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Editorial

Fifty Years of Dementia: A Transdisciplinary and Intergenerative Lifelong Learning Adventure in the Field

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Fifty years ago, I started my journey into the Alzheimer's field, both personally and professionally. My mother's pleas to "not let me get like that" referring to my elderly grandmother's perseverations echoed as I embarked on my health and cognitive neuroscience education at Johns Hopkins University. My grandmother, a late-life immigrant from Scotland, lived out her life without a formal diagnosis of dementia in her own apartment cared for by family, friends, and local shopkeepers who knew her well and were aware of her cognitive challenges. Those were the days.

As an undergraduate at Brown University, I had taken advantage of its progressive curriculum and explored a wide range of topics from philosophy to ecology. During that time, I was inspired by my father's own life's work in pediatric behavioral neurology and both my parent's contributions as educators. I was well prepared for my MD-PhD program and eventual neurology residency at Hopkins. During my neuropathology rotation, opportunities

emerged to research basic brain mechanisms underlying dementia. The nucleus basalis of Meynert (cholinergic basal forebrain) became a ticket to rapid career advancement. I developed wide-ranging research and scholarship interests including history, genetics, cognitive neuroscience, pharmacology, outcomes, and eventually ethics and public health. I developed a clinical practice which extended for most of my career. In 1986, I moved to Case Western Reserve University in Cleveland as founding director of the soon to be NIMH and NIA-funded Alzheimer Center. In 1993, I helped develop cholinesterase inhibitors, and celebrated albeit rather half-heartedly, their approval as the first symptomatic drugs for dementia. It was quite a ride!

My gratitude to the many mentors over the years is profound. Oliver Sacks inspired me to narrative; Van Rensselaer Potter deepened my bioethics; Sid Katz introduced me to long-term care and quality of life; Bob Butler to geriatrics; and many others modelled academic behaviors (most for good, some for ill). I paid them back through reciprocating mentorship for and with others.

But over time, I grew concerned. People with cognitive challenges did not seem to fit into the boxes I was taught to apply. The field kept extending the labeling process earlier in the evolution of the symptoms and even before symptoms with

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biomarkers. And we were still unsure of the relationships between aging and various neurodegenerative processes. Overlaps among vascular and degenerative conditions became apparent. Danny George and I summarized our concerns in *The Myth of Alzheimer's: What You Aren't Being Told About Today's Most Dreaded Diagnosis* (St. Martin's Press, 2008). With respect to the subtitle, what people were and are not even today being told is that experts are confused by the labels and relationships among them. Faced with increasing complexity in the field, I continued my lifelong learning with degrees and educational experiences in bioethics, health systems management, and organizational development.

The loosely structured Alzheimer's field coalesced largely through the efforts of the Alzheimer's Association and the National Institute on Aging as a powerful and more tightly controlled "Alzheimer's Empire" that pushed fundraising through promises of cure. Their exaggerated and often deceptive and dehumanizing (e.g., zombie-like language to refer to people living with dementia) claims that cure (or an end) for this devastating disease was imminent (by 2010, then, 2020, then 2025) effectively increased stigma, while at the same they called for ending stigma. Pharma pushed drug treatment approaches, many of which were unproven (off-label) and some dangerous. Their business models included illegal and immoral behaviors designed to maximize profits (the resultant billions in fines were nothing compared to their profits). I contributed to some of this labeling frenzy and therapeutic optimism, but eventually I came to feel that I was in the belly of the beast and wanted out by seeking a healthier way to think of individual and societal responses to dementia. In 2008, I quit consulting and published an article explaining why.

Alzheimer's was clearly more than a brain chemistry to improve or a molecular problem to fix. Over my career, I moved from leadership positions in neurological and psychiatric organizations to geriatrics and then public health. I saw the problem of Alzheimer's as bigger than just Alzheimer's and hence ironically more hopeful. The idea that Alzheimer's provided a glimpse of the great pathologies in our society drove me into transdisciplinary endeavors. I came to see dementia as a potential lever for cultural change. As part of this transition, I began to view the climate crisis as the greatest threat to quality of life of people with cognitive impairment because it is the greatest threat to all of us, especially vulnerable children, and elders. Hence, I saw

that dementia could help us understand our own limitations as human beings and the importance of social solidarity and relationships to nature. Understanding dementia as more than a technological problem to fix or even more than just a "problem" or a "conundrum" made it a source of potential humility and wisdom.

Recently, relative rates of dementia in some rich countries with resources to improve the environment and reduce poverty were found to be decreasing. Education was consistently found to be a leading protective factor against cognitive decline. Inspired by the benefit of learning for people of all ages and by our own commitment to lifelong learning, my wife, Catherine Whitehouse, and I started intergenerational schools in Cleveland to foster cognitive health across the life course. Our programs, like reading mentoring and field trips into nature included people with dementia as mentors. Learning is key to so-called "brain health" but also essential to addressing social problems more serious than dementia like income/wealth inequity, social injustice, and the environmental degradation. And ironically, addressing these bigger issues will lead to improved collective brain health and more importantly perhaps the wisdom to design a course to a more sustainable future.

But our continued fixation with narrow reductionistic, profit-driven medical approaches led Danny and I in our second book together to diagnose our society as having a "cultural dementia" (*American Dementia: Brain Health in an Unhealth Society*, Johns Hopkins University Press, 2021). We forget important lessons from the past, plan poorly, attend to the wrong priorities, and are doing badly with our activities of daily living (water, food, waste production). "American dementia" is not unique to the United States, but we are the prime example and are purveyors of a political-economic model (i.e., "neoliberalism") that has infested the world via globalization. At its core, this represents an individual-focused, money-driven political system in which social unrest is increasing in the face of deepening inequality and falling living standards for working people and democracy seems to be failing. Health "systems" mirror the larger cultural pathologies and the Alzheimer field is a caricature of the worst of neoliberal and scientific fanciful thinking and impoverished valuing.

As a result, my own current work is focusing on value-based ecopsychosocial models of health and understanding design and innovation processes more deeply. Putting "eco" as a prefix in front of psychosocial health instead of the usual biopsychosocial allows the inventor of the term, me, to

point out that biomedical researchers and physicians got the biology wrong—it should not be molecular reductionistic, but environmental systems focused. Biological relativism, which finds purpose in the different levels of organization in living creatures, is challenging sterile, simplistic Neo Darwinian conceptions of genes and their linear unidirectional cascades of metabolic effects.

My principal life goal is nothing short of innovating and designing features of civilizations that move from our hypercognitive, unfair, and ecologically destructive current societies. Modern ways of life are unsustainable and incompatible with human flourishing and even survival as a species. The climate crisis is accelerating as we see in the fires, droughts, floods, and storms in the news every day. Food and water insecurities are growing as we destroy the very soil and water upon which our lives depend. Income and health inequity are growing. Social injustice has become so much more visible as has its deep ties to unevenly distributed environmental devastations. Addressing all these interlinked wicked social/economic/political problems through transdisciplinary approaches promises to be a more effective means for addressing the challenges of dementia (both clinical and cultural) than biomedicine. When we talk of progress in the Alzheimer's field, we often focus on limited goals, like modifying biology. We need new conceptions of health and wealth beyond biomarkers and money. And yet where does our attention and money go thanks to the irresponsible claims of never-ending progress, but never quite arriving ultimate success, from the Alzheimer's Association with the too-often-uncritical acquiescence from the National Institute on Aging.

We need to reenchanted our civilizations and create what I and others call "cosmodernity". Modernity with its hyperrationality, command and control arrogance, siloed knowledge, and distorted values lacks wisdom. Once again enriching our civilizations with cosmologies of awe and wonder would promote a humility which is key to wisdom. A major component of cultural change is the arts (and humanities), so I have been working as a visual performing artist. I have become a Tree Doctor (Sylvanus) who asks humans what we can learn about health from trees and forests. The answer is a whole lot, ecologically, metaphorically, and culturally. Sylvanus (the transdisciplinary character is named for the Roman god of forests and their boundaries) explores the epistemological and ethical limitations of modern medicine. Stories are critical to health individually and

collectively. Drug companies are better at story creation and dissemination (marketing and lobbying) than they are at developing new innovative and cost-effective biological products. Anecdotes (hidden stories) are to be valued as antidotes to the epistemological poisonous belief that we can only act in the world if we have evidence from Randomized Controlled Trials. Many, if not most, things of value in life and health are incommensurable, unblindable, and perhaps even possibly unrandomizable.

So what do these concerns about society and culture have to do with dementia and brain health? Cognitive capability has been and remains a key to human success individually and collectively, especially to addressing our troubled future. So threats to our thinking go to one essence of our humanity. More importantly than cognition itself, however, are individual caring relationships and social solidarity based on enduring values like trust. Dementia threatens our economics but also wellbeing more generally. They are such a threat that they require vastly different ways of thinking about how we live and die together. Particularly tragically, dementia creates anxiety and fear (intentionally as a strategy by the Alzheimer's empire, even as they decry the stigma they help create) and this emotional angst shuts off thinking, particularly to new ways that could in and of themselves lead to innovative and sustainable change. The existence of rare autosomal dominant forms of "Alzheimer's" and rare people who live into their 100s without apparent dementia does not prove that "Alzheimer's" is not a part of normal aging for most of us. It is wrong to say that our cognition does not change with age (to variable degrees). It is mal-intent to lump such age-related heterogeneity into one label and claim that with enough funding we will cure it.

It is time we rehumanize ourselves, our communities, and cultures. Ironically, people with dementia can teach us more about our humanity than perhaps we can teach them! They can teach us about the value of the life of the mind (and spirit) beyond rationality and of the essential importance of relationships to quality of life. We also need to renaturalize ourselves by deconstructing our ideas about human exceptionalism and decolonizing our minds from the false modern belief that we are separate from nature and able to control it. As a lever for social change, dementia can shift our worldview. Why is it that we dehumanize people with dementia only then to expose them to music, art, community, dance, and other enjoyable social activities that make us human while at the same demanding high-level

evidence that these activities we all do somehow need to be proven valuable for people who are labeled with a diagnosis? Person-centered (and better labeled relationship-based) care should be built on knowing individual preferences, passions, and purposes in life (their story). The Alzheimer's field is full of genetic deterministic ideas for precision or personalized treatments and cures based on DNA being our human essence. "Care today cure tomorrow" (a current slogan for advocacy organizations) is a frequently used phrase that seems to suggest no need for caring after the magic bullet arrives. And labels are viewed as the first step in starting the journey to happy and healthy, likely drug-induced, outcomes, including "cure." The field seems to believe we all need a label. The latest "clinical" label that the Alzheimer's Association is introducing into public health (of all places) is Subjective Cognitive Decline—in other words, complain that your memory is getting worse and you have got it.

During the time I was writing this reflective essay, rather surprisingly to me (and many others), aducanumab, an anti-amyloid biologic, was approved by the FDA using an accelerated mechanism where only biomarker data was required. The science was inadequate to support approval—well, at least to all but the most egregiously coopted or ill-informed. Amyloid imaging had been oversold for years and had not been adequately validated as predictive of clinical progression. But the politics was enough to drive a bad FDA decision. For years I had been warning that advocacy groups who have been promising an end to Alzheimer's for years needed an approval to maintain their short-term credibility. I was concerned that fame-seeking experts wedded to their ideas and funding streams, highly paid so-called Key Opinion Leaders, and profit-seeking companies could push ineffective drugs on the market. Suffice to say the main argument from those who advocate approval seems to be that although aducanumab is not much (if anything), it is something (maybe) that will open the floodgates of innovation (or perhaps actually close them). If there is ever a case of false hope, then this is it. With the first wave of symptomatic drugs the initial approval of weak drugs led to more mostly me-too drugs. The approval of aducanumab will indeed flood us with desperate individuals, high costs, and wasted opportunities (in public health, for example). Most importantly, it will encourage the dominant reductionistic thinking about Alzheimer's we are suffering from now.

Biogen priced the drug far beyond what most people considered reasonable. The FDA's use of Accelerated Approval process was unwisely based on the dominant fear message, the failing so-called amyloid hypothesis, and unvalidated biomarker data. The FDA did not require demonstrating clinical value for approval. The FDA says it will require post-marketing clinical studies and would consider taking the drug off the market if those studies did not show clinical benefit, but their track record on monitoring such Phase IV studies is poor. Meanwhile the company announced it will take nine years to do the study—how much profit can they make from a quite possibly completely ineffective drug during that time? Fortunately, several major health systems, including the Veterans Affairs Administration, are refusing to offer the medicine and payers are resisting the high cost of not only the drug but the physician and PET and MRI imaging charges. In complete contradiction to what the Alzheimer's Association and some "experts" are touting, this decision will set the field back, potentially lead to many more ineffective medications, and confirm the institutional corruption and irresponsible innovation in the Alzheimer's field. I believe that this decision may live in infamy!

I personally do not want to be buried in the "field" of dementia. Humans have been cultivating fields for 10,000 years or more and today we have big agriculture, monoculture crops, species extinction, soil loss, infestations with pests, food production and distribution issues, and water shortages. The Alzheimer's field is a microcosm with similar immoral and ineffective practices as the field of Big Agriculture and its allied multinational energy companies. Consistent with the ethos of the Tree Doctor, I see myself moving into a more natural meadow of opportunities looking for ways to enhance resilience and create paths to sustainable futures for my grandchildren and those not yet born, human and other living creatures. Let's raise a toast to life-long learning about the Big Picture of human existence in the universe and to some deep unlearning in the cognitively and ethically challenged Alzheimer's micro-world. I would say goodbye, but I actually left a long time ago. But then again, I am "still here."

DISCLOSURE STATEMENT

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