Declarative memory consolidation dynamics: new time windows and its implications for clinical application

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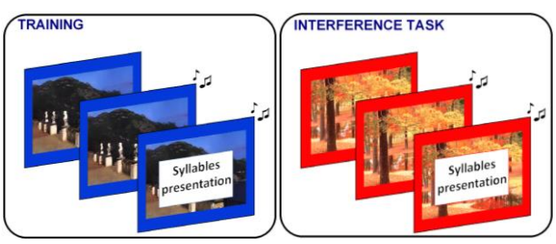
INTRODUCTION

After encoding, memories go through a labile state followed by a stabilization process known as consolidation[1]. Once consolidated they can enter a new labile state after the presentation of a reminder (cue) of the original memory, followed by a period of re-stabilization (reconsolidation)[2]. In both processes, once stabilization/re-stabilization is accomplished the memory cannot be modified[3]. Currently there are studies that show a rapid stabilization after 30 min[4,5], while others studies show that stabilization occurs after 6h[3]. However, there are no studies evaluating short and long delays simultaneously. Knowing that there are spontaneous waves of destabilization (without the re-exposure to keys linked to learning) on which the consolidation and memory persistence depend[6], here we investigate whether declarative memories in humans suffer spontaneous labilization/stabilization processes after learning or if they only pass through a single time window of lability.

METHODS

Online Experiment: Basic Protocol

DAY 1		DAY 3
Training	Interference Task	Testing



We used the Gorilla Experiment Builder (www.gorilla.sc) to create and host our experiment.

TRAINING (L1-memory). 10 trials: In the first trial 5 pairs of syllables were presented and in the following 9 trials the subjects had to complete them.

INTEFERENCE (L2-memory). 10 trials similar to training (red background color, image of a forest and classical music). The L2 was formed by five different pairs of syllables.

TESTING. 4 trials with feedback.

An impaired performance at L2-testing is attributed to Retrieval-Induced Forgetting effect (RIF). It shows that the act of remembering L1-memory can temporarily block a late retrieval of L2-memory[11].

Low number of L2 errors at testing	High number of L2 errors at testing
⇩	⇩
NO RIF EFFECT	RIF EFFECT
⇩	⇩
L1-Memory IMPAIRED	L1- Memory INTACT

The study began during the Argentinean COVID-19 quarantine. Therefore some additional tests and questionnaires were included:

- Beck Depression Inventory-II (Test BDI-II)[7]
- State-Trait Anxiety Inventory (Test STAI)[8]
- Pittsburgh Sleep Quality Index (PSQI)[9]
- Morningness–Eveningness Questionnaire (MEQ)[10]

DEPENDENT VARIABLES

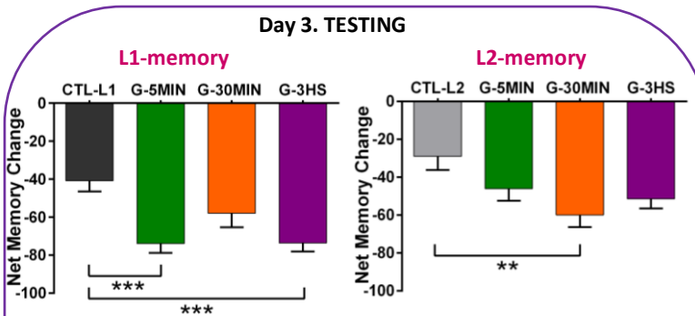
Absolute Memory Change = % Correct responses Trial 1Testing – % Correct responses Trial 10Training

Net Memory Change $= \frac{\text{nº Correct responses Trial 1Testing} - \text{nº Correct responses Trial 10Training} \times 100}{\text{nº correct responses Trial 10Training}}$

RESULTS

GROUP	DAY 1	DAY 3
G-5min	Training — 5 min — Interference task	Testing
G-30min	Training — 30 min — Interference task	Testing
G-3h	Training — 3 hours — Interference task	Testing
Control L1-memory	Training	Testing
Control L2-memory	Interference task	Testing

Day 3. TESTING



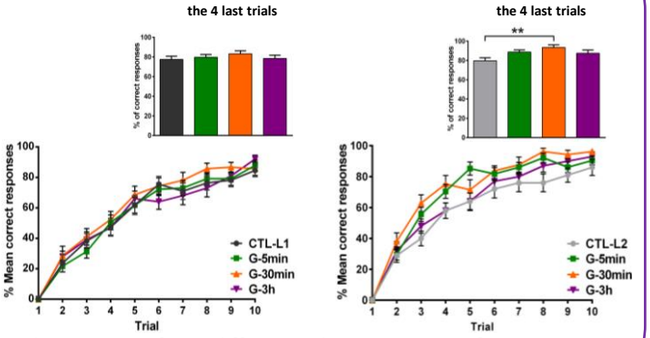
L1- Memory: The memory was impaired only when the interference task was presented immediately after or 3 hours after learning. When the interference task was presented 30 min after learning, the memory was not impaired.

L2- Memory: Only the G-30min group showed an impaired performance compared to the CTL-L2 group. This indicates that L1 memory is intact (RIF Effect).

Therefore, immediately after learning, the memory is labile, it then goes through a rapid stabilization 30 min later, where it is temporally protected against interference and, after 3 hours, is labile again.

	ABSOLUTE MEMORY CHANGE L1-MEMORY	ABSOLUTE MEMORY CHANGE L2-MEMORY
CTL-L1	-33,64 ± 5,16	
CTL-L2		-26,50 ± 6,17
G-5min	-63,48 ± 4,10 ***	-42,61 ± 6,21
G-30min	-50,00 ± 9,17	-57,00 ± 8,56**
G-3h	-69,00 ± 5,12 ***	-48,00 ± 5,11
p value	p <0,0001	p= 0,005

Day 1. TRAINING



There are significant differences beetwen groups for List 2 training. So, we use a new dependent variable: Memory Change.

TEST AND QUESTIONNARIES

	BDI II	STAI: TRAIT	STAI: STATE	PSQI	MEQ
CTL-L1	14,27 ± 2,23	41,09 ± 2,56	38,36 ± 2,06	7,68 ± 0,79	43,64 ± 2,29
CTL-L2	14,00 ± 2,37	43,10 ± 2,06	37,80 ± 1,78	6,40 ± 0,68	44,60 ± 2,17
G-5min	12,96 ± 1,37	39,70 ± 1,87	38,22 ± 1,66	6,61 ± 0,69	45,83 ± 2,21
G-30min	11,85 ± 1,34	38,15 ± 1,96	36,70 ± 1,43	7,40 ± 0,75	46,60 ± 1,88
G-3h	10,63 ± 1,32	35,11 ± 2,11	35,26 ± 1,27	6,16 ± 0,56	45,11 ± 2,54
p value	p= 0,63	p= 0,11	p= 0,68	p= 0,49	p= 0,87

We did not find any correlation between the evaluated variables and memory processes.

DISCUSSION

We found that the dynamics of declarative memory consolidation seem not to be an all or nothing process. We suggest that, within about 30 minutes, a rapid stabilization independent of protein synthesis occurs. It has been observed that these early consolidation processes take place within about 30 minutes and induce a fast increase in synaptic strength[12, 13], possibly resulting in protection of these memory traces against interference at short-term. However, these early changes are transient and decay after about 90 minutes[14].

Further studies should be done to test if similar waves of lability exist after cued memory reactivation. Knowing the different time windows susceptible to interferences becomes fundamental for the design of new psychotherapy treatments for anxiety disorders such as phobias and post traumatic stress disorder.

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