

communicating the nitty-gritty of your research to the lay public, but my point is that if the experimental scientists themselves feed this collective perception that science leads to discovering the truth by “selling” each other their findings, then we’re screwed because the same feeling can only leak out and reinforce the public’s blind faith in science. I was reading this article¹ in *The Scientist* the other day, and the author goes: “As a proposition about history, Wallace’s hypothesis ultimately cannot be proved.” There! The author is suggesting the hypothesis cannot be proved because you can’t go back in time and run tests, but otherwise hypotheses can be proved just fine. And the guy is writing for scientists presumably. I just think you should be more aware and careful of the way you conduct science and conclude from your experiments. As a graduate student in science, you should learn to appreciate the philosophy behind how you carry out your experiments in your quest to logically and truthfully advance scientific knowledge. Surely the data are

important, and surely science has done tremendous things for us; but again I wonder if the way other scientists in your field think and what they say about science has any impact on the eventual outcome of our scientific progress. Would their strong, over-the-edge comments have got in the way of how we would have advanced over the years? You said it’s the pressure to excel in a tough, competitive environment. I don’t know, man, perhaps it’s just nature to do so for human beings,” Phil pondered.

At this point, both Bill and Phil realized that the bar was about to close. They quickly paid for their drinks and briskly walked into the street to start a whole new discussion on human nature in the cold early morning.

References

1. D. Steinberg, *The Scientist* 18:28 (2004). For further reading see J.F. Allen, *Bioessays* 23:104 (2001) and A.S. Wilkins, *Bioessays* 23:1-2 (2001).

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ARTICLE

Love the Rock.

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If you are familiar with the many stories told in Greek mythology you would know that the ancient gods, while sometimes caring and compassionate, were mostly a cruel and nasty lot. Dare cross these folk and, like Atlas (condemned to hold the world on his shoulders) and Prometheus (chained to a cliff and eaten by a bird), their wrath upon you was likely to be swift, brutal, and in many cases, eternal. The story of Sisyphus, whose suffering

was popularized by the famous French philosopher Albert Camus, is no exception. Influenced by other existentialist¹ writers, Camus was of the rather dreary opinion that humans fundamentally lack definition and that life was without meaning. The paradox, he explains, is that despite this meaninglessness we still struggle to find meaning in our lives. Camus calls this absurd. In his book *The Myth of Sisyphus*, he defines the *absurd* and uses

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the story of Sisyphus as a metaphor to explain that only by becoming *conscious* of the absurd struggle and by *choosing* to continue it anyway - despite the absurdity – is it possible to escape the inherent futility of the situation itself.

This discussion offers only a small sample of Camus' message and its purpose is not to dissect or evaluate views on either the absurd or human existence. Instead its intent is to take some of the key issues raised by Camus' work and determine if they can be applied to other struggles and burdens, admittedly more mundane than the topic of existence, but important nonetheless. In particular I wonder how can an individual face a burden or struggle deemed to be absurd, i.e. one that is dreaded, feared, seemingly insurmountable, and yet must be completed? Numerous examples can be used to illustrate this point but probably the best place to start is with Camus' example of the story of Sisyphus.



The Myth of Sisyphus

In the myth itself, Sisyphus is a man who dies and awakes to find himself in the underworld. Not happy with this, he convincingly laments to the gods that he would like to return to earth, if only for a short while, to sort out some unfinished business. The gods agree, albeit conditionally, so Sisyphus is allowed to make the journey back. However soon after reuniting with the many pleasures of earth - the sun, wind, and sea – he abandons his promise of return to the underworld. The gods, not to be trifled with, are decidedly upset by this deception and force Sisyphus to return to the darkness where upon they exact a most horrible punishment. Every day, for all eternity, Sisyphus is condemned to the onerous task of pushing an immense rock up a hill where, once at the top, he must wait for it to roll down so that he can start the task all over again.

The Absurd Hero

Sisyphus's spurning of both the gods and death earned him the punishment of having to expend every ounce of his energy for a task that accomplishes absolutely nothing. For Camus this endless futile toiling is representative of the absurdity of human existence. Worse still, says Camus, is that this isn't even the most horrible part. The real tragedy is in those rare moments when Sisyphus becomes *conscious* of the futility of his struggle.

"Then Sisyphus watches the stone rush down in a few moments toward that lower world whence he will have to push it up again toward the summit...I see that man going back down with a heavy yet measured step toward the torment of which he will never know the end...The workman of today works everyday in his life at the same tasks, and his fate is no less absurd. But it is tragic only at the rare moments when it becomes *conscious*. Sisyphus, proletarian of the gods, powerless and rebellious, knows the whole extent of his wretched condition..."

The Absurd Victory (or 'Defeating the Rock')

Although Sisyphus seems trapped in this meaningless existence, Camus presents his thesis that there is a means of escape and that consciousness of the absurd is the most important first step. Once becoming aware of the futility inherent within his task, Camus suggests that Sisyphus can overcome the absurdity of his fate by *choosing* to face his struggle – to push the rock anyway - despite its futility. Therefore, even though the rock itself is still being pushed, the critical components of 'consciousness' and 'choice' allow for control of the situation to be placed in Sisyphus' hands.

"A person who has become conscious of the absurd is for ever bound to it. A man devoid of hope and conscious of being so has ceased to belong to the future. That is natural. But it is just as natural that he should strive to escape the universe of which he is the creator...I fancy Sisyphus returning toward his rock, when the images of earth cling too tightly to memory, when the call of happiness becomes too insistent, it happens that melancholy arises in man's heart: this is the rock's victory, this is the rock itself. The boundless grief is too heavy to bear...[However] happiness and the absurd are two sons of the same earth. They are inseparable... At each of those moments when he leaves the heights and gradually sinks toward the lairs of the gods, he is superior to his fate. He is stronger than his rock...if this myth is tragic, that is because its hero is conscious...All Sisyphus' silent joy is contained therein. His fate belongs to him. His rock is his thing... The struggle itself toward the heights is enough to fill a man's heart. One must imagine Sisyphus happy".

For Camus, Sisyphus' choice is the key to changing his fate from one of misery to one of happiness. Faced with absurdity, Sisyphus makes the absurd choice. Rather than hate the rock and dread pushing it, he instead chooses to advance on his struggle with passion

and resolve. By choosing his burden, he revolts against it. Rather than despising and loathing his rock, Sisyphus instead chooses to love it.

Love the Struggle

Admittedly this might be a controversial extrapolation of Camus' view, but I see merit in thinking of this interpretation as a possible recipe for facing a struggle that *has* to be completed. It can be a dreaded, loathed, or seemingly doomed-to-failure task, or just one link in a long chain of things that needs to be done to finish something. It is important to note though that Sisyphus' struggle, like existence, is meant to represent a burden that *must* be continued. For Camus, 'quitting' is not an option when it comes to existence (in fact, this point is the main purpose of his book). So this example is most definitely an extreme one and may be difficult to compare to other struggles. Or is it? Is it not fair to say that some struggles faced everyday, ranging from both the great to the mundane, are nevertheless often viewed in the same extreme way? If so, are they no less absurd? Recall the question that was initially raised. How can an individual face an absurd struggle? Can Camus' view be applied? To take one example, consider an individual who faces a dreaded task with loathing and passivity, but at the same time still feels compelled (at least in their view) to complete it. Since this represents an absurd struggle, what could be said to the individual? Following Camus' example, the person must first become *conscious* of the absurdity inherent in their task and second, must make the choice to throw all energies, all passions, actively into the struggle – even while acknowledging and accepting that the task may not be completed in the end. In effect, we would ask them to love their struggle – to love their rock. But does this make any sense? Consider the following example.

Mary the Geneticist

Mary wants to be a scientist but in order to be one, Mary must face a subject that she fears. In this case the subject is Genetics. Mary doesn't understand genetics, doesn't know much about genetics, and for this reason, Mary hates and fears genetics. However, genetics is the one thing that Mary must master in order to complete a greater task that she likes very much (i.e., research into a disease) so she accepts that the subject of genetics is going to be her struggle. Since she is compelled to complete this task while at the same time not wanting to, she is aware that this struggle is an absurd one. Conscious of this absurdity, Mary makes the absurd choice to put all her energies into learning Genetics. She still hates it, but she devotes every moment to learning something new about it. Hours turn to days, days turn to months, and all the while she continues to put all her passions and resolve into accumulating more knowledge

about genetics. Over time, this learning becomes easier and easier and soon she realizes that she knows a great deal more about genetics than anyone else. In fact, she becomes recognized as an expert and people from around the world come to hear her views on the subject. At this point, Mary makes a stark realization. In the beginning she chose to love her struggle – despite the absurdity – but inwardly thought that she actually hated it. But now she realizes that her struggle is no longer a struggle; now she thinks she actually does *love* genetics.

But what's love got to do with it?

The interesting thing about Camus' analogy of the rock is that the struggle, no matter what it is, will continue whether you want to do it or not. So this begs the question. Why bother with the 'love' bit? After becoming conscious of an absurd struggle (i.e. being compelled to complete a task and not wanting to), why would one *choose* to 'passionately', and 'actively' complete it? Why not just *choose* to complete it? Admittedly, this is a more difficult question to answer but I think that ultimately this is the thing that is most intriguing. If we take the case of Mary, the fact that she devoted everything to genetics seems the main reason why she became good at it. If she merely chose to passively or half-heartedly pursue her topic, she may have also fulfilled her obligations, but she would have still completed a task that she didn't want to complete. Her struggle would have remained absurd - despite completion. Therefore, it could be argued that her choice to passionately pursue her absurd struggle is the very thing that removed the absurdity. By loving her struggle, her struggle ceased to exist.

The PhD Rock

For some it might be a brief fleeting feeling while for others it might be a long deep foreboding dread, but for a number of people there is no quagmire of hopeless futility quite like the pursuit of a PhD. Although the roots of this can be debated *ad nauseam* (i.e., topic, supervisor, person, discipline, luck, desire, etc.) the fact that this perception is known to all, openly admitted by some, and secretly held by many others, is probably testament to its seeming universality. Of course it must be granted that some disciplines have far fewer students gripped by this torment. Some have very structured requirements with a very structured focus (e.g. research into a specific disease) where a dissertation is a gradual ever-evolving entity with a real focus. Thus many students might never come to view their PhD as an absurd struggle. But the notion of the absurd PhD nonetheless exists. Just look at the numerous websites and focus groups dedicated to talking about doctoral hardships and struggles for some examples². If this is the case, then another question might be raised. If you feel yours is truly an absurd PhD, can the analogy of the rock be of any help?

Many thanks go to Alexandra Haninec for her brilliant illustration (above) and critical review of this piece.

Notes

1. A sort of anti-philosophy philosophy. Existentialists believe human existence has no meaning but nonetheless try to find some sort of meaningful inner meaning in all the assorted meaninglessness.

2. Crippled by the seemingly senseless futility of your thesis? Visit www.deadthesissociety.org

REVIEW**The Alzheimer's Alarm Clock**

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Alzheimer's disease is a progressive neurological disorder characterized by memory loss and confusion, and is the most prevalent age-dependent dementia¹. The major risk factor of Alzheimer's disease is age. Less than two percent of all people inflicted with Alzheimer's disease are below the age of forty-five. This increases to approximately ten percent over the age of sixty-five, and jumps dramatically to forty-seven percent in the over eighty-five population². The familial forms of Alzheimer's disease account for less than ten percent of all affected individuals, and the majority of these cases become affected after the age of sixty³. This signifies a biological alarm clock that appears to awaken this dormant disease after the age of fifty in most individuals, and the mechanism responsible still remains unclear.

One of the most prevalent neuropathological features of Alzheimer's disease is the deposition of amyloid in the brain, in addition to selective neuronal loss and neurofibrillary tangles. Amyloid accretions exist as either amorphous, diffuse deposits or as a dense senile plaques, which stain positive with Congo red⁴. The principle constituent of the amyloid deposits is a peptide denoted amyloid β ($A\beta$), which varies from 39 to 43 amino acids in length, the most abundant forms being 40 and 42 amino acids ($A\beta_{40}$ and $A\beta_{42}$, respectively)⁵. The $A\beta$ protein is normally cleaved from the proteolytic processing of the amyloid precursor protein (APP) by two enzymes, β secretase and α secretase (Figure 1).

β -secretase, also known as β -site APP cleaving enzyme (BACE), leads to the production of $A\beta$ peptide after β -secretase cleavage, whereas α -secretase cleavage produces the non-toxic P3 peptide⁴. Both $A\beta_{40}$ and $A\beta_{42}$ can form amyloid fibrils, but are also associated with other structural forms in the progression to the fibril state. The monomeric form of the $A\beta$ peptide has generally been considered to not be a neurotoxic species.

It has been shown that the density of senile plaques does not increase with age, rather, patients switch from a plaque-free state to plaque-bearing³. The amyloid plaques develop from initially being non-neurotoxic into mature, senile neuritic plaques. The number of these senile neuritic plaques increases after the process is first

initiated, with the number approximating to the degree of cognitive impairment³.

Thus the question still remains as to what major physiological change(s) occur which allow for the initiation of Alzheimer's disease. One possibility is that a regulatory change occurs, leading to the usage of different signaling pathways, hormones and transcriptional regions. This process can be clearly defined in women as menopause, which typically occurs between the ages of forty-five and fifty. A similar change may also occur in men around the same time period. This may be the natural winding down of the human clock that inadvertently awakens the processes leading to Alzheimer's disease. Greater understanding of the changes that occur later in life is required for prevention of age-dependent diseases such as Alzheimer's. Prevention will not be possible until the factors that initiate the clouds of plaques in the brain are clarified; this leaves only symptomatic treatment for Alzheimer's sufferers. However, recent findings have shed light on possible methods for treatment.

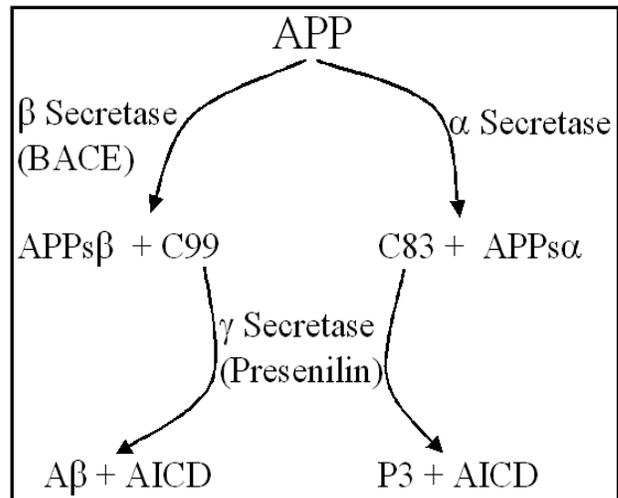


Figure 1: β -Secretase and α -secretase compete for the amyloid precursor protein (APP) to produce either of their respectful large extracellular fragments termed APPs. The C-terminal fragments remaining in the membrane are cleaved by γ -secretase in the transmembrane region, to release either $A\beta$ or P3 peptides and the intracellular release of the APP intracellular domain (AICD).