Hippocampal morphology mediates biased memories of chronic pain

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\section*{ABSTRACT}

Experiences and memories are often mismatched. While multiple studies have investigated psychological underpinnings of recall error with respect to emotional events, the neurobiological mechanisms underlying the divergence between experiences and memories remain relatively unexplored in the domain of chronic pain. Here we examined the discrepancy between experienced chronic low back pain (CBP) intensity (twice daily ratings) and remembered pain intensity (n = 48 subjects) relative to psychometric properties, hippocampus morphology, memory capabilities, and personality traits related to reward. 77\% of CBP patients exaggerated remembered pain, which depended on their strongest experienced pain and their most recent mood rating. This bias persisted over nearly 1 year and was related to reward memory bias and loss aversion. Shape displacement of a specific region in the left posterior hippocampus mediated personality effects on pain memory bias, predicted pain memory bias in a validation CBP group (n = 21), and accounted for 55\% of the variance of pain memory bias. In two independent groups (n = 20/group), morphology of this region was stable over time and unperturbed by the development of chronic pain. These results imply that a localized hippocampal circuit, and personality traits associated with reward processing, largely determine exaggeration of daily pain experiences in chronic pain patients.

\section*{Introduction}

Everyday existence is a mixture of experiences and memories, the confluence and interaction of which guide future behaviors, and likely reflect adaptations critical for enhancing survival of the organism. Unraveling biological mechanisms regarding the relationship between experiences and the memories of those experiences is a cornerstone from which neuroscience can inform and advance psychology. Yet, the neurobiological mechanisms that determine or control such interactions remain minimally known. The emotional context (including mood and motivation) during an experience or recall significantly influences subsequent declarative and non-declarative memories (Murty et al., 2010). Moreover, memories may be enhanced to various degrees with valence and levels of arousal (Miron-Shatz et al., 2009; Murty et al., 2010; Miranda and Toffalini, 2016), and there is also evidence that emotional context (including mood and motivation) during an experience or recall significantly influences subsequent declarative and non-declarative memories (Murty et al., 2010). Memory distortions (Winocur, 1985), and both its anatomical structure and associated neurophysiology are implicated in memory distortions (Ramirez et al., 2013; Liu et al., 2014b; Kim et al., 2017). Numerous studies have shown that the hippocampus is a key region for emotional memory processing, including the production of false or incorrect memories (Ramirez et al., 2013; Liu et al., 2014b; Kim et al., 2017), memory interferences (Winocur, 1985), and both its anatomical structure and associated neurophysiology are implicated in memory distortions (Ramirez et al., 2013; Liu et al., 2014b; Kim et al., 2017; Leal et al., 2017).

Here we examine the topic from the viewpoint of the daily experience of patients suffering from chronic pain, a severe pathology that remains undertreated, poorly understood and a primary source of disability worldwide (Murray and Lopez, 2013). In addition to the intrinsic difficulty in describing and quantifying pain, it has been repeatedly shown that memories for painful events are inaccurate - when asked to recall a past painful event, people tend to overestimate their pain, with the intensity usually reported more severe than actually experienced (Salovey and Smith, 1997). The magnitude and direction of the discrepancy between remembered pain and actual pain seem to depend upon many...
of the hippocampus in memory encoding and retrieval, its role in the actual pain intensity they experienced while rating and that this bias in time and relative to other kinds of memories.

Morbid chronic pain, neurological, or psychiatric conditions was also least 6 months. No report or evidence of substance abuse or additional co-

Participants

The data presented here are from two separate studies investigating neural mechanisms of chronic pain and its relief. The memory-based (primary) dataset was taken from the initial baseline period of a clinical trial investigating brain mechanisms and biomarkers of placebo response in chronic pain. 72 participants with chronic low back pain (CBP) who completed at least the primary dataset to study the in...
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