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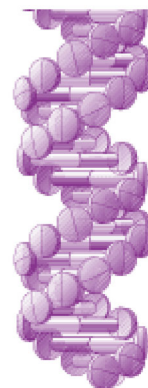
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Pharmacogenomics



Research Article

No impact of eight *NTRK2* genetic polymorphisms on 6-month antidepressant efficacy in depressed patients

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Aim: *NTRK2* is the main receptor of the brain derived neurotrophic factor, which is involved in antidepressant efficacy. We assessed the impact of eight *NTRK2* SNPs pertaining to response and remission after antidepressant treatment in depressed patients. **Patients & methods:** In a naturalistic study, 569 patients with a major depressive episode requiring a new antidepressant treatment were genotyped for eight *NTRK2* SNPs (rs1187352, rs1439050, rs1778933, rs2289656, rs2289657, rs2289658, rs3824519, rs56142442) and prospectively assessed for response and remission after 6 months of treatment. **Results:** No association was shown between the *NTRK2* SNPs and response/remission. **Conclusion:** There is no benefit to assess these eight *TRKB* SNPs to predict response/remission after antidepressant treatment in depressed patients.

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Keywords: antidepressant • genetic polymorphism • major depressive disorder • major depressive episode • NTRK2 • pharmacogenetics • remission • response • TRKB

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Half of the patients with major depressive episodes (MDE) in major depressive disorder (MDD) do not respond to antidepressant treatment, while two-thirds do not achieve remission after 3 months [1]. Identifying biomarkers at baseline for future response and remission after administering antidepressant medication, could improve the efficacy of treatment for depressed patients [2]. Among these potential biomarkers, pharmacogenetic biomarkers are particularly interesting in a personalized medicine approach [3].

NTRK2 is the main receptor of BDNF, which is involved in antidepressant efficacy [4,5]. Its activation by BDNF increases neuronal survival, plasticity, neurogenesis and synaptic connectivity [6]. In preclinical studies, NTRK2 is indirectly activated by antidepressants and some NTRK2 agonists have antidepressant effects [4]. Moreover, the lack of this receptor in hippocampal cells decreases antidepressant efficacy [6,7]. In human studies some *NTRK2* genetic polymorphisms are associated with an increased risk of depression [8–10]. And the impact of some *NTRK2* SNPs on response or remission, after antidepressant treatment, has been assessed in depressed patients [11–14] (Table 1). In particular, Dong *et al.* [11] showed an association between rs2289656, rs2289657, rs2289658 and rs56142442 and the 8-week response and remission rates after antidepressant treatment in a sample of 272 Mexican–American depressed patients. However, due to the high number of genetic variants assessed in this study and the sample size, these *NTRK2* SNPs did not reach statistical significance after correction for multiple tests. Furthermore, in this study, the allelic frequencies of these SNPs differed regarding ethnicity: the minor allelic frequencies of rs2289656, rs2289657 and rs2289658 in Mexican–Americans versus Caucasians were respectively: 9 versus 17%, 10 versus 6% and 15.6 versus 4% [15].

Hence, our primary aim was to assess the association of these *NTRK2* SNPs with response and remission after antidepressant treatment in a larger population of depressed patients.

Our second aim was to assess the same association in the homogeneous ethnic sample of Caucasian patients.

Patients & methods

Design

In a 6-month prospective, real-world treatment study in psychiatric settings [16], patients with a current MDEs were assessed at the beginning of antidepressant treatment, as well as 1, 3 and 6 months later. Clinical assessments were performed blind to genotyping results. This study was registered by the French National Agency for Medicine and Health Products Safety and the Commission Nationale de l'Informatique et des Libertés, was approved by the Ethics Committee of Paris-Boulogne, France, and conformed to international ethical standards (ClinicalTrials.gov identifier: NCT00526383) [16].

Patients

Five hundred and sixty-nine in- or out-patients, aged 18–65 years, with a diagnosis of MDE in the context of MDD based on the Mini International Neuropsychiatric Interview, were included in these psychiatric settings [16]. Five hundred and twenty one (92%) patients were

Caucasians, in other words, had two Caucasian parents. A minimum depression score of 18 on the 17-item Hamilton Depression Rating Scale (HAMD) was required to ensure that patients qualified for MDE. To be included, patients required the initiation of a new antidepressant treatment. This clinical decision, the drug and its dose, were left to the treating psychiatrist, using 'real world' treatment options. Patients with DSM-IVTR bipolar disorders, psychotic disorders, current substance abuse or dependence, pregnancy, breast feeding, organic brain syndromes or unstable medical conditions were excluded. Patients receiving antipsychotics or mood stabilizers before inclusion and/or for 4 months or more during the last year were excluded. All patients signed a written informed consent for study participation and for genetic analyses.

SNP selection & genotyping methods

Eight SNPs of *NTRK2* were selected. Four were based on the results of Dong *et al.* [11], who showed their possible association with antidepressant efficacy in a sample of Mexican-American depressed patients: rs2289656, rs2289657, rs2289658 and rs56142442. And the other four were based on the results of the study of Perroud *et al.* [17], who evidenced their possible association with the outcome of suicidal ideation in depressed Caucasian patients treated with antidepressants: rs1187352, rs1439050, rs1778933 and rs3824519. These candidate SNPs were located on the *NTRK2* gene (*NTRK2* gene location: 87283417–87641985 in GRCh37) (Table 1). To the best of our knowledge, there was no known functional variant in *NTRK2*.

Genomic DNA was extracted from circulating blood leukocytes by Gentra[®] Puregene[®] Blood Kits, following the manufacturer's protocol (Qiagen, MN, USA) and stored at -20°C. The genotyping was performed by the IntegraGen company (Evry, France) using the Fluidigm[®] BioMark[™] HD system (Fluidigm Corporation, CA, USA). Some genetic results were not available depending on each SNP, ranging from 16 to 37 patients, due to a lack of amplification and low call rates (Table 1). All SNPs had a call rate >97%, except rs2289658 (96.5%) and rs1439050 (94%). To identify linkage disequilibrium between SNPs, a haplotype analysis was performed with THESIAS 3.1 [18]. Moderate linkage disequilibrium was defined by D' criteria absolute value between 0.50 and 0.75. High linkage disequilibrium was defined by D' criteria absolute value between 0.75 and 1.

Antidepressants

An antidepressant monotherapy was chosen by the psychiatrist, using 'real world' treatment options. The antidepressant medication belonged to one of four antidepressant classes (SSRI, SNRI, tricyclics and others). SSRI (n = 220) and SNRI (n = 220) were the two most prescribed antidepressant drug classes.

Concomitant treatments

Antipsychotics, mood stabilizers and stimulants were not permitted during the study. Benzodiazepines, at the minimum effective dose and for the minimum time period, were allowed as well as psychotherapies.

Antidepressant efficacy

The HAMD scale [19] was rated by trained clinicians at baseline, followed by 1 month, 3 months and 6 months after the beginning of antidepressant treatment.

HAMD total scores, response and remission rates were assessed after 1, 3 and 6 months of antidepressant treatment. The response rate was defined by a decrease of the HAMD total score of at least 50% from baseline to follow-up [20]. The remission rate was defined by a HAMD total score of 7 or less at follow-up [20,21] and was the primary end point.

Statistical analysis

Statistical analyses were performed with the R 3.2.2 software.

After testing the Hardy–Weinberg equilibrium using χ^2 tests, each SNP was studied in three groups (two homozygote and one heterozygote groups) and in two groups (the heterozygote group being associated with one of the homozygote groups to test dominant and recessive models).

Both ‘intent to treat’ (main analyses) and ‘last observation carried forward’ methods were applied. All the time points were analyzed (baseline, 1, 3 and 6 months).

Due to the number of SNPs studied and to take into account the increased risk of false-positive results due to the high number of comparisons. Bonferroni's corrections were applied, the threshold for significance being $0.05/8 = 0.00625$. For the primary objective, intergenotypic comparisons were computed using χ^2 for response and remission rates and ANOVAs for repeated measures for the HAMD total score. If the number of patients in any group was below 20, nonparametric Kruskal–Wallis and Wilcoxon tests were computed. Multivariate analyses (i.e., logistic regressions for response and remission and linear regressions for HAMD total score) were performed to control for potential confounders among demographic and clinical variables. Indeed, covariables of the multivariate models were selected on the basis of a significant association ($p < 0.05$) with at least one SNP at baseline. For the secondary objective, the primary analysis was performed in a subgroup of Caucasian patients.

The *a priori* power estimation, which took into account the estimated attrition rate (40% at 3 months and 60% at 6 months) was performed with G*Power 3.1.9.2. The power to detect a 10% response/remission difference between two groups of genotypes, with an alpha risk of 5%, was 93% at 3 months and 79% at 6 months.

Results

Sample characteristics

The 569 patients were mainly women (69.6%). Their mean age was 46.2 years (standard deviation = 13.2). Their mean HAMD score at baseline was 24.6 (standard deviation = 5.0). Of these patients, 86.8% were hospitalized at baseline and 74.8% had a recurrent MDD. Five hundred and twenty one (92%) patients were Caucasian, in other words, had two Caucasian parents.

Patients who prematurely dropped out from the study (123 [21.6%] patients after 1 month, 246 [42.2%] after 3 months and 328 [57.6%] after 6 months) did not significantly differ from completers for age, sex, HAMD score at baseline, presence of recurrent MDEs, antidepressant treatment classes and allelic frequencies of the eight *NTRK2* polymorphisms. The dropout reasons were: discontinuation of the antidepressant medication studied (30.1%), prescription of unauthorized drugs (9.9%), change of diagnosis not compatible with the study (5.3%), patient's decision (5.8%), lost during follow-up (41.1%), and others (7.8%).

Table 2 shows the allelic repartition of the eight *NTRK2* SNPs. Since there were no homozygous patients for the minor allele and only two heterozygous patients for the rs56142442, this SNP was not analyzed. There was a deviation from the Hardy–Weinberg equilibrium for two other SNPs (rs2289658 and rs3824519). The haplotype analysis

(Supplementary Table 1) showed that rs1439050, rs1187352 and rs1778933 were in moderate linkage disequilibrium and that rs2289658, rs2289657, rs2289656 and rs3824519 were in high linkage disequilibrium. The demographic and clinical features of the cohort according to each SNP are described in Table 3. The genotype groups (analyzed either in three or in two groups) did not significantly differ for these demographic and clinical features, neither in the whole sample and Caucasian patients.

Outcome of depression after antidepressant treatment

In the whole sample, the intent to treat analysis showed that three out of eight SNPs, in other words, rs1187352, rs1439050 and rs3824519 were associated with at least one efficacy outcome in bivariate analyses ($p < 0.05$). Rs1187352 was associated with remission rates after 1 month, rs1439050 with the HAMD total score decreasing after 3 months, and rs3824519 with the remission rates after 6 months (Table 4). However, these associations were not statistically significant after Bonferroni's corrections, and after multivariate analyses controlling for age, sex, educational level and previous antidepressant treatment. Accordingly, the last observation carried forward analyses confirmed previous results. Additionally, the analysis of completers using an ANOVA for repeated measures, confirmed previous results. A *posteriori* statistical power estimations, taking attrition into account, were performed for the bivariate tests which had a p -value < 0.05 . The power estimations evidenced a 99.9% power for rs1187352 based on the remission rate after one month, a 93.5% power for rs3824519 based on remission rates after 6 months and a 63% power for rs1439050 based on the HAMD total score after 3 months.

In the subgroup of Caucasian patients, no significant association was observed between the eight *NTRK2* polymorphisms and outcome of depression after antidepressant treatment.

Discussion

This study fails to show an association between the eight *NTRK2* SNPs selected (rs1187352, rs1439050, rs1778933, rs2289656, rs2289657, rs2289658, rs3824519 and rs56142442) and the response and remission rates after antidepressant treatment in depressed patients. Our results confirm, in a greater sample, those of Dong *et al.* [11] for rs2289656, rs2289657, rs2289658 and rs56142442. They also confirm, with a greater follow-up duration, those of Hennings *et al.* [12] for rs1439050, rs1778933, rs2289656 and rs3824519.

Regarding the four *NTRK2* genetic polymorphisms which were previously associated with suicidal ideation in depressed Caucasian patients treated with antidepressants (rs1187352, rs1439050, rs1778933 and rs3824519) [17], we fail to show their association with response and remission rates of depression post-treatment. This difference could be explained by the number of symptoms taken into account for the definition of response/remission as compared with suicidal ideation assessed alone. Of note, to the best of our knowledge, there are no published data beyond major depression, in other psychiatric or nonpsychiatric disorders, and with other drug treatments, showing a relevance of the assessment of some *NTRK2* SNPs to predict treatment response.

Results of the haplotype analyses, showing that rs1439050, rs1187352 and rs1778933 were in linkage disequilibrium, are in line with those of Perroud *et al.* [17] in Caucasians. Indeed, they reported a linkage disequilibrium for rs1187352 and rs1778933 in a same haplotype bloc. We also show a high linkage disequilibrium for rs2289658, rs2289657, rs2289656 and rs3824519, which is in line with the results of Dong *et al.* [11] in Mexican-

American. They report that rs2289657, rs2289656 and rs3824519 were in linkage disequilibrium and determined an haplotype bloc.

The main strengths of this study are its large sample size, its long-term follow-up (6 months), and an homogenous sample in terms of diagnosis (MDD patients only), with a majority of Caucasian patients and an analysis of the Caucasian subgroup. Nevertheless, this study has some limitations. It is a nonrandomized naturalistic open study, the treatment being chosen by the psychiatrist according to his clinical assessment and own experience. The first limit of this study is the high attrition rate (42.2% after 3 months and 57.6% after 6 months), although similar to the one of other cohorts of MDD patients such as the STAR*D cohort [1]. In this study, comorbid anxiety, hormonal changes, life events or low income were not specifically assessed. However, they may predict antidepressant response. Thus, their potential associations with the *NTRK2* SNPs or potential confounding effects on outcome were not tested. Moreover, the study is underpowered to draw firm conclusions regarding the genetic effect of this gene. In addition, for the *NTRK2* gene, the approach based on candidate SNPs is limited by the poor rationale to identify candidate SNPs since their functionality is unknown. Finally, since *NTRK2* is involved in the mechanisms of action of antidepressant drugs [4], new studies could be useful in this field. Beyond powerful genome-wide association studies, searching for rare variants in the *NTRK2* gene may also be a promising strategy.

Conclusion

Despite its moderate power, this study in depressed patients fails to show an impact of eight *NTRK2* SNPs on response and remission after 6 months of antidepressant treatment, suggesting that there is no benefit to genotype these *NTRK2* SNPs in daily practice to predict outcomes after antidepressant treatment in depressed patients.

Table 1. Published studies with *NTRK2* SNPs and outcome after antidepressant treatment in depressed patients. (Table view)

| Study (year) | Patients (n) | Ethnicity | Diagnosis | Bipolar patients | Cohort Identification | Follow-up (week) | Antidepressant | Design |
|-------------------------------|--------------|------------------|---------------|------------------|-----------------------|------------------|---|-----------------------------|
| Dong <i>et al.</i> (2009) | 142 | Mexican–American | MDE MDD | Excluded | UCLA PPRG | 8 | Fluoxetine (n = 74) Desipramine (n = 68) | Double blind random control |
| Hennings <i>et al.</i> (2013) | 894 | Caucasian | MDE MDD/BD | 11% | MARS/Muenster | 5 | All marketed AD | Prospective open |
| Li <i>et al.</i> (2013) | 948 | Asian | MDE MDD | Excluded | OPERATION/CARE | 12 | SSRI (n = 603) SNRI (n = 267) Others (n = 78) | Prospective open |

AD: Antidepressant; BD: Bipolar disorder; HAMD: Hamilton Depression Rating Scale; MDD: Major depressive disorder; MDE: Major depressive episode; Remission: Hamilton Depression Rating Scale <8; Resistance: lack of response after two or more trials of antidepressants from different classes with adequate dosages and treatment durations; Response: At least 50% reduction of Hamilton Depression Rating Scale; SNRI: Serotonin and norepinephrine reuptake inhibitor; SSRI: Selective serotonin reuptake inhibitor.

Table 2. Allelic repartition of eight NTRK2 genetic polymorphisms and Hardy–Weinberg equilibrium in our sample of depressed patients. (Table view)

| SNP | Location and function | Position GRCh37 | Major allele | Minor allele | MAF HapMap CEU | Available genotypes (n) | Homozygous for the major allele, n (%) | Heterozygous, n (%) | H | fo | a |
|------------|-----------------------|-----------------|--------------|--------------|----------------|-------------------------|--|---------------------|---|----|---|
| rs1439050 | Intron | 87288192 | G | T | 33% | 532 | 194 (36.4) | 265 (49.8) | 7 | | |
| rs1187352 | Intron | 87293456 | G | A | 36% | 548 | 266 (48.5) | 223 (40.7) | 5 | | |
| rs1778933 | Intron | 87324410 | T | C | 35% | 551 | 280 (50.8) | 215 (39.0) | 5 | | |
| rs2289658 | Exon synonymous | 87563369 | A | G | 4% | 547 | 504 (92.1) | 39 (7.1) | 4 | | |
| rs2289657 | Intron | 87563459 | G | T | 6% | 553 | 514 (92.9) | 37 (6.7) | 2 | | |
| rs2289656 | Intron | 87563561 | C | T | 17% | 547 | 340 (62.2) | 181 (33.1) | 2 | | |
| rs3824519 | Intron | 87570003 | C | T | 8% | 552 | 468 (84.8) | 75 (13.6) | 9 | | |
| rs56142442 | Exon synonymous | 87636264 | C | T | – | 553 | 551 (99.6) | 2 (0.4) | 0 | | |

*Significant deviation from Hardy–Weinberg equilibrium.
MAF: Minor allele frequency; n: Number of patients.

Table 3. Demographic and clinical features at baseline according to the NTRK2 genetic polymorphisms studied. (Table view)

| | rs1439050 | | | rs1187352 | | | rs1778933 | | | rs2289658 | | | rs2289657 | | |
|---------------------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----------------|-------------|-------------|-----------|-------------|-------------|------------|-------------|-------------|-------------|
| Genotype | GG | GT | TT | GG | GA | AA | TT | TC | CC | AA | AG | GG | GG | GG | CC |
| Patients (n) | 194 | 265 | 73 | 266 | 223 | 59 | 280 | 215 | 56 | 504 | 39 | 4 | 514 | 37 | 3 |
| Caucasian patients (n) | 190 | 236 | 60 | 243 | 204 | 56 | 252 | 196 | 55 | 467 | 31 | 2 | 475 | 28 | 2 |
| Age (m [SD]) | 45 (13.3) | 46.5 (13.1) | 49 (13.0) | 45.7 (12.8) | 46.4 (13.6) | 47.9 (12.6) | 45.7 (12.7) | 47.4 (13.5) | 44.7 (13) | 46.2 (13.3) | 45.6 (11.3) | 58.1 (1.7) | 46.2 (13.2) | 46.2 (13.2) | 46.2 (13.2) |
| Women (%) | 71.6 | 69.4 | 68.5 | 69.9 | 71.7 | 64.4 | 68.6 | 72.6 | 69.6 | 71.4 | 59 | 50 | 70.6 | 69.4 | 69.4 |
| Recurrent MDD (%) | 76.2 | 74 | 75.3 | 73.6 | 75.3 | 81.4 | 71.7 | 78.1 | 78.6 | 75.5 | 74.4 | 50 | 75 | 75 | 75 |
| High educational level (%) | 53.1 [†] | 36.4 [†] | 47.9 [†] | 47.2 [‡] | 37.7 [‡] | 61 [‡] | 57.1 | 39.1 | 46.2 | 44.3 | 53.8 | 0 | 44.4 | 53.1 | 53.1 |
| HAMD-17 (m [SD]) | 24.2 (5.0) | 24.6 (4.7) | 24.9 (5.3) | 24.3 (4.8) | 24.7 (5.0) | 25 (4.8) | 24.6 (5.0) | 24.3 (4.8) | 25 (4.9) | 24.5 (4.9) | 25.1 (5.5) | 23 (3.6) | 24.5 (4.9) | 24.5 (4.9) | 24.5 (4.9) |
| Previous antidepressant treatment (%) | 77.7 | 79.6 | 76.7 | 74.7 | 83.4 | 78 | 74.6 | 84.2 | 76.8 | 79.1 | 71.8 | 100 | 78.6 | 78.6 | 78.6 |
| Current antidepressant: | | | | | | | | | | | | | | | |
| SSRI (%) | 40 | 39 | 38 | 41 | 39 | 27 | 40 | 38 | 38 | 39 | 49 | 25 | 39 | 39 | 40 |
| SNRI (%) | 36 | 40 | 38 | 39 | 36 | 44 | 39 | 38 | 41 | 38 | 36 | 50 | 38 | 38 | 40 |
| Others (%) | 24 | 21 | 24 | 20 | 25 | 29 | 21 | 24 | 21 | 23 | 15 | 25 | 23 | 23 | 21 |

[†]p = 0.001 (bivariate analysis) for intergenotypic comparisons (three groups).

[‡]p = 0.003 (bivariate analysis) for intergenotypic comparisons (three groups).

HAMD-17: Hamilton Depression Rating Scale 17 items at baseline; m: Mean; MDD: Major depressive disorder; SNRI: Serotonin and norepinephrine reuptake inhibitor; SSRI: Selective serotonin reuptake inhibitor.

Table 4. Antidepressant efficacy after 1, 3 and 6 months of treatment, according to the NTRK2 genetic polymorphisms studied. (Table view)

| | rs1439050 | | | rs1187352 | | | rs1778933 | | | rs2289658 | | | rs2289657 | | | |
|------------------------------------|-------------------------|-------------------------|-------------------------|-------------------|-------------------|-------------------|------------|------------|------------|------------|------------|-------------|------------|------------|-------------|-------|
| | GG | GT | TT | GG | GA | AA | TT | TC | CC | AA | AG | GG | GG | GT | TT | |
| After 1 month of treatment | | | | | | | | | | | | | | | | |
| Attrition (%) | 17.5 | 23.8 | 19.2 | 20.3 | 22 | 22 | 19.3 | 22.8 | 25 | 21.2 | 20.5 | 0 | 21.6 | 18.9 | 0 | 2 |
| HAMD-17 (m [SD]) | 13.7 (6.7) | 14.8 (6.6) | 15.3 (7.2) | 14.2 (7.1) | 15 (6.7) | 13.5 (6.9) | 14.7 (7.0) | 14.3 (6.5) | 14.1 (7.9) | 14.4 (6.8) | 16 (7.5) | 11.8 (6.7) | 14.4 (6.9) | 15.9 (7.6) | 8 (8.5) | 1 (7) |
| Response (%) | 42.5 | 38.1 | 33.9 | 40.6 | 37.9 | 41.3 | 39.4 | 38.6 | 40.5 | 40.3 | 25.8 | 25 | 40.4 | 23.3 | 50 | 3 |
| Remission (%) | 21.9 | 15.3 | 15.3 | 22.6 [†] | 12.1 [‡] | 26.1 [‡] | 19 | 15.1 | 26.2 | 18.6 | 16.1 | 25 | 18.9 | 16.7 | 50 | 1 |
| After 3 months of treatment | | | | | | | | | | | | | | | | |
| Attrition (%) | 40.2 | 44.2 | 47.9 | 41 | 46.2 | 44.1 | 41.8 | 46 | 41.1 | 42.5 | 61.5 | 0 | 42.4 | 59.5 | 0 | 4 |
| HAMD-17 (m [SD]) | 11.3 [†] (6.5) | 13.6 [†] (7.9) | 11.7 [†] (8.4) | 12.6 (7.3) | 12.9 (8.0) | 11.5 (7.9) | 13 (7.8) | 12.3 (7.2) | 11.8 (8.4) | 12.7 (7.6) | 10.5 (7.8) | 11.5 (6.8) | 12.8 (7.6) | 10.3 (7.0) | 8.5 (6.4) | 1 (7) |
| Response (%) | 55.2 | 50 | 60.5 | 49.7 | 55.8 | 54.5 | 49.7 | 56 | 57.6 | 51.7 | 66.7 | 75 | 51.4 | 66.7 | 100 | 5 |
| Remission (%) | 30.2 | 25.7 | 31.6 | 26.1 | 26.7 | 42.4 | 27 | 25.9 | 39.4 | 26.9 | 46.7 | 25 | 26.7 | 40 | 50 | 2 |
| After 6 months of treatment | | | | | | | | | | | | | | | | |
| Attrition (%) | 53.1 | 59.2 | 60.3 | 54.5 | 60.5 | 57.6 | 56.8 | 56.3 | 62.5 | 56.9 | 66.7 | 25 | 57.2 | 64.9 | 0 | 5 |
| HAMD-17 (m [SD]) | 10.1 (8.1) | 11.5 (7.8) | 10.2 (7.2) | 10.5 (8.1) | 10.7 (7.4) | 12.5 (8.6) | 10.8 (8.2) | 10.6 (7.0) | 12.3 (9.6) | 10.8 (7.9) | 10.2 (7.7) | 16.3 (10.5) | 10.8 (7.9) | 11.3 (7.5) | 16.5 (14.8) | 1 (8) |
| Response (%) | 65.9 | 63.9 | 69 | 62.8 | 71.6 | 60 | 63.6 | 70.2 | 57.1 | 65 | 76.9 | 33.3 | 65.5 | 69.2 | 50 | 6 |
| Remission (%) | 47.3 | 37 | 41.4 | 42.1 | 43.2 | 36 | 41.3 | 42.6 | 38.1 | 41.9 | 30.8 | 33.3 | 42.3 | 23.1 | 50 | 4 |

[†]p = 0.038 (bivariate analysis) for inter-genotypic comparisons (three groups).

[‡]p = 0.012 (bivariate analysis) for inter-genotypic comparisons (three groups).

[§]p = 0.04 (bivariate analysis) for inter-genotypic comparisons (three groups).

HAMD-17: Hamilton Depression Rating Scale 17 items; m: Mean.

Executive summary

Introduction

- NTRK2 is the main receptor of the BDNF, which is involved in antidepressant efficacy.
- We assessed the impact of eight NTRK2 SNPs on response/remission after antidepressant treatment in depressed patients in a naturalistic study.

Patients & methods

- 569 patients with a current major depressive episode requiring a new antidepressant treatment were prospectively assessed for response and remission after 1, 3 and 6 months of treatment.
- Eight *NTRK2* SNPs were genotyped at baseline: rs1187352, rs1439050, rs1778933, rs2289656, rs2289657, rs2289658, rs3824519 and rs56142442.

Results

- These *NTRK2* SNPs were not associated with response/remission.

Conclusions

- There is no benefit to assess these eight *NTRK2* SNPs to predict response/remission after antidepressant treatment in depressed patients.

Financial & competing interests disclosure

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Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

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