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Perspective

Unraveling the Gender Code in Neurological Diseases: A Call for Sex-Specific Medicine

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DESCRIPTION

For decades, the medical model has treated men and women as physiologically interchangeable an approach increasingly shown to be dangerously outdated, especially in the realm of neurological disease. Disorders such as ischemic stroke, Parkinson's Disease (PD) and Multiple Sclerosis (MS) not only exhibit striking differences in prevalence and symptomatology between sexes, but also diverge significantly in underlying pathophysiological mechanisms. Despite this, sex-specific considerations are still largely absent in research, diagnostics and treatment protocols.

This blind spot has real-world consequences. Women are more likely to be misdiagnosed, less likely to receive optimal treatment and often experience poorer outcomes. To truly address the burden of neurological disease, we must elevate biological sex from a marginal variable to a core element in personalized medicine.

Ischemic stroke disproportionately affects women in older age, largely due to hormonal transitions associated with menopause. Estrogen, a neuroprotective hormone during reproductive years, enhances cerebral blood flow and reduces inflammation. Post-menopause, the sharp decline in estrogen removes these protective effects, increasing susceptibility to stroke and diminishing recovery potential.

Beyond biology, sociocultural factors compound the risk. Older women are more likely to live alone, receive delayed care and face barriers to rehabilitation. These realities underscore the importance of integrating both biological and social determinants into stroke management strategies.

Parkinson's disease: A tale of two sexes

Parkinson's disease occurs nearly twice as frequently in men, who often experience earlier onset and more severe motor symptoms. Conversely, women with PD typically show later onset and more pronounced non-motor symptoms such as anxiety, depression and fatigue. Estrogen again plays a likely neuroprotective role, shielding dopaminergic neurons in the substantia nigra.

Furthermore, the gut-brain axis a bidirectional communication pathway involved in PD pathogenesis appears to function differently across sexes. These differences may alter disease trajectory and response to emerging therapies, including microbiome-modulating treatments. Yet, current diagnostic criteria remain biased toward the male presentation, resulting in delayed or inadequate treatment for many women.

Multiple sclerosis: A case study in sex-based susceptibility

MS exemplifies the gender gap in autoimmune neurological disease, affecting women nearly three times more than men, particularly during reproductive years. This pattern implicates sex hormones such as estrogen and progesterone in disease susceptibility and activity. Unlike their role in stroke or PD, these hormones may actually exacerbate autoimmune reactivity in MS.

Women's immune systems are inherently more prone to hyper activation, a factor further influenced by hormonal fluctuations and X-linked genetic expression. Despite this, most MS treatments are developed and tested without rigorous sex-based stratification, leaving therapeutic blind spots that fail to meet the needs of the majority female patient population.

Recent research into the gut microbiome offers a compelling new lens through which to understand neurological disease. Microbial composition, diversity and function differ significantly between sexes and may modulate disease risk, progression and treatment efficacy. These microbes influence neuroinflammation, neurotransmitter synthesis and even hormone metabolism all of which are key factors in stroke, PD and MS.

Yet, microbiome research and therapeutic development continue to underrepresent sex as a primary variable. This omission limits the potential of microbiota-targeted interventions, which could offer new pathways for sex-specific neuromodulation.

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CONCLUSION

The mounting evidence for sex-based differences in neurological diseases demands a reevaluation of current research and treatment models. Conditions like stroke, Parkinson's disease and multiple sclerosis exhibit unique biological, hormonal and immunological characteristics across sexes yet conventional medicine continues to generalize based on male-dominant data sets.

To close this gap, we must mandate sex-stratified data analysis in clinical research, improve female representation in trials and educate clinicians to recognize sex-specific presentations and therapeutic responses. As our understanding of sex-based physiology deepens particularly in the realms of immunity and microbiota it is increasingly clear that gender is not a superficial difference, but a fundamental determinant of brain health.

By centering sex-specific medicine, we stand to unlock more accurate diagnoses, safer treatments and better outcomes for all patients. The future of neurology must be personalized and that means acknowledging that when it comes to the brain, gender is deeply encoded in our cells, our hormones and our microbes.