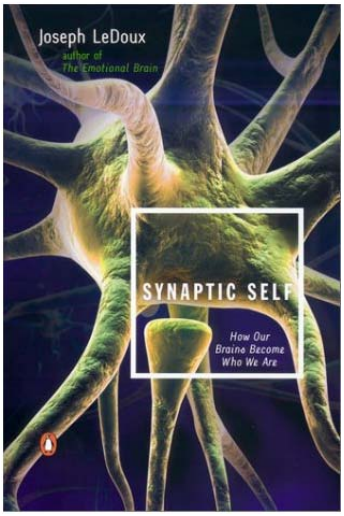
Nick Murray
PSY385: Neuroscience Capstone
Dr. Jan Wotton
25 February 2010

Q. Who are you?

A. *The Synaptic Self, How Our Brains Become Who We Are*

- by Joseph LeDoux Ph. D



"There is no such thing as learning" (87).

Um…what?

Unsettling as this reads, it captures one flavor (i.e. *unlearning* by a process of elimination) of the intricately balanced learning arguments Joseph Le-Doux describes in *The Synaptic Self* (Penguin Books 2003; Paperback for $11.05 new on Amazon). Although the book is over seven years old, it remains current, and there is no other text at present that clearly address similar foci as *The Synaptic Self.* It consists of 324 pages of text complemented by a 67 page notes and works cited section and a useful index. This molds the book into a crossover between a textbook on learning and memory and a long review paper containing solutions to wide range of questions you and I might have regarding what makes up ourselves, our personality on a neuronal basis.

The chapters are laid out to describe what is known about the synaptic components of self in memory, brain development, neuronal physiology and brain plasticity, emotions and motivation, and synaptic imbalances that result in disease states. In doing so it covers a broad scope, providing initial perspective on (1) *what a synapse is* and through accumulated inferences gathered throughout the book to end with a final chapter that adequately answers (2) *who one is.* Yes, it sounds a bold move, but in reality the literature provides sufficient support for such conclusions.

LeDoux, professor of neuroscience at New York University, draws on his then 20 (now 28) years of studying emotion and fear modulation to begin the book and details how historical investigations of brain anatomy and physiology have contributed to the findings of the last half century

which conclusively show, on a molecular scale, how neurons develop and change to create each of us. And in doing so he answers the question of who each of us is based on the ever changing strengthening and weakening of the physical structure of the brain. In short, the take home message of *The Synaptic Self* is: you are your synapses.

Synapses, simply, are spatial clefts that bridge the physical components of the communication structures of separate neurons. Communication across the synapse is how messages are delivered and how brain systems interact throughout our body.

For those with backgrounds in basic psychology and biochemistry, the flow of writing is easily followed. If not, the book will be a challenge, but not an insurmountable one. LeDoux brings together current understanding of the mind and brain into an extensive, integrated theory of neuronal synapse alteration or *plasticity*. Readers will appreciate his use of the same popular lay person language as in his 1996 text *The Emotional Brain.* This allows one, as it did for me, freedom to read the book similarly to a textbook to browse specific concepts that do not necessarily follow right after each other. I discovered that *The Synaptic Self* caters toward chapter and section hopping for quick reference for questions on how the mind, brain and their unified influence exerts itself on species specific and individual personality. Despite the facilitated section hopping structure, the text is not a self-help or pop psychology book. Parsimonious line drawings and frequent figures that explain concepts fundamental to learning, such as early and late long term potentiation (LTP) and the receptors involved are appropriately used. The LeDoux Lab Home Page (www.cns.nyu.edu/home/ledoux) provides current laboratory information and perspective on topics of interest.

OK, so *The Synaptic Self* is tailored toward a specific, well-informed audience and supplemental material is of no short supply. But since you are probably reading this to grasp on the content of the book, let us return to that discussion.

Following the introductory pages, LeDoux establishes the concepts of self *and* synaptic self. He first describes how classical Greek logic has inevitable shortfalls in truly getting down to the core of what makes the 'self' of each of us. As expected, LeDoux successfully conceptualizes

'self' with a simple section on what are from psychological standpoints (e.g. Nativist, behavioralist, etc.), what neurons physically are, and psychology and neurons each function (in a parallel manner, which is discussed later) to allow for sensation, perception, and cognition.

To answer what really makes us who we are (i.e. the age-old nature vs. nurture controversy), LeDoux provides a simple explanation that while genes make us all the same (humans) and distinguish us from each other, environmental influences manipulate the expression of these genes to modify synapses. LeDoux summarizes, or perhaps tries to end, the nature nurture question of personality arguing that learning involves the nurturing of nature. Therefore, genetic factors can constrain neuronal structure via the innate ability we each have to make (and break) synapses. This process dictates personality to some extent. He suggests that the literature (previous to 2003) does not provide insight into what makes one conscious and gives each a personality, so the "big one question" will remain unanswered.

Due to the lack of answers to questions that have plagued psychologists for ages, he prudently sets expectations for the reader, stating "…we can't, at this point, go all the way in formulating a complete synaptic theory of personality…but even a partial understanding of the synaptic basis of who we are is, for me, an acceptable goal" (3). That goal of understanding the personality and nature of consciousness questions to the greatest possible extent is, however, achieved by the end of the book.

In addressing these questions, *The Synaptic Self* is different from previous texts, which address the relation of the self to the brain via the conscious self. Here the book explores this relationship on a biological mechanisms platform. With this platform LeDoux is able to reach out to a diverse set of audiences. For example: a spiritual and theological audience. He reiterates that even though the Vatican decreed in 2000 that the soul is non-material, it is biologically implied that spiritual intervention robustly links the soul to the physical world (i.e. any influence the soul or intervention of God on *thought* inevitably affects neuronal structure). That conclusion suggests that a combination of the biological with a classical Christian spiritual mindset may not be possible. Theologians acknowledge the relationship between the mind and the brain to explain spiritual intervention and synaptic change simply as part of a master plan since God created the

principles of physics that underlie plasticity. So perhaps a traditional Christian viewpoint can be melded with biology in some way.

Next, LeDoux builds a foundation for action potentials, development of signaling circuits, and gross brain structures. He draws on studies, such as those of David Hubel and Torsten Wiesel in the 1960s on visual system development. Their experiment used cats to investigate how cortical cells were assigned to the visual field. Hubel and Wiesel used test closure of one eye of a kitten immediately after birth that resulted in the alternate eye remapping and expanding its cortical terminals into the region that would have be used with the covered eye. The exact same covering of an eye to give an adult cat mono-vision did not result in remapping, indicating that there is a capacity for redevelopment of synaptic circuitry that is only receptive during certain early life stages. This process of remapping explained in the book helps the reader to grasp the concept of cellular pruning and regrowth through biochemical modification of neuronal circuits from experience and genetics.

In organismal development the principle of "use it or lose it" is applied to neuronal interactions by the Hebbian method of wiring by firing. This results in select synapses being selected for preservation or further development, or in other words, the strengthening of that aspect of memory or even trait that gives us characteristics of our personality. Experts are quoted heavily throughout the book by LeDoux, especially in this section. One is that of Mark Johnson who commented that "…early years of [human] development are crucial not because the window of opportunity closes but because what is learned at this time becomes the foundation for subsequent learning" (96). LeDoux follows this with the insight that often new memories are made out of old ones, as each new experience is dependent on the one before it.

Often, fundamental aspects of daily life are overlooked, such as the gatekeeper function of memory to one's entire self, reason, feeling, and action. LeDoux illustrates the work of Brenda Milner, who showed what happens when we lose memory function with the patient H.M. H.M. had his hippocampus removed as a treatment for epilepsy and he subsequently could no longer form new episodic memories. Retrieval of formed memory in (normal) humans is detailed in the text with a nomadic perspective in that "many researchers believe that explicit memories are

stored in the cortex systems that are involved with the initial processing of the stimulus, and that the hippocampus is needed to direct the storage process [and perhaps the retrieval process as well]" (107). As with nearly every concept presented in the book, a counter argument is too, here LeDoux shares the current view that only some kinds of memory depend on the hippocampus.

Due to waning interest toward explaining intricate molecular biology in book reviews, my brief comment on the "Small Change" molecular neurobiology chapter is a short forewarning that it could conveniently be used in a *university level* neurobiology classroom. Hint: it is intense. (If you need a mental break during reading, listen to the neuroscience-themed rock band, The Amygdaloids http://www.amygdaloids.com/, of which LeDoux is a guitarist)

But, the chapter is strongly written and covers research published by the star players in the study of learning (and, in an awkward manner, the results of past accomplishments of some Ph. D. students in the LeDoux lab) and thus has potential to build comprehension for if and when memory enhancement products come up for testing. Some already have, if genetic manipulation counts, in the gene modified Doogie mice (i.e. they have unregulated NMDA receptor subunit expression) created by the Joe Tsien laboratory.

The following mental trilogy chapter elaborates on cognition, emotion, and motivation. The construction of a framework for a final discussion in the last chapter brings the reader at this point to information on: working memory, top-down and bottom-up *and* natural methods of reinforcement in emotional processing (with extensive detail on the neuronal replay of emotions and fear). The transition to synaptic sickness, or disorders (e.g. depression, Parkinson's, etc), makes for captivating clinical case studies when the phenotypic results of synaptic function go awry. This chapter will most likely be of great interest to university students (or anyone interested in neuronal health) due to in-depth coverage one is unlikely to find elsewhere.

And to be completely honest, I read that chapter for relaxation on a Friday evening.

For example, the progress of treating the complex dopaminergic circuits involved in Schizophrenia is addressed. LeDoux provides media, chemical company, and neuroscientist responses to serotonin modulation in the 1980s in clinical depression as selective serotonin reuptake inhibitor (SSRI). He quotes an advertisement about SSRIs, which describes them as "science [that] will let you change your personality with a pill." I am particularly impressed with the variety of backgrounds pulled into *The Synaptic Self* to provide perspective here. LeDoux himself suggest that either the 'enhance your personality' selling point above of SSRIs worked or, because neuronal side effects are limited, more borderline depressed individuals felt comfortable using the drug.

To conclude, LeDoux synthesizes the plethora of literature previously mentioned into the final chapter to answer the question of how synapses make you who you are. Really, the bulk of novel synthesis occurs here. LeDoux argues that seven principles are explanatory of who you are (even though viewing or listening to electrophysiological recordings of brain activity indicates that the brain is just an unruly mob of tissue).

In a nutshell, LeDoux repeats that *parallel plastic*, thus interlinked brain systems, experience many of the same external environmental inputs (i.e. all the information acquired during a specific activity for each system) which synchronizes activity to release neuromodulators (e.g. neurotransmitters or hormones) that influences the electrical activity of post-neuronal circuits in various parts of the brain. Particular regions of the brain are specialized signal convergence centers (e.g. the limbic system; hypothalamus, hippocampus) that can integrate signals to amplify them or inhibit their further effects.

Fortunately, information provided in the text is relatively current according to PubMed literature searches conducted in February 2010.

In case you wish to pursue more current literature on the subjects detailed in *The Synaptic* Self, the papers published LeDoux lab continue to focus on auditory induced short term and long term LTP on cortical and thalamic inputs to amygdala in the fear learning system. In January of 2010

they reported that *in vivo* stimulation pulses elicited stronger LTP in the cortical inputs than thalamic inputs.

They also have taken account of Joe Tsien's 1999 work on upregulation of NMDA receptors and showed in their own 2009 paper that NR2B-containing NMDARs (NR2Bs) in the lateral amygdala are required for fear memory extinction acquisition.

Other papers in 2009 and 2010 reflect their lab's transition to work on preventing traumatic fear memory recall in humans. In 2009 the LeDoux team used a reconsolidation blockade that recruits a US-CS behavioral design that destabilizes fear memory without the use of potentially toxic drugs. They were able to permanently attenuate the fear memory. In late January 2009 to the present it appears as if they are exploring a non-invasive pharmacological manipulation procedure for human fear memory erasure. During reconsolidation of fear memories they target the labile nature of the synaptic circuit to disrupt it (a paper on this topic was published in Nature on January 7th).

My final suggestion: purchase *The Synaptic Self*, read it, and share it with a neuroscience leaning friend.

-Nick Murray
February 25, 2010

"That the self is synaptic can be a curse—it doesn't take much to break it apart. But it is also a blessing, as there are always new connections waiting to be made. You are your synapses. They are who you are."

-Joe LeDoux