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Depressed Caucasians with Met allele of BDNF Val66Met polymorphism have more deleterious metabolic changes after antidepressant treatment than Val/Val

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INTRODUCTION

- In mice, the Brain Derived Neurotrophic factor (BDNF) is involved in response to antidepressant drugs (1) and metabolism regulation (2).
- In humans, the BDNF Val66Met polymorphism is associated with response to antidepressant drugs in depressed patients (3) and with metabolic abnormalities after antipsychotic drug treatment (4).
- Since metabolic effects have been described in depressed patients treated with antidepressants (5), the aim of this study was to assess the association between the BDNF Val66Met polymorphism and metabolic changes after antidepressant treatment in depressed patients.

MATERIALS AND METHODS

- This study was performed in the METADAP cohort, a 6-month prospective observational cohort in real life psychiatry settings, of patients with a current unipolar major depressive episode (MDE) (DSM IV-TR) requiring the beginning of a new antidepressant treatment (5).
- Patients were genotyped for the Val66Met polymorphism and assessed for depression severity and metabolic parameters, at baseline and after 3 (M3) and 6 months (M6) of antidepressant treatment.
- The main outcome was insulin resistance, the core phenomenon of Metabolic Syndrome, assessed by the « Homeostasic Model Assessment for Insulin Resistance » (HOMA-IR) index. Secondary outcomes were the incidence of central obesity and other metabolic syndrome criteria regarding International diabetes Federation definition (6).
- Genotypes were compared for variations of quantitative metabolic changes using repeated measures ANOVA, and for incidence of metabolic criteria using χ^2 tests.

RESULTS

- 515 caucasian patients were analyzed, of whom 181 (35.2%) were Met carriers and 334 (64.8%) were homozygous Val/Val. There was no difference between genotypes at baseline for major depression and metabolic parameters. 52 (28.7%) Met carriers and 96 (28.7%) Val/Val were completers.

Table 1: Evolution of insulin resistance during antidepressant treatment in completers (n=148)

	M0	M3	M6
FBIL (pg/mL) (m±sd)			
Val/Val	287.2±247.9	233.9±163.8	261.2±163.7
Met	317.2±216.3	311.9±224.1	355.5±321.9
FBGL (g/L) (m±sd)			
Val/Val	0.90±0.19	0.93±0.21	0.92±0.13
Met	0.89±0.12	0.90±0.11	0.99±0.35

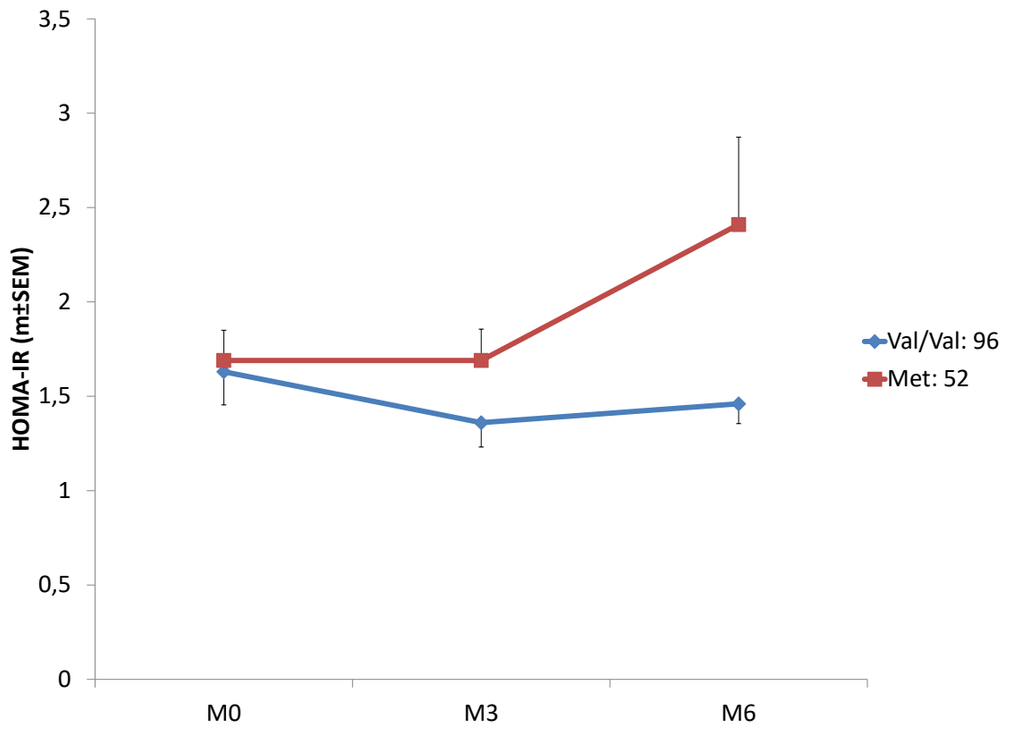
FBIL: Fasting Blood Insulin Level, FBGL: Fasting Blood Glucose Level, m: mean value, sd: standard deviation

Evolution of insulin resistance

In completers, significant genotype x time interactions were shown for HOMA-IR and fasting blood glucose levels (p=0.02 and p=0.01 respectively), significant time effects were shown for HOMA-IR and fasting blood glucose levels (p=0.04 and p=0.003 respectively), and significant genotype effects were shown for HOMA-IR and fasting insulinemia levels (p=0.05 and p=0.03 respectively). Indeed, HOMA-IR values tended to decrease in Val/Val subjects and increase in Met carriers, along with increase of fasting blood glucose levels in Met carriers, fasting insulinemia levels being higher in Met carriers than in Val/Val patients.

(Table 1 - Figure 1)

Figure 1: Evolution of HOMA-IR during antidepressant treatment in completers (n=148)



m= mean value, SEM= standard error of the mean

Incidence of central obesity

In patients without central obesity at baseline (n=189, 123 (65.1%) Val/Val, 66(34.9%) Met), the incidence of central obesity after 6 months of treatment was also higher in Met than in Val/Val patients (Met: 58.3%, Val/Val: 27.8%, p=0.01). Finally, there was no impact of remission on these results, suggesting that they were not explained by improvement of depressive symptoms.

Incidence of other metabolic syndrome criteria

Regarding incidence of other metabolic syndrome criteria, no difference was found between Met carriers and Val/Val.

CONCLUSION

Depressed Caucasian patients with the Met allele of the Val66Met BDNF polymorphism have more deleterious metabolic changes after antidepressant treatment than those with the Val/Val genotype. These results are consistent with those in mice. If they could be confirmed, they suggest that Met carriers could benefit from specific monitoring of metabolism and preventive measures.

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There is no potential conflict of interest