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Protein synthesis and memory¹

Paul E. Gold

Department of Psychology and Psychiatry, Neuroscience Program and Institute for Genomic Biology, University of Illinois at Urbana-Champaign, Champaign, IL 61820, USA, Fax: 217-244-5876, E-mail address:pgold@uiuc.edu

Introduction

This special issue of *Neurobiology of Learning and Memory* is devoted to the question of the role of protein synthesis in learning and memory. Prospective authors with very different views on this subject were invited to contribute to the special issue. Happily, most of those invited quickly agreed to participate. All papers were peer-reviewed and most were revised prior to publication. The result is a collection of papers representing significant diversity of opinion regarding the role of protein synthesis in memory formation. The authors took different approaches to represent their views of the role of protein synthesis in memory, with formats including broad reviews, targeted reviews, and experimental papers.

The goal of collecting these papers was not to find a single clear view, laying to rest one alternative view or another—a rather delusional goal at best. Instead, the attempt was to provide a venue through which different perspectives could appear together, with the understanding that all contributors are interested in a common purpose, to identify the ways in which brains make and hold new memories.

When approached with a description of the theme for this special issue, the authors were also provided with some general questions that they might use to guide the preparation of their papers.

- What current data provide the best evidence for and against the view that memory formation passes through protein synthesis dependent and independent stages?
- What is the significance of observations of different rates for onset of amnesia, as well as for decay of LTP, within and across laboratories and procedures?
- What future data are needed to provide the best evidence for and against the view that memory formation passes through protein synthesis dependent and independent stages?

Across these papers, there is agreement on the basic findings. All authors agree that proteins and protein synthesis are important to memory formation, but disagree on the question of whether new protein synthesis specifically triggered by an event is important for the formation of memory for that event. Some of the alternatives suggested include protein synthesis needed to maintain cell integrity, to replenish proteins ‘consumed’ by plasticity mechanisms, and to

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provide particular proteins that might be modified by experience, with long-lasting modification perhaps themselves representing cellular memory.

The authors also agree that protein synthesis inhibitors impair memory but disagree about whether such findings reveal a core mechanism of memory formation. There is related disagreement regarding whether the loss of protein synthesis following inhibition is responsible for the amnesia. In part, the different views stem from the idea that the mechanisms of amnesia need not be the inverse of the mechanisms of memory. Some of the opposing views are based on the distinction between mechanisms of amnesia and mechanisms of memory. A second issue is whether inhibition of protein synthesis is a primary cause of amnesia produced by protein synthesis inhibitors or a side effect of these drugs. An extension of the latter view is that inhibition of protein synthesis induces neural responses to the challenge, and these responses then produce amnesia, i.e., that the mechanisms of amnesia are initiated by protein synthesis inhibition but the inhibition, *per se*, does not cause amnesia.

Embedded in the various perspectives offered here are very different ideas about the significance of timing. Some writers see relatively fixed times for retrograde and anterograde amnesia after administration of protein synthesis inhibitors and other treatments, taking this evidence to imply two-process—e.g., early/late, short-term/long-term—theories of memory formation. Other writers see widely variable times for retrograde and anterograde amnesia, taking this as evidence for high-order multiple processes of memory formation. Still others compare the slow times of onset of amnesia and decay of LTP to the fast times of synaptic physiological and anatomical plasticity and suggest that the molecular changes occur after the plasticity is complete, and therefore attempt to assign other functional roles to the molecular changes triggered by experiences.

The diversity of opinion collected in this special issue, and briefly summarized here, offers an opportunity for readers to examine how different researchers, each sharing a common goal of understanding how memories are made, can view the same data set and come away with disparate opinions. In this way, the readers may find this discourse useful in identifying the important questions, if not the answers, surrounding the roles of protein synthesis in memory.