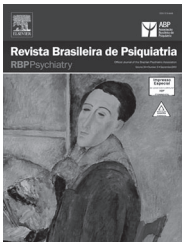
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Letter to the Editors

Negligible impact of a *HTR1A* gene promoter variant on suicidal behavior

Dear Editors,

I have read with great interest the recent meta-analysis of rs6295 effects on suicidal behavior conducted by Angles et al.[1] Praise to the authors for having rigorously selected eligible studies prior to embarking on their analysis. The message is clear. Unfortunately, the calculations are in error as alleles were muddled in one of the four investigations on which the random effects model was based: Lemonde et al.[2] examined the transcribed DNA strand, whereas the remaining studies refer to the anti-parallel strand. When this is overlooked, G and C alleles are exchanged and the G allele becomes risk-enhancing rather than protective. Even if the data in question are dropped on the grounds of heterogeneity, I have counted four additional studies of which at least one[3] warrants inclusion in the model. After correcting for these confounders, the pooled odds ratios obtained are 0.86 (0.7-1.2) and 0.97 (0.8-1.1), respectively (Figure 1). No significant association with suicidal behavior emerges which is in line with a further, more recent publication.[4]

The main concern with present and past research in the field remains, however, the lack of adequate specification of genetic exposure that precludes all verifications of this kind. A growing number of studies has referred to rs6295 without providing experimental details on the DNA strand amplified and the allele actually called. Literally, such data make little sense and cannot be used for aggregating results across examinations to increase statistical power.[5] It appears unlikely, therefore, that larger samples will shed more light on the role of rs6295 in candidate phenotypes unless genotyping procedures are routinely reported in full detail to help decrypt this information.

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Disclosure

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Employment: *University of Regensburg, Germany.*

** Modest*

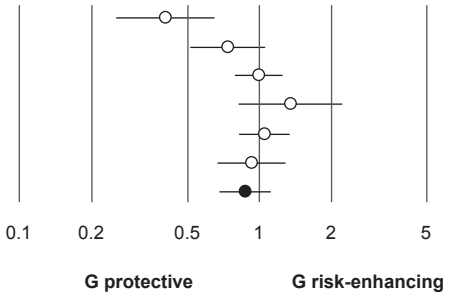
*** Significant*

**** Significant: Amounts given to the author's institution or to a colleague for research in which the author has participation, not directly to the author. The funding sources had no role in the study design, collection, analysis and interpretation of data, writing of the report, and decision to submit the paper for publication.*

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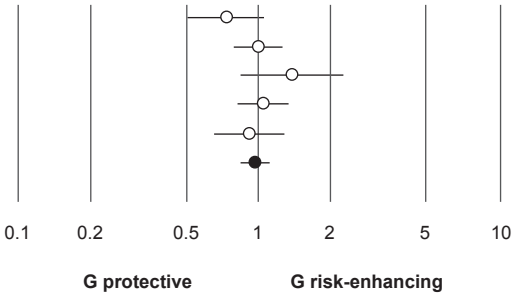
(a)

	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Lemonde et al.[2]	0.402	0.253	0.638	-3.865	0.000
Serretti et al.[6]	0.734	0.511	1.055	-1673	0.094
Serretti et al.[6]	0.993	0.787	1.254	-0.055	0.956
Sawiniec et al.[3]	1.364	0.833	2.232	1.233	0.218
Videtic et al.[7]	1.034	0.802	1.333	0.259	0.796
Yoon et al.[8]	0.920	0.658	1.286	-0.488	0.626
Random effects model	0.866	0.670	1.118	-1.103	0.270



(b)

	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Serretti et al.[6]	0.734	0.511	1.055	-1673	0.094
Serretti et al.[6]	0.993	0.787	1.254	-0.055	0.956
Sawiniec et al.[3]	1.364	0.833	2.232	1.233	0.218
Videtic et al.[7]	1.034	0.802	1.333	0.259	0.796
Yoon et al.[8]	0.920	0.658	1.286	-0.488	0.626
Random effects model	0.973	0.842	1.126	-0.363	0.716



Circles and horizontal lines correspond to the study-specific OR and 95% confidence intervals (CI). The filled circle represents the pooled OR under a random effects model.

Figure 1 Forest plots of odds ratios (OR) for the rs6295 G allele assuming a codominant mode of inheritance with (a) and without (b) the initial study by Lemonde et al.[2]

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