Body Mass Index and Brain Structure Association in Mexican Twins

I.M. Espinosa-Méndez[1,5], T.V. Román-López[1], D. Ramírez-González[1,], C.I. Sánchez-Moncada[1], X. Díaz-Téllez[3,5], C.A. Domínguez-Frausto[1], V. Murillo-Lechuga[1], X.J. López-Camaño[1], G. E. Guzmán-Tenorio[1], G. D. Robles-Rodríguez[1], E. B. Ortiz-Tapia[1], A. Piña-Hernández[1,5], O. Aldana-Assad[3], A. Medina-Rivera[3], A.E. Ruiz-Contreras[2], M. Rentería[4], S. Alcauter[1]

[1]Instituto de Neurobiología, Universidad Nacional Autónoma de México, Querétaro, México; [2]Facultad de Psicología, Universidad Nacional Autónoma de México, Ciudad de México, México; [3]Laboratorio Internacional de Investigación sobre el Genoma Humano, Universidad Nacional Autónoma de México, Querétaro, México; [4]QIMR Berghofer Medical Research Institute, Brisbane, Australia; [5]Escuela Nacional de Estudios Superiores Juriquilla, Universidad Nacional Autónoma de México, Querétaro, México.

Introduction

Variations in obesity among individuals can be predominantly attributed to genetic differences (Locke el al., 2015). It has been observed that genes associated with obesity are more prominently expressed in the brain (Vainik et al., 2018). However, the mechanism by which these brain-expressed genes contribute to obesity remains unclear. While there have been studies investigating the connection between BMI and brain structure in a Mexican-American sample (Curran et al., 2013), there is currently a dearth of research on this topic within the context of Mexican twins.

Objective

To examine the relationship between total cortical volume and body mass index, as well as to assess the heritability and genetic/phenotypic correlations of these two characteristics, we conducted a study using data from the Mexican Twin Registry (TwinsMX).

Methods

For this study, we had a sample of 65 pairs of twins (41 MZ and 24 DZ) from the Mexican twin registry, TwinsMX (Leon-Apodaca et al., 2019) who underwent magnetic resonance imaging at the *Laboratorio Nacional de Imagenología por Resonancia Magnética* (LANIREM). The study included acquiring high-resolution T1-weighted images covering the whole brain, which were processed with FreeSurfer's recon-all pipeline. BMI was calculated automatically by dividing the participants weight (kg) by the square of the height (m) using the OMRON Digital Scale (HBF-514C). A bivariate ACE model estimated the heritability and genetic cross-trait correlations of both phenotypes. Analyses were performed with umx (Bates, Maes & Neale, 2019), and OpenMX (Boker et al, 2011) R v4.2.1 packages.

Results

The heritability for the BMI and total cortical volume were 85.19% and 49.14%, respectively. On the other hand, the cross-trait genetic correlation between traits was rA = -0.242 and they had a phenotypic correlation of rP = -0.230. The whole sample BMI and total cortical volume correlation was -0.255 (p = 0.003).

Conclusions

The heritability of BMI was similar to meta-analysis estimates (75%, Elks et al., 2013), but cortical total volume was considerably lower than reported. We found a considerable genetic and phenotypic correlation between both phenotypes, showing that there is a genetic

overlap between the two phenotypes. The negative correlations indicate that an increased BMI is associated with a reduction in total cortical volume and this is plausibly regulated by a common set of genes, which is consistent with literature. However, these relations may vary between anatomic structures and between different cortical measurements (e.g. mean thickness, surface area). Therefore, subsequent analyses in specific cortical areas rather than global measures and with different measurements, are necessary to determine whether this genetic/phenotypic overlap is maintained.

Acknowledgments: We are grateful to the twins that participate in TwinsMX. We also thank Leopoldo González Santos, Luis Alberto Aguilar Jair García for technical assistance, Erick Pasaye for his technical support during MRI acquisitions, LANIREM and the Laboratorio Nacional de Visualización Científica Avanzada (LAVIS), UNAM, for the imaging and computing resources. This work was supported by CONACYT grant CF-2019-6390

References

- Bates, T. C., Maes, H., & Neale, M. C. (2019). umx: twin and path-based structural equation modeling in R. Twin Research and Human Genetics, 22(1), 27-41.Curran, J. E., McKay, D. R., Winkler, A. M., Olvera, R. L., Carless, M. A., Dyer, T. D., ... & Glahn, D. C. (2013). Identification of pleiotropic genetic effects on obesity and brain anatomy. Human heredity, 75(2-4), 136-143.
- Elks, C. E., Den Hoed, M., Zhao, J. H., Sharp, S. J., Wareham, N. J., Loos, R. J., & Ong, K. K. (2012). Variability in the heritability of body mass index: a systematic review and meta-regression. Frontiers in endocrinology, 3, 29.
- Leon-Apodaca, A. V., Chiu-Han, E., Ortega-Mora, I., Román-López, T. V., Caballero-Sánchez, U., Aldana-Assad, O., ... & Medina-Rivera, A. (2019). TwinsMX: uncovering the basis of health and disease in the Mexican population. Twin Research and Human Genetics, 22(6), 611-616.
- Locke, A. E., Kahali, B., Berndt, S. I., Justice, A. E., Pers, T. H., Day, F. R., ... & Lindström, J. (2015). Genetic studies of body mass index yield new insights for obesity biology. Nature, 518(7538), 197-206.
- Posthuma, D. (2009). Multivariate genetic analysis. In Handbook of behavior genetics (pp. 47-59). New York, NY: Springer New York.
- Vainik, U., Baker, T. E., Dadar, M., Zeighami, Y., Michaud, A., Zhang, Y., ... & Dagher, A. (2018). Neurobehavioral correlates of obesity are largely heritable. Proceedings of the National Academy of Sciences, 115(37), 9312-9317.