B)**  **Lower-Upper** |
| **Verbal Memory** | -0.786 | 0.256 | 0.002 | 2.193† | 1.328\*-3.623† |
| **Severity** | 0.237 | 0.161 | 0.142 | 1.268 | 0.924-1.740 |
| **Constant** | -2.015 | 0.455 | <0.001 | 0.133 |  |

†Those values represent 1/0.456 and CI (1/0.276-1/0.753)