

Understanding the boundary conditions of memory reconsolidation

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Hardwicke et al.'s article (1) challenges the concept that reactivating human memories, by way of retrieval, returns them to a labile form requiring reconsolidation. Several lessons emerge from their study. Although the authors replicate the majority of our original observations (2) (learning, offline consolidation), they observed no evidence for memory lability following retrieval. Three methodological differences suggest potential explanations for this partial failure to replicate.

First, subjects in our study (2) underwent learning and retrieval at 1:00 PM, whereas Hardwicke et al.'s (1) subjects were assessed across a wide range of circadian phases (9:00 AM to 6:00 PM), and hence, after an equally wide range of prior wakefulness (potentially 1–11 h). Both factors influence memory processing. The ability to instigate memory lability through reactivation is diminished after extended time awake (3). Furthermore, memory lability and the mechanisms underlying memory reactivation, consolidation, and reconsolidation all vary with circadian phase (4).

Second, Hardwicke et al. (1) used older subjects (18–52 y) than we did (18–27 y). This difference is key, as contextual reminders fail to trigger reactivation and thus memory lability in older rats and older humans (5).

Finally, Hardwicke et al. (1) altered the original memory task. Their first two experiments replicated our instructions to tap “as quickly and accurately as possible” (1). However, subjects in their last two experiments were told to “tap as quickly as you can!” (1), removing our equal emphasis on accuracy, which is precisely where we saw reconsolidation effects and they did not.

Did such differences lead to Hardwicke et al.'s (1) failed replication? Discrepancies in their own experimental data, which were unable to establish internal replication, suggest this is possible. Hardwicke et al.'s

last three experiments showed the expected overnight improvement in motor-skill speed (mean ~19%, P 's < 0.001). However, their first “replication experiment” found no significant off-line improvement for either of two motor sequences tested (mean ~4.5%, P 's > 0.14): this is a significant 4.3-fold discrepancy in motor-skill improvement across Hardwicke et al.'s own experiments (ANOVA P 's = 0.003 and 0.023 for first and second sequences).

More generally, how should the concept of memory reconsolidation be viewed in light of these data? Hardwicke et al. (1) suggest that memory reactivation and reconsolidation may be less robust than previously assumed. However, the existence of two independent replications of our original finding of motor memory reconsolidation (6, 7) suggests such reconsolidation is not uncommon. Indeed, almost two dozen human studies and over 900 animal studies have reported reconsolidation. Hardwicke et al.'s study (1), by itself, does not establish the absence of reconsolidation (a null result cannot obviate an effect).

Instead, Hardwicke et al.'s (1) study suggests that, when using small numbers of subjects, behavioral (rather than electrical or pharmacological) manipulations of reactivation may less reliably produce measurable reconsolidation. Indeed, our own report of motor reconsolidation using purely behavioral methods, had only a moderate effect size (Cohen's $d = 0.59$) and power (69%) (2); that is, one could expect a one-in-three chance of failing to observe a significant effect in a similarly sized replication study.

In conclusion, the thoughtful report by Hardwicke et al. (1) provides an important replication of our earlier work and, through contrasting design features, suggests nuanced limits to measurable human motor memory reconsolidation.

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