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Hippocampus, Temporal Context and Taste Memories

Milagros Gallo

Department of Experimental Psychology and Physiology of Behavior and Institute of Neurosciences F. Oloriz, University of Granada, Granada-18071, Spain

Correspondence to be sent to: Milagros Gallo, e-mail: mgallo@ugr.es

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Human research points to the relevance of the hippocampus for episodic memory, i.e. the ability to remember unique events that took place at a particular time and place (Tulving, 2002). The study of the hippocampal involvement in animal models of episodic memory faces several pitfalls (Eichenbaum and Fortin, 2003). As an alternative animal model, episodic-like taste memories may be studied using taste recognition memory tasks (Bermúdez-Rattoni, 2004). As it is required for an animal model of episodic memory, taste memories are bound to the context in which learning occurred. This has been shown both for safe and aversive taste memories. On one hand, the contextual dependency of latent inhibition (LI), i.e. the fact that previous taste exposure without consequences interferes with later learning (Lubow, 1989), indicates that the safe taste memory includes contextual cues. A context change between pre-exposure and conditioning disrupts LI (Hall and Channell, 1986). On the other hand, retrieval of an aversive taste memory may be context-dependent (Bonardi *et al.*, 1990; Loy *et al.*, 1993), mainly when the taste was previously exposed without consequences (Puente *et al.*, 1988; Boakes *et al.*, 1997). This conditional discrimination task shows that context cues may facilitate retrieval either of the safe or the aversive taste memory trace.

There is evidence using other learning tasks that supports a hippocampal involvement both in the contextual dependency of LI and in conditional learning (Honey and Good, 1993; Holland and Bouton, 1999; Maren and Holt, 2000). In these studies context frequently refers to a particular place. A good model of episodic memory, however, should include not only the external but also the temporal context (Bouton, 1993).

We reported that the time of day may act as a context which modulates either LI (Manrique *et al.*, 2004) or conditioned taste aversions retrieval (Morón *et al.*, 2002) in Wistar rats. Both phenomena have been tested using the same behavioral procedure that included two non-reinforced saline preexposures before conditioning and testing (Table 1). Animals were assigned to one of two conditions, animals in the 'Same' condition were pre-exposed, aversively conditioned to saline (i.p. injections of lithium chloride after saline intake) and tested (one-bottle test) in their home cages during the evening drinking session. Animals in the 'Different' condition were aversively conditioned to saline during the morning drinking session while preexposure and testing took place in the evening session.

Subtle modifications of the procedure (Table 1) seem to drastically modify the role of the temporal context. By increasing the duration of the previous habituation training to drink water twice a day and also allowing the animals to drink freely during the conditioning session, the ability of a change of the time of day for disrupting LI becomes evident (Manrique *et al.*, 2004). Thus, 'Different' groups exhibit stronger aversions than 'Same' groups because the change of time of day interferes with LI. However, if the procedure includes only two days of previous habituation and restricted drinking during the conditioning session, 'Same' groups show stronger aversions than 'Different' groups. This may be due to the fact that the same time-of-day of conditioning facilitates retrieval of the aversive taste memory (Morón *et al.*, 2002). Thus, the results are opposite.

Using these behavioral procedures, the effect of NMDA induced lesions of the dorsal hippocampus in both roles of the temporal context was explored. In a series of two experiments using only preexposed groups (see Table 1) the performance of male Wistar rats with hippocampal (experiment 1, $n = 18$; experiment 2, $n = 20$) and amygdala (experiment 1, $n = 18$; experiment 2, $n = 19$) lesions was compared. Amygdala lesioned rats were used as control groups. Although the amygdala has been related with taste recognition memory (Bermúdez-Rattoni, 2004), there are conflicting results concerning the effect of amygdala lesions on taste aversion learning (Bermúdez-Rattoni and Yamamoto, 1998). Damage to this area did not disrupt taste aversion learning using the lesion and behavioral procedure applied in these experiments.

The results indicated that the excitotoxic damage of the amygdala did not impair any of the temporal context effects, showing similar patterns to those reported in intact rats. As can be seen in Figure 1, a long habituation training to the temporal contexts (experiment 1, upper panel) led to significantly higher aversion rates in the 'Different' group than in the 'Same' group. A short habituation training to the drinking temporal context (experiment 2, lower panel) led to significant differences in the opposite direction, i.e. higher aversion rates in the 'Same' group than in the 'Different' group.

Excitotoxic lesions of the dorsal hippocampus, however, selectively disrupted the effect of a temporal context change in the long-

Table 1 Behavioral procedure

		Habituation	Pre-exposure	Conditioning	Test
Experiment 1		**5 days**	2 days	**Free amount**, 1 day	1 day
Experiment 2		**2 days**	2 days	**Limited amount**, 1 day	1 day
	Same	Water, am/pm	Saline (1%), pm	Saline (1%), LiCl (0.15 M, 2% body wt), pm	Saline (1%), pm
	Different	Water, am/pm	Saline (1%), pm	Saline (1%), LiCl (0.15 M, 2% body wt), am	Saline (1%), pm

Differences between experiments 1 and 2 are highlighted in bold letters. Water drinking sessions during pre-exposure, conditioning and testing are not represented. All the sessions lasted 15 min. (am, 10 h; pm, 20 h; LiCl, lithium chloride)

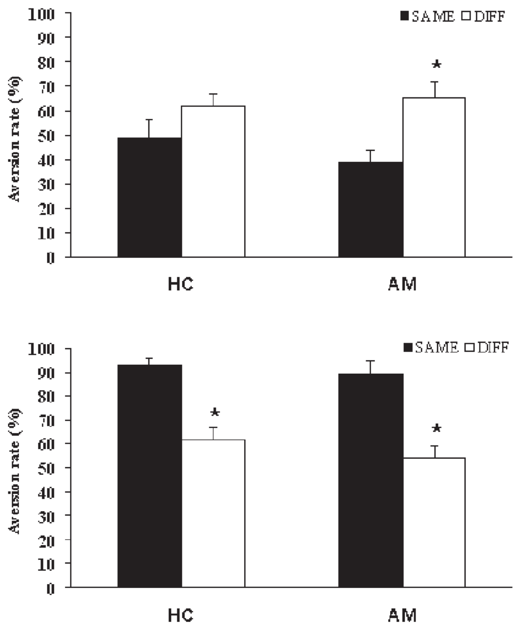

Figure 1 Effect of NMDA-induced lesions of the hippocampus (HC) and amygdala (AM) on mean (±SEM) taste aversion rates (saline intake during conditioning/sum of saline intake during conditioning and testing × 100) in experiment 1 (upper panel) and experiment 2 (lower panel). A rate of 100 means maximal aversion, the rats avoiding drinking saline during testing. Hippocampal lesions disrupt the effect of a context change between pre-exposure and conditioning in the experiment 1 (*$P < 0.05$; Newman–Keuls *post hoc* comparisons. DIFF, Different).

habituation procedure (upper panel) as there were no differences between 'Same' and 'Different' groups, but not in the short-habituation procedure (lower panel). This fact rules out an interpretation of the time dependency of LI disruption by hippocampal lesions in terms of time-detection or circadian rhythms deficits.

In all, the results demonstrate a hippocampal role in the temporal context-dependency of LI, but not in conditional learning using taste recognition memory tasks. This is consistent with evidence obtained using other learning tasks showing a similar hippocampal role in the external context-dependency of LI (Honey and Good, 1993) and no role of the hippocampus nor amygdala in conditional learning using places as contexts (Skinner *et al.*, 1994, 2000).

The present evidence can be interpreted according to a two-trace model of taste recognition memory that proposes dissociable neural mechanisms for safe and aversive taste memories (Bermúdez-Rattoni, 2004). It is possible that the temporal context may independently modulate the retrieval of the safe and the aversive trace memory, the hippocampus being selectively involved in the time cues modulation of safe taste memories.

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References

Bermúdez-Rattoni, F. (2004) *Molecular Mechanisms of taste-recognition memory*. Nat. Rev. Neurosci., 5, 209–217.

Bermúdez-Rattoni, F. and **Yamamoto, T.** (1998) *Neuroanatomy of conditioned taste aversion, lesion studies*. In Bures, J., Bermudez-Rattoni, F. and Yamamoto, T. (eds), Conditioned Taste Aversion, Memory of a Special Kind. Oxford University Press, Oxford, pp. 26–45.

Boakes, R.A., Westbrook, R.F., Elliot, M. and **Swinbourne, A.L.** (1997) *Context dependency of conditioned aversions to water and sweet tastes*. J. Exp. Psychol. Anim. Behav. Proc., 23, 56–67.

Bonardi ,C., Honey, R.C. and **Hall, G.** (1990). *Context specificity of conditioning in flavor-aversion learning, extinction and blocking tests*. Anim. Learn. Behav., 18, 29–237.

Bouton, M.E. (1993) *Context, time and memory retrieval in the interference paradigms of pavlovian learning*. Psychol. Bull., 114, 80–99.

Eichenbaum, H. and **Fortin, N.** (2003) *Episodic memory and the hippocampus, it's about time*. Curr. Dir. Psychol. Sci., 12, 53–57.

Hall, G. and **Channell, S.** (1986) *Context specificity of latent inhibition in taste aversion learning*. Q. J. Exp. Psychol., 38B, 121–139.

Holland, P.C. and **Bouton, M.E.** (1999) *Hippocampus and context in classical conditioning*. Curr. Opin. Neurobiol., 9, 195–202.

Honey, R.C. and **Good, M.** (1993) *Selective hippocampal lesions abolish the contextual specificity of latent inhibition and conditioning*. Behav. Neurosci., 107, 23–33.

Loy, I., Alvárez. R., Rey, V. and **López, M.** (1993) *Context–US associations rather than occasion setting in taste aversion learning*. Learn. Motiv., 24, 55–72.

Lubow, R.E. (1989) Latent Inhibition and Conditioned Theory. Cambridge University Press, Cambridge.

Manrique, T., Molero, A., Ballesteros, M.A., Morón, I., Gallo, M. and **Fenton, A.** (2004) *Time of day-dependent latent inhibition taste aversion learning in rats*. Neurobiol. Learn. Mem., 82, 77–80.

Maren, S. and **Holt, W.** (2000) *The hippocampus and contextual memory retrieval in Pavlovian conditioning*. Behav. Brain Res., 110, 97–108.

Morón, I., Manrique, T., Molero, A., Ballesteros, M.A., Gallo, M. and **Fenton, A.** (2002) *The contextual modulation of conditioned taste aversions by the physical environment and time of day is similar*. Learn. Mem., 9, 218–223.

Puente, G.P., Cannon, D.S., Best, M.R. and **Carrell, L.E.** (1988) *Occasion setting of fluid ingestion by contextual cues*. Learn. Motiv., 19, 239–253.

Skinner, D.M., Martin, G.M., Harley, C., Kolb, B., Pridgar, A., Bechara, A. and **Van der Kooy, D.** (1994) *Acquisition of conditional discrimination in hippocampal lesioned and decorticated rats, evidence for learning that is separate from both simple classical conditioning and configural learning*. Behav. Neurosci., 108, 911–926.

Skinner, D.M., Clarke, H.A. and **Van der Kooy, D.** (2000) *Amygdala lesions impair context aversions but not the ability of contexts to serve as occasion setters*. Psychobiology, 28, 67–80.

Tulving, E. (2002) *Episodic memory, from mind to brain*. Annu. Rev. Psychol., 53, 1–25.