

**Table 2. The changes of histamine or histamine receptor in epilepsy animal model.**

Animal model	Seizure type	Species	Histamine changes	Reference
PTZ	General myoclonic seizure	Rats <sup>a,b,c</sup> <sub>e,f</sub> Mice <sup>d</sup>	<sup>a</sup> Histamine in hippocampus and striatum does not change. <sup>b,c,e,f</sup> Histamine decrease in hippocampus, thalamus and hypothalamus. <sup>d</sup> Brain histamine decrease in lamotrigine-resistant PTZ mice.	<sup>a</sup> (Szyndler et al., 2006), <sup>b</sup> (Zhang, Ma & Li, 2006), <sup>c</sup> (Chen, Ren, Zhang & Hu, 2012), <sup>d</sup> (Singh, Pillai & Mehndiratta, 2014), <sup>e</sup> (Zhang, Chen, Chen, He & Hu, 2017), <sup>f</sup> (Alachkar et al., 2020)
KA	Temporal lobe epilepsy	Rats <sup>a,b</sup>	<sup>a</sup> The mRNA of H1R and H3R transiently decrease in the midline areas with decrease H1R mRNA in the ventral thalamus; H3R mRNA increase in the ventral posterior and geniculate nuclei after 1 week. <sup>b</sup> KA increases brain histamine and histamine immunoreactive nerve fibers in piriform cortex and amygdala.	<sup>a</sup> (Jin, Lintunen & Panula, 2005), <sup>b</sup> (Lintunen, Sallmen, Karlstedt & Panula, 2005)
Pilocarpine	Temporal lobe epilepsy	Rats	Histamine extracellular levels in hippocampus increased.	(Enrique et al., 2019)
Amygdala kindling	Focal seizure	Rats	Histamine in the amygdala decrease.	(Kamei, Ishizawa, Kakinoki & Fukunaga, 1998)
MES	General tonic-clonic seizure	Rats	Lesion of the TMN E2-region decreases histamine in the cortex, hippocampus, brainstem and hypothalamus.	(Jin et al., 2007)

Transauricular kindling	Chronic seizure	Rat	Histamine in the hippocampus decreased.	(Li, Liu, Zhu, Zhou & Chen, 2006)
6-Hz Stimulation	Partial seizure	Mice	The brain histamine decreased.	(Jahan, Pillai & Vohora, 2017)
Audiogenic model	Audiogenic seizure	Mice	The histamine level in hypothalamus of DBA/2 mice decreases with age.	(Tuomisto, Sturman, Freeman & Tarhanen, 2003)
Hyperthermia	Febrile seizure	Rat	Hyperthermia induces a decrease of blood histamine level.	(Gholipour, Saboory, Roshan-Milani & Fereidoni, 2013)
Genetic epilepsy-prone animal	Absence epilepsy	Rat <sup>a, b</sup>	<sup>a</sup> Histamine levels in the striatum, hippocampus, amygdala, midbrain, thalamus and hypothalamus are lower. <sup>b</sup> The H1R density increases in superior colliculus, central grey, nucleus interpositus and pontine nuclei of WAG/Rij rats.	<sup>a</sup> (Onodera, Tuomisto, Tacke & Airaksinen, 1992), <sup>b</sup> (Midzyanovskaya & Tuomisto, 2003)