HORIZON 2020

A Cross-Species Investigation of Memory Replay During Reconsolidation

Rendicontazione

Informazioni relative al progetto

ReconsolidationDynamics

ID dell'accordo di sovvenzione: 659221

Sito web del progetto

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Progetto chiuso

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Periodic Reporting for period 2 - ReconsolidationDynamics (A Cross-Species Investigation of Memory Replay During Reconsolidation)

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Sintesi del contesto e degli obiettivi generali del progetto

Learned fear responses and memories contribute to psychiatric disorders that constitute a significant socio-economic burden. Primary treatment methods teach patients to control fear responses. When learning to control fear responses a new safety memory forms that inhibits the expression of the old fear memory. Learning to control fear responses does, however, not get rid of the memory itself. The persistence of the fear memory explains why many patients experience a return of fear even after initially successful treatment. This return of fear highlights the need to discover robust treatments that persist.

One potentially promising approach is to alter the original fear memory, as opposed to inhibiting it, by targeting memory reconsolidation. Recent research shows that reactivating an old memory results in a period of memory flexibility and requires stabilization processes, or reconsolidation, for the memory to persist. This reconsolidation period provides a brief time-window during which it is possible to modify a specific fear memory. Renewal of memory flexibility following reactivation holds great clinical potential as it allows targeting and changing of specific memories that contribute to psychiatric disorders.

To live up to its clinical potential it is necessary to understand how to most effectively utilize paradigms targeting reconsolidation. The proposed research attempts to address this issue by providing a neural measure of the reconsolidation process itself. This will be achieved by determining whether dynamic patterns of neural network activity that occur during initial learning re-occur during offline ‘rest’ periods, and test whether this ‘replay’ of memory is linked to reconsolidation. The first objective is to identify and quantify a neural marker of reconsolidation. The second objective is to use this neural marker to determine how context serves as one potential critical boundary condition to inducing reconsolidation. To achieve the objectives an innovative cross-species approach, testing both humans and rats, using similar behavioural tasks and complementary recording techniques (functional magnetic resonance imaging and intracranial electrophysiological recordings).

The identification and quantification of a neural marker of reconsolidation can be used bridge the gap between animal and human studies and help to optimize approaches targeting reconsolidation to develop more optimal treatment methods for patients. State-of-the art techniques will be developed during this project and be shared with the scientific community. Findings are expected to provide novel insight into the neural mechanisms that underlie the persistent flexible nature of memory.

Lavoro eseguito dall’inizio del progetto fino alla fine del periodo coperto dalla relazione e principali risultati finora ottenuti

W1 aims to identify and quantify a neural marker of reconsolidation in humans. we set-up (M1.1) completed data acquisition (M1.2) and completed analyses of behavioural and physiological data but not yet of neural data (M1.3) after which we plan to publish (M1.4). The first public presentations regarding the work of the project have been held (PE1).

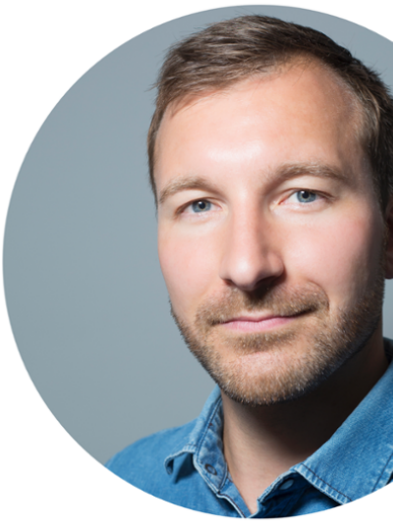
W2 aims to identify and quantify a neural marker of reconsolidation in rats. We set-up (M2.1) and completed behavioural data acquisition (M1.2) but did not replicate previous publications and are working to optimize the behavioural paradigm.

W3 aims to determine how context serves as one critical boundary condition to inducing reconsolidation in rats. This study has not been started as it awaits positive behavioral results in W2.

W4 aims to determine how context serves as one critical boundary condition to inducing reconsolidation in humans. We have created and published a novel immersive Virtual Reality contextual fear-conditioning paradigm. This paradigm will be used to reach the aim of W4.
In extending the project, we discovered that the intensity of aversive experiences limit the effectiveness of reconsolidation-interventions to modify fear memories. That the effectiveness of reconsolidation-interventions is limited for generalized fear and that such interventions can inadvertently enhance explicit fear memories. And that the reason it is difficult to modify fear memories may be that the ongoing stream of episodic experiences is segmented into distinct memory traces dependent on event boundaries during a consolidation period, which protects fear memories from interference by competing experiences of safety.

Progressi oltre lo stato dell’arte e potenziale impatto previsto (incluso l’impatto socioeconomico e le implicazioni sociali più ampie del progetto fino ad ora)

The research within the fellowship has discovered mechanisms underlying the modification of fear memories during reconsolidation. We have identified opportunities, limitations, and potential risks of targeting reconsolidation to modify unwanted memories. This has clear implications for the development of potential novel treatment strategies for fear- and anxiety-related disorders. Furthermore, the fellowship has led to the development of novel research paradigms that we made freely available to the scientific community.



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