Rapid Communication

Consolidation of object recognition memory requires simultaneous activation of dopamine D₁/D₅ receptors in the amygdala and medial prefrontal cortex but not in the hippocampus

Janine I. Rossato^{a,b}, Andressa Radiske^{a,c}, Cristiano A. Kohler^a, Carolina Gonzalez^d, Lia R. Bevilacqua^{a,b}, Jorge H. Medina^d, Martín Cammarota^{a,b,c,*}

^a Memory Research Laboratory, Brain Institute (ICe), Federal University of Rio Grande do Norte (UFRN), Natal, RN 59056-450, Brazil

^b Laboratory of Behavioral Neurobiology, Biomedical Research Institute, Porto Alegre, RS 90610-000, Brazil

^c Post-Graduate Research Program in Biomedical Gerontology, Pontifical Catholic University of Rio Grande do Sul (PUCRS), Porto Alegre, RS 90610-000, Brazil

^d Memory Research Laboratory, Institute for Cell Biology & Neuroscience (IBCyN), School of Medical Sciences, University of Buenos Aires (UBA), 1121ABG Buenos Aires, Argentina

ARTICLE INFO

Article history:

Received 3 June 2013

Revised 26 June 2013

Accepted 12 July 2013

Available online 24 July 2013

Keywords:

Dopamine

Object recognition memory

Ventral tegmental area

Amygdala

Hippocampus

Medial prefrontal cortex

ABSTRACT

The mesocorticolimbic dopaminergic system includes the ventral tegmental area (VTA) and its projections to the amygdala (AMY), the hippocampus (HIP) and the medial prefrontal cortex (mPFC), among others. Object recognition (OR) long-term memory (LTM) processing requires dopaminergic activity but, although some of the brain regions mentioned above are necessary for OR LTM consolidation, their possible dopamine-mediated interplay remains to be analyzed. Using adult male Wistar rats, we found that posttraining microinjection of the dopamine D₁/D₅ receptor antagonist SCH23390 in mPFC or AMY, but not in HIP, impaired OR LTM. The dopamine D₂ receptor agonist quinpirole had no effect on retention. VTA inactivation also hindered OR LTM, and even though this effect was unaffected by co-infusion of the dopamine D₁/D₅ receptor agonist SKF38393 in HIP, mPFC or AMY alone, it was reversed by simultaneous activation of D₁/D₅ receptors in the last two regions. Our results demonstrate that the mesocorticolimbic dopaminergic system is indeed essential for OR LTM consolidation and suggest that the role played by some of its components during this process is much more complex than previously thought.

© 2013 Elsevier Inc. All rights reserved.

The mesocorticolimbic dopaminergic pathway originates in the ventral tegmental area (VTA) and controls motivated behavior and movement initiation strategies as well as attention, reward processing, fear, and novelty detection (Cole & Robbins, 1989; Beninger & Miller, 1998; Nader & LeDoux, 1999; Granon et al., 2000; Schultz, 2002). This pathway includes several brain areas essential for learning and memory, such as the amygdala (AMY), the hippocampus (HIP) and the medial prefrontal cortex (mPFC). Indeed, it has been hypothesized that a functional loop including VTA-hippocampus dopamine connections regulates the influx of information into long-term memory (LTM; Lisman & Grace, 2005). We previously demonstrated that, in order to persist, fear memories require activation of this pathway (Rossato, Bevilacqua, Izquierdo, Medina, & Cammarota, 2009). Here, we investigated whether VTA function is also needed for consolidation of object recognition (OR) LTM. Since different brain regions are necessary for discriminating objects

(Bussey, Muir, & Aggleton, 1999; Hotte, Naudon, & Jay, 2005; Tinsley et al., 2011; Zhu, McCabe, Aggleton, & Brown, 1997), and AMY, mPFC and HIP seem to serve distinct functions during OR memory processing, including, respectively, arousal, judgment of recency and familiarity (Akirav & Maroun, 2006; Barker, Bird, Alexander, & Warburton, 2007; Barker & Warburton, 2008; Roozendaal, Castello, Vedana, Barseganyan, & McGaugh, 2008; Balderas et al., 2008; Nelson, Cooper, Thur, Marsden, & Cassaday, 2011; Werenicz et al., 2012; Cross, Brown, Aggleton, & Warburton, 2012; Albasser, Amin, Lin, Iordanova, & Aggleton, 2012; Fortress, Fan, Orr, Zhao, & Frick, 2013), there are good reasons to expect that dopaminergic influence on OR LTM may differ in these brain areas. Therefore, we also examined the possible dopamine-mediated interplay between these regions. To address these questions, male Wistar rats (3-month-old) implanted with 22-gauge guides aimed to the VTA [stereotaxic coordinates AP −4.8/LL ±1.0/DV −9.0], CA₁ region of the dorsal HIP [stereotaxic coordinates AP −4.2/LL ±3.0/DV −3.0], the basolateral nucleus of AMY [stereotaxic coordinates AP −2.4/LL ±5.1/DV −8.1], and/or the pre-limbic sub-division of the mPFC [stereotaxic coordinates AP +3.2/LL ±0.8/DV −4.0] (Paxinos & Watson, 1986)] were trained in the novel object recognition task

* Corresponding author at: Memory Research Laboratory, Brain Institute (ICe), Federal University of Rio Grande do Norte (UFRN), Natal, RN 59056-450, Brazil. Fax: +55 84 32152709.

E-mail address: mcammara@terra.com.br (M. Cammarota).

Fig. 1. Reversible inactivation of the VTA hinders OR LTM consolidation. **A:** On day 1, rats were exposed to two different objects (A and B) for 5 min and immediately or 360 min after that received bilateral infusions (0.5 μ l/side) of vehicle (VEH; 0.1% DMSO in saline) or muscimol (MUS; 0.1 μ g/side) in VTA. On day 2, animals were exposed to a familiar (A) and a novel object (C) for five extra minutes to evaluate OR LTM. **B:** Animals were treated exactly as in A, except that immediately or 360 min after training they received bilateral infusions of VEH or AP5 (1.0 μ g/side) in VTA. Data (mean $\pm$ SEM) are presented as percentage of total exploration time. *** P < 0.001, ** P < 0.01, and * P < 0.05 in one-sample Student's t -test with theoretical mean = 50; n = 8–10 per group.

(NOR), a novelty-preference learning paradigm based on the rats' natural preference to explore novel objects involving a 5-min exposure to two novel stimuli objects in an open field arena (Dix & Aggleton, 1999; Ennaceur & Delacour, 1988; Ennaceur, Neave, & Aggleton 1997), which is susceptible to dopaminergic modulation (de Lima et al., 2011). Before that, the animals were habituated to the training arena by allowing them to freely explore it during 20 min per day for 4 days in the absence of any other behaviorally relevant stimulus. The stimuli objects were made of metal, glass or glazed ceramic, and their role (familiar or novel) and relative position were counterbalanced and randomly permuted for each experimental animal. Exploration was defined as sniffing or touching the stimuli objects with the muzzle and/or forepaws. Sitting on or turning around the objects was not considered exploratory behavior. Approximately 4% of the animals did not accumulate at least 20 s of object exploration during the training session and, consequently, were excluded from the experiments.

To analyze the involvement of the VTA in OR LTM consolidation, rats trained in the NOR task received bilateral intra-VTA infusions of the GABA_A receptor agonist muscimol (MUS; 0.1 μ g/side), the NMDA receptor antagonist AP5 (1 μ g/side) or vehicle (VEH; 0.1% DMSO in saline) immediately or 360 min after training. Retention was assessed 24 h later. During the test session, the animals were exposed to one of the stimuli objects presented in the training session together with a novel one. Rats that received VEH explored the novel object longer than the familiar one (p < 0.05; $t(8)$ = 2.483, in one-sample Student's t -test with theoretical mean = 50). In contrast, animals that received MUS or AP5 immediately but not 360 min after training spent the same amount of time exploring the novel and the familiar objects (Fig. 1A and B, respectively; p < 0.01; $t(7)$ = 4.255 for MUS and p < 0.001; $t(7)$ = 5.177 for AP5, in one-sample Student's t -test with theoretical mean = 50). Neither

MUS nor AP5 affected the animals' performance in the plus-maze or the open field tasks when given in VTA 24 h before the respective behavioral session (Table 1). The VTA sends projections to several brain regions known to participate in OR memory processing, including AMY (Roosendaal et al., 2008), mPFC (Mitchell & Laiacona, 1998), and HIP (Fortress et al., 2013). Therefore, we investigated whether dopamine receptors regulate OR LTM consolidation in any of these regions. When given in AMY (Fig. 2A; p < 0.01, $t(7)$ = 3.497 for VEH; p < 0.001, $t(7)$ = 7.798 for SCH) or mPFC (Fig. 2B; p < 0.05, $t(6)$ = 2.689 for VEH; p < 0.01, $t(7)$ = 3.160 for SCH) immediately but not 360 min after training, the dopamine D₁/D₅ receptor antagonist SCH23390 (1.5 μ g/side) impaired OR LTM. SCH23390 did not affect retention when injected in HIP at any post-training time analyzed (Fig. 2C; p < 0.001,

Table 1

Intra-VTA infusions of muscimol and AP5 have no effect on locomotor and exploratory activities or anxiety. VEH, MUS (0.1 μ g/side) or AP5 (1 μ g/side) were infused in VTA 24 h before Open Field or Plus Maze behavioral sessions. Data are expressed as mean ($\pm$ SEM) of the total number of entries and the percentage of time spent in the open arms (Plus Maze) or of the number of crossings and rearings (Open Field); n = 10 per group. VEH = vehicle. A different set of animals was used for each behavioral test.

	VEH	AP5	MUS
<i>Plus maze</i>			
Total entries	20.3 $\pm$ 1.9	18.3 $\pm$ 2.9	23.3 $\pm$ 2.9
Entries in the open arms	8.2 $\pm$ 0.9	7.2 $\pm$ 1.9	8.2 $\pm$ 1.3
% Time in the open arms	25.6 $\pm$ 4.1	21.6 $\pm$ 5.1	27.6 $\pm$ 5.1
<i>Open field</i>			
Crossings	77.3 $\pm$ 6.8	80.3 $\pm$ 7.8	81.3 $\pm$ 9.9
Rearings	18.8 $\pm$ 2.0	21.8 $\pm$ 3.0	21.0 $\pm$ 2.0

Fig. 2. Activation of dopamine D_1/D_5 receptors in AMY and mPFC, but not in HIP is necessary for OR LTM consolidation. A–C: On day 1, rats were exposed to two different objects (A and B) for 5 min and immediately or 360 min after that received bilateral infusions of vehicle (VEH; 0.1% DMSO in saline) or of the dopamine D_1/D_5 receptor antagonist, SCH23390 (1.5 μ g/side) in AMY (A; 0.5 μ l/side), mPFC (B; 1 μ l/side) or HIP (C; 1 μ l/side). On day 2, animals were exposed to a familiar (A) and a novel object (C) for five extra minutes to evaluate long-term memory retention. D: Animals were treated exactly as in A–C, except that immediately after training they received bilateral infusions of VEH or quinpirole (QUIN; 3.0 μ g/side) in AMY, mPFC or HIP. Data (mean $\pm$ SEM) are presented as percentage of total exploration time. *** $P < 0.001$, ** $P < 0.01$, and * $P < 0.05$ in one-sample Student's t -test with theoretical mean = 50; $n = 7$ –12 per group.

$t(11) = 5.139$ for VEH; $p < 0.01$, $t(11) = 3.892$ and $p < 0.01$, $t(7) = 3.458$ for SCH). Posttraining microinjection of the dopamine D_2 receptor agonist quinpirole (3.0 μ g/side) in AMY, mPFC or HIP had no effect on LTM (Fig. 2D; $p < 0.05$, $t(8) = 2.562$ for VEH; $p < 0.01$, $t(8) = 3.394$; $p < 0.001$, $t(8) = 6.462$; $p < 0.01$, $t(8) = 3.420$ for QUIN in AMY, mPFC and HIP respectively, in one-sample Student's t -test with theoretical mean = 50). We also found that co-infusion of the dopamine D_1/D_5 receptor agonist SKF38393 (12.5 μ g/side) in AMY, mPFC or HIP did not affect the amnesia caused by intra-VTA MUS (Fig. 3A) or intra-VTA AP5 (Fig. 3B). Likewise, concomitant administration of SKF38393 in HIP and AMY, or in HIP and mPFC, did not reverse the amnesic effect of intra-VTA MUS (Fig. 3C) or intra-VTA AP5 (Fig. 3D). Conversely, simultaneous co-infusion of SKF38393 in AMY and mPFC totally reversed the amnesia induced by intra-VTA administration of MUS (Fig. 3E $p < 0.05$, $t(12) = 2.475$ for VEH and $p < 0.01$, $t(7) = 3.478$ for co-infusion, in one-sample Student's t -test with theoretical mean = 50) and AP5 (Fig. 3F; < 0.05 , $t(10) = 2.549$ for VEH and $p < 0.05$, $t(8) = 2.345$ for co-infusion, in one-sample Student's t -test with theoretical mean = 50).

Taken together, our results suggest that early posttraining stimulation of the VTA controls OR memory consolidation, and that simultaneous activity of D_1/D_5 dopamine receptors in AMY and mPFC is not only necessary but sufficient to mediate this effect. This conclusion is based on 3 sets of data. Firstly, intra-VTA administration of MUS or AP5 hindered OR LTM in a time-dependent manner without affecting the animals' behavior on the plus maze and open field tasks 24 h post-administration, thus indicating that the amnesic effect of VTA inactivation is not due to a protracted and unspecific effect on performance, exploratory activity or anxiety at the time of OR retrieval but, instead, to impairment of the memory consolidation process. Secondly, intra-AMY and intra-mPFC, but not intra-HIP, infusion of the D_1/D_5 antagonist SCH23390 impeded OR LTM retention, showing that activation of these receptors is indeed necessary for OR LTM formation. Thirdly,

and most importantly, co-infusion of the D_1/D_5 receptor agonist SKF38393 in AMY, mPFC or HIP alone, at a dose known to enhance memory processing (Rossato et al., 2009), was unable to reverse the amnesic effect of VTA inactivation. However, when SKF was given concurrently in AMY and mPFC, but not in AMY and HIP or in mPFC and HIP, it totally overturned the amnesia caused by intra-VTA MUS and intra-VTA AP5.

Dopamine modulates the excitability of AMY and mPFC neurons (Dong & White, 2003; Kröner, Rosenkranz, Grace, & Barrionuevo, 2005) and regulates the balance between excitatory and inhibitory neurotransmission in AMY-mPFC circuits (Floresco & Tse, 2007). In fact, it is known that the mPFC-mediated suppression of spontaneous and sensory driven activity in AMY is reversed by dopamine receptors activation and that this activation allows for plasticity (Grace & Rosenkranz, 2002). Indeed, memory-relevant interactions between AMY and mPFC cortex are well documented. For example, it has been reported that transfer of information between BLA and mPFC guides response selection in rats (Floresco & Ghods-Sharifi, 2007) and that AMY-mPFC functional interactions are essential for enabling the effect that glucocorticoids have on working memory and LTM consolidation (Roosendaal, Hahn, Nathan, de Quervain, & McGaugh, 2004; Roosendaal et al., 2009) as well as on the behavioral responses to fear and stress (Akirav, Raizel, & Maroun, 2006; Marek, Strobel, Bredy, & Sah, 2013; Stevenson & Gratton, 2003; Vouimba & Maroun, 2011). Moreover, coincident neuronal activity in AMY and mPFC modulates perirhinal cortex functionality as well as its interaction with the entorhinal cortex (Paz, Bauer, & Paré, 2009; Pelletier, Apergis-Schoute, & Paré, 2005) which are essential for OR memory formation (Banks, Bashir, & Brown, 2012; Deshmukh, Johnson, & Knierim, 2012; Albasser et al., 2013; Hunsaker, Chen, Tran, & Kesner, 2013). Although we and others have previously shown that HIP plays a key role in OR LTM, and normal functionality of VTA-HIP dopamine neurotransmission is essential for the formation and storage of several other memory types (Wittmann, Schiltz, Boehler, & Düzel, 2008; Martig

Fig. 3. Simultaneous activation of D1/D5 receptors in AMY and mPFC reverses the amnesia induced by VTA inactivation. **A:** On day 1 rats were exposed to two different objects (A and B) for 5 min and immediately after that received bilateral infusions of VEH or muscimol (MUS; 0.1 μ g/side) in VTA + SKF38393 (SKF; 12.5 μ g/side) in AMY, mPFC or HIP. On day 2, animals were exposed to a familiar (A) and a novel object (C) for five extra minutes to evaluate LTM. **B:** Animals were treated as in A, except that immediately after training they received bilateral infusions of VEH or AP5 (1 μ g/side) in VTA + SKF in AMY, mPFC or HIP. **C:** Animals were treated as in A, except that immediately after training they received bilateral co-infusions of MUS + SKF in both BLA and HIP. **D:** Animals were treated as in C, except that immediately after training they received bilateral co-infusions of AP5 + SKF. **E:** Animals were treated as in A, except that immediately after training they received bilateral co-infusions of MUS + SKF in both BLA and mPFC. **F:** Animals were treated as in E, except that immediately after training they received bilateral co-infusions of AP5 + SKF. Data (mean $\pm$ SEM) are presented as percentage of total exploration time. *** P < 0.001, ** P < 0.01, and * P < 0.05 in one-sample Student's t -test with theoretical mean = 50; n = 8–12 per group.

& Mizumori, 2011; Nazari-Serenjeh, Rezayof, & Zarrindast, 2011), we failed to detect any involvement of HIP D1/D5 receptors in OR consolidation. These results are in agreement with earlier findings demonstrating that exposure to a novel environment does not increase dopamine in HIP (Guzmán-Ramos et al., 2012) and that blockade of dopamine D1 receptors in HIP does not affect OR LTM acquisition (Balderas, Moreno-Castilla, & Bermudez-Rattoni, in Press), but are at odds with a recent report showing that SCH23390 abolished OR LTM retention when given in HIP 30 min before training (de Bundel et al., 2013). Methodological differences, such as the use of pre-training pharmacological interventions as well as the number and duration of pre-training habituation sessions and/or the length of the training session, which can substantially modify the behavioral characteristics as well as the neurochemical and neuroanatomical requirements of OR memory consolidation (Okuda, Roozendaal, & McGaugh, 2004; Roozendaal, Okuda, Van der Zee, & McGaugh, 2006; Roozendaal et al., 2008), could help explain the discrepancies between our results and those reported by de Bundel et al., 2013.

Acknowledgements

This work was supported by grants from National Council for Scientific & Technological Development (CNPq, Brazil), Rio Grande do Sul State Foundation for Scientific Development (FAPERGS, Brazil) and Rio Grande do Norte State Foundation for Scientific Development (FAPERN, Brazil) to MC; National Agency for the Advancement of Science & Technology (ANPCyT, Argentina) to JHM, and International Brain Research Organization (IBRO) to JHM and MC.

References

- Akirav, I., & Maroun, M. (2006). Ventromedial prefrontal cortex is obligatory for consolidation and reconsolidation of object recognition memory. *Cerebral Cortex*, 16, 1759–1765.
- Akirav, I., Raizel, H., & Maroun, M. (2006). Enhancement of conditioned fear extinction by infusion of the GABA(A) agonist muscimol into the rat prefrontal cortex and amygdala. *European Journal of Neuroscience*, 23, 758–764.
- Albasser, M. M., Amin, E., Lin, T. C., Iordanova, M. D., & Aggleton, J. P. (2012). Evidence that the rat hippocampus has contrasting roles in object recognition memory and object recency memory. *Behavioural Neuroscience*, 126, 659–669.

- Albasser, M. M., Olarte-Sánchez, C. M., Amin, E., Horne, M. R., Newton, M. J., Warburton, E. C., et al. (2013). The neural basis of nonvisual object recognition memory in the rat. *Behavioural Neuroscience*, 127, 70–85.
- Balderas, I., Moreno-Castilla, P., & Bermudez-Rattoni, F. (2013). Dopamine D1 receptor activity modulates object recognition memory consolidation in the perirhinal cortex but not in the hippocampus. *Hippocampus* (in Press).
- Balderas, I., Rodríguez-Ortiz, C. J., Salgado-Tonda, P., Chavez-Hurtado, J., McGaugh, J. L., & Bermudez-Rattoni, F. (2008). The consolidation of object and context recognition memory involve different regions of the temporal lobe. *Learning and Memory*, 15, 618–624.
- Banks, P. J., Bashir, Z. I., & Brown, M. W. (2012). Recognition memory and synaptic plasticity in the perirhinal and prefrontal cortices. *Hippocampus*, 22, 2012–2031.
- Barker, G. R., Bird, F., Alexander, V., & Warburton, E. C. (2007). Recognition memory for objects, place, and temporal order: A disconnection analysis of the role of the medial prefrontal cortex and perirhinal cortex. *Journal of Neuroscience*, 27, 2948–2957.
- Barker, G. R., & Warburton, E. C. (2008). Critical role of the cholinergic system for object-in-place associative recognition memory. *Learning and Memory*, 16, 8–11.
- Beninger, R. J., & Miller, R. (1998). Dopamine D1-like receptors and reward-related incentive learning. *Neuroscience and Biobehavioral Reviews*, 22, 335–345.
- Bussey, T. J., Muir, J. L., & Aggleton, J. P. (1999). Functionally dissociating aspects of event memory: The effects of combined perirhinal and postrhinal cortex lesions on object and place memory in the rat. *Journal of Neuroscience*, 19, 495–502.
- Cole, B. J., & Robbins, T. W. (1989). Effects of 6-hydroxydopamine lesions of the nucleus accumbens septi on performance of a 5-choice serial reaction time task in rats: Implications for theories of selective attention and arousal. *Behavioral Brain Research*, 33, 165–179.
- Cross, L., Brown, M. W., Aggleton, J. P., & Warburton, E. C. (2012). The medial dorsal thalamic nucleus and the medial prefrontal cortex of the rat function together to support associative recognition and recency but not item recognition. *Learning and Memory*, 20, 41–50.
- de Bundel, D., Femenia, T., Dupont, C. M., Konradsson-Geuken, A., Feltmann, K., Schilström, B., et al. (2013). Hippocampal and prefrontal dopamine D1/5 receptor involvement in the memory-enhancing effect of reboxetine. *International Journal of Neuropsychopharmacology*, 14, 1–11.
- de Lima, M. N., Presti-Torres, J., Dornelles, A., Scalco, F. S., Roesler, R., Garcia, V. A., et al. (2011). Modulatory influence of dopamine receptors on consolidation of object recognition memory. *Neurobiology of Learning and Memory*, 95, 305–310.
- Deshmukh, S. S., Johnson, J. L., & Knierim, J. J. (2012). Perirhinal cortex represents nonspatial, but not spatial, information in rats foraging in the presence of objects: comparison with lateral entorhinal cortex. *Hippocampus*, 22, 2045–2058.
- Dix, S. L., & Aggleton, J. P. (1999). Extending the spontaneous preference test of recognition: evidence of object-location and object-context recognition. *Behavioral Brain Research*, 99, 191–200.
- Dong, Y., & White, F. J. (2003). Dopamine D1-class receptors selectively modulate a slowly inactivating potassium current in rat medial prefrontal cortex pyramidal neurons. *Journal of Neuroscience*, 23, 2686–2695.
- Ennaceur, A., & Delacour, J. (1988). A new one-trial test for neurobiological studies of memory in rats. 1: Behavioral data. *Behavioral Brain Research*, 31, 47–59.
- Ennaceur, A., Neave, N., & Aggleton, J. P. (1997). Spontaneous object recognition and object location memory in rats: the effects of lesions in the cingulate cortices, the medial prefrontal cortex, the cingulum bundle and the fornix. *Experimental Brain Research*, 113, 509–519.
- Floresco, S. B., & Ghods-Sharifi, S. (2007). Amygdala-prefrontal cortical circuitry regulates effort-based decision making. *Cerebral Cortex*, 17, 251–260.
- Floresco, S. B., & Tse, M. T. (2007). Dopaminergic regulation of inhibitory and excitatory transmission in the basolateral amygdala-prefrontal cortical pathway. *Journal of Neuroscience*, 27, 2045–2057.
- Fortress, A. M., Fan, L., Orr, P. T., Zhao, Z., & Frick, K. M. (2013). Estradiol-induced object recognition memory consolidation is dependent on activation of mTOR signaling in the dorsal hippocampus. *Learning & Memory*, 20, 147–155.
- Grace, A. A., & Rosenkranz, J. A. (2002). Regulation of conditioned responses of basolateral amygdala neurons. *Physiological Behavioral*, 77, 489–493.
- Granon, S., Passetti, F., Thomas, K. L., Dalley, J. W., Everitt, B. J., & Robbins, T. W. (2000). Enhanced and impaired attentional performance after infusion of D1 dopaminergic receptor agents into rat prefrontal cortex. *Journal of Neuroscience*, 20, 1208–1215.
- Guzmán-Ramos, K., Moreno-Castilla, P., Castro-Cruz, M., McGaugh, J. L., Martínez-Coria, H., LaFerla, F. M., et al. (2012). Restoration of dopamine release deficits during object recognition memory acquisition attenuates cognitive impairment in a triple transgenic mice model of Alzheimer's disease. *Learning and Memory*, 19, 450–453.
- Hotte, M., Naudon, L., & Jay, T. M. (2005). Modulation of recognition and temporal order memory retrieval by dopamine D1 receptor in rats. *Neurobiology of Learning and Memory*, 84, 85–92.
- Hunsaker, M. R., Chen, V., Tran, G. T., & Kesner, R. P. (2013). The medial and lateral entorhinal cortex both contribute to contextual and item recognition memory: A test of the binding of items and context model. *Hippocampus*, 23, 380–391.
- Kröner, S., Rosenkranz, J. A., Grace, A. A., & Barrionuevo, G. (2005). Dopamine modulates excitability of basolateral amygdala neurons in vitro. *Journal of Neurophysiology*, 93, 1598–1610.
- Lisman, J. E., & Grace, A. A. (2005). The hippocampal-VTA loop: controlling the entry of information into long-term memory. *Neuron*, 46, 703–713.
- Marek, R., Strobel, C., Bredy, T. W., & Sah, P. (2013). The amygdala and medial prefrontal cortex: Partners in the fear circuit. *Journal of Physiology*, 591, 2381–2391.
- Martig, A. K., & Mizumori, S. J. (2011). Ventral tegmental area disruption selectively affects CA1/CA2 but not CA3 place fields during a differential reward working memory task. *Hippocampus*, 21, 172–184.
- Mitchell, J. B., & Laiacina, J. (1998). The medial frontal cortex and temporal memory: Tests using spontaneous exploratory behaviour in the rat. *Behavioral Brain Research*, 97, 107–113.
- Nader, K., & LeDoux, J. E. (1999). Inhibition of the mesoamygdala dopaminergic pathway impairs the retrieval of conditioned fear associations. *Behavioral Neuroscience*, 113, 891–901.
- Nazari-Serenjeh, F., Rezayof, A., & Zarrindast, M. R. (2011). Functional correlation between GABAergic and dopaminergic systems of dorsal hippocampus and ventral tegmental area in passive avoidance learning in rats. *Neuroscience*, 24, 104–114.
- Nelson, A. J., Cooper, M. T., Thur, K. E., Marsden, C. A., & Cassaday, H. J. (2011). The effect of catecholaminergic depletion within the prelimbic and infralimbic medial prefrontal cortex on recognition memory for recency, location, and objects. *Behavioral Neuroscience*, 125, 396–403.
- Okuda, S., Roozendaal, B., & McGaugh, J. L. (2004). Glucocorticoid effects on object recognition memory require training-associated emotional arousal. *Proceedings of National Academy of Sciences of U S A*, 101, 853–858.
- Paxinos, G., & Watson, C. (1986). *The rat brain in stereotaxic coordinates* (2nd ed). San Diego: Academic Press.
- Paz, R., Bauer, E. P., & Paré, D. (2009). Measuring correlations and interactions among four simultaneously recorded brain regions during learning. *Journal of Neurophysiology*, 101, 2507–2515.
- Pelletier, J. G., Apergis-Schoute, J., & Paré, D. (2005). Interaction between amygdala and neocortical inputs in the perirhinal cortex. *Journal of Neurophysiology*, 94, 1837–1848.
- Roozendaal, B., Castello, N. A., Vedana, G., Barseganyan, A., & McGaugh, J. L. (2008). Noradrenergic activation of the basolateral amygdala modulates consolidation of object recognition memory. *Neurobiology of Learning and Memory*, 90, 576–579.
- Roozendaal, B., Hahn, E. L., Nathan, S. V., de Quervain, D. J., & McGaugh, J. L. (2004). Glucocorticoid effects on memory retrieval require concurrent noradrenergic activity in the hippocampus and basolateral amygdala. *Journal of Neuroscience*, 24, 8161–8169.
- Roozendaal, B., McReynolds, J. R., Van der Zee, E. A., Lee, S., McGaugh, J. L., & McIntyre, C. K. (2009). Glucocorticoid effects on memory consolidation depend on functional interactions between the medial prefrontal cortex and basolateral amygdala. *Journal of Neuroscience*, 29, 14299–14308.
- Roozendaal, B., Okuda, S., Van der Zee, E. A., & McGaugh, J. L. (2006). Glucocorticoid enhancement of memory requires arousal-induced noradrenergic activation in the basolateral amygdala. *Proceedings of National Academy of Sciences of USA*, 103, 6741–6746.
- Rossato, J. I., Bevilacqua, L. R., Izquierdo, I., Medina, J. H., & Cammarota, M. (2009). Dopamine controls persistence of long-term memory storage. *Science*, 325, 1017–1020.
- Schultz, W. (2002). Getting formal with dopamine and reward. *Neuron*, 36, 241–263.
- Stevenson, C. W., & Gratton, A. (2003). Basolateral amygdala modulation of the nucleus accumbens dopamine response to stress: role of the medial prefrontal cortex. *European Journal of Neuroscience*, 17, 1287–1295.
- Tinsley, C. J., Fontaine-Palmer, N. S., Vincent, M., Endean, E. P., Aggleton, J. P., Brown, M. W., et al. (2011). Differing time dependencies of object recognition memory impairments produced by nicotinic and muscarinic cholinergic antagonism in perirhinal cortex. *Learning and Memory*, 18, 484–492.
- Vouimba, R. M., & Maroun, M. (2011). Learning-induced changes in mPFC-BLA connections after fear conditioning, extinction, and reinstatement of fear. *Neuropsychopharmacology*, 36, 2276–2285.
- Werenicz, A., Christoff, R. R., Blank, M., Jobim, P. F., Pedrosa, T. R., Reolon, G. K., et al. (2012). Administration of the phosphodiesterase type 4 inhibitor rolipram into the amygdala at a specific time interval after learning increases recognition memory persistence. *Learning and Memory*, 19, 495–498.
- Wittmann, B. C., Schiltz, K., Boehler, C. N., & Düzel, E. (2008). Mesolimbic interaction of emotional valence and reward improves memory formation. *Neuropsychologia*, 46, 1000–1008.
- Zhu, X. O., McCabe, B. J., Aggleton, J. P., & Brown, M. W. (1997). Differential activation of the rat hippocampus and perirhinal cortex by novel visual stimuli and a novel environment. *Neuroscience Letters*, 229, 141–143.