BOOK AND FILM REVIEWS

Margaret Lock, *The Alzheimer Conundrum: Entanglements of Dementia and Aging*. Princeton, NJ: Princeton University Press, 2013. Hardcover, 328 pp., $29.95. ISBN: 9780691149783.

In her book *The Alzheimer Conundrum: Entanglements of Dementia and Aging,* Margaret Lock traces the history and politics of research on Alzheimer's disease (AD). She begins with the discovery of the disease by Alois Alzheimer and its creation as a disease category (chapter 1) and then describes efforts to standardize AD given the continuous anomalies between neuropathology and symptoms (chapter 2). Lock analyses the shift towards the assessment of risk, especially through the identification of mild cognitive impairment (MCI, chapter 3), prodromal AD (chapter 4), genetic biomarkers (chapter 5), and genome-wide associations (chapter 6). She examines the effects of this focus on risk assessment on offspring of Alzheimer patients (chapter 7) and its role in the current interest in epigenetics (chapter 8). The first four chapters show, in detailed excerpts from scientific articles and quotations from interviews with researchers, the highly unsettled ontological status of AD: What is Alzheimer's? When is something pathological? The later chapters describe a somewhat hesitant shift towards prevention.

In her analysis Lock focuses on the role of uncertainty and (high-tech biomedical) reductionism in AD research. In particular, she examines the dominant and enduring position of localization theory, which tries to locate AD in changes in the brain and relate the disease to specific neuropathology. Investigators, consciously or unconsciously, embed this localization theory in their research. Lock describes how localization grounds the most prominent hypothesis on AD, the amyloid cascade theory, which posits that the accumulation of amyloid β (Aβ) protein in plaques is the first sign of AD that triggers deposition of tangles that eventually leads to symptoms.

Lock traces the predominance of this hypothesis and its grounding in localization theory through an impressive exposé of AD research and discussions with prominent researchers. Lock shows that although attention has now shifted to twenty years prior to first symptoms, with research on MCI, genetic and epigenetic processes, and the hunt for biomarkers to identify disease (onset), this research is still based on the amyloid cascade hypothesis. In the tracing of research she demonstrates that AD research is primarily conducted in the United States, and addresses the precarious balance with research subjects in developing countries, especially when it comes to experimental

pharmaceutical interventions. One such example is a randomized controlled trial of a pharmaceutical intervention involving families in Antioquia, Colombia. This group of families carries a specific gene mutation that results in about one third among them developing early onset AD (manifest around the age of forty-five). Lock discusses the ethical dimensions of this trial as it relates to 'the expanding universe of drug trials in which "naïve" subjects … often living in economically deprived conditions are systematically recruited for trials' (p. 140). In these trials it is often unclear whether participants will benefit from the developments that they co-create. In the case of the Colombian trial, participants were asked to sign up for information and attend extensive information sessions, and the pharmaceutical company agreed that if a medicine would be developed the Colombian families would receive it.

The Colombian trial is by some considered 'a treasure trove' in which studying predisposed, quite exceptional individuals will lead to a fuller understanding of the pathway of the disease, and in the end, make or break the amyloid cascade hypothesis. This is illustrative for the Alzheimer field that seems to be constantly anticipating a 'breakthrough' and looking for 'silver bullets'. Some frame the hesitant move toward prevention as a Kuhnian paradigm shift, but Lock convincingly shows that research efforts in fact are a continuation of thinking within the framework of the amyloid cascade hypothesis; such a paradigm shift is actually nonexistent. Furthermore, uncertainty still pervades the research field.

In the sidelines of *The Alzheimer Conundrum* lingers a critique of localization theory, the effects of a genetic focus on patients and family members, and the sometimes somewhat limited self-reflection of the researchers. She hints at a dogmatic following of localization theory and an unrelenting belief in the amyloid cascade hypothesis, almost as an implicit rationale within the AD community. However, Lock does this with utmost respect; she sees the vigorous activity, the efforts, and the well-hearted attempts, but at the same time raises ethical and philosophical questions. Particularly revealing is chapter 7 in which she interviews individuals who, in a clinical trial project, come to know about their genetic risk for AD. With laudable honesty she shows how this new information is integrated with previous ideas about their risk for and experience with the disease. For most participants knowledge of their genetic predisposition does not change how they perceive the risk of the disease. Rather, they envision their risk of genetic predisposition – and by extension, of disease – on the basis of likeness in character and appearance to a family member with the disease (p. 195).

This is an illuminating analysis of how people think about genetics and integrate genetic knowledge, and is of relevance to the wider scientific public dealing with biotechnological innovation.

Throughout the book, Lock shows how decontextualized AD research is (although a glimpse of the contrary becomes visible now) and how environmental factors are rarely explicitly considered because the basic scientists (and perhaps funders) that lead AD research favor a more reductionist – localized – approach. As a result, the issues of caring for AD patients and environmental factors in AD remain neglected. But this point is not taken to the fullest. As decontextualized as the research feels, as decontextualized the book itself sometimes feels. Anthropologists might long for what is behind the stories, the human touch, the ordinary life, instead of interview excerpts and quotations from scientific articles. But then again, this is not what the book promises to do, and Lock's approach to look at researchers themselves and trace the history of AD has rarely been accomplished in such a thorough way.

We do not learn much about general processes that seem to be looming large: of a disease orientation, of a genetic focus, and of the money-making machine that seems to be intertwined with research on AD. These processes, and the involvement of pharmaceutical companies in medicine at large, remain decontextualized in the book and perhaps deserved some more attention. Lock shows deep understanding of AD research, but her findings could have been more embedded in wider developments showing the 'entanglements' of AD research.

Lock also raises more general questions such as: What is 'normal' aging? Where and how do we draw boundaries? How do we place the continuous search for stabilizing disease markers throughout medicine, especially in light of aging and how we approach disease at later age? Similarly, how do we explicate the predominance of reductionism in research and funding that support it? The questions are there, but only touched upon, leaving the reader wishing for closer scrutiny of these kinds of questions.

However, Lock's social scientific critique is outstanding. She maintains analytical distance without neglecting the human burden of the disease and the genuine efforts that are made to understand and explore the disease. She never just critiques, and her call in the last chapter for attention to 'social, political and environmental factors, including poverty, inequality, discrimination and racism' (p. 229)

in the approach to AD is one that shows her engagement with the AD field and her concern for the people involved.

Jolanda Lindenberg
Social Anthropology, Leyden Academy on Vitality & Ageing, Leiden University