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Propranolol's effects on the consolidation and reconsolidation of long-term emotional memory in healthy participants: a meta-analysis

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Abstract

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Background

Considering the pivotal role of negative emotional experiences in the development and persistence of mental disorders, interfering with the consolidation/reconsolidation of such experiences would open the door to a novel treatment approach in psychiatry. We conducted a meta-analysis on the experimental evidence regarding the capacity of the β-blocker propranolol to block the consolidation/reconsolidation of emotional memories in healthy adults.

Methods

Selected studies consisted of randomized, double-blind experiments assessing long-term memory for emotional material in healthy adults and involved at least 1 propranolol and 1 placebo condition. We searched PsycInfo, PubMed, Web of Science, Cochrane Central, PILOTS, Google Scholar and clinicaltrials.org for eligible studies from the period 1995–2012. Ten consolidation (n = 259) and 8 reconsolidation (n = 308) experiments met the inclusion criteria. We

calculated effect sizes (Hedges *g*) using a random effects model.

Results

Compared with placebo, propranolol given before memory consolidation reduced subsequent recall for negatively valenced stories, pictures and word lists (Hedges $g = 0.44$, 95% confidence interval [CI] 0.14–0.74). Propranolol before reconsolidation also reduced subsequent recall for negatively valenced emotional words and the expression of cue-elicited fear responses (Hedges $g = 0.56$, 95% CI 0.13–1.00).

Limitations

Limitations include the moderate number of studies examining the influence of propranolol on emotional memory consolidation and reconsolidation in healthy adults and the fact that most samples consisted entirely of young adults, which may limit the ecological validity of results.

Conclusion

Propranolol shows promise in reducing subsequent memory for new or recalled emotional material in healthy adults. However, future studies will need to investigate whether more powerful idiosyncratic emotional memories can also be weakened and whether this weakening can bring about long-lasting symptomatic relief in clinical populations, such as patients with posttraumatic stress or other event-related disorders.

The role of consolidation in memory

"**Consolidation**" is a term that is bandied about a lot in recent memory research. Here's my take on what it means.

Becoming a memory

Initially, information is thought to be encoded as patterns of neural activity — cells "talking" to each other. Later, the information is coded in more persistent molecular or structural formats (e.g., the formation of new synapses). It has been assumed that once this occurs, the memory is "fixed" — a permanent, unchanging, representation.

With new techniques, it has indeed become possible to observe these changes (you can see **videos** here). Researchers found that the changes to a cell that occurred in response to an initial stimulation lasted some three to five minutes and disappeared within five to 10 minutes. If the cell was stimulated four times over the course of an hour, however, the **synapse** would actually split and new synapses would form, producing a (presumably) permanent change.

Memory consolidation theory

The hypothesis that new memories consolidate slowly over time was proposed 100 years ago, and continues to guide memory research. In modern consolidation theory, it is assumed that new memories are initially

'labile' and sensitive to disruption before undergoing a series of processes (e.g., **glutamate** release, protein synthesis, neural growth and rearrangement) that render the memory representations progressively more stable. It is these processes that are generally referred to as “consolidation”.

Recently, however, the idea has been gaining support that stable representations can revert to a labile state on reactivation.

Memory as reconstruction

In a way, this is not surprising. We already have ample evidence that retrieval is a dynamic process during which new information merges with and modifies the existing representation — memory is now seen as reconstructive, rather than a simple replaying of stored information

Reconsolidation of memories

Researchers who have found evidence that supposedly stable representations have become labile again after reactivation, have called the process “reconsolidation”, and suggest that consolidation, rather than being a one-time event, occurs repeatedly every time the representation is activated.

This raises the question: does reconsolidation involve *replacing* the previously stable representation, or the establishment of a new representation, that coexists with the old?

Whether reconsolidation is the creating of a new representation, or the modifying of an old, is this something other than the reconstruction of memories as they are retrieved? In other words, is this recent research telling us something about consolidation (part of the encoding process), or something about reconstruction (part of the retrieval process)?

Hippocampus involved in memory consolidation
The principal player in memory consolidation research, in terms of brain regions, is the hippocampus. The hippocampus is involved in the recognition of place and the consolidation of contextual memories, and is part of a region called the medial **temporal lobe** (MTL), that also includes the perirhinal, **parahippocampal**,and entorhinal cortices. Lesions in the medial temporal lobe typically produce amnesia characterized by the disproportionate loss of recently acquired memories. This has been interpreted as evidence for a memory consolidation process.
Some research suggests that the hippocampus may participate only in consolidation processes lasting a few years. The **entorhinal cortex**, on the other hand, gives evidence of temporally graded changes extending up to 20 years, suggesting that it is this region that participates in memory consolidation over decades. The entorhinal cortex is damaged in the early stages of Alzheimer's disease.
There is, however, some evidence that the hippocampus can be involved in older memories — perhaps when they are particularly vivid.
A recent idea that has been floated suggests that the entorhinal cortex, through which all information passes on its way to the hippocampus, handles "incremental learning" — learning that requires repeated experiences. "Episodic learning" — memories that are stored after only one occurrence — might be mainly stored in the hippocampus.
This may help explain the persistence of some vivid memories in the hippocampus. Memories of emotionally arousing events tend to be more vivid and to persist longer than do memories of neutral or trivial

events, and are, moreover, more likely to require only a single experience.

Whether or not the hippocampus may retain some older memories, the evidence that some memories might be held in the hippocampus for several years, only to move on, as it were, to another region, is another challenge to a simple consolidation theory.

Memory more complex than we thought

So where does all this leave us? What **is** consolidation? **Do** memories reach a fixed state?

My own feeling is that, no, memories don't reach this fabled "cast in stone" state. Memories are subject to change every time they are activated (such activation doesn't have to bring the memory to your conscious awareness). But consolidation traditionally (and logically) refers to encoding processes. It is reasonable, and useful, to distinguish between:

- the initial encoding, the "**working memory**" state, when new information is held precariously in shifting patterns of neural activity,
- the later encoding processes, when the information is consolidated into a more permanent form with the growth of new connections between nerve cells,
- the (possibly much) later retrieval processes, when the information is retrieved in, most probably, a new context, and is activated anew

I think that "reconsolidation" is a retrieval process rather than part of the encoding processes, but of course, if you admit retrieval as involving a return to the active state and a modification of the original representation in line with new associations, then the differences between retrieval and encoding become less evident.

When you add to this the possibility that memories might "move" from one area of the brain to another after a certain period of time (although it is likely that the triggering factor is not time *per se*), then you cast into disarray the whole concept of memories becoming stable.

Perhaps our best approach is to see memory as a series of processes, and consolidation as an agreed-upon (and possibly arbitrary) subset of those processes.

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