

Adjourning Alzheimer's

Synopsis - The Road To Diagnosing Alzheimer's (Day 53)

We've covered a **lot of material** in this second month. It's time to do a recap!

(1) Memory

Memories are emergent phenomena that arise from **interactions between neurons** as they send and receive signals to and from each other. Most memories are **episodic** (personal experiences that occurred in a specific place and time) or **semantic** (facts about the world learned independently of personal experience). Memories are **created** in a process that spans wakefulness and sleep; in **wakefulness**, they are **encoded** into the hippocampus, and in **non-rapid eye movement (NREM) sleep**, they are **consolidated** into the cerebral cortex. Memories are **utilized** in a process that also spans both wakefulness and sleep; in **wakefulness**, they are **retrieved and reassembled** by the hippocampus, in either realistic or imagined ways, so that they may form our perspectives and guide our actions, and in the dreams of **rapid eye movement (REM) sleep**, they are **semi-randomly relayed** to the hippocampus, forming our perspectives and guiding our actions in subtle ways. The creation and utilization of episodic and semantic memories is a constant to-and-fro between hippocampus and cerebral cortex; a **cognitive dance** in which memories are continuously refined and modified. This dance forms our inner model of the world.

(2) The 5-Step Alzheimer's Approach

Since there is no definitive test that can identify the pathological process in Alzheimer's, a person with long-term cognitive impairment can only be diagnosed with Alzheimer's after excluding alternative possibilities, followed by applying clinical criteria for Alzheimer's. A variety of disorders can produce long-term cognitive impairment; to discover which is responsible, a **5-step approach** can be useful. The 5-step approach includes a **corroborated history, focused examination, cognitive and functional scales, laboratory tests** (usually blood tests, rarely lumbar puncture), and **brain imaging** (usually CT or MRI scans, rarely PET scans).

(3) Mild Cognitive Impairment

In 2001, neurologist Ronald Petersen came up with the concept of **mild cognitive impairment (MCI)** to describe an intermediate state between normal aging and mild Alzheimer's. MCI is now defined as a **decrease in cognition**, which includes a decrease in one or more of **memory, attention, concentration, language, visuospatial skills** (interpret spatial relationships), or **executive function** (plan, judge, decide), exceeding that of normal aging. People with MCI **retain the ability to function**, working and socializing virtually normally. MCI does not necessarily mean a person will develop Alzheimer's, but it does increase their risk of eventually being diagnosed with Alzheimer's compared to a person without MCI, by ten-fold.

(4) Dementia Mimics

Roughly **10%** of all dementia cases are classified as **dementia mimics**, disorders with the capacity to mimic Alzheimer's. Common dementia mimics include **depression, medications, organ disorders, vitamin deficiencies, infections, and brain lesions**. It is important to use the 5-step approach to exclude dementia mimics, for some of them are reversible, although looking at the numbers, less than 1% of all dementia cases are actually partly or wholly reversible. Still, a slim chance is better than no chance at all.

(5) Non-Alzheimer's Dementias

Roughly **20-30%** of all dementia cases result from a **non-Alzheimer's pathological process**, the most common of which are **vascular dementia, Lewy body dementia, and frontotemporal dementia**. Each non-Alzheimer's dementia represents a **signature pathological process** marked by **hallmark clinical features**. Vascular dementia is ischemic, and marked by step-by-step cognitive decline. Lewy body dementia is neurodegenerative involving Lewy bodies, and marked by fluctuating alertness, visual hallucinations, and parkinsonism. Frontotemporal dementia is neurodegenerative involving tau, and marked by disinhibited social conduct and blunted emotional responses. Using the 5-step approach, a non-Alzheimer's dementia can usually be diagnosed - but sometimes, it's hard.

(6) Alzheimer's

Roughly **60-70%** of all dementia cases are due to **Alzheimer's**. The Alzheimer's pathological process has no hallmark clinical features, nor can we use any test or scan to identify it; therefore, the best we can do is diagnose a person with **probable Alzheimer's**. In 2011, neurologist Guy McKhann published the currently used criteria for diagnosing a person with probable Alzheimer's. The revised McKhann criteria are **80-90% accurate** for diagnosing Alzheimer's, yet many people with mild Alzheimer's remain undiagnosed - some may be unaware that something is amiss, others are aware but explain it away (or have it explained away), and still others are aware yet choose to turn a blind eye.

Clearly, the road to diagnosing Alzheimer's is **not an easy road**, for anyone. Yet it is a crucial road to travel, for several reasons:

(1) First, an undiagnosed disorder, the unseen adversary, is often more frightening to deal with than a known disorder. When a person can put a name to the disorder that ails them so, that knowledge provides a **degree of relief**. No more wondering, "What is going on?" Finally, there is an answer.

(2) Second, a diagnosis can provide a person with **clarity of vision** as to what they want to do with their life - Australian **Greg Kelly**, who was diagnosed with one of the forms of dementia in his 50s, chose to change his life based on that diagnosis and rode his motorcycle around Australia and New Zealand, raising money for dementia research along the way.

(3) Third, being diagnosed early on provides a person with the **ability to tackle the disorder earlier**. I believe that the trajectory of Alzheimer's can be altered; we just have to find out how.



Greg Kelly rode around Australia and New Zealand to raise money for dementia research.

Thus, if we choose to look at things in a more positive light, being diagnosed with Alzheimer's provides a degree of relief, clarity of vision, and the ability to tackle the disorder earlier. Surely, these are great things. However, it is also vital to realize that the diagnosis itself is not the end of the road; rather, it is a **gateway to a new one**.

The diagnosis of Alzheimer's empowers a person with **knowledge**; they can hone in on the condition, learn about it, embrace it. Yet knowledge alone is not enough. If the knowledge is not applied to reality, or viewed in a negative light, it is nothing. However, if the knowledge is applied to reality, then slowly, methodically, and rigorously, the combination of **knowledge plus action** can become something else entirely...

...it can become **power**.

Matt (Neurologist, Waikato Hospital).