

# 5-ht<sub>7</sub> receptor stimulation and blockade: a therapeutic paradox about memory form...

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## Overview

Mammalian memory involves multiple brain areas and neurotransmitter systems; both at the receptor and post-receptor level ( [Meneses, 2014a, b](#) ). Investigations of serotonin (5-hydroxytryptamine, 5-HT) involvement in memory ( [Meneses, 2013](#) ) have been significantly enhanced by the identification, classification, and cloning of multiple receptors ( [Hoyer et al., 1994, 2002](#) ) and studies at the post-receptor level ( [Raymond et al., 2001](#) ). Emergent investigation of 5-HT <sub>7</sub> receptor is growing but contradictory. Hence, major current questions include (1) the paradox that 5-HT <sub>7</sub> receptor agonists and antagonists in behavioral memory tasks are revealing promnesic and anti-amnesic effects; (2) 5-HT <sub>7</sub> and 5-HT <sub>1A</sub> receptors interaction (and other 5-HT receptors), and neural markers associated to these cognitive processes and individual differences. In this work recent data are briefly revised.

## 5-HT <sub>7</sub> Receptor Stimulation

[Freret et al. \(2014\)](#) reported that with a 2-h delay, (post-training) administration of the 5-HT <sub>7</sub> receptor antagonist SB-269970 (3 and 10 mg/kg, sc) impaired the discrimination of the novel object; but with a 4-h delay, while control mice were not able to discriminate the novel object, mice treated with the agonist 5-carboxamidotryptamine (5-CT; displaying affinity for several receptors including 5-HT <sub>7</sub> ; [Hoyer et al., 1994](#) ) showed a significant discrimination. This promnesic effect was blocked by SB-269970, but not by WAY-100135 or GR-127935 (5-HT <sub>1A</sub> or 5-HT <sub>1B/1D</sub> receptor antagonists, respectively; [Hoyer et al., 1994](#) ). [Freret et al. \(2014\)](#) conclude

that 5-HT<sub>7</sub> receptor tonically modulates cognitive processes involved in consolidation performances in object recognition and therefore, it could be a promising target to treat memory dysfunctions (especially episodically related deficits) or pathological aging. Notably, [Stahl \(2010\)](#) suggests that 5-HT<sub>7</sub> receptor (blockade) as a novel therapeutic target for antidepressant and pro-cognitive effects. [Nikiforuk et al. \(2013\)](#) also conclude that antagonism of 5-HT<sub>7</sub> receptor may represent a useful pharmacological approach in the treatment of cognitive deficits and some negative schizophrenia symptoms. Also, [Tajiri et al. \(2012\)](#) and [Gasbarri and Pompili \(2014\)](#) propose that the 5-HT<sub>7</sub> receptor is a rational target for the treatment of psychiatric disorders. Certainly, more research is necessary about 5-HT<sub>7</sub> receptor, its functional complexity in memory formation and abnormal memory as well timing of drug administration ( [McGaugh, 1989](#) ; [Monleón et al., 2008](#) ).

Pre-training elevation of 5-HT by the selective serotonin reuptake inhibitor (SSRI) fluoxetine had no effect by itself, but facilitated passive avoidance when combined with the 5-HT<sub>1A</sub> receptor antagonist NAD-299 and this facilitation was blocked by SB-269970 ( [Eriksson et al., 2012](#) ). Likewise [Eriksson et al. \(2012\)](#) reported that a reduced activation of the 5-HT<sub>1A</sub> receptor was resulting in enhanced stimulation of the 5-HT<sub>7</sub> receptor but 5-HT<sub>7</sub> receptor agonists LP-44 or AS19 failed to facilitate passive avoidance performance; and according with these authors LP-44 and AS19 have low efficacy to stimulate protein phosphorylation of 5-HT<sub>7</sub> receptor-activated signaling cascades. Notably, in the mutant mouse brain (lacking pituitary adenylate cyclase, an experimental mouse model for psychiatric disorders) 5-HT<sub>7</sub> protein expression did not differ from wild-type mice but in primary <https://assignbuster.com/5-ht-7-receptor-stimulation-and-blockade-a-therapeutic-paradox-about-memory-formation-and-amnesia/>

embryonic hippocampal neurons AS-19 increased neurite length and number ([Tajiri et al., 2012](#)). Likewise, LP-211 and 8-OHDPAT affect neurites in embryonic cultures ([Speranza et al., 2013](#)). Certainly, [Eriksson et al. \(2012\)](#) propose that retention (in passive avoidance) is mediated through hippocampal 5-HT<sub>1A</sub> receptor activation, while the 5-HT<sub>7</sub> receptor appears to facilitate memory processes in a broader cortico-limbic network and not the hippocampus alone. Notably, LP-211 rescued diverse defective performances, including memory in the novelty preference task as well as the abnormal activation of PAK and cofilin (key regulators of actin cytoskeleton dynamics) and of the ribosomal protein (rp) S6, whose reduced activation in MECP2 mutant neurons is responsible for the altered protein translational control ([De Filippis et al., 2014](#)). [De Filippis et al. \(2014\)](#) indicate that pharmacological targeting of 5-HT<sub>7</sub> receptor improves specific behavioral and molecular manifestations and these data are a first step toward the validation of an innovative systemic treatment to disorders associated with intellectual disability.

Importantly, either AS-19 or LP-211 or the dual 5-HT<sub>1A/7</sub> receptor agonist, 8-OHDPAT, facilitated memory consolidation in an associative memory task and increased cAMP production ([Pérez-García et al., 2006](#); [Meneses, 2013](#); [Meneses et al., 2014](#)) which were reversed by SB-269970. Certainly, an association between memory and cAMP production exists ([Kandel, 2001](#); [Izquierdo et al., 2006](#)). It should be noted however that memory formation in an autoshaping learning ([Pérez-García and Meneses, 2008](#)) showed that cAMP production was decreased by 8-OHDPAT if memory was improving but the opposite occurred in absence of memory. In autoshaping task, trained

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animals are food-restricted (at 85% of *ad-libitum*), receiving one autoshaping training and are tested at 1.5 h for short-term memory (STM) and at 24 and 48 h for consolidation of long-term memory (LTM) ( [Meneses, 2013](#) ). Why 8-OHDPAT improved memory (consolidation, 48 h) and increased cAMP in cortex and hippocampus ( [Manuel-Apolinar and Meneses, 2004](#) ) or decremented ( [Pérez-García and Meneses, 2008](#) ) hippocampal cAMP production? Importantly, the new 5-HT<sub>7</sub> receptor agonist LP-211 did not affect STM; nonetheless, at 0.5 and 1.0 mg/kg it improved LTM. The 5-HT<sub>7</sub> receptor antagonist SB-269970 (10.0 mg/kg) alone had no effect but it reversed the LP-211 (1.0 mg/kg) LTM facilitation. The scopolamine (0.2 mg/kg) induced-decrement in CR was accompanied by significant increased cAMP production. Scopolamine-induced amnesia and increments in cAMP, are significantly but not completely reversed by LP-211 ( [Meneses et al., 2014](#) ). Hence, prefrontal cortex, cAMP production and improved memory formation seem to be associated; however, this association is complex and dependent on the basal level (e. g., prevalent expression of either of 5-HT<sub>1A</sub> or 5-HT<sub>7</sub> receptors). For instance, the time-course (0–120 h) of autoshaped responses revealed progressive performance and mRNA 5-HT<sub>1A</sub> or 5-HT<sub>7</sub> receptors are monotonically augmented or declined in prefrontal cortex, hippocampus and raphe nuclei, respectively ( [Perez-Garcia and Meneses, 2009](#) ). Moreover, 5-HT<sub>1A</sub> receptor is increased, whereas 5-HT<sub>7</sub> receptor levels are decreased by aging ( [Saroja et al., 2014](#) ). Also, they showed significant correlation with the time spent in target quadrant; hence according with [Saroja et al. \(2014\)](#) these are two key parameters of memory

retrieval which in turn unambiguously links the serotonergic receptor system to spatial memory performance.

## **5-HT<sub>7</sub> Receptor Blockade: Cognitive Demand or Memory Impaired**

[Gasbarri et al. \(2008\)](#) showed that SB-269970 improved memory, decreasing the number of errors in test phase and, thus, affecting reference memory, while no effects in working memory; postulating that 5-HT<sub>7</sub> receptor blockade had procognitive effect, when the learning task implicated a high degree of difficulty. In addition, the 5-HT<sub>7</sub> receptor antagonists, SB-269970 or DR 4004 alone had no effect but reversed amnesia induced by scopolamine and dizocilpine ( [Meneses, 2004](#) ). Hence, 5-HT<sub>7</sub> receptor antagonism plays an important role under poor memory or when the learning or memory is complex.

## **5-HT<sub>7</sub> Blockade and Promiscuous Affinity**

In recent time, it has become evident that 5-HT<sub>7</sub> blockade and drugs displaying promiscuous affinity have interesting effects. For instance, lurasidone (affinity for several receptors including 5-HT<sub>7</sub>) and the selective 5-HT<sub>7</sub> receptor antagonist, SB-656104-A improved learning and memory deficits by dizocilpine (or MK-801), in the rat passive avoidance test, and AS-19 (3 mg/kg) completely blocked the attenuating effects of lurasidone (3 mg/kg); AS-19 (1–10 mg/kg) pre-training administration had no effects ( [Horisawa et al., 2013](#) ). SB-269970 (30 but not 10 mg/kg) pre-training administration produces both anti-psychotic-like (amphetamine- or phencyclidine-induced hyperactivity tests) and pro-cognitive (novel object

discrimination test) activity in preclinical animal models ( [Waters et al., 2012](#) ); these authors conclude that SB-269970 is more a potent inverse agonist than SB-258741, which might be a potential explanation for the conflicting profiles *in vivo* (for references see [Waters et al., 2012](#) ). Importantly, [Huang et al. \(2014\)](#) reported that 5-HT<sub>1A</sub> and 5-HT<sub>7</sub> receptors contribute to lurasidone-induced dopamine efflux, concluding that, at least partially, 5-HT<sub>1A</sub> agonist and 5-HT<sub>7</sub> antagonist properties may contribute to reversing schizophrenia-like effects. Chronic stress impaired performance on the extra-dimensional (ED) set-shifting stage of the frontal-dependent attentional set-shifting task and amisulpride (3 mg/kg) before testing reversed this restraint-induced cognitive inflexibility and improved ED performance of the unstressed control group ( [Nikiforuk and Popik, 2013](#) ). AS-19 (10 mg/kg) pre-training alone had no effect but abolished the pro-cognitive efficacy of amisulpride ( [Nikiforuk and Popik, 2013](#) ). [Nikiforuk et al. \(2013\)](#) also reported that acute administration of SB-269970 (1 mg/kg) or amisulpride (3 mg/kg) ameliorated ketamine-induced cognitive inflexibility and novel object recognition deficit in rats; both compounds were also effective in attenuating ketamine-evoked disruption of social interactions. In contrast, neither SB-269970 nor amisulpride affected ketamine-disrupted prepulse inhibition; ketamine is a glutamatergic antagonist ( [Neill et al., 2010](#) ). Importantly, in contrast to the negative regulatory effects of long-term activation of 5-HT<sub>7</sub> receptors on NMDA receptor signaling ( *in vitro* ) acute activation of 5-HT<sub>7</sub> receptors promotes NMDA receptor activity ( [Vasefi et al., 2013](#) ). Hence, these findings highlight the potential for temporally differential regulation of NMDA receptors by the 5-HT<sub>7</sub> receptor. While some inconsistencies might be

related to the opposite action exerted by 5-HT<sub>1A</sub> and 5-HT<sub>7</sub> receptors over cAMP production ( [Renner et al., 2012](#) ; [Meneses, 2014a, b](#) ); certainly, in different protocols of training/testing (memory consolidation vs. STM and LTM), various brain areas and neurotransmission systems interaction might be also implicated.

## **5-HT<sub>1A</sub> and 5-HT<sub>7</sub> Receptors**

The functional significance of 5-HT<sub>1A</sub> and 5-HT<sub>7</sub> receptors dimerization is has been revised ( [Matthys et al., 2011](#) ; [Gellynck et al., 2013](#) ; [Herrick-Davis, 2013](#) ); indicating that it differentially regulates receptor signaling and trafficking ( [Renner et al., 2012](#) ). But still we do not know the implications of this in memory formation and amnesic conditions; hence, the study of signaling associated to 5-HT<sub>7</sub> receptor in memory formation, amnesia and forgetting might provide significant insights ( [Meneses, 2014a, b](#) ). For instance, while the association of 5-HT<sub>7</sub> receptor stimulation, improved memory and increased cAMP seems to be reliable findings; certainly factors such as differential regulation of hippocampal expression as well as individual differences might be important (see [Meneses, 2013](#) ). In addition, a biphasic and brain-region selective down-regulation of cAMP concentrations is observed supporting object recognition in the rat ( [Hotte et al., 2012](#) ). [Wang et al. \(2013\)](#) have noted that while it is relatively well established that cAMP signaling is involved in the mediation of memory, the reports on its role to date are inconsistent. One hypothesis is that overactive cAMP signaling impairs working memory in the aged prefrontal cortex (PFC) or activation of the cAMP signaling in the frontal cortex is necessary for working memory; the explanations for this discrepancy may include: (i) <https://assignbuster.com/5-ht-7-receptor-stimulation-and-blockade-a-therapeutic-paradox-about-memory-formation-and-amnesia/>



activation of cAMP signaling within the PFC and an inverted U-shape dose-response on working memory and memory optimum range of cAMP rather than an overmuch or scanty production; (ii) the continuous and dynamic updating of cAMP levels occurs at the different time-course of memory formation; (iii) cAMP activation might be beneficial for working memory under conditions that require hippocampal–PFC interactions ( [Wang et al., 2013](#) ). Given the complexity of cAMP-dependent responses; hence studies of brain areas and individual differences remain to be reported at both behavioral and cellular levels (see [Wang et al., 2013](#) ).

Evidence exists of individual differences regarding memory ( [Ballaz et al., 2007a](#) , [b](#) ; [Fitzpatrick et al., 2013](#) ; [Flagel et al., 2014](#) ) and forgetting ( [Tellez et al., 2012](#) ); hence, it seems reasonable to suggest that in autoshaping (or sign-tracking; see [Meneses, 2003](#) ) the increment ( [Manuel-Apolinar and Meneses, 2004](#) ) or decrement ( [Pérez-García and Meneses, 2008](#) ) cAMP production might be involving individual differences (e. g., [Meneses, 2014a](#) , [b](#) ). Notably, individual variation in the magnitude and influence of cue reactivity over behavior in humans and animals suggest that cue-reactive individuals may be at greater risk for the progression to addiction and/or relapse ( [Anastasio et al., 2014](#) ).

Also, an important implication is that 5-HT<sub>7</sub> (and/or 5-HT<sub>1A</sub>) receptors stimulation increased or decreased cAMP production (e. g., [Hoyer et al., 1994](#) ) and improved memory ( [Meneses et al., 2014](#) ). Likewise, evidence indicates that 5-HT<sub>7</sub> splice variants constitutively activate adenylyl cyclase ( [Leopoldo et al., 2011](#) ). It should be crucial to confirm if memory formation,

amnesia, or forgetting by themselves and/or plus drugs modify adenylyl cyclase.

Hence, (1) memory requires restricted or selective cAMP production ( [Pérez-García and Meneses, 2008](#) ; [Meneses, 2013](#) ); (2) a major and consistent emerging finding is that 5-HT <sub>7</sub> receptor stimulation seems to facilitate memory formation and reverse memory impairment; (3) expression of 5-HT <sub>7</sub> (and 5-HT <sub>1A</sub> ) receptors are accompanying memory; (4) the 5-HT <sub>7</sub> antagonism alone had no effect but reversed memory deficits. Notably, a combination of neural and cognitive processes may contribute an early and specific marker of disorders associated to dysfunctional cognitive skills or memory in psychiatric disorders ( [Millan et al., 2012](#) ), including Alzheimer's disease progression ( [Ibanez and Parra, 2014](#) ).

## Conclusions

Behavioral and molecular studies may be particularly insightful and timely in view of the apparently contradictory notion that either 5-HT <sub>1A</sub> or 5-HT <sub>7</sub> receptor agonists or antagonists are useful in the treatment of learning and memory disorders. Also, the distinction about normal memory or impaired memory, timing of drug administration and individual differences are providing important insights about 5-HT <sub>1A</sub> or 5-HT <sub>7</sub> receptors stimulation and blockade.

## Conflict of Interest Statement

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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## References

Anastasio, N. C., Liu, S., Maili, L., Swinford, S. E., Lane, S. D., Fox, R. G., et al. (2014). Variation within the serotonin (5-HT) 5-HT<sub>2C</sub> receptor system aligns with vulnerability to cocaine cue reactivity. *Transl. Psychiatry* 4: e369. doi: 10.1038/tp.2013.131

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

Ballaz, S. J., Akil, H., and Watson, S. J. (2007a). The 5-HT<sub>7</sub> receptor: role in novel object discrimination and relation to novelty-seeking behavior. *Neuroscience* 149, 192–202. doi: 10.1016/j.neuroscience.2007.07.043

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

Ballaz, S. J., Akil, H., and Watson, S. J. (2007b). Analysis of 5-HT<sub>6</sub> and 5-HT<sub>7</sub> receptor gene expression in rats showing differences in novelty-seeking behavior. *Neuroscience* 147, 428–438. doi: 10.1016/j.neuroscience.2007.04.024

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

De Filippis, B., Nativio, P., Fabbri, A., Ricceri, L., Adriani, W., Lacivita, E., et al. (2014). Pharmacological stimulation of the brain serotonin receptor 7 as a novel therapeutic approach for Rett syndrome. *Neuropsychopharmacology*. doi: 10.1038/npp.2014.105. [Epub ahead of print].

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

Eriksson, T. M., Holst, S., Stan, T. L., Hager, T., Sjögren, B., Ogren, S. Ö., et al. (2012). Ce5-HT1A and 5-HT7 receptor crosstalk in the regulation of emotional memory: implications for effects of selective serotonin reuptake inhibitors. *Neuropharmacology* 63, 1150–60. doi: 10.1016/j.neuropharm.2012.06.061

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

Fitzpatrick, C. J., Gopalakrishnan, S., Cogan, E. S., Yager, L. M., Meyer, P. J., Lovic, V., et al. (2013). Variation in the form of pavlovian conditioned approach behavior among outbred male Sprague-Dawley rats from different vendors and colonies: sign-tracking vs. goal-tracking. *PLoS ONE* 8: e75042. doi: 10.1371/journal.pone.0075042

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

Flagel, S. B., Waselus, M., Clinton, S. M., Watson, S. J., and Akil, H. (2014). Antecedents and consequences of drug abuse in rats selectively bred for high and low response to novelty. *Neuropharmacology* 76(pt B), 425–436. doi: 10.1016/j.neuropharm.2013.04.033

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

Freret, T., Paizanis, E., Beaudet, G., Gusmao-Montaigne, A., Nee, G., Dauphin, F., et al. (2014). Modulation of 5-HT7 receptor: effect on object recognition performances in mice. *Psychopharmacology (Berl)* . 231, 393–400. doi: 10.1007/s00213-013-3247-x

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

<https://assignbuster.com/5-ht-7-receptor-stimulation-and-blockade-a-therapeutic-paradox-about-memory-formation-and-amnesia/>

Gasbarri, A., Cifariello, A., Pompili, A., and Meneses, A. (2008). Effect of 5-HT7 antagonist SB-269970 in the modulation of working and reference memory in the rat. *Behav. Brain Res.* 195, 164–170. doi: 10.1016/j.bbr.2007.12.020

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Gasbarri, A., and Pompili, A. (2014). Serotonergic 5-HT7 receptors and cognition. *Rev. Neurosci.* 25, 311–323. doi: 10.1515/revneuro-2013-0066

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Gellynck, E., Heyninck, K., Andressen, K. W., Haegeman, G., Levy, F. O., Vanhoenacker, P., et al. (2013). The serotonin 5-HT7 receptors: two decades of research. *Exp. Brain Res.* 230, 555–568. doi: 10.1007/s00221-013-3694-y

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Herrick-Davis, K. (2013). Functional significance of serotonin receptor dimerization. *Exp. Brain Res.* 230, 375–386. doi: 10.1007/s00221-013-3622-1

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Horisawa, T., Nishikawa, H., Toma, S., Ikeda, A., Horiguchi, M., Ono, M., et al. (2013). The role of 5-HT7 receptor antagonism in the amelioration of MK-801-induced learning and memory deficits by the novel atypical antipsychotic drug lurasidone. *Behav. Brain Res.* 244, 66–69. doi: 10.1016/j.bbr.2013.01.026

<https://assignbuster.com/5-ht-7-receptor-stimulation-and-blockade-a-therapeutic-paradox-about-memory-formation-and-amnesia/>

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Hotte, M., Dauphin, F., Freret, T., Boulouard, M., and Levallet, G. (2012). A biphasic and brain-region selective down-regulation of cyclic adenosine monophosphate concentrations supports object recognition in the rat. *PLoS ONE* 7: e32244. doi: 10.1371/journal.pone.0032244

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Hoyer, D., Clarke, D. E., Fozard, J. R., Hartig, P. R., Martin, G. R., Mylecharane, E. J., et al. (1994). International Union of Pharmacology classification of receptors for 5-hydroxytryptamine (Serotonin). *Pharmacol. Rev.* 46, 157–203.

[Pubmed Abstract](#) | [Pubmed Full Text](#)

Hoyer, D., Hannon, J. P., and Martin, G. R. (2002). Molecular, pharmacological and functional diversity of 5-HT receptors. *Pharmacol. Biochem. Behav.* 71, 533–554. doi: 10.1016/S0091-3057(01)00746-8

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Huang, M., Panos, J. J., Kwon, S., Oyamada, Y., Rajagopal, L., and Meltzer, H. Y. (2014). Comparative effect of lurasidone and blonanserin on cortical glutamate, dopamine, and acetylcholine efflux: role of relative serotonin (5-HT)<sub>2A</sub> and DA D<sub>2</sub> antagonism and 5-HT<sub>1A</sub> partial agonism. *J. Neurochem.* 128, 938–949. doi: 10.1111/jnc.12512

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

<https://assignbuster.com/5-ht-7-receptor-stimulation-and-blockade-a-therapeutic-paradox-about-memory-formation-and-amnesia/>

Ibanez, A., and Parra, M. A. (2014). Mapping memory binding onto the connectome's temporal dynamics: toward a combined biomarker for Alzheimer's disease. *Front. Hum. Neurosci.* 8: 237. doi: 10.3389/fnhum.2014.00237

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

Izquierdo, I., Bevilaqua, L. R., Rossato, J. I., Bonini, J. S., Medina, J. H., and Cammarota, M. (2006). Different molecular cascades in different sites of the brain control memory consolidation. *Trends Neurosci.* 29, 496–505. doi: 10.1016/j.tins.2006.07.005

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

Kandel, E. R. (2001). The molecular biology of memory storage: a dialogue between genes and synapses. *Science* 294, 1030–1038. doi: 10.1126/science.1067020

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

Leopoldo, M., Lacivita, E., Berardi, F., Perrone, R., and Hedlund, P. B. (2011). Serotonin 5-HT<sub>7</sub> receptor agents: structure-activity relationships and potential therapeutic applications in central nervous system disorders. *Pharmacol. Ther.* 129, 120–148. doi: 10.1016/j.pharmthera.2010.08.013

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

Manuel-Apolinar, L., and Meneses, A. (2004). 8-OH-DPAT facilitated memory consolidation and increased hippocampal and cortical cAMP production. *Behav. Brain Res.* 148, 179–184. doi: 10.1016/S0166-4328(03)00186-4

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Matthys, A., Haegeman, G., Van Craenenbroeck, K., and Vanhoenacker, P. (2011). Role of the 5-HT7 receptor in the central nervous system: from current status to future perspectives. *Mol. Neurobiol.* 43, 228–253. doi: 10.1007/s12035-011-8175-3

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

McGaugh, J. L. (1989). Dissociating learning and performance: drug and hormone enhancement of memory storage. *Brain Res. Bull.* 23, 339–345. doi: 10.1016/0361-9230(89)90220-7

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Meneses, A. (2003). A pharmacological analysis of an associative learning task: 5-HT(1) to 5-HT(7) receptor subtypes function on a pavlovian/instrumental autoshaped memory. *Learn. Mem.* 10, 363–372. doi: 10.1101/lm.60503

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Meneses, A. (2004). Effects of the 5-HT7 receptor antagonists SB-269970 and DR 4004 in autoshaping Pavlovian/instrumental learning task. *Behav. Brain Res.* 155, 275–282. doi: 10.1016/j.bbr.2004.04.026

<https://assignbuster.com/5-ht-7-receptor-stimulation-and-blockade-a-therapeutic-paradox-about-memory-formation-and-amnesia/>



[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Meneses, A. (2013) 5-HT systems: emergent targets for memory formation and memory alterations. *Rev. Neurosci.* 24, 629–664. doi: 10.1515/revneuro-2013-0026

1515/revneuro-2013-0026

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Meneses, A. (2014a). Memory formation and memory alterations: 5-HT<sub>6</sub> and 5-HT<sub>7</sub> receptors, novel alternative. *Rev. Neurosci.* 25, 325–356. doi: 10.1515/revneuro-2014-0001

1515/revneuro-2014-0001

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Meneses, A. (2014b). “ Neurotransmitters and memory: cholinergic, glutamatergic, gabaergic, dopaminergic, serotonergic, signaling, and memory,” in *Identification of Neural Markers Accompanying Memory*, ed A. Meneses (San Diego, CA: Elsevier), 5–45.

Meneses, A., Perez-Garcia, G., Liy-Salmeron, G., Lacivita, E., and Leopoldo, M. (2014). Effects of the 5-HT<sub>7</sub> receptor agonist LP-211 during memory formation and amnesia. *Psychopharmacology*.

Millan, M. J., Agid, Y., Brüne, M., Bullmore, E. T., Carter, C. S., Clayton, N. S., et al. (2012). Cognitive dysfunction in psychiatric disorders: characteristics, causes and the quest for improved therapy. *Nat. Rev. Drug Discov.* 11, 141–168. doi: 10.1038/nrd3628

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

<https://assignbuster.com/5-ht-7-receptor-stimulation-and-blockade-a-therapeutic-paradox-about-memory-formation-and-amnesia/>

Monleón, S., Vinader-Caerols, C., Arenas, M. C., and Parra, A. (2008). Antidepressant drugs and memory: insights from animal studies. *Eur. Neuropsychopharmacol.* 18, 235–248. doi: 10.1016/j.euroneuro.2007.07.001

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Neill, J. C., Barnes, S., Cook, S., Grayson, B., Idris, N. F., McLean, S. L., et al. (2010). Animal models of cognitive dysfunction and negative symptoms of schizophrenia: focus on NMDA receptor antagonism. *Pharmacol. Ther.* 128, 419–432. doi: 10.1016/j.pharmthera.2010.07.004

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Nikiforuk, A., Kos, T., Fijał, K., Hołuj, M., Rafa, D., and Popik, P. (2013). Effects of the selective 5-HT7 receptor antagonist SB-269970 and amisulpride on ketamine-induced schizophrenia-like deficits in rats. *PLoS ONE* 8: e66695. doi: 10.1371/journal.pone.0066695

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Nikiforuk, A., and Popik, P. (2013). Amisulpride promotes cognitive flexibility in rats: the role of 5-HT7 receptors. *Behav. Brain. Res.* 248, 136–140. doi: 10.1016/j.bbr.2013.04.008

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Pérez-García, G., Gonzalez-Espinosa, C., and Meneses, A. (2006). An mRNA expression analysis of stimulation and blockade of 5-HT7 receptors during

<https://assignbuster.com/5-ht-7-receptor-stimulation-and-blockade-a-therapeutic-paradox-about-memory-formation-and-amnesia/>

memory consolidation. *Behav. Brain Res.* 169, 83–92. doi: 10.1016/j.bbr.2005.12.013

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Pérez-García, G., and Meneses, A. (2008). *Ex-vivo* study of 5-HT<sub>1A</sub> and 5-HT<sub>7</sub> receptor agonists and antagonists on cAMP accumulation during memory formation and amnesia. *Behav. Brain Res.* 195, 139–146. doi: 10.1016/j.bbr.2008.07.033

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Perez-Garcia, G., and Meneses, A. (2009). Memory time-course: mRNA 5-HT<sub>1A</sub> and 5-HT<sub>7</sub> receptors. *Behav. Brain Res.* 202, 102–113. doi: 10.1016/j.bbr.2009.03.027

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Raymond, J. R., Mukhin, Y. V., Gelasco, A., Turner, J., Collinsworth, G., Gettys, T. W., et al. (2001). Multiplicity of mechanisms of serotonin receptor signal transduction. *Pharmacol. Ther.* 92, 179–212. doi: 10.1016/S0163-7258(01)00169-3

[Pubmed Abstract](#) | [Pubmed Full Text](#) | [CrossRef Full Text](#)

Renner, U., Zeug, A., Woehler, A., Niebert, M., Dityatev, A., Dityateva, G., et al. (2012). Heterodimerization of serotonin receptors 5-HT<sub>1A</sub> and 5-HT<sub>7</sub> differentially regulates receptor signalling and trafficking. *J. Cell Sci.* 125, 2486–2499. doi: 10.1242/jcs.101337

<https://assignbuster.com/5-ht-7-receptor-stimulation-and-blockade-a-therapeutic-paradox-about-memory-formation-and-amnesia/>

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

Saroja, S. R., Kim, E. J., Shanmugasundaram, B., Höger, H., and Lubec, G. (2014). Hippocampal monoamine receptor complex levels linked to spatial memory decline in the aging C57BL/6J. *Behav. Brain Res.* 264, 1–8. doi: 10.1016/j.bbr.2014.01.042

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

Speranza, L., Chambery, A., Di Domenico, M., Crispino, M., Severino, V., Volpicelli, F., et al. (2013). The serotonin receptor 7 promotes neurite outgrowth via ERK and Cdk5 signaling pathways. *Neuropharmacology* 67, 155–167. doi: 10.1016/j.neuropharm.2012.10.026

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

Stahl, S. M. (2010). The serotonin-7 receptor as a novel therapeutic target. *J. Clin. Psychiatry* 71, 1414–1415. doi: 10.4088/JCP.10bs06601gry

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

Tajiri, M., Hayata-Takano, A., Seiriki, K., Ogata, K., Hazama, K., Shintani, N., et al. (2012). Serotonin 5-HT<sub>7</sub> receptor blockade reverses behavioral abnormalities in PACAP-deficient mice and receptor activation promotes neurite extension in primary embryonic hippocampal neurons: therapeutic implications for psychiatric disorders. *J. Mol. Neurosci.* 48, 473–481. doi: 10.1007/s12031-012-9861-y

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

<https://assignbuster.com/5-ht-7-receptor-stimulation-and-blockade-a-therapeutic-paradox-about-memory-formation-and-amnesia/>

Tellez, R., Gómez-Viquez, L., Liy-Salmeron, G., and Meneses, A. (2012). GABA, glutamate, dopamine and serotonin transporters expression on forgetting. *Neurobiol. Learn. Mem.* 98, 66–77. doi: 10.1016/j.nlm.2012.05.001

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

Vasefi, M. S., Yang, K., Li, J., Kruk, J. S., Heikkila, J. J., Jackson, M. F., et al. (2013). Acute 5-HT<sub>7</sub> receptor activation increases NMDA-evoked currents and differentially alters NMDA receptor subunit phosphorylation and trafficking in hippocampal neurons. *Mol. Brain* 6: 24. doi: 10.1186/1756-6606-6-24

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

Wang, Z. Z., Zhang, Y., Liu, Y. Q., Zhao, N., Zhang, Y. Z., Yuan, L., et al. (2013). RNA interference-mediated phosphodiesterase 4D splice variants knock-down in the prefrontal cortex produces antidepressant-like and cognition-enhancing effects. *Br. J. Pharmacol.* 168, 1001–1014. doi: 10.1111/j.1476-5381.2012.02225.x

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

Waters, K. A., Stean, T. O., Hammond, B., Virley, D. J., Upton, N., Kew, J. N., et al. (2012). Effects of the selective 5-HT<sub>7</sub> receptor antagonist SB-269970 in animal models of psychosis and cognition. *Behav. Brain Res.* 228, 211–218. doi: 10.1016/j.bbr.2011.12.009

[PubMed Abstract](#) | [PubMed Full Text](#) | [CrossRef Full Text](#)

<https://assignbuster.com/5-ht-7-receptor-stimulation-and-blockade-a-therapeutic-paradox-about-memory-formation-and-amnesia/>