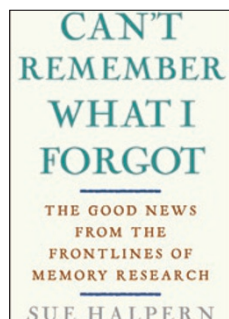


## Worried about your memory?



### Can't Remember What I Forgot: The Good News from the Front Lines of Memory Research

Sue Halpern

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Reviewed by Howard Eichenbaum

Am I beginning to lose my memory? Will I get Alzheimer's disease? These are questions Sue Halpern worries about in *Can't Remember What I Forgot*. She shares this anxiety with many members of the baby boomer generation, educated nonscientists who would like to visit the luminaries of memory research and ask these questions. Halpern saves them the trouble and describes in this book her odyssey to discover what science is doing about memory loss.

Halpern likes to tell stories. She tells stories about memory, about the brain, about memory disorder researchers, and about the many efforts to discover preventions and treatments. She's especially fascinated with the people who study memory disorders, providing a physical description and biography of each person she interviews and highlighting their unique personalities. Each research program is a story, too, a narrative of a protagonist (the scientist), a plot (the hypothesis) and an uncertain ending (the progress).

This book does not do a good job of describing how memory works. There is mention of some of the key brain structures that are involved in regulating memory, along with a description of the different types of memory and stories about key discoveries. But, as a basic scientist, I was disappointed that Halpern seems uninterested in the brain circuitry that encodes memories. I think knowledge about normal brain circuits will turn out to be critical to understanding how they fall apart in aging and disease. But current research, as reflected in this book, prefers to leap from molecules to behavior, skipping the brain circuits in between.

Instead, the book focuses on two key questions: how do we diagnose memory disorders, and what are we doing about them? With regard to the first question, Halpern does a marvelous job of explaining why there are so many studies showing brain correlates of memory loss or disease, and yet it is very difficult to diagnose or predict memory disorders in an individual. But Halpern never comes right out and tells us that the difficulty involves the fundamental distinction between population statistics and individual identification. The measures of disorders and of the normal brain are variable and involve a large distribution of every measure, so that the distributions of normal and abnormal scores overlap substantially.

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The other key question ("What are we doing?") is addressed in a comprehensive overview of all the ways scientists and hucksters (and sometimes it's difficult to tell the difference) are suggesting that memory loss might be cured or prevented. Each of these stories begins with potential insight and promise but ends in failure or, at best, a question mark. There are many books describing memory exercises and tricks to improve memory, mostly telling us that practice, elaboration and organization are the best strategies. There is substantial evidence that more physical exercise and less stress benefit the brain as they do the body. So keeping in good shape is a good strategy—but this advice is working about as well for brain fitness as it is for our national crisis in obesity. How about mental exercise, highlighted in the mental aerobics captured in new videogames? Unfortunately, mental exercise enhances connections only in the brain areas that are exercised and only for the tasks that are involved in the exercise. Our best hope along this line is that high educational level is a reflection of the most general variety of mental exercise and, correspondingly, is a good predictor of avoiding memory disorder.

There are also many stories about the possible roles of food products in maintaining memory. The candidates include cocoa, ginkgo, red wine, fish oil and more (I personally like the chocolate idea). Each has a rationale in metabolism and an associated link to aging or disease. Each has some relevant anecdote or full-fledged study showing a correlation. At the same time, either the nature of the evidence is questionable or the positive study is complemented by another study showing no correlation.

Most fascinating, and perhaps least widely known, are the efforts at drug development. These are, of course, pursued intensively by big pharma, but those stories are not told here (perhaps Halpern couldn't penetrate corporate secrecy). Rather, the focus is on scientists who have formed drug companies. Each case begins with a rational approach highlighting a molecule that plays a prominent role in their research. The story of Sention is illustrative and perhaps the most titillating. The company received \$13 million in venture capital to discover the next "Viagra for the brain." They focused on a molecule known by the cryptic name C105 and soon proved that it was safe and exciting enough to move into large-scale clinical trials. Then, well...nothing. We don't know what happened, but obviously it was not good news for C105. Perhaps the problem with drug discovery is that all such efforts are based on the questionable hypothesis that a single molecule is at fault or at least a major part of the cause—and maybe the situation is just more complicated. Then there's the problem of side effects: because memory uses molecules that are critical to many bodily functions, a major challenge is to influence that molecule in the critical brain site and not muck up its functions elsewhere.

So, is Halpern accurate in her subtitle, asserting that there is "good news from the front lines of memory research"? Having read the book, whose findings are consistent with my own knowledge of memory and memory disorders, one has to conclude that Halpern is an optimist. True, a cure or prevention *could* be just 5 years down the road. And there is a lot of activity and "smoke" in the findings. But the stories of current research could just as well lead us to conclude that we would be better off to drop the anxiety and enjoy our senior moments, while awaiting a more sophisticated approach.