Revista Brasileira de Psiquiatria. 2014;36

LETTERS TO THE EDITOR

HMNC1 gene polymorphism associated with postpartum depression

Rev Bras Psiquiatr. 2014;36:96–97
doi:10.1590/1516-4446-2013-3507

Postpartum depression (PPD) is a frequent condition with major consequences for both mother and child.[1] A genetic determinant for PPD has been suggested by several reports. The first genome-wide study of PPD was recently published, and showed that the hemicentin-1 (*HMNC1*) gene had the strongest association with postpartum mood symptoms.[2] This gene encodes an extracellular protein that contains four estrogen receptor-binding sites and is involved mainly in cell migration, protein anchorage, and the formation of hemidesmosomes in the epidermis.[3]

In view of this finding, we genotyped the rs2891230 single-nucleotide polymorphism (TaqMan® SNP genotyping assay, Applied Biosystems Inc, Foster City, CA, USA) of the *HMCN1* gene using a 7500 Real-Time PCR System (Applied Biosystems Inc, Foster City, CA, USA), in allelic discrimination mode. Association analysis was performed using UNPHASED software (v.3.0.14). All tests were two-tailed and the results were considered significant when $p \leqslant 0.05$. At least 10% of the samples were retyped for quality control. Sociodemographic categorical variables were analyzed by the chi-square test, and continuous variables, by analysis of variance (ANOVA).

A sample of 110 randomly selected, unrelated Brazilian women of European descent who had given birth was assessed. All subjects completed the Edinburgh Postpartum Depression Scale (EPDS) and a structured psychiatric interview (MINI PLUS 5.0), conducted by a psychiatrist, 8 weeks after delivery. The local ethics committee approved this study, and all participants signed a written informed consent form.

Following the structured psychiatric interview, 34 women (30.9%) were diagnosed with PPD. Although high, this prevalence is consistent with some previous Brazilian studies, such as those of Lobato et al.[4] and Ruschi et al.[5] No significant statistical differences in terms of sociodemographic data were observed between depressed (PPD+) and non-depressed women (PPD-). Sociodemographic data, diagnosis, and EPDS scores are shown in table 1.

The genotypic frequencies in PPD+/PPD- women were as follows: AA (0.03/0.21), GA (0.74/0.33) and GG (0.23/0.46). Genotype distribution was in Hardy-Weinberg equilibrium ($p = 0.69$). The GA genotype was associated with the presence of depressive symptoms in the postpartum period (chi-square = 15.64; $p < 0.01$; df = 2).

To the best of our knowledge, this is the first association study based on a candidate gene approach to confirm that a *HMCN1* polymorphism (rs2891230) is associated with PPD diagnosis. Heterozygosity (GA) for this SNP was associated with an increased risk of PPD. This could be an example of the phenomenon of molecular heterosis, defined as a situation in which heterozygous display a lesser or greater effect on the trait than homozygous groups. One possible explanation is an interaction with other genetic or nongenetic risk factors that causes a hidden stratification of the study population. Some limitations of our study must be considered, not least the sample size of only 110 women, but our finding confirms and provides more evidence of the importance of the *HMCN1* gene in PPD. Keeping this limitation in mind, we studied a homogeneous sample of women using a structured diagnostic interview (Mini International Neuropsychiatric Interview, MINI-PLUS). We suggest that the role of *HMCN1* in PPD should be further investigated and clarified, preferably in studies with larger samples.

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Submitted Apr 09 2013, accepted Apr 17 2013.

Acknowledgements

MARS has received a grant from the National Science and Technology Institute for Molecular Medicine (FAPEMIG: CBB-APQ-00075-09; CNPq: 573646/2008-2).

Table 1 Demographic characteristics and health status during and after pregnancy stratified by genotype, mean ± standard deviation or n (%)

	GG (n=43)	GA (n=50)	AA (n=17)
Age (years)	29.44±6.07	30.78±5.23	31.0±6.48
Higher education	22.0 (51.16)	19.0 (38)	11.0 (64.71)
Married	35.0 (81.4)	42.0 (84.0)	13.0 (76.47)
Previous pregnancies	1.53±0.99	1.68±0.73	1.52±0.60
Previous deliveries	1.33±0.64	1.48±0.61	1.41±0.49
Working out of home	30.0 (69.77)	35 (70.0)	10.0 (58.82)
EPDS score	7.93±6.2	10.32±6.75	5.94±3.06
Timing of interview (days after delivery)	58.67±11.40	59.32±12.76	57.29±8.26

Disclosure

The authors report no conflicts of interest.

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