Programme of the 29th ECNP Congress - Vienna 2016

BACK TO MY SEARCH RESULTS

Presentation No: P.1.a.001

Session title: Basic and clinical neuroscience - Genetics and epigenetics

Session type: Poster session

The role of gender in the effect of folate pathway-related MTHFD1L gene on ruminative response style


(1) Semmelweis University, Department of Pharmacodynamics, Budapest, Hungary
(2) The University of Manchester, Neuroscience and Psychiatry Unit- School of Community Based Medicine, Manchester, United Kingdom

Our previous results recently demonstrated that the rs11754661 polymorphism A allele, situated in the folate-related MTHFD1L gene, increases the risk of ruminative response style (depressive rumination, or shortly rumination) in a European white population, and this association completely explains the risk that the A allele confers to depression [1]. Although it has been shown that gender differences in rumination play a considerable part in explaining the gender differences in depressive symptoms [2], data on gender differences in the effect of the MTHFD1L gene on neuropsychiatric [3] or neural [4] outcomes are lacking. Our present aim was to explore the role of gender in the association between rs11754661 and rumination.

N=2120 white European adults (aged 18–60 years) from Budapest and Manchester filled out the 10-item Ruminative Responses Scale and were genotyped for MTHFD1L rs11754661. We built linear regression models separately in women and men, with population and age as covariates, to test the effect of the A allele of rs11754661 on rumination score. We also ran a
linear regression model on rumination in the total sample, with population, age, rs11754661 A allele, gender, and the interaction term of rs11754661 A allele and gender as predictors. The Bonferroni-corrected threshold of significance for these three tests was \( p = 0.0167 \).

Our results show that the presence of the A allele of rs11754661 increases rumination in both genders but this effect was only significant in females but not in males (see Table 1).

Table 1. Effect of the rs11754661 A allele on rumination score, in a linear regression model, with population and age as covariates, separately in females and males.

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>β</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td>14850</td>
<td>0.153</td>
<td>3.414</td>
<td>0.0007</td>
</tr>
<tr>
<td>Males</td>
<td>635</td>
<td>0.048</td>
<td>0.672</td>
<td>0.502</td>
</tr>
</tbody>
</table>

To follow up the results of separate analyses in females and males, an analysis was run in the total sample (as mentioned above) which showed that the interaction effect of the rs11754661 A allele and gender proved to be nonsignificant (\( \beta = 0.117; t = 1.388; p = 0.165 \)) suggesting that despite the observed difference in effect strength of the A risk allele between females and males it could not cause significant interaction in this model.

Our findings suggest that gender does not modify the direction in which the rs11754661 A allele exerts its effect on rumination, even though this effect was stronger and only significant in females. It should be further investigated if the lack of significance in males can be attributable to decreased power in statistical testing or to real underlying biological differences. If real biological differences exist between women and men in the effect of the \( MTHFD1L \) gene on rumination, this may have numerous consequences regarding the possibilities of folate supplementation in the prevention of mental disorders having been linked to rumination, e.g. depression, anxiety, substance abuse and eating disorders [5].

References


**Disclosure statement:** The study was supported by the Sixth Framework Program of the European Union, NewMood, LSHM-CT-2004–503474 by the National Institute for Health Research Manchester Biomedical Research Centre by the TAMOP-4.2.1.B-09/1/KMR-2010–0001 by the Hungarian Brain Research Program (Grant KTIA_13_NAP-A-II/14) and National Development Agency (Grant KTIA_NAP_13–1–2013–0001) by the Hungarian Academy of Sciences (MTA-SE Neuropsychopharmacology and Neurochemistry Research Group) and by the Hungarian Academy of Sciences and the Hungarian Brain Research Program – Grant No. KTIA_NAP_13–2–2015–0001 (MTA-SE-NAP B Genetic Brain Imaging Migraine Research Group). Xenia Gonda is recipient of the Janos Bolyai Scholarship of the Hungarian Academy of Sciences. Prof. Deakin has variously performed consultancy, speaking engagements, and research for Bristol-Myers Squibb, AstraZeneca, Eli Lilly, Schering Plough, Janssen-Cilag, and Servier (all fees are paid to the University of Manchester to reimburse them for the time taken) he also has share options in P1vital. Prof. Anderson has received consultancy fees from Servier, Alkermes, Lundbeck/Otsuka and Janssen, an honorarium for speaking from Lundbeck and grant support from Servier and AstraZeneca. Rebecca Elliott has received consultancy fees from Cambridge Cognition and P1vital. The other authors report no conflict of interest. The sponsors funded the work, but had no further role in the design of the study, in data collection or analysis, in the decision to publish, or in the preparation, review, or approval of the manuscript.

**Keywords:**
Genetics / Molecular genetics
Depression: basic
ruminative response style