NEURODEGENERATIVE DISEASES ARE NOT CURABLE (IN 2015)

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Are neurodegenerative diseases curable? As of now, I would have to say “No”. At some point in the future, the answer may indeed be “Yes”. But in the meantime, I believe the answer has to be that neurodegenerative diseases are “potentially controllable”.

Why not “curable”? In order to cure a disease or condition, the treating physician must be able to remove the offending agent that is causing the problem. Our present understanding tells us that a) causation of all but a tiny fraction of cases of neurodegenerative disorders is likely to be multi-factorial, involving multiple gene, pathways, epigenetic and environmental influences and b) the process that results in the manifestations of neurodegenerative diseases begins (with the possible exception of ALS) several years, if not decades, before symptoms appear.

We currently somewhat arbitrarily classify potential therapeutic agents for NDDs as “symptomatic” or “disease modifying”. We tend to believe that the efficacy of the former wanes over time, whereas the effects of the latter is to “slow progression” of disease. Yet the effectiveness of our currently available drugs is small. Cholinesterase inhibitors for Alzheimer’s disease produce an average improvement of 2-4 points on the 70-point ADAS–cog scale. In the post-hoc analysis of the combined solanezumab trials in the subset of mild AD patients, treated patients declined approximately 1.3 points less than controls on the same scale over 18 months. Yet this small difference represented an approximately 30% slowing of the rate of cognitive loss. Traditionally, “disease modification” trials have been designed to be able to detect differences in this range. Yet we are surprised when the magnitude of change, even after 18 months, is small in absolute terms relative to that seen with “symptomatic” agents.

But solanezumab is an antibody directed against beta-amyloid, only one of the many aspects of the pathological chain of events believed to underlie the relentless march of AD. New agents on the horizon will target the tau pathway, neuro-inflammation, and other aspects of the disease process. Eventually we will have to test these agents in combination, as has been done in the field of oncology. Perhaps the outcome of these studies will lead us to be able to truly arrest (control) or eradicate the cause and reverse the clinical damage from (cure) neurodegenerative diseases.