Memory and emotions in Alzheimer’s disease.

Visiting a patient with Alzheimer can be frustrating, both for the person making the visit and the patient itself. Talking with a close family member, with whom you may have shared many different experiences over the course of your life, and realizing he or she no longer remembers your name, is probably an extenuating feeling. Adding even more to the already wearisome situation is the fact that the visited person may not even recall you came in at all a few hours after you depart. These problems tend to elicit questions regarding the usefulness, and objective, of visiting patients with this kind of disease. Do they have any effect on their mood and quality of life, or do they only leave painful memories on their family members and friends? This essay will ponder over these questions, providing, at the same time, a simple background to gain a better understanding of memories, as well as the link between them and personal emotions.

What is memory?

We use memory all the time, whether we are conscious of it or not. It is one of the most complex and useful aspects of the human mind, helping us to remain in contact with past experiences, learn from mistakes, and recognize our surroundings. Without it we would be looking at our everyday life situations as something unusual, and foreign. We don’t usually value having it, but for a person affected with Alzheimer, or any other kind of memory impairment, it makes the difference between a fully functional life and one filled with constant confusion. But what exactly is memory?

Memory, according to a textbook definition, is “the persistence of learning over time through the storage and retrieval of information”.\(^1\) Although this gives us a general idea of what memory is, we will quickly find out that the real, in-depth exploration of the topic involves much more than just storing and recalling events. One general misconception that people tend to have about the function of memory is the belief that previous events are saved in a “general storing place” inside the brain. Different aspects of memory are processed by different parts of the brain, rather than analyzed by a single, identifiable unit.\(^2,7\) the exact mechanism of it is still not fully understood, making it difficult to find an actual cure for memory related diseases.

Memory can be classified in many distinct ways. The two most general (and, concerning the theme of this essay, most important ones are the following:

**Short term memory:** Short term memory, as the name implies, is the ephemeral capacity of holding small amounts of information in our mind.\(^1,2\) Our most recent experiences and details are
first processed by our short-term memories, remaining there for a small amount of time (usually a matter of seconds) until they are processed, destined to be either forgotten or definitely embedded in our more permanent, long term memories. We are constantly receiving inputs from our surroundings, our short term memories being constantly updated. Processing new information into the memory system is called encoding, and it is the first crucial step for the formation of new memories.\textsuperscript{1, 2}

**Long term memory:** It is the memory of all the past events and experiences that happen in the course of our lives, remaining stored in our brain system until they are consciously recalled, or retrieved.\textsuperscript{1, 2} At the first stages of the Alzheimer’s disease, many patients still conserve some of their long-term memories intact, their ability to make short-term memories the only thing damaged (able to recall old events, but unable to store new ones).\textsuperscript{3} As the condition deteriorates, however, the patients lose their long-term memories as well, reaching a point where recognition of family members, or the ability to perform simple, every day actions, is no longer possible.\textsuperscript{3}

Since long-term memories are so broad, they are further divided into several categories:

**Types of long term memory:**

**Declarative or explicit memory:** Our conscious, available memories. These are subdivided into two other main categories, episodic (concerning our personal memories, and specific events in time) and semantic (memories unrelated to specific past experiences, considered “general knowledge”, like an historical fact or the meaning of a word). These memories are mainly processed on the hippocampus.\textsuperscript{1, 2}

**Non declarative, or implicit:** These are all the kinds of non-conscious memories, in which we perform actions, or react to a certain situation, without necessarily recalling the event that made us learn it. Walking, for example, is a kind of non declarative memory, since we perform it every day in a “mechanical” way.\textsuperscript{1, 2}

There are diverse medical conditions that can result in temporary or permanent loss of memory. The most common, and often most fatal, is Alzheimer’s disease. We will analyze its origins and symptoms in more detail, in order to have an appropriate background to answer the main question of this essay.

**What is Alzheimer’s disease?**
Alzheimer’s disease is the most common type of **dementia**, a group of brain disorders that cause progressive loss of intellectual and social skills due to an abundant death of brain cells. This disease has no known cure, and it is known to be fatal. 3

It was first described by neurologist Alois Alzheimer in 1906, when observing the progressive loss of a woman’s memory and mental faculties before the age that would characterize it as senile dementia. 4 The defining characteristic that distinguishes Alzheimer from other kinds of dementia is the abundance of two specific proteins in the brain: **plaques** and **tangles**.3,4 Plaques are starch-like proteins better known as “beta-amyloids”, which, when accumulated in large quantities inside the brain, interfere with the ability of neurons to communicate with each other. Tangles are deposits of a protein known as “tau”. Although “tau” is normally present inside neurons, during Alzheimer’s disease this protein tends to abnormally coil with itself, forming unusual knots. The exact role of plaques and tangles is still heavily debated within the scientific community, although their abundance in patients with Alzheimer is irrefutable. 3,4...

**Causes:**

Scientists are not entirely sure of what the conditions that cause the disease are, mainly due to its own complexity. It has been speculated that the disease may be generated by multiple factors, rather than a single cause. Family history, age, heart problems, and a particular race can be some common risk factors contributing to the acquirement of the disease, but it is not always the case. 3

**Solutions:**

Although there has been a lot of research on the matter, no known cure has been found. There are, however, common prevention methods (like staying mentally active, exercising and having a healthy diet), as well as medications that help to slow down the degenerative rate of the disease once acquired. The road leading to its eradication, it seems, still remains in shadows. 3

One of the first symptoms of Alzheimer is damage to the hippocampus (a fundamental component of the brain, which allows us, amongst other things, to create new memories), getting worse as it progresses. If the patients cannot make new memories and aren’t able to recall whether or not they have received a visit from a loved one, to what degree are they affected by them in the first place? Could visits provide a small window for Alzheimer patients to re-experience the real world, or are they nothing more than a blank page on their never formed memories?
Memory and emotion: How much do Alzheimer’s patients actually feel, or remember, after visiting hours?

Memories and emotions seem to share a mutual, almost unbreakable link with each other. Specific events can make us feel a certain way, the emotion coming back to us when the memory is recalled. It is also well known, not only because of detailed research but from our own experiences, that specific moments characterized by a particularly strong feeling (a wedding, a funeral, or even a sad movie) are the ones that stay deeply ingrained in our memories. Both concepts may appear, at first glance, completely inseparable. But what happens when one of the main strands is separated from the other? When you can no longer recall - is it possible for the emotional load it generated to remain?

In a recent study patients with dementia were presented with a series of emotional films portraying themes of sadness (loss and death), and happiness (humorous situations) in two subsequent experiments. Moments later, the amnesic patients still manifested an emotional response to the film, despite having little or no recollection of its contents. The results of these experiments show that emotions can endure long after the conscious memory of the event itself is lost. Another surprising result of this experiment is that sad emotions, in contrast to happy ones, remained longer on the subconscious of the patient, even longer than in the healthy controls. (Fig 1) The reason as to why this happened is debatable; it is believed that, due to the frustration of the patient not knowing why he or she is having a negative feeling, the sensation increases.

This was not the only recorded case. In 1911, a Swiss neurologist named Edouard Claparede decided to make an experiment with one woman that suffered of progressive amnesia, making her unable to create new memories. In this simple experiment, Claparede decided to hide a pin between his fingers as he greeted her with a handshake. The pin, as expected, elicited a painful response in the patient. Although the event was forgotten within minutes, the woman refused to shake Claparede’s hand, not exactly understanding the cause of her mistrust. One of the most interesting results of this experiment is that the discomfort of the patient would last a very long amount of time, sometimes during an entire day. This experiment also seems to suggest that negative emotions remain on the subconscious of the patient long enough after the specific event has been forgotten.
Fig 1. The graph on the left shows the amount of details recalled of a particular sad film by patients with amnesia (red bar), compared to those remembered by healthy controls (blue bar). The graph on the right shows the level of sadness reported both by healthy controls and amnesiacs after they saw the film, and after the memory of it was faded. It can be seen that people with severe amnesia tended to manifest a higher level of sadness than the healthy individuals, even after the concrete facts of the film were forgotten by both groups of subjects.

Not only do negative emotions seem to remain longer, but sometimes the event itself isn’t that easily forgotten if it carries a very tragic emotion. In 1995, a very strong earthquake, known as the “Kobe Earthquake” swept a great part of the southern territory of Japan. In an experiment to see how much these kind of events remain on the memories of people with some kind of dementia disorder, experimenters asked patients that had acquired Alzheimer’s previous to the earthquake how much did they remember. Surprisingly, almost all of them seemed to recall the earthquake, although facts such as dates remained elusive. A similar case happened after the events of September 11th, 2001, where patients with the already acquired condition of Alzheimer could accurately recall the main events of such tragic episode. It has also been shown that patients with a memory condition that have been victims of a crime tend to provide a precise description of the episode, more accurately remembered than other mundane, daily events.
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Science through film and fiction

The fact that negative emotions are preserved in a greater magnitude than positive ones can be considered as one strong evidence supporting the importance of visiting, and showing concern, to patients with this kind of mind disorders. If visitors, or even caretakers, of Alzheimer’s patients show an attitude that make them feel uncomfortable, or confused, the feeling will persist long after the visitors are gone. As shown by Claparede’s experiment, they can last not only hours, but even days after the main event is forgotten. This clearly affects the life quality of the patients; an unpleasant experience will leave them feeling depressed, emotion that will only magnify as the memories of the experience fade. Refusal to eat, or to share any kind of company, can be the result of this seemingly unknown depression, feeding it even more and probably accelerating the degenerative rate of the disease. A positive attitude towards them, however, can trigger the opposite effect. Although the scene itself will be forgotten, the mood of the patients will significantly improve if they were previously treated in a way that made them feel comfortable.

It is known that patients with any kind of dementia tend to present several and sudden mood changes, as well as a mild impassiveness to other’s emotions. Three recent articles published by the “The Journal of Neuropsychiatry and Clinical Neurosciences” seemed to confirm this notion, revealing that patients with Alzheimer tend not to feel or recognize emotions as strongly as a healthy person would. The first study showed them pictures of different facial expressions, asking them to match the expression with the emotion they believed was the most adequate. The second study showed pictures to the subjects, who then had to rate in a scale from one to ten how emotional did they consider them. The results of both studies showed that people with Alzheimer condition had a more faded response to them than the controls.

How can we explain the noticeable differences between one study and the other? Is the amount of damage caused by the disease an important factor that should be considered?

**The hippocampus and the amygdala: connection between emotions and memories.**

In order to understand the relationship between memory and emotions, and to answer the previous question, we first need to know the essential brain parts involved in these two processes. Something that should be clarified, however, is that the functions of these sections of the brain are not just limited to those discovered and explained on this essay: the human mind is far too complex for it to restrict single functions to specific areas.

**Hippocampus:** Although it was previously clarified that memory isn’t located in a specific part of the brain, one of the main processing units in terms of long term memory is the hippocampus. This major component of the human brain helps to encode and process incoming memories. The relationship between the hippocampus and the formation of new memories has been...
proved with several experiments made to patients with damage in that part of the brain. One commonly known example is that of a patient known as HM. After a surgery that removed almost all of his hippocampus, it was discovered that he was unable to form new declarative memories.

Amygdala: The amygdala is a nuclear complex located on the temporal lobe of the brain. One of its most fundamental functions—amongst many others—is the enhancement of emotional memories. Several investigations have proven that, thanks to the amygdala, the most deeply emotional events in our life are the ones that more quickly become embedded as permanent, long-term memories. This suggests that the amygdala and the hippocampus play a very intrinsic role together, with the amygdala influencing the encoding and storage of long-term memories. This role can be proven by several experiments made to patients that had a lesion on their amygdala, or their hippocampus, and comparing their responses.

In one of them, called the “Blue square shock” three groups of patients (a healthy control, one with damage in their amygdala and the other with damage in their hippocampus) were presented with different images, one of them being a blue square, while the experimenters measured their brain activities. Before the experiment begun, the experimenters told the subjects that they would receive a slight shock in the wrist whenever the blue square appeared in the screen. Although no actual shock was presented, the three groups showed different reactions whenever the blue square came into view. The control group, in anticipation for an imminent shock, demonstrated high levels of anxiety, as well as increased levels of activity in their amygdala. The patients with damage in their amygdala, however, failed to show any response at all, even though they knew—and showed a complete understanding—of what consequences would bring the appearance of the blue square. The third group, which showed damage on their hippocampus, showed an emotional response whenever they saw the blue square, without being able to point out the exact reason for their reaction. The results of this experiment can clearly show the link between the amygdala (which regulates the emotional reactions of the patient, in response to any verbal stimulus or association) and the hippocampus (which is a main component in the formation of new memories.)

After seeing the roles of these two important complexes, it is easier to suggest an explanation for the differences between the experiments showing prolonged emotional response on Alzheimer patients, and those showing no response at all. In Alzheimer’s disease, one of the first complexes to be damaged is the hippocampus itself, rendering the affected person from making new memories. In the early stages of the disease, the already established long-term memories, as well as the functionality of the amygdala is kept intact. This makes it possible for the emotions of an event to
be preserved, regardless of the memories of the event itself. However, as the disease progresses and the amygdala deteriorates, the ability of the patients to recognize or differentiate emotions turns out to be more difficult. It has been observed that patients with a more developed stage of the disease ( ) tend to have drastic mood changes with no apparent reason, fail to communicate pain, and, in the late-stage of the disease, become unable to respond to their environment.

The answer as to whether or not the visits affect patients with Alzheimer may depend, as previously demonstrated, on the stage of the disease itself. If the mental condition is in its early or medium stages, visits from family and friends may generate a positive emotion in the patients receiving them, easily contrasted with those who are mistreated or ignored by their relatives. As the condition worsens, however, it might be possible that the affected patients no longer recognize any external stimuli, remaining completely and forever separated from the world. Although that doesn’t mean external visits should stop at these advanced stages, it is highly possible that patients in their terminal phase are no longer affected by the presence or absence of familiar faces, or the treatment they are receiving. Those who have relatives or friends with these conditions should continue to perform the visits, no matter how advanced the disease. That way, you not only attempt to generate some recognition, or inadvertently make some improvement on the quality of life of your loved ones, but also show them that you will always be there for them, even when they no longer remember.
Bibliography:


   <http://www.alz.org/national/documents/Facts_Figures_2011.pdf>. This is a full, well written report about the most recent facts of Alzheimer’s disease. A great part of my background research for this project was taken from this report, located on the Alzheimer’s Association webpage.


   ..<http://www.pnas.org/content/107/17/7674.full>. More detail about the experiment that showed emotions can endure long after the memory of an event is lost.


