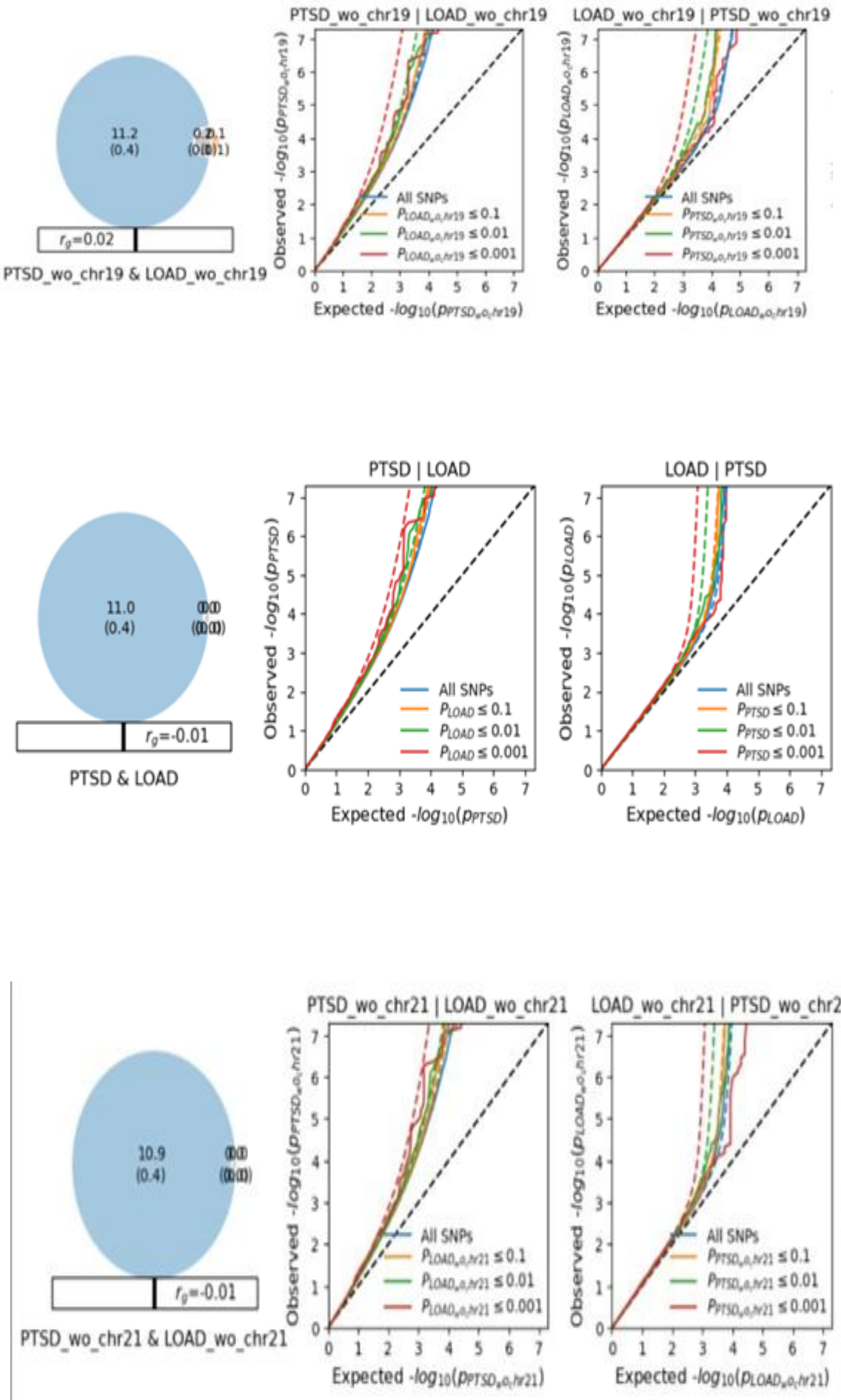


Shared Genetics Between PTSD And LAOD

Disease With The MiXeR Toolset

P4-03

Vinicius Boaventura¹, Victor Borin Centurion Biruel^{2,3}, João Paulo Oliveira Braga⁴, Gustavo Melo de Andrade Lima¹, Eugênio Horácio Grevet⁵, Paulo Henrique Ferreira Bertolucci¹, Carolina Muniz Carvalho⁶.
¹Neurology, Universidade Federal de São Paulo, São Paulo, Brazil, ²Microbial Genetics, Univesidade de Campinas, São Paulo, Brazil, ³Interdisciplinary Laboratory of Clinical Neurosciences (LiNC), Universidade Federal de São Paulo, São Paulo, Brazil, ⁴Center for Teaching and Research in Brain Aging, Universidade Federal de São Paulo, São Paulo, Brazil, ⁵Psychiatry, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil, ⁶Pós-graduação em Biologia Estrutural e Funcional, Universidade Federal de São Paulo, São Paulo, Brazil.

Limited genome-wide genetic correlation between PTSD and LOAD, even after removing major-effect loci				
INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
Genetic and neurobiological factors changes may influence the development of Posttraumatic Stress Disorder (PTSD) and Late-Onset Alzheimer’s Disease (LOAD)¹. Large-effect loci, particularly those involving the <i>APOE</i> and <i>APP</i> genes, may disproportionately influence estimates of genetic overlap between disorders. We hypothesized that excluding chromosomes 19 and 21 may help in a better understanding of whether the genetic relationship between PTSD and LOAD is supported by broad and shared biological mechanisms or depends predominantly on large-effect loci². This study aims to evaluate a shared genetic conditioning between PTSD and LOAD under different analytic scenarios to assess potential masking effects related to <i>APOE</i> and <i>APP</i>.	We used publicly availablegenome-wide association studies (GWAS) summary statistics for PTSD and LOAD^{3,4}. MiXeR was used to analyze the shared genetic between these conditions. MiXeR analyses were used in three separate scenarios: (1) including chromosome 19 (containing the <i>APOE</i> region) and 21 (containing the <i>APP</i> region), (2) excluding chromosome 19 to evaluate potential masking effects due to <i>APOE</i> and (3) excluding chromosome 21 to evaluate potential masking effects attributable to <i>APP</i>.		These findings suggest limited genome-wide genetic correlation between PTSD and LOAD, even after removing major-effect loci, supporting the hypothesis that any shared genetic architecture is modest and distributed across the Genome.	1- Kuring, J. K., Mathias, J. L. & Ward, L. Risk of Dementia in persons who have previously experienced clinically-significant Depression, Anxiety, or PTSD: A Systematic Review and Meta-Analysis. <i>Journal of Affective Disorders</i> vol. 274 247–261 Preprint at https://doi.org/10.1016/j.jad.2020.05.020 (2020). 2-Lutz, M. W., Luo, S., Williamson, D. E. & Chiba-Falek, O. Shared genetic etiology underlying late-onset Alzheimer’s disease and posttraumatic stress syndrome. <i>Alzheimer’s and Dementia</i> 16, 1280–1292 (2020). 3- Kunkle, B. W. <i>et al.</i> Genetic meta-analysis of diagnosed Alzheimer’s disease identifies new risk loci and implicates Aβ, tau, immunity and lipid processing. <i>Nat. Genet.</i> 51, 414–430 (2019). 4-Nievergelt, C. M. <i>et al.</i> Genome-wide association analyses identify 95 risk loci and provide insights into the neurobiology of post-traumatic stress disorder. <i>Nat. Genet.</i> 56, 792–808 (2024).
CONTACT				vinicius.Boaventura@unifesp.br  ALZHEIMER'S ASSOCIATION AAIC 26