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Review

Human reconsolidation: A reactivation and update

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ABSTRACT

The reconsolidation hypothesis states that memories, when reactivated, enter a transient, labile state followed by a re-stabilization termed reconsolidation. By affecting the reconsolidation process, memory persistence can be influenced, leading to memory enhancement or decrement. This is a time-dependent process and the result of modulating reconsolidation is present only after the reconsolidation process is completed. Historically, reconsolidation research has been performed on non-human animals, since the methods originally used for reconsolidation disruption are not safe. However, there now exist several techniques safe for humans, and consequently, in recent years, papers on human reconsolidation have emerged. Here, the existing literature on human reconsolidation is reviewed and discussed, including studies on fear memories, appetitive memories, procedural memories, and declarative memories. Methods of memory reactivation are compared between studies, and the consistency and lack of consistency in results over reactivation methods and memory types are discussed. These results provide future challenges, both experimental and clinical, in defining the boundary conditions and mechanisms governing the reconsolidation phenomenon.

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Contents

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1. Introduction

A newly formed memory becomes a stable memory trace through a consolidation process that follows encoding. The process of consolidation is dependent on protein synthesis and is modulated by components of a stress reaction, such as noradrenaline and glucocorticoids, in a process in which the amygdala is vital (McGaugh, 2000). However, a consolidated memory is not set forever. Recalled or reactivated memories can under certain circumstances enter a transient labile phase followed by a new stabilization process termed reconsolidation. Thus, reconsolidation seems to be a time-dependent process and the effects of reconsolidation modulation should be observable after concluded reconsolidation, and not immediately upon administration. Reconsolidation is a phenomenon found in a range of species and types of memory, making it appear as an often employed memory strategy in nature (Alberini, 2005). During reconsolidation, memories can be enhanced (Rodriguez et al., 1999), impaired (Nader et al., 2000), or updated with new information (Lee, 2008). The term 'reconsolidation' is perhaps unfortunate; since the reconsolidation process appears to be something else than a simple repeat of the consolidation that follows directly on encoding. The differences and similarities in the molecular mechanisms of consolidation and reconsolidation are comprehensively discussed elsewhere (Alberini, 2005; Tronson and Taylor, 2007). However, the term 'reconsolidation' has firmly established itself within the scientific community and is unlikely to be replaced.

Studies on reconsolidation have mostly been performed on animals. The first methods used to disrupt reconsolidation were electroconvulsive shocks (Misanin et al., 1968) and the administration of protein synthesis inhibitors (Nader et al., 2000). The first study to experimentally examine the reconsolidation process in humans used electroconvulsive shocks for reconsolidation disruption. Participants encoded a set of pictures of items and a set of word pairs which were tested with recognition memory tests. On these tests, it seemed that consolidation could be disrupted by electric shocks, but no effect of electroconvulsive shocks on reconsolidation was found. The study also tested the subject's memories of TV shows, watched years before the study. These older memories were not affected by the shocks at all (Squire et al., 1976). Also, early clinical trials used electroconvulsive therapy (ECT) and disrupted the reconsolidation in patients with OCD and hallucinations with some success (Rubin, 1976). Still, ECT is deemed too risky for general experimental use and protein synthesis inhibitors are also not safe for humans. However, memory enhancement and erasure by affecting reconsolidation have recently been shown, by use of pharmacological manipulations that are safe for humans (Brunet et al., 2008; Kindt et al., 2009), and behavioural means (Schiller et al., 2010; Walker et al., 2003). Consequently, the last few years have produced quite a few studies on human reconsolidation and the present paper aims at summarizing what we have learned.

Reconsolidation processes are typically studied with a three-day experimental design (Fig. 1). On the first experimental day, encoding takes place. On experimental day 2, the memory is reactivated, and manipulated. Usually, there is a control group that does not receive the manipulation, or receive the manipulation after a delay, when the reconsolidation process is supposed to be concluded. There is also typically a control group that do not receive a reactivation, showing that the effect of manipulation is dependent on a memory reactivation. Finally, on experimental day 3, there is a test of memory strength. Sometimes, there are further follow up tests. In clinical studies, the patients are viewed as already possessing the memories, and instead of experimental day 1, baseline measures are obtained, and then the subjects proceed directly to experimental day 2.

1.1. Methods of reconsolidation manipulation

The results below will be structured according to method of reconsolidation manipulation and type of memory. Listed below are the methods used for reconsolidation manipulation in humans, along with the rationale on why these methods are used, drawing on the literature on rodent consolidation, rodent reconsolidation, and human consolidation.

1.1.1. Propranolol

The most frequently used pharmacological manipulation is the administration of the drug propranolol, a β-adrenergic antagonist. Its presumed function on memory is through adrenergic β receptors coupled with the adenylyl cyclase-linked G-protein receptors governing the cAMP cascade that leads to protein synthesis-dependent long-term memory formation (Przybyslawski et al.,

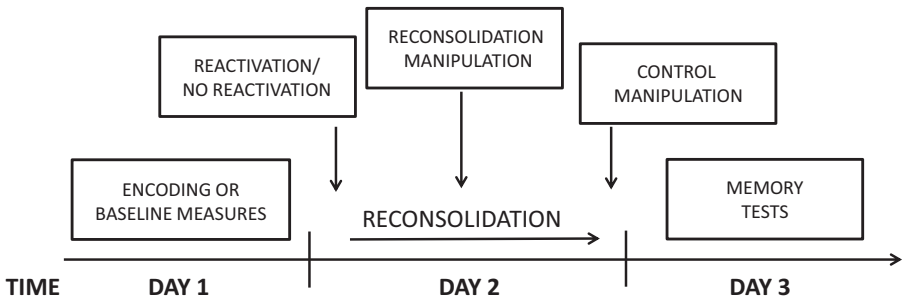

Fig. 1. Typical three-day experimental design for the study of human reconsolidation. On day 1, subjects participate in an encoding session. On day 2, the memory is reactivated, triggering a reconsolidation process. A control group, in which the memory is not reactivated, is often included. The on-going reconsolidation process is then manipulated. An additional control group does not receive this manipulation, or receives a control manipulation after the reconsolidation process is concluded. Finally, on day 3, the memory is tested. In clinical trials, the encoding of day 1 is replaced by baseline measurements of the traumatic memory to be treated.