Adjourning Alzheimer's

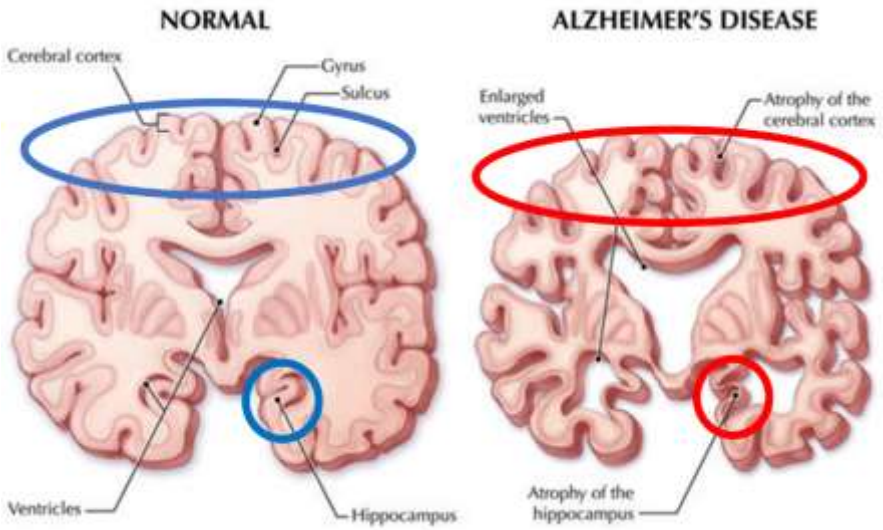
Neuron Loss (Day 8)

What **is** Alzheimer's? This is a very good question.

To answer it, it helps to realize that Alzheimer's is probably not a single event, but **a long chain of pathological events**. We know several facts about the end of that chain, but not too many about its beginning. Thus, to elucidate the origins of Alzheimer's, we will start by describing the facts that characterize the disorder in its latter stages, and then work backwards.

If we compare the brain of a cognitively normal person to that of a similarly-aged person with late-stage Alzheimer's, we see pronounced areas of **atrophy** (decreased size) in the latter. This atrophy is a consequence of **neuron loss**; many of the neurons in these areas have died. Neuron loss is not an inevitable feature of aging; cognitively normal 115-years-olds have the same number of neurons as cognitively normal 60-year-olds. Yet a person with late-stage Alzheimer's shows an astounding **70% loss of neurons** in their cerebral cortex compared to a cognitively normal person of similar age.

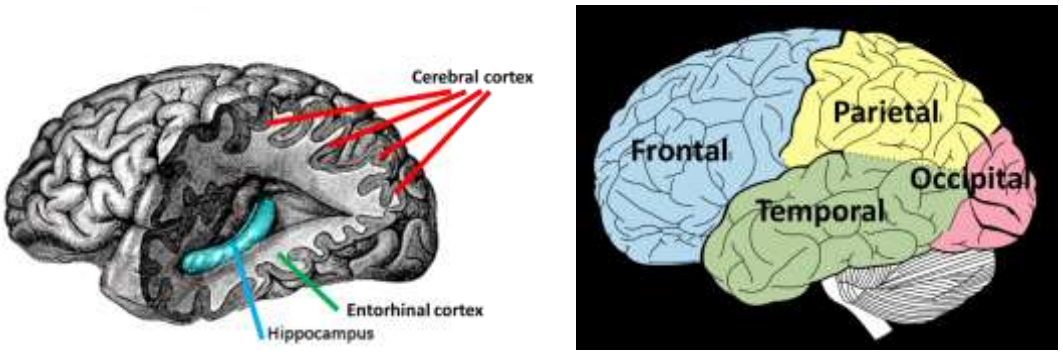
In Alzheimer's, the atrophy is particularly pronounced in two brain structures, the hippocampus and cerebral cortex. The **hippocampus** consists of a pair of small, seahorse-shaped structures; it is vital for forming and using memories. The **cerebral cortex** which is a thin, 2-3 mm sheet of 30 billion neurons that envelops most of the rest of the brain; it stores the memories.



In Alzheimer's (right figure), the hippocampus (small circles) and cerebral cortex (large circles) are severely atrophied.

The hippocampus and cerebral cortex are hit hard by Alzheimer's. However, brain structures such as the **thalamus** (keeps us awake and attentive) and **amygdala** (generates emotions) are also affected. Interestingly, there are other brain structures, such as the **basal nuclei** (selects which movements and thoughts are most appropriate for a given situation) and **cerebellum** (allows us to perform them with proficiency), that remain largely unaffected by Alzheimer's.

Neuron loss in Alzheimer's does not happen all at once; it happens **slowly**, years before the diagnosis of Alzheimer's is even made, and in a **particular order**. Neuron loss initially occurs in the **hippocampus** and a tiny adjacent region of cerebral cortex, the **entorhinal cortex**. Typically, neuron loss then proceeds along the remaining regions of cerebral cortex, afflicting the temporal and parietal regions, followed by the frontal region, with the occipital region involved last.



Neuron loss starts in the hippocampus and entorhinal cortex (left figure) before afflicting the remaining regions of the cerebral cortex (right figure).

To sum up, the pathological feature most directly responsible for the clinical symptoms of Alzheimer's is **neuron loss**; this is what truly defines the disorder, at least in its latter stages. Neuron loss is not an inevitable consequence of aging; rather, it is a process that takes such a **long time** to occur, it tends to appear in old age. Moreover, neuron loss does not afflict the entire brain, but is **selective** for the hippocampus and certain regions of cerebral cortex. However, it would be a mistake to think that neuron loss is the first event in Alzheimer's. Neuron loss is merely the final event in a long chain of pathological events, one that stretches back several decades, at least.

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References

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(3) Rivera et al. 2005. Insulin and insulin-like growth factor expression and function deteriorate with progression of Alzheimer's disease: Link to brain reductions in acetylcholine. J Alz Dis 8, 247-268.