Imaging recent to very remote object-in-place memories in the medial temporal lobe and prefrontal cortex

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BACKGROUND

The consolidation of very remote memories has mainly been investigated in highly emotionally arousing tasks like fear conditioning. Results show that cortical regions become increasingly engaged over time, however, whether the hippocampus remains engaged or not remains controversial. We have recently showed that while CA1 is recruited during the retrieval of up to 1-year-old contextual fear memories in mice (comparable to 40 years in humans based on life expectancy), CA3 is no longer recruited for the retrieval of very remote memories see Fig.3 ; Lux et al., *elife*, 2016). Further, MTL areas were also increasingly engaged over time. However, little is known about the relative contribution of these regions to the retrieval of early remote/very remote memories devoid of fear content. Here, **we tested whether the disengagement of CA3 for the retrieval of very remote memories and the increasing contribution of cortical regions in MTL and mPFC over time reflect a general mechanism subserving memory consolidation.** To this end, we developed a task devoid of fear content to investigate the specific contribution of MTL and mPFC areas to the retrieval over up to 6 months memories using *Arc* imaging.

APPROACH

We developed an object-in-place task (based on Ennaceur & Delacour, 1988; Beer et al., 2013 and Melani et al., 2017) for the detection of very remote memories using immediate early gene imaging (Sauvage et al., 2019) in the MTL and PFC regions

METHODS

Object-in-place memory remembering recent to very remote

Fig.2 Locations of the counting frames

Fig.3 Persistent engagement of CA1 and disengagement of CA3 for very remote memories in a contextual fear conditioning task (Lux et al., *elife*, 2016)

IMAGING RESULTS (N=2)

CA1 remains recruited while CA3 is disengaged during very remote retrieval of a non-fearful event

Unlike in fear conditioning PER and LEC are maximally engaged during early remote memory retrieval

ACC is also recruited for the retrieval of non-fearful remote memory

BEHAVIORAL RESULTS

Memory performance is comparable across delays

Non-mnemonic processes or memory strength across delays unlikely to account for the observed different Arc activity patterns

Similar exploration time of objects during study phase

CONCLUSIONS

Preliminary data indicate that the time-limited engagement of CA3, the persistent engagement of CA1 and the over time recruitment of cortical areas, such as ACC in the neocortex and LEC and PER in the parahippocampal areas, are a general mechanism supporting retrieval of remote memory for events independent of its emotional content.

FUTURE PLANS

- + Whether the contribution of CA1 and CA3 reflect the contributions of trisynaptic and temporoammonic pathways.
- + Whether the time-limited contribution of CA3 translates to human memory retrieval (7T fMRI).

(Adapted from Deng et al., 2010)

REFERENCES

1. Lux et al., *Elife*, 2016
2. Beer et al., *Hippocampus*, 2013
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6. Melani et al., *Neurosci*, 2017