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LETTERS TO THE EDITORS

Analyzing leukocyte telomere length in bipolar disorder

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I have read with interest the article by Barbé-Tuana et al. entitled "Shortened telomere length in bipolar disorder: a comparison of the early and late stages of disease."[1] This is the first study addressing leukocyte telomere length (LTL) in a sample of euthymic bipolar disorder (BD) patients in the early and late stages of the disorder.

Although the sample size was small, the authors found a significant difference between the LTL of 14 BD patients in early stages compared to 15 controls ($p = 0.002$), and a marginal difference between 12 late-stage BD patients vs. 19 controls ($p = 0.058$ in Table 1).[1] Their results support the theory of accelerated aging in BD, even present since the early stages of the disease.

This study also raises some questions. First, the authors did not mention the presence of any comorbidities in the participants; however, considering that late-stage BD patients are older and have more mood episodes and worse functioning scores (Table 1[1]), one would expect a greater significant difference of LTL in late-stage BD patients vs. controls, as has been documented for other psychiatric disorders.[2] A possible explanation for this may be the modulation of telomere length (TL) by other factors, such as psychotropic medications. The authors reported that all but three patients were on polytherapy, but due to the sample size they could not explore LTL and type/number of medications.[1]

Second, is this "propensity" for shorter LTL at early stages of BD genetically predetermined? The family history of patients is not mentioned in this article. For instance, Gotlib et al. showed that children at familial risk of developing major depressive disorder (MDD) had shorter LTL compared to controls, even before manifesting an onset of depression.[3] Michalek et al. analyzed genetic polymorphisms of telomerase components (*TERT* and *TERC*) as predictors of LTL to demonstrate that shortened telomeres might increase risk for early-onset recurrent MDD in a large sample of cases and controls.[4] In this context, shortened TL was considered as a susceptibility marker for MDD that is present before illness onset. On the contrary, shortened TL might be an early consequence of the increased stress/inflammation sensitivity of individuals with BD. Wolkowitz et al. showed that accelerated aging at the level of LTL progresses in proportion to lifetime depression exposure, and that telomere shrinking does not antedate depression and is not an intrinsic feature.[5]

TL is modulated by additional factors not considered in this study, such as physical activity, eating habits, polypharmacy, and smoking. Thus, to answer these questions, a prospective analysis of LTL in individuals at genetic risk for BD will be required to evaluate these variables in relation to LTL at different stages of the disease.

Finally, it will also be necessary to investigate whether LTL in patients with BD is a trait that can be reversed by modifying factors, e.g. lithium. This will determine whether development of new TL-based therapeutic targets is warranted for opportune and preventive interventions at the early stages of the disease, when there is a better response to treatment than at later stages.

Nancy Monroy-Jaramillo[1,2]
[1]*Translational Psychiatry Program, Department of Psychiatry and Behavioral Sciences, McGovern Medical School, University of Texas Health Science Center at Houston (UTHealth), Houston, TX, USA.*
[2]*Departamento de Genética, Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez, Ciudad de México, Mexico*

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Disclosure

The author reports no conflicts of interest.

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