Environmental and Geo-Social Factors in Alzheimer's Disease and Related Dementia Development

Gabrielle Husted, M.A.
Susan Cassels, Ph.D.
Elizabeth Ackert, Ph.D.
Barbara Bendlin, Ph.D.

Corresponding Author: Please address all correspondence to Gabrielle Husted gabrielle604@ucsb.edu.

Short Abstract

Background: As the world experiences a rapid demographic shift toward longer lifespans, the proportion of older adults is rising, as are the cases of Alzheimer's Disease and Related Dementias (ADRD). This demographic aging trend is concurrent with ongoing industrialization and increased pollution. Environmental toxicants and neighborhood resources encompass modifiable risk factors for healthy aging. *Objective:* This work investigates the connection between plastics and ADRD, a topic that has only recently gained attention in the broader research community. The approach of this paper bridges multiple disciplines (Geography, Neuroscience, Nursing) and methodologies (spatial statistics, biomarker biochemical analysis, neighborhood effects) to create a nuanced understanding of the public-scale modifiable risk factors that impact ADRD risk. *Methods:* Geocoded socio-demographic data captured by the Panel Study of Income Dynamics (PSID) is paired with geocoded data from the Environmental Protection Agency (EPA) Toxic Release Inventory (TRI), years 2017-2021, multi-level models analyze ADRD risk in association with phthalate industry density and proximity, and demographic and social characteristics, which serve as a proxy for resources to mitigate the harms of exposure to toxic industries. *Results:* Individuals with lower socioeconomic status, reduced access to resources, and greater exposure to plastics in their communities have higher prevalence of ADRD risk.

Extended Abstract

Introduction

There are many potential points of intervention to explore in pursuit of ameliorating Alzheimer's disease and related dementias (ADRD), and to identify health behaviors and policies that can reduce the incidence of ADRD in communities. This paper aims to identify the relationship between nationally representative socio-demographic characteristics of individuals with ADRD risk and proximity to toxic chemical waste.

Background

The term "dementia" refers to a clinical syndrome which includes decline in cognitive abilities that is substantial enough to disrupt activities of daily living. Alzheimer's disease (AD) accounts for 60-80% of dementia cases (Alzheimer's Association, 2020; Alzheimer's Disease International, 2020; Alzheimer's Association, 2024). It is a progressive neurodegenerative disease defined by the accumulation of abnormal proteinopathies (amyloid plaques and neurofibrillary tangles) with a prolonged silent phase of disease development, and eventual progressive loss of cognitive function, changes in behavior and physical challenges like swallowing. In the United States, nearly 7 million people are living with Alzheimer's, and even more that are not diagnosed or captured in the statistics. In 2020, the economic toll of Alzheimer's was estimated at $305 billion (Wong, 2020; Milken Institute, 2022). However, this figure doesn't encapsulate the broader societal repercussions of Alzheimer's and related dementias (ADRD), nor the most profound consequence of Alzheimer's—the deprivation of precious quality time with loved ones. ADRD pathology accumulates many years before a clinical diagnosis of Alzheimer's, and while factors like older age and genetics are unmodifiable, there are twelve well-established potentially-modifiable risk factors for dementia: less education, hypertension, hearing impairment, smoking, obesity, depression, physical inactivity, diabetes, low social contact, alcohol consumption, traumatic brain injury (TBI), and air pollution, collectively accounting for roughly 40% of population attributable worldwide dementias (Livingston et al., 2020). Reduced exposure to environmental risk factors, such as air pollution, is associated with reduction in neuropathological damage (amyloid or tau-mediated, vascular, or inflammatory), and dementia prevention (Livingston et al., 2020; Zetterberg, H. & Bendlin, B. B., 2021). The 2020 Lancet Commission Report on Dementia Prevention, Intervention, and Care calls for a better understanding of how dementias are related to social-determinants of health across the life course, in order to identify and mitigate inequalities, protect people with dementia, and adapt interventions for different cultures and environments (2020). Our work will focus on exposure to phthalate pollution via proximity to toxic industries.

Exposure to phthalate chemicals alters the gut microbiome and related neurodevelopment, potentially ADRD. Phthalates are chemicals used to make plastics flexible and durable. Key components in plastics are phthalates and since the creation of plastics in the 1940s, they've become hidden in a variety of daily use items, such as flooring materials and toys. Phthalates can make their way into bodies through ingestion, inhalation, and dermal absorption, and exposures may differ by socio-economic status, e.g., ability to avoid plastic items (Wang, Y. & Qian, H., 2021; Zarus et al., 2021). However, there is a lack of sufficient oversight regulating phthalate production and use, despite evidence on the omnipresence of phthalates in human bodies, and research documenting phthalate toxicity to endocrine, respiratory, and nervous systems (Wang, Y. & Qian, H., 2021). More studies are urgently needed to understand the potential harm caused by phthalates and motivate public policy, given the increasingly common presence of phthalates in our daily lives. While there are disputes about measurement, the crucial takeaway is that phthalates are pervasive in our bodies and we do not have adequate systems in place to protect humans from exposure (Pletz, 2022; Sadeghzadeh, C., 2024).

The social determinants of health framework can inform expectations for how phthalate levels may differ by socio-demographic factors, and concomitantly impact the gut microbiome and brain health. Social determinants of health refers to the upstream factors - those that are occurring prior to health care interventions - that contribute to health outcomes (CDC, 2022). The gut microbiome reflects inter-individual and intra-individual differences throughout the life process (Subramanian, 2014; Rinninella et al., 2019). Possibly, this is the mechanism that would enable one gut microbiome to be more resilient amidst exposure to phthalates than another gut microbiome, and in turn limit cognitive impairment. This paper explores these concepts of social determinants of health by analyzing the relationships between proximity to toxic facilities, socio-demographic characteristics, and cognitive health outcomes.

In this study, we will investigate the presence of an association between density of toxic industries in a neighborhood and ADRD pathology. This research aims to identify populations and communities that require additional resources, support, and interventions at both neighborhood and policy levels. By intervening in the pre-clinical causal pathway leading to ADRD, we seek to reduce preventable cognitive decline, enhance societal well-being, optimize healthcare resources, foster social connections, and maintain a healthy workforce, ultimately promoting individual, societal, and economic health on a broader scale (Farsetta, 2020).

Research Questions

Our research question is:

(1) How does cognition and Alzheimer's neuropathology vary within the U.S. population in relation to geo-social determinants of health, specifically locations of and pollutants released by industries?
   (a) Does greater density of phthalate polluting industries increase the predicted probability of individuals in that geographic area having cognitive health challenges, such as ADRD?
   (b) Do certain compositional, contextual, and collective characteristics of geographic areas moderate the risk posed by phthalate polluting industries on cognitive health?

Data and Measures

The research in this proposal will harness the power of the socio-demographic data captured by Panel Study of Income Dynamics (PSID)and pair it with data from the Environmental Protection Agency Toxic Release Inventory (EPA TRI). We've chosen the years 2017-2021 as our study timeframe because our key outcome variable, AD8 Dementia Screen score, was added to the PSID in 2017. While this brief measure is intended to identify older adults at risk of developing Alzheimer's disease and related dementias (ADRD), there are many other variables in the PSID that have merit in this realm as well, such as general health and well-being, educational attainment, and employment. Our work will utilize the geocoded PSID data, and the geocoded TRI data in order to analyze the prevalence of ADRD in association with phthalate industry density and proximity and demographic and social characteristics, which serve as a proxy for resources to mitigate the harms of exposure to toxic industries.

The Population Study of Income Dynamics (PSID) is the longest running longitudinal household study in the world. It began in 1968 and has collected data annually from 1968-1997, and biennially 1997 onward (PSID, 2017). The panel began with data collection from 5,000 families and 18,000 individuals, however, through the PSID 'natural refreshment' design, the sample has grown to roughly 30,000 individuals in 2021. We utilize geographic identifiers available under a restricted contract from the PSID in order to identify residential neighborhoods of respondents. The restricted PSID Geocode Match files contain the Census Tract, Block-Group, and Block data necessary to link data from the PSID annual family files to Census data – the characteristics of the geographic area in which individuals and families lived (e.g., the neighborhood and/ or the labor market area) to the PSID individual, or family-level data. We use the block level data and create a buffer around the toxic industry (EPA TRI data) point source – 0.5 mile, 1 mile, and 5 mile buffers (Wilson et al., 2012). The data from the Environmental Protection Agency (EPA) Toxic Release Inventory (TRI) documents toxic chemical releases (into air, water, land) and pollution prevention activities reported by industrial and federal facilities (EPA, 2017). They publish new data each year in July, and update the database throughout the year. The CDR gathers manufacturer information every four years regarding the types, amount, uses, and exposure to chemicals in commerce.

The PSID has been instrumental in previous work examining health disparities related to air pollution. Existing research shows that social groups in the U.S. have different exposures to industrial hazards. Social disadvantages, lack of environmental assets (i.e., green space, urban heat islands), and health vulnerabilities combine to produce racial stratification of disproportionate exposure to pollution through the environment. Historic redlining, zoning, urban planning and development, and industry regulation have varying impacts on individuals in relation to their socio-demographics (Wilson et al., 2012; Frey, 2022). For example, even amidst nationwide declines in pollution levels, on average, Blacks and Latinos are exposed to greater amounts of nitrogen dioxide (NO2) and particulate matter, PM2.5 and PM10 (Kravitz-Wirtz et al., 2016). This work lays the foundation for our exploration of the socio-demographic patterning of phthalate exposure via toxic industries, and motivates the validity of our health outcome of interest: Alzheimer's Disease and related dementias.

Research Methods

We use distance decay modeling to create variables of spatial exposure to TRI. Next, we run multilevel models, with individuals grouped at the block level to assess the relationship between proximity to toxic phthalate industries and cognitive health, measured with the PSID AD8 survey variable [ER34590] indicating whether an individual has endorsed two or more cognitive impairments. We also take into account the density of toxic phthalate industries within the three buffers previously described.

The multi-level modeling approach is a technique designed to handle hierarchical data structures. This approach allows us to account for the nested nature of the data, where individuals are nested within households, and households are nested within communities. By employing multi-level modeling, we aim to examine how individual-level factors, household characteristics, and community-level variables interact to influence outcomes related to Alzheimer's Disease and Related Dementias (ADRD). This methodology will enable a comprehensive understanding of the complex relationships within the dataset, offering insights into the broader social and environmental determinants of ADRD prevalence and outcomes.

Exposure levels will be predictors in the multilevel model. Interactions between exposure levels and other predictors will be explored, in addition to nonlinear relationships between the exposure and outcomes. We can examine fixed effects of exposure levels on our outcomes, random effects to analyze variation in the impact of exposure across the different geographic units, and we will explore cross-level interactions (such as varying exposure related to individual socioeconomic status factors).

Descriptive statistics for the continuous variables in our sample are provided in table 1, and the descriptive statistics for the categorical variables are in table 2.

Variable	Mean	Linearized Std. Error	N
Age	40.237	0.337	81,259
Total Releases (per State)	26558.590	1946.875	77,607
Number of Industries (per State)	9.692	0.415	77,607
	Percent	**Linearized Std. Error**	**N**

Table 1: Weighted Descriptive Statistics for Panel Study of Income Dynamics (PSID) and Environmental Protection Agency Toxic Release Inventory (EPA TRI) Continuous Variables, 2017-2021

Variable		Percent	Linearized Std. Error	N
Sex				81,322
	male	49	0.48	
	female	51	0.48	
Currently has health insurance				81,322
	Yes	86	0.45	
	No	10	0.37	
	Inap.; NA; Refused	4	0.17	
Whether Attended College				81,322
	Yes	47	0.85	
	No	24	0.78	
	Inap.; NA; Refused	29	0.64	
Whether individual is 65 years of age or older				81,322
	65 years of age or older	0.58	0.05	
	64 years of age or younger; DK/NA age	18.5	0.6	
	Inap	80.92	0.6	
Whether change in decision making				81,322
	Yes, a change	2.13	0.12	
	No, no change	16.2	0.56	
	Inap.; NA; Refused	81.67	0.64	
Whether change in interest for activities/hobbies				81,322
	Yes, a change	4.17	0.19	
	No, no change	14.18	0.53	
	Inap.; NA; Refused	81.66	0.64	
Whether change in repeating stories, questions, etc.				81,322
	Yes, a change	2.4	0.14	
	No, no change	15.93	0.59	
	Inap.; NA; Refused	81.68	0.65	
Whether change in learning				81,322
	Yes, a change	1.95	0.13	
	No, no change	16.38	0.58	
	Inap.; NA; Refused	81.69	0.64	
Whether change in remembering dates				81,322
	Yes, a change	1.56	0.1	
	No, no change	16.8	0.58	
	Inap.; NA; Refused	81.63	0.64	
Whether change in handling money				81,322
	Yes, a change	1.28	0.1	
	No, no change	17.02	0.57	
	Inap.; NA; Refused	81.7	0.65	
Whether change in remembering appointments				81,322
	Yes, a change	2.41	0.14	
	No, no change	15.95	0.55	
	Inap.; NA; Refused	81.65	0.64	
Whether change in daily thinking/memory				81,322
	Yes, a change	3.08	0.17	
	No, no change	15.27	0.55	
	Inap.; NA; Refused	81.66	0.64	
Whether two or more problems endorsed				81,322
	Yes, two or more endorsed	3.85	0.18	
	No, fewer than two problems endorsed	14.65	0.54	
	Inap.; NA; Refused	81.5	0.6	

Table 2: Weighted Descriptive Statistics for Panel Study of Income Dynamics (PSID) and Environmental Protection Agency Toxic Release Inventory (EPA TRI) Categorical Variables, 2017-2021

Expected findings

We expect that individuals with lower measures of socioeconomic status and access to resources (as measured by proxy variables) will have higher exposure to EPA TRI phthalate pollution, and higher prevalence of ADRD risk (as measured by endorsing two or more memory problems within the PSID AD8 survey). Based on existing literature and preliminary analyses, we expect to find a significant positive relationship between increased industrial exposure (number of phthalate industries) and cognitive health outcomes. We also anticipate that individuals endorsing two or more problems will show a greater vulnerability to social resource availability and industrial exposures, resulting in worse cognitive health and other negative health outcomes. Additionally, we expect to observe significant variation in industrial exposures and cognitive outcomes across different neighborhoods (census block groups) and states, with some states showing consistently higher exposure levels. Temporal analysis across 2017, 2019, and 2021 is expected to reveal changes in exposure and health outcomes, potentially reflecting shifts in environmental policies and socio-economic conditions. These findings will have important implications for public health interventions aimed at reducing disparities in environmental exposures and promoting cognitive health across diverse populations.

Figure 1 depicts the predicted probability of experiencing 2+ memory problems in relation to the number of industries, stratified by years of education. There's a negative relationship between the number of industries and the probability of experiencing 2+ memory problems. As the number of industries increases, the probability of memory problems decreases for all education levels. The graph shows three lines representing different education levels: 8th grade, 12th grade, and 4 years of college. Surprisingly, those with more education (4 years of college) have a slightly higher predicted probability of reporting 2+ memory problems across all industry levels compared to those with less education. The probability of experiencing 2+ memory problems ranges from about 5% (0.05) when there are no industries to about 1% (0.01) when there are 100 industries. This suggests a relatively small but noticeable effect. As the number of industries increases, the effect of education on memory problems becomes less pronounced in areas with more industries. The negative relationship between the number of industries and memory problems is somewhat counterintuitive. We anticipated that more industries could lead to more pollution and thus more health problems, but this graph suggests the opposite. The slightly higher probability of memory problems for those with more education is also intriguing. This could be due to various factors such as increased awareness and reporting of memory issues among more educated individuals, or confounding variables not captured in this analysis.

The effect of education on memory problems is complex. There seems to be a protective effect associated with living in areas with more industries, which warrants further investigation. This could be related to other factors like better healthcare access or higher socioeconomic status in more industrialized areas. The relationship between industries and memory problems is most pronounced in areas with fewer industries, suggesting that other factors may become more influential in highly industrialized areas. Further analysis and consideration of potential confounding factors is necessary to better understand these patterns.

As we continue this work, we will be incorporating many more control variables, and also refining our geographic scale (we are in the process of getting the restricted PSID block level data – anticipated to receive October 2024, however, these preliminary findings reflect the state level).

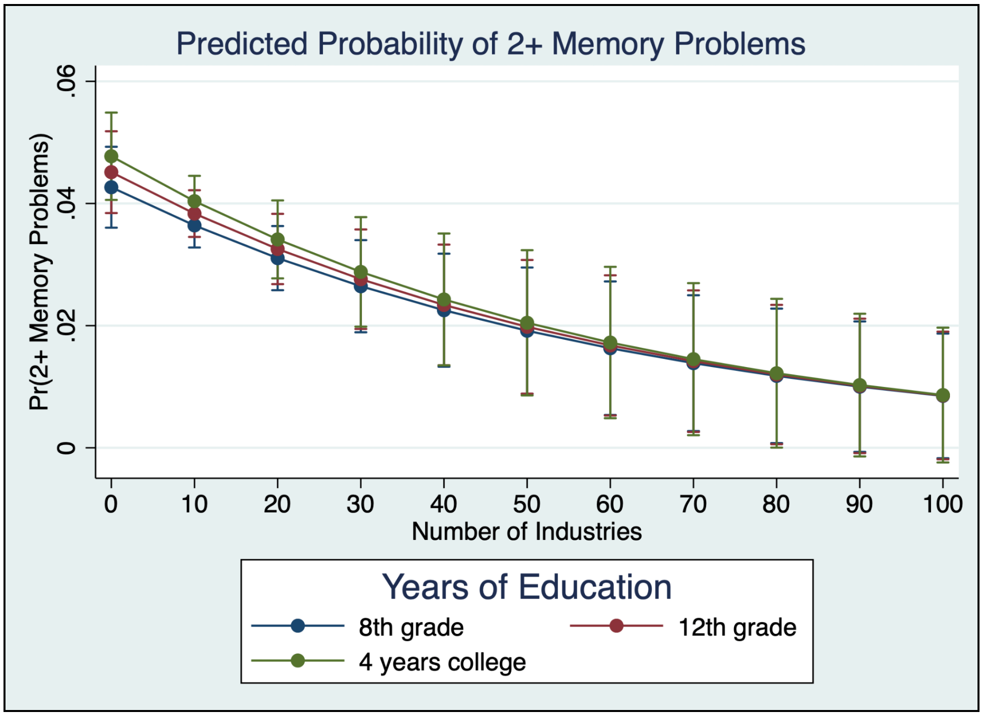

Figure 1: The predicted probability of experiencing 2+ memory problems in relation to the number of industries, stratified by years of education.

Discussion

To be added to as this research progresses.

Conclusion

In this study we rigorously evaluate the factors contributing to ADRD over space and time by studying exposure to phthalates in various spatial and social levels. Our methodology enables a comprehensive understanding of the complex relationships within the dataset, offering insights into the broader social and environmental determinants of ADRD prevalence and outcomes.

Limitations & Future Work

A limitation of my work will be that the PSID doesn't capture early onset Alzheimer's/ADRD in the AD8 as it is only asked to 65+ year old individuals. Additionally, we will not be able to identify the mechanism of exposure in our work. We will be conducting analyses of association between TRI facilities and cognitive outcomes measured in the PSID.

This work is part of a broader project that focuses on the preclinical pathway leading to ADRD. Our follow up study utilizes microdata and fecal samples for a subset of the US population to explore whether greater access to favorable neighborhood resources – assessed in terms of income, education, employment, and housing quality – is linked to a resilient gut microbiome, and therefore less detrimental impact by phthalates on cognitive health. We use nationally representative data, comprehensive microdata, and perform lab analysis to craft a research agenda that captures the phthalate-gut-brain nexus.

Our work highlights the omnipotent nature of plastics prevalence in society and investigates the insidious harm related to these chemicals making their way into human bodies. Our work contributes new data points in our pursuit of answering the research question: How do environmental exposures and geo-social determinants of health impact development and prevalence of ADRD?

References

Alzheimer's Association. (2020). The number of Americans living with Alzheimer's is growing and growing fast. https://aaic.alz.org/downloads2020/2020_Facts_and_Figures_Fact_Sheet.pdf

Alzheimer's Association. (2024). Alzheimer's disease facts and figures. [Ebook]. Chicago. Retrieved from https://www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf

Alzheimer's Disease International. (2020). Dementia Statistics. Alzheimer's Disease International. https://www.alzint.org/about/dementia-facts-figures/dementia-statistics/

Centers for Disease Control and Prevention. (2022). Social Determinants of Health at CDC. Centers for Disease Control and Prevention. Retrieved from https://www.cdc.gov/about/sdoh/index.html

Environmental Protection Agency. (2017). Toxics Release Inventory (TRI) Data for the year 2017. Retrieved from https://www.epa.gov/toxics-release-inventory-tri-program/tri-basic-data-files-calendar-years-1987-2017

Farsetta, D. (2020, October 27). Taking Stress in STRIDE: Learning How to Support Brain Health. Center for Aging Research and Education; UW Madison School of Nursing. https://care.nursing.wisc.edu/2020/10/27/taking-stress-in-stride-learning-how-to-support-brain-health/

Frey, Christopher H., 2022, EPA Researchers Release Cumulative Impacts Report, Prioritizing Environmental Justice in New Research Cycle. Environmental Protection Agency. Science Matters.

Kravitz-Wirtz, N., Crowder, K., Hajat, A., & Sass, V. (2016). THE LONG-TERM DYNAMICS OF RACIAL/ETHNIC INEQUALITY IN NEIGHBORHOOD AIR POLLUTION EXPOSURE, 1990–2009. Du Bois Review : Social Science Research on Race, 13(2), 237–259. https://doi.org/10.1017/S1742058X16000205

Livingston, G., Huntley, J., Sommerlad, A., Ames, D., Ballard, C., Banerjee, S., Brayne, C., Burns, A., Cohen-Mansfield, J., Cooper, C., Costafreda, S. G., Dias, A., Fox, N., Gitlin, L. N., Howard, R., Kales, H. C., Kivimäki, M., Larson, E. B., Ogunniyi, A., … Mukadam, N. (2020). Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. The Lancet, 396(10248), 413–446. https://doi.org/10.1016/S0140-6736(20)30367-6

Milken Institute, Projected Prevalence and Cost of Dementia: 2022 Update Highlights, Diane Ty and Rajiv Ahuja, link: https://milkeninstitute.org/sites/default/files/2022-11/Projected%20Prevalence%20and%20Cost%20of%20Dementia%202022%20Update_Highlights_FINAL_Nov.pdf

Panel Study of Income Dynamics, public use dataset. Produced and distributed by the Survey Research Center, Institute for Social Research, University of Michigan, Ann Arbor, MI (2017)

Pletz, M. (2022). Ingested microplastics: Do humans eat one credit card per week? Journal of Hazardous Materials Letters, 3, 100071. https://doi.org/10.1016/j.hazl.2022.100071

Rinninella E, Raoul P, Cintoni M, Franceschi F, Miggiano GAD, Gasbarrini A, Mele MC. What is the Healthy Gut Microbiota Composition? A Changing Ecosystem across Age, Environment, Diet, and Diseases. Microorganisms. 2019 Jan 10;7(1):14. https://doi.org/10.3390/microorganisms7010014. PMID: 30634578; PMCID: PMC6351938

Sadeghzadeh, C. (2024, January 29). We inhale a credit card's worth of microplastics each week. BBC.com. https://www.bbc.com/reel/video/p0h7vcts/we-inhale-a-credit-card-s-worth-of-microplastics-each-week

Subramanian, S. et al. Persistent gut microbiota immaturity in malnourished Bangladeshi children. Nature. 510, 417–421 (2014).

Wang, Y., & Qian, H. (2021). Phthalates and Their Impacts on Human Health. Healthcare (Basel, Switzerland), 9(5), 603. https://doi.org/10.3390/healthcare9050603

Wilson, S. M., Fraser-Rahim, H., Williams, E., Zhang, H., Rice, L., Svendsen, E., & Abara, W. (2012). Assessment of the Distribution of Toxic Release Inventory Facilities in Metropolitan Charleston: An Environmental Justice Case Study. American Journal of Public Health, 102(10), 1974–1980. https://doi.org/10.2105/AJPH.2012.300700

Wong W. (2020). Economic burden of Alzheimer disease and managed care considerations. The American journal of managed care, 26(8 Suppl), S177–S183. https://doi.org/10.37765/ajmc.2020.88482

Zarus, G., Muianga, C., Hunter, C. M., & Pappas, R. S. (2021). A review of data for quantifying human exposures to micro and nano-plastics and potential health risks. Science of The Total Environment, 756, 144010. https://doi.org/10.1016/j.scitotenv.2020.144010

Zetterberg, H., & Bendlin, B. B. (2021). Biomarkers for Alzheimer's disease – preparing for a new era of disease-modifying therapies. Molecular Psychiatry, 26(1), 296–308. https://doi.org/10.1038/s41380-020-0721-9