Population Neuroscience: An Arranged Marriage

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In recent years, the term "population neuroscience" has been seen more widely in the literature.

Where did it come from? What does it mean? What is its utility?

The term population neuroscience, introduced in 2010 by neuroscientist Dr Tomas Paus,[1] refers to the "marriage" of traditional basic/clinical neuroscience with population sciences such as epidemiology and demography. It can be said that Dr Paus arranged this marriage because he saw the potential benefits of melding the perspectives of the two broad scientific disciplines.

While basic and clinical neuroscientists focus on understanding everything about neuroanatomy, neurobiology, neurochemistry, and neurophysics—every detail of a person's brain structure and function—they are typically unconcerned with the rest of that person's physiology, let alone the person's developmental and personal characteristics, history, environment, and community. Yet, all of these factors play roles in how brain structure eventually manifests as behavior and brain disorders.

Further, these studies are typically conducted in small samples of convenience, most often WEIRD (Western Educated Industrialized Rich Democracies) samples and tell us very little about whether the findings generalize to the rest of the world's population.

Meanwhile, population scientists who are experts in all these additional factors treat the brain like a "black box" and do not attempt to relate their findings to neural structure and function. I strongly encourage readers to read a lucid exposition on this topic by Dr Emily Falk.[2]

Paus[3] makes the case that merging genetics and epidemiology with neuroscience allows us to gain new knowledge about the "processes leading to a particular state of brain structure and function," and that this knowledge can be used to "predict the risk (and resilience) of an individual for developing a brain disorder." He argues that these goals are best achieved "by espousing a developmental perspective that acknowledges the importance of the time dimension (within and across generations) when studying multilevel factors shaping the human brain." Paus himself has focused on the relationship between developmental science and population neuroscience using examples of brain imaging in people with autism.

However, this perspective extends far beyond autism and the neuroscience of the developing brain. It can be applied, e.g., to dementias in late life, as discussed in a commentary by a group of epidemiologists who study dementia.[4] They recommended that the field of dementia epidemiology should be reframed as the population neuroscience of dementia, a perspective which would allow their studies to strongly advance precision medicine and population health. Specific directions they suggested were:

- Investigating expanded phenotypes of dementia and mild cognitive impairment (e.g., studying the neural underpinnings of their behavioral manifestations which are typically ignored by most dementia researchers who focus solely on cognitive deficits).
- Investigating links between disease patterns and the modifiable macroenvironment (e.g., the relationships between dementia, brain changes, and air and water quality).
- Further developing molecular epidemiology by incorporating multilevel omics; where possible, obtaining brain autopsies in population-based studies.
- Investigating epidemiology across the life course, e.g., the timing and duration of various exposures, such as the effect of early childhood environment, or mid-life diabetes, on the risk of late-life dementia.
- Investigating trends in disease and risk factors across successive birth cohorts (e.g., trends showing dementia incidence rates decreasing in more recent cohorts in high-income countries).

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- Using novel approaches to investigate risks and manifestations of dementia in coming generations, e.g., social media for recruitment, mobile assessments embedded in wearable technologies, smartphone applications, and gaming applications.
- Expanding investigations of inadequately studied populations where novel risk and protective factors might be found, e.g., in low- and middle-income countries, and in ethnic minorities or remote areas of high-income countries, who might have exposures to different toxins such as pesticides or heavy metals or dietary toxins.
- Expanding the scope of interventional epidemiology, e.g., embedding clinical trials in representative populations, rather than conducting trials in volunteers from upper socioeconomic strata in major urban areas.
- Using Big Data (data science) approaches in very large datasets where it is appropriate to do so, such as electronic health record data for objective measures such as blood pressure; or biochemistry values like blood sugar and cholesterol; or prescription drugs.
- Judiciously combining datasets from different studies for pooled or coordinated analysis.

Many of these recommendations are ripe for being carried out in low- and middle-income countries (LMIC) where members of the general population thus far show greater inclination to accept invitations to participate in research than in high-income countries. Many in rural areas and poor urban areas welcome the opportunity for free health checkups, if those are included as part of the study design and provided ethically.

In India, population studies have been conducted in many states[5] with thousands of individuals who have undergone standardized clinical assessments. Potentially, all studies can collect and bank blood and saliva specimens. Not all regions have the facilities to provide neuroimaging, but many can transport selected study participants to urban centers where a CT or MRI or even a PET scan can be carried out.

Ideally, multicenter studies could be conducted using identical protocols across sites if logistical and political challenges can be overcome. A collaborative approach could be more feasible in which studies are independent but agree to use a core shared protocol. This would allow datasets from different sites to be combined for pooled analysis, or coordinated analyses, in which each site keeps its own data but conducts identical analyses which can then be combined. Apart from the technical challenges, a frequent obstacle is a lack of trust and experience in collaborations between centers.

As listed above, epidemiologists and demographers have many opportunities to invite basic and clinical neuroscientists to collaborate with them in bringing more neuroscience hypotheses and assessments into population studies.

But marriage is a two-way street. Neuroscientists are being offered, in essence, a new laboratory in the world outside. They would be well advised to appreciate the opportunity and reach out to population researchers to offer their ideas and expertise.

As in an arranged marriage, the two parties of neuroscience and population science have relatively little prior acquaintance with each other. On the other hand, as in any relationship, a process of mutual education based in mutual trust and respect is likely to reap the best rewards. "Love" is not a prerequisite but rather a desired outcome!

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