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Hiding in Plain Sight—Neighborhood Versus Individual Determinants of Psychological Outcomes in Patients With Epilepsy

Association of Neighborhood Deprivation With Cognitive and Mood Outcomes in Adults With Pharmacoresistant Temporal Lobe Epilepsy

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Background and objectives: Temporal lobe epilepsy (TLE) is the most common adult form of epilepsy and is associated with a high risk of cognitive deficits and depressed mood. However, little is known about the role of environmental factors on cognition and mood in TLE. This cross-sectional study examined the relationship between neighborhood deprivation and neuropsychological function in adults with TLE. Methods: Neuropsychological data were obtained from a clinical registry of patients with TLE and included measures of intelligence, attention, processing speed, language, executive function, visuospatial skills, verbal/visual memory, depression, and anxiety. Home addresses were used to calculate the Area Deprivation Index (ADI) for each individual, which were separated into quintiles (i.e., quintile 1 = least disadvantaged and quintile 5 = most disadvantaged). Kruskal-Wallis tests compared quintile groups on cognitive domain scores and mood and anxiety scores. Multivariable regression models, with and without ADI, were estimated for overall cognitive phenotype and for mood and anxiety scores. Results: A total of 800 patients (median age 38 years; 58% female) met all inclusion criteria. Effects of disadvantage (increasing ADI) were observed across nearly all measured cognitive domains and with significant increases in symptoms of depression and anxiety. Furthermore, patients in more disadvantaged ADI quintiles had increased odds of a worse cognitive phenotype ($p = 0.013$). Patients who self-identified as members of minoritized groups were overrepresented in the most disadvantaged ADI quintiles and were 2.91 (95% CI 1.87-4.54) times more likely to be in a severe cognitive phenotype than non-Hispanic White individuals ($p < 0.001$). However, accounting for ADI attenuated this relationship, suggesting neighborhood deprivation may account for some of the relationship between race/ethnicity and cognitive phenotype (ADI-adjusted proportional odds ratio 1.82, 95% CI 1.37-2.42). Discussion: These findings highlight the importance of environmental factors and regional characteristics in neuropsychological studies of epilepsy. There are many potential mechanisms by which neighborhood disadvantage can adversely affect cognition (e.g., fewer educational opportunities, limited access to health care, food insecurity/poor nutrition, and greater medical comorbidities). Future research will seek to investigate these potential mechanisms and determine whether structural and functional alterations in the brain moderate the relationship between ADI and cognition.

Commentary

Seizure reduction represents a critical endpoint for patients with epilepsy. But is far from the only one. Likewise, antiseizure medications have important benefits but are not the only modifiable lever determining health outcomes for patients with epilepsy. Studying the effects of a person's neighborhood or community, independent of personal characteristics, has several appealing features.

First, there is high face validity that context matters. Studies began emerging in the 1980's suggesting the importance of a person's physical and social environment.[1] There are an enormous number of ways by which a person's environment might affect their health: pollution, healthy food availability, occupational and recreational opportunities, transportation, violence and other stressors, behavioral norms, social connections, and plenty more.

Second, findings may lead to actionable results. While change is slow, urban planners control the built environment, and governments prioritize use of limited resources. While discrimination is pervasive, change is possible over time, and many have at least some control over where they live and work.

Busch et al (2023) recently examined the association between neighborhood deprivation with cognitive/mood outcomes.[2] They noted that studies of social determinants of brain health are limited, particularly regarding the implications of neighborhood deprivation for neuropsychological function. They identified 800 patients at least 16 years old with pharmacoresistant temporal lobe epilepsy, who underwent neuropsychological evaluation as part of presurgical workup at the Cleveland Clinic, between 1986 and 2021. Their main exposure was the Area Deprivation Index (ADI)—a weighted sum of 17 markers (eg, % with high school diploma, employed, below the poverty line, households with a car or telephone, median family income or home value) for every census block group in the United States (each typically consists of several hundreds to thousands of people).

Worse ADI correlated with poorer unadjusted neuropsychological scores. For example, the median IQ was 100 in the best ADI quintile compared with 86 in the worse ADI quintile, nearly a 1 standard deviation [SD] difference (SD = 15). Other subdomains (eg, attention, processing language, visuospatial skills, memory) showed 0.3 to 0.9 SD worsening as well. When considering the number of "abnormal" (at least 1.5 SD below average) subdomains, more disadvantage quintiles had ~1.3 to 1.4 times odds of having one additional abnormal subdomain compared with the least disadvantaged quintile after adjusting for individual factors (eg, age, sex, race). Non-Hispanic whites had 2.9-fold lower odds of having one additional abnormal subdomain compared to others, which was only partially attenuated (only 1.8-fold lower) after adjusting for ADI. Beck Depression and Anxiety Inventories were also slightly worse in the most disadvantaged versus least disadvantaged ADI quintile.

These results are unsurprising. Lower socioeconomic status, less education, manual employment, higher body mass index during midlife and decreasing body mass index in older age, food insecurity, living in economically disadvantaged neighborhoods, lesser social engagement, higher stress levels, early-life adversity, and residential segregation have all been previously associated with greater risk of Alzheimer disease and related dementias.[3] Other work has implicated early neighborhood poverty in reduced brain volumes in children, relevant to later-life disadvantage.[4] There is no real reason to think that patients specifically with epilepsy would fare any better when subjected to these stressors. Still, socioeconomic barriers are increased in people with epilepsy, in addition to unique cognitive hindrances from neurological polypharmacy, seizures or interictal discharges, epilepsy etiologies, depression/anxiety, and sleep disturbances. Busch et al have added fuel to the fire with a large sample size over an impressively long period of time and detailed, expert cognitive assessments, to extend the bad news—these more transcendent socioeconomic factors may serve to magnify disparities faced by people with epilepsy beyond their disease-specific issues. However, interpretation requires caution.

First, one-time cross-sectional data cannot distinguish causation (how neighborhoods affect people) from reverse causation (how people choose neighborhoods) or disentangle the effect of early life versus later life or current exposures. This leads to confusing relationships. For example, it is plausible that race could affect neuropsychological outcomes in ways other than by neighborhood disparities and vice versa. However, less plausible is that current age was uncorrelated with cognitive impairment, raising questions about interpretating other parameters. Many strategies exist to improve causation in future studies. Longitudinal observational data applying marginal structural models can distinguish effects of past versus current exposures and avoid reverse causation bias, provided sufficient individual-level confounders have been measured.[5] Quasi-experiments have exploited natural variation, such as refugees randomly sorted into neighborhoods of various degrees of poverty,[6] community-wide changes in food retail policies,[7] or distance from highways influencing other exposures.[8] True randomized trials have assessed the effects of providing income/housing vouchers.[9,10] These examples highlight some of many analytic approaches and study designs to guide future inquiry, leveraging natural variation and/or longitudinal follow-up particularly when randomization is not feasible.

Second, analyzing the ADI as the exposure does not inform which of its 17 components drive outcomes, if any. The ADI also lacks potentially more causal factors such as pollution, healthy food, social cohesion, or city planning, among many others.

Third, even defining a "neighborhood" is not straightforward, and census block groups are not the only way to group people or social networks. Census groups do not tell the whole story of what people or institutions we interact with in our online, globalized society, and a low ADI neighborhood next to a high ADI neighborhood is probably different than a low ADI neighborhood with less favorable spatial dependencies.

Fourth, multilevel models are key when testing the effects of group (neighborhoods) versus individual characteristics to correct standard errors and quantify within-neighborhood correlations.[11,12] As an example, multilevel models assessing factors predicting readmissions after seizure-related hospitalizations found that only 0.4% of variation in hospital readmissions was explained by differences between hospital ZIP code as a surrogate for neighborhood.[13] This was true regardless of adjustment for individual, hospital, and/or ZIP code aggregate characteristics (eg, smoking, obesity, uninsurance, unemployment, inadequate social support, illiteracy, primary care availability, household income). Though this also highlights that geographic differences likely matter more for some outcomes than others.

Structural racism and inequity are unfortunately difficult to eradicate. Social worker services represent key complementary interventions to physician interventions. Still, providers may have little control over many ADI metrics for their patient (let alone for their community). This work is a call for more research—we cannot know exactly what policies to advocate for or why, without a clearer understanding of the most important modifiable exposures. This is an important reminder that

we should evaluate our patients holistically rather than focused purely on seizure reduction—it is clear by now that medications and non-medication interventions go hand in hand.

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Declaration of Conflicting Interests

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