

## Accepted Manuscript

NMDA receptors and BDNF are necessary for discrimination of overlapping spatial and non-spatial memories in perirhinal cortex and hippocampus

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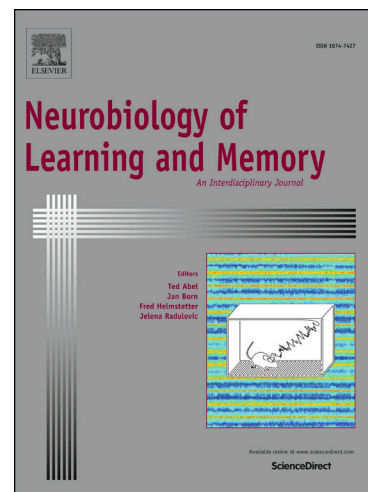
PII: S1074-7427(18)30213-2  
DOI: <https://doi.org/10.1016/j.nlm.2018.08.019>  
Reference: YNLME 6929

To appear in: *Neurobiology of Learning and Memory*

Received Date: 12 March 2018  
Revised Date: 3 July 2018  
Accepted Date: 29 August 2018

Please cite this article as: Miranda, M., Kent, B.A., Facundo Morici, J., Gallo, F., Saksida, L.M., Bussey, T.J., Weisstaub, N., Bekinschtein, P., NMDA receptors and BDNF are necessary for discrimination of overlapping spatial and non-spatial memories in perirhinal cortex and hippocampus, *Neurobiology of Learning and Memory* (2018), doi: <https://doi.org/10.1016/j.nlm.2018.08.019>

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***NMDA receptors and BDNF are necessary for discrimination of overlapping spatial and non-spatial memories in perirhinal cortex and hippocampus*****Magdalena Miranda<sup>1</sup>, Brianne A. Kent<sup>2</sup>, Juan Facundo Morici<sup>1</sup>, Francisco Gallo<sup>1</sup>, Lisa M. Saksida<sup>3,4</sup>, Timothy J. Bussey<sup>3,4</sup>, Noelia Weisstaub<sup>1</sup> and Pedro Bekinschtein<sup>1</sup>.**

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**Abstract**

Successful memory involves not only remembering information over time but also keeping memories distinct and less confusable. Discrimination of overlapping representations has been investigated in the dentate gyrus (DG) of the hippocampus and largely in the perirhinal cortex (Prh). In particular, the DG was shown to be important for discrimination of overlapping spatial memories and Prh was shown to be important for discrimination of overlapping object memories. In the present study, we used both a DG-dependent and a Prh-dependent task and manipulated the load of similarity between either spatial or object stimuli during information encoding. We showed that N-methyl-D-aspartate-type glutamate receptors (NMDAR) and BDNF participate of the same cellular network during consolidation of both overlapping object and spatial memories in the Prh and DG, respectively. This argues in favor of conserved cellular mechanisms across regions despite anatomical differences.

**Introduction**

Memory is often thought of as the ability to remember information over time. However, the ability to separate memories of similar experiences into distinct representations that are resistant to confusion is crucial for accurate retrieval (Dickerson et al., 2010). This has been simulated in computational models by a process termed 'pattern separation' that transforms similar inputs into output representations that are less correlated with each other and there is electrophysiological evidence of such transformation in the DG (Leutgeb et al., 2007) and Prh (Ahn et al., 2017). The study of this process may be relevant to understanding memory loss in aging and pathological conditions. For example, it has been reported that patients with schizophrenia or Alzheimer's disease show memory deficits related to the inability to keep memories distinct (Ally et al., 2013; Das et al., 2014; Llorens-Martin et al., 2014). The DG of the hippocampus (HC) was proposed as crucial for this cognitive function (Ranganath, 2010), and adult neurogenesis in the DG was shown to be necessary for normal behavioral pattern separation (Bekinschtein et al., 2014b; Clelland et al., 2009). However, previous

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