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Book Review

Alzheimer's Disease: Are We There Yet?

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Alzheimer's Disease Research: What Has Guided Research So Far and Why It Is High Time for a Paradigm Shift by Christian Behl, 2023, Springer, Cham, Switzerland, 677 pp.

Vacationing with children or remembering our own childhood, the common question is, 'are we there yet'? Until our brain develops perspective, time and distance are seemingly infinite. Behl's treatise is written to place in mature perspective where we have been for over a century and the dominance of the amyloid and tau cascade on most research. Behl's work differs from prior books/articles on the lack of progress for an effective therapeutic by taking a circumspect and agnostic approach. Extensive facts are creatively intertwined with history and psychology to reveal new truths. The depth of facts and explanatory figures will enlighten experts in Alzheimer's disease (AD) research, students, and journalists. We know of no other work that reaches the scope of scholarship of this volume.

Beginning even before Emil Kraepelin, the foundations of modern AD research on clinicopathological correlation were established. People with young onset AD have amyloid plaques and neurofibrillary tangles and normal people of that age do not. Correlative logic extends to genetics where mutations in the amyloid-β (Aβ) pathway are linked to AD. However, based on the lack of clinical benefit from plaque removal, Aβ is not the primary driver of AD. We cannot but think within Behl's book a solution to what AD is and how to treat it are already known, if only we do as Max Planck suggested: "If you change the way you look at things, things you look at change."

While the 1980–1990 s might be the golden age of AD research, in Behl's words, it was also a period of technical and conceptual shortcuts that hindered development. As Behl comments, plaques are more than Aβ and similarly, neurofibrillary tangles are not equivalent to paired helical filaments produced as an artifact of isolation. Methodologies purporting synapse loss rely almost completely on synaptic vesicle loss, rather than an examination of synapse structure. Brain atrophy and neuronal loss are variable in AD and correlate poorly with dementia. These and numerous other artifacts linger and cannot be corrected by the most sophisticated analyses. Behl concludes that only by replacing incremental research with more disruptive research that leads to new understanding, can we move forward.

Arrival is long past due.

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