Asian J Biol Life Sci., 2026; 15(1):9-14.
https://ajbls.com

Review Article

Acetylcholine: The Master Messenger of the Nervous System

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ABSTRACT

Acetylcholine is the major neurotransmitter, whose role in mediating synaptic interactions between neurones in the central nervous system as well as in the peripheral nervous system is well characterized. In human beings acetylcholine system regulates multiple physiological processes not only in neuronal tissues but also in nonneuronal tissues. However, since the concept of the "nonneuronal cholinergic system" has been proposed, the role of the acetylcholine system in nonneuronal tissues has received increasing attention. A growing body of research shows that the acetylcholine system also participates in modulating inflammatory responses, regulating contraction and mucus secretion of respiratory tracts, and influencing the metastasis and invasion of lung cancer. In addition, the susceptibility and severity of respiratory tract infections caused by pathogens such as *Mycobacterium tuberculosis* and the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can also correlate with the regulation of the acetylcholine system. So, acetylcholine as an excitatory neurotransmitter not only affect many neuronal processes, development of nervous system, plasticity of nervous system, cope up with stress, neuroprotection but it also influences other systems respiratory, cardiovascular, gastrointestinal as well.

Keywords: Acetylcholine, Nonneuronal Cholinergic System, Central Nervous System, Peripheral Nervous System.

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Received: 19-01-2026;
Revised: 04-03-2026;
Accepted: 28-04-2026.

INTRODUCTION

Acetylcholine (Ach) is a small molecule plays a crucial role in maintaining homeostasis and brain functions by acting as a neurotransmitter or chemical messenger, that functions in both central and peripheral nervous systems (Picciotto *et al*., 2012). Acetylcholine was the first neurotransmitter to be identified. The name acetylcholine is derived from its structure. It is a chemical compound made up of acetic acid and choline. It is synthesized by choline acetyltransferase enzyme with choline and acetyl coenzyme- as a substrate. Acetylcholine released from nerve-endings upon nerve excitation and is rapidly degrade by acetylcholinesterase into choline and acetic acid. The neurotransmitter acetylcholine is excitatory at the neuromuscular junction in skeletal muscle, causing the muscle to contract. In contrast, it is inhibitory in the heart, where it slows heart rate. Acetylcholine is known to play an important role in memory and learning and to be inadequately available in Alzheimer's disease. Acetylcholine is a neurotransmitter at various synapses, nerves, and at the motor nerve plate of vertebrate muscles (Suryanarayanan, 2014). As a first-discovered neurotransmitter, it regulates movements, heartbeat, digestion, and breathing, as well as other autonomic functions between neurones and nonneural tissues. However, ACh can also be found in the Nonneuronal Cholinergic System (NNCS). The concept of the "NNCS" was first proposed by Sastry and Sadavongvivad in the 1970s (Sastry and Sadavongvivad, 1978). In addition, the NNCS have been detected in reproductive organs (ovary, placenta, and amnion), immune cells, airway, and alimentary epithelial cells, as well as in cancers such as lung cancer, and breast cancer (Grando *et al*., 2003).

History

Naturally occurring acetylcholine was first isolated in 1913 by English chemist Arthur James Ewins, at the urging of his colleague, physiologist Sir Henry Dale. Henry Dale described the chemical action of acetylcholine. The functional significance of acetylcholine was first established in 1921 by German physiologist Otto Loewi. Loewi demonstrated that acetylcholine is liberated when the vagus nerve is stimulated, causing slowing of the heartbeat. Subsequently he and others showed that the chemical is also liberated as transmitter at the motor end plate of striated (Voluntary) muscles of vertebrates. It subsequently identified as transmitter a many neural synapses and in may invertebrate system as well. Due to work of Dale's and Loewi's acetylcholine became the first neurotransmitter to be identified and characterized. For this work both the scientist shared the

DOI: 10.5530/ajbls.20260103

Nobel Prize in Physiology or Medicine and medicine in 1936 (Sir Henry Dale- facts).

Acetylcholine Receptors

The acetylcholine receptors are proteins, that after binding with acetylcholine undergo a conformational transition which result in membrane permeability (Nachmansohn, 1955). There are two types of acetylcholine receptors.

- Metabotropic muscarinic receptors
- Ionotropic nicotinic receptors

Both types of receptors being activated by endogenous neurotransmitter Acetylcholine (ACh) and they are expressed by both neuronal and nonneuronal cells throughout the body (Albuquerque *et al*., 1995; Dani and Bertrand, 2007; Eglen *et al*., 2004).

Muscarinic acetylcholine Receptors or mAChRs are acetylcholine receptors that form G-protein coupled receptor complexes, in the cell membranes of certain neurones (Eglen, 2006). Muscarinic receptors are so named because they are more sensitive to muscarine than nicotine. Activation of muscarinic acetylcholine receptor is relatively slow millisecond to cAMP, and free calcium. They play several roles, including acting as the main end- receptor stimulated by acetylcholine released from postganglionic fibres in the parasympathetic nervous system (Eglen, 2005).

The other subtype of acetylcholine receptors is the fast ionotropic cationic receptor channel (nAChR). These receptors are sensitive to activation by nicotine and have ion channels whose activity is induced in the micro-to submicrosecond range.

Functions

Acetylcholine has functions both in the peripheral nervous system and in the central nervous system (CNS) as a neuromodulator. In the peripheral nervous system, acetylcholine activates muscles, and it is major neurotransmitter in the autonomic nervous system. In the CNS, acetylcholine and the associated neurones form a neurotransmitter system, the cholinergic system, which tends to cause excitatory actions.

In Peripheral Nervous System

In the peripheral nervous system, acetylcholine activates muscles, and is a major neurotransmitter in the autonomic nervous system as well. When acetylcholine binds to acetylcholine receptors on skeletal muscle fibres, it opens ligand gated sodium channels in the cell membrane. Sodium ions then enter the muscle cell, stimulating muscle contraction. Acetylcholine, while inducing contraction of skeletal muscle, instead induces decreased contraction in cardiac muscle fibres. This distinction is attributed to differences in receptors structure between skeletal and cardiac fibres.

In Central Nervous System

In the central nervous system, the cholinergic neurones are widely distributed in various brain areas like spinal cord, hindbrain, medial habenula, mesopontine region, basal forebrain, striatum, olfactory tubercle and island of Cajella complex (Armstrong *et al*., 1983; Houser *et al*., 1983; Woolf, 1991; Woolf and Butcher, 2011). In central nervous system acetylcholine has a variety of effects as a neuromodulator. Within the brain acetylcholine has involvement in memory, motivation, arousal and attention (Christian and Bruno, 2023). Acetylcholine has an important role in the enhancement of alertness when we wake up (Jones, 2005), in sustaining attention (Himmelheber *et al*., 2000) and in the learning and memory (Ridley *et al*., 1984).

In Development of Nervous System

Acetylcholine neurotransmitter plays an important role in developing tissues and primitive organism, as it is released from growing axons, regulates growth, differentiation and plasticity of developing central nervous system neurones (Lauder and Schambra, 1999). One study discusses the evidence that the nicotinic acetylcholine receptors have additional function during development that may be unrelated to their role in cholinergic neurotransmission in the vertebrate brain. It means nicotinic acetylcholine receptors support in neural developmental process such as neurite outgrowth and differentiation (Andrea and Torraoluiz, 2002). One more study support that acetylcholine is found in the first moment of developing the ectodermal system (neural plate), as its action is fundamental for the differentiation of neural cells. So, the neurotransmitter acts as a morphogen (Christian and Bruno, 2023). Thus, neurotransmitter acetylcholine may play important role during development of nervous system.

Learning and Memory

The acetylcholine neurotransmitter plays an important role in supporting learning (Fine *et al*., 1997; Miranda and Bermúdez-Rattoni, 1999) and memory processes in the hippocampus (Parent and Baxter, 2004). As degeneration of central cholinergic neurones impairs memory, and enhancement of cholinergic synapses improves cognitive processes (Maurer and Williams, 2017). It also plays an important role in cognitive functions as-working memory, attention, episodic memory and spatial memory function. It also shows modulatory influences on the cellular physiology of hippocampal and cortical neurones (Newman *et al*., 2012). Study done by Hasselmo and Bower (1993) clearly indicated that both muscarinic and nicotinic acetylcholine receptors have a role in encoding new memories. Another study have demonstrated that endogenous acetylcholine is important for modulation of acquisition (Blokland *et al*., 1992), encoding (Winters and Bussey, 2005), consolidation (Power *et al*., 2003), reconsolidation (Boccia *et al*., 2004), extinction (Boccia *et al*., 2009) and retrieval of memory (Boccia *et al*., 2003).

In Stress

Stress can be defined as brain-body reaction toward stimuli arising from the environment or from internal cues that are interpreted as a disruption of homeostasis. It is a natural, physical and mental reaction to life experiences. It is normal human reaction that happens to everyone. Acetylcholine neurotransmitter may have some role during stress. Acetylcholine is released by nerve cells in the brain when people or mice are mild stress or concentrating on learning something new (Science News Staff, 1998). Acute stress leads to elevated hippocampal acetylcholine (Stillman *et al*., 1997), and may induce hyper excitation of cholinergic circuits (Zimmerman and Soreq, 2006) particularly in the hippocampus (Pavlovsky *et al*., 2012). Different study showed that mild stressor (handling) increases the extracellular concentration of dopamine and acetylcholine in prefrontal cortex (Del Arco *et al*., 2007b; Laplante *et al*., 2004; Mark *et al*., 1996; Segovia *et al*., 2008b). Studies also showed that there is increased release of acetylcholine in hippocampus region of brain under different situation of stress (Imperato *et al*., 1991).

Acetylcholine in Neuroprotection

Neuroprotection is an effect that may result in salvage, recovery or regeneration of the nervous system, its cells, structure and function. Neuroprotective effects induced by long-term nAChR stimulation indicate that CNS nAChRs play important roles in promotion of neuronal survival under pathophysiological conditions such as brain ischaemia and neurodegenerative diseases (Akaike *et al*., 2018). α7 nicotinic acetylcholine receptors (α7nAChR) are expressed in neurones, neuroglia, and endothelial cells of the mammalian brain (Duris *et al*., 2011; Lightfoot *et al*., 2008; Takada-Takatori *et al*., 2006). In addition to their effects as ligand-gated ion channels, α7nAChR stimulation attenuates neuronal apoptosis (Shaw *et al*., 2002).

In Gastrointestinal Tract

In the enteric nervous system, acetylcholine is the most common neurotransmitter to induce gastrointestinal smooth muscle contraction. The muscarinic M2 acetylcholine receptors is the major muscarinic receptors subtype expressed by smooth muscle tissue in the gastrointestinal tract (Iino and Nojyo, 2006). According to the Hansen (2003), acetylcholine is the major excitatory neurotransmitter of the enteric nervous system, and its excitatory effect on intestinal smooth muscle is mediated through the muscarinic type of acetylcholine receptors. In the gastrointestinal system, acetylcholine also increases the peristaltic movement of stomach and amplitude of digestive contraction.

On Cardiovascular System

Acetylcholine neurotransmitter also affects cardiovascular system. The autonomic nervous system controls heart rate and contractility through sympathetic and parasympathetic inputs to the cardiac tissue with acetylcholine and Nor-adrenaline as the chemical transmitters (Arie *et al*., 2012). Acetylcholine released by parasympathetic nerves regulates the minute-to-minute changes in heart rate and contractility required for proper cardiovascular function via muscarinic receptors opposing the activity of the sympathetic nervous system (Levy, 1997). Acetylcholine slows the heart rate by activating the muscarinic receptor (M2) (Robin *et al*., 2018). It also regulates atrial activity and plays multiple roles in ventricular function (Kanazawa *et al*., 2010; Lara *et al*., 2010). A reduction in acetylcholine release is associated with the early onset of cardiovascular disease, and increasing evidence support the protective roles of Ach against cardiovascular disease (Ming *et al*., 2024). Additionally, Mahmoud *et al*., (2015) demonstrated that inhibition of the cholinergic nerve during cardiac injury in neonatal mice and zebrafish leads to incomplete heart regeneration, causing a significant decrease in neonatal cardiac cell proliferation. Some studies suggest that implicate Ach act as a major regulator of cardiac remodelling and provide support for the notion that enhancing cholinergic signalling in human patients with cardiac disease can reduce morbidity and mortality.

Effect on Eye

ACh is a major retinal neurotransmitter that modulates visual processing through a large repertoire of cholinergic receptors expressed on different retinal cell types (Elgueta *et al*., 2015). Muscarinic acetylcholine receptor belong to the superfamily of G-protein coupled receptors and it is widely expressed in the eye and its adnexa (Hutchins and Hollyfield, 1984; Lind and Cavanagh, 1995) and exert multiple functions, such as- modulation of tear secretion, regulation of pupil size, modulation of intraocular pressure, participation in cell to cell signalling and modulation of vascular diameter in the retina (Ruan *et al*., 2021) as the activation and blockade of muscarinic acetylcholine receptors (mAChRs) affects retinal ganglion cell light responses and firing rates (Strang *et al*., 2010). Due to this variety of functions, abnormalities in mAChR signalling may contribute to the development of various ocular diseases. By contrast, mAChR ligands have been used in ophthalmology to treat dry eye disease, myopia and glaucoma.

In Alzheimer's Disease

ACh has an important role in cognitive processes, the cholinergic system is pointed as an important factor in many forms of dementia, including Alzheimer's disease (Muir, 1997; Wilcock *et al*., 1982). Cholinergic neurones located in the basal forebrain, including the neurones that form the nucleus basalis of Meynert, are severely lost in Alzheimers disease. Alzheimers disease is the most ordinary cause of dementia affecting 25 million people worldwide. The hallmarks of the disease are the accumulation of neurofibrillary tangled and amyloid plaques. Synaptic loss is the main correlation of disease progression and loss of cholinergic neurones contributes to memory and attention deficits (Talita *et al*., 2016). Evidence exists for both cholinergic and glutamatergic involvement in the aetiology of Alzheimer's disease. ACh, a

neurotransmitter essential for processing memory and learning, is decreased in both concentration and function in patients with Alzheimer's disease (Francis, 2005).

Acetylcholine in Respiratory System

Acetylcholine produced and released by both neuronal and nonneuronal sources acts through muscarinic receptors to regulate many important physiological processes. It contracts airway smooth muscle to control tone and regulate potency of the conducting airways. In blood vessels, acetylcholine causes smooth muscle relaxation and vasodilation. At mucosal glands and epithelial cells, acetylcholine regulates mucus secretion and, via ciliary beat frequency, mucus clearance.

Acetylcholine, released by parasympathetic nerves acts directly at muscarinic receptors on airway smooth muscle to cause bronchoconstriction. Therefore, as with vagotomy, muscarinic receptor antagonists decrease smooth muscle tone (Kesler and Canning, 1999; Severinghaus and Stupfel, 1955; Sheppard *et al*., 1982) and prevent bronchoconstriction induced by electrical stimulation of the vagus nerves.

Plasticity

ACh is involved with synaptic plasticity, specifically in learning and short-term memory. Acetylcholine has been shown to enhance the amplitude of synaptic potentials following long-term potentiation in many regions, including the dentate gyrus, CA1, piriform cortex, and neocortex. One more study supports that acetylcholine plays a major role in inducing plasticity in archi-, palaeo-, and neocortex (Rasmusson, 2000). This effect most likely occurs either through enhancing current through NMDA receptors or indirectly by suppressing adaptation. The suppression of adaptation has been shown in brain slices of regions CA1, cingulate cortex, and piriform cortex, as well as in vivo in cat somatosensory and motor cortex by decreasing the conductance of voltage-dependent M currents and Ca2+-dependent K+ currents.

Excitability

Acetylcholine also has other effects on excitability of neurones. The cholinergic system in the brain modulates neuronal excitability, synaptic transmission, and synaptic plasticity, playing a significant role in many physiological functions (Picciotto *et al*., 2012). Its presence causes slow depolarization by blocking a too ionically-active K+ current, which increases neuronal excitability. One study suggests that acetylcholine neurotransmitter modulate the neuronal excitability by interacting with specific chemoreceptor molecules, changing the permeability of the membrane to specific ions, and producing an excitatory effect (Wanke and Ferroni, 1988). Andrei B. Belousov *et al*., 2015 (Belousov *et al*., 2001) suggest that in the absence of glutamate excitation in the hypothalamus in vitro, ACh, neurotransmitter becomes the major excitatory neurotransmitter and supports the excitation/inhibition balance. The increase in excitatory ACh transmission during a decrease in glutamate excitation may represent a novel form of neuronal plasticity that regulates activity and excitability of neurones during the glutamate/GABA imbalance.

CONCLUSION

Acetylcholine is a versatile and essential neurotransmitter with both neuronal and nonneuronal functions. It plays a crucial role in the central nervous system by regulating cognition, memory, learning, and motor control, and in the peripheral nervous system by mediating neuromuscular transmission and autonomic-nervous-system activities. Beyond the nervous system, acetylcholine also exerts significant effects on nonneuronal tissues, influencing cardiovascular functions such as heart rate and vascular tone, respiratory functions including bronchoconstriction and mucus secretion, and gastrointestinal activities like motility and secretion. Thus, acetylcholine acts as a key signalling molecule integrating neural and nonneural processes, highlighting its broad physiological importance in maintaining normal body function and homeostasis. In addition, acetylcholine is essential for normal eye function, particularly in pupil constriction and accommodation. Its deficiency and dysfunction are strongly associated with neurological disorders such as Alzheimer's disease, where reduced cholinergic activity contributes to memory loss and cognitive decline. Alterations in acetylcholine signalling have also been linked to coronary (cardiac) diseases through their influence on autonomic regulation of the heart. Thus, acetylcholine acts as a key signalling molecule integrating neural and nonneural processes, highlighting its broad physiological importance in maintaining normal body function and homeostasis.

ACKNOWLEDGEMENT

None.

ABBREVIATIONS

ACh: Acetylcholine; **NNCS:** Nonneuronal cholinergic system; **SARS-CoV-2:** Severe Acute Respiratory Syndrome Coronavirus 2; **PNS:** Peripheral Nervous System; **CNS:** Central Nervous System; **cAMP:** Cyclic Adenosine Monophosphate; **mAChRs:** Muscarinic Acetylcholine Receptors; **nAChR:** Nicotinic Acetylcholine Receptor; **ENS:** Enteric Nervous System; **CVD:** Cardiovascular Disease; **NMDA:** N-methyl-D-aspartate; **GABA:** Gamma-aminobutyric acid.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

REFERENCES

Akaike, A., Shimohama, S., & Misu, Y. Nicotinic acetylcholine Receptors signaling in neuroprotection. Library. Oapen. org. (2018).

Albuquerque, E. X., Pereira, E. F., Castro, N. G., Alkondon, M., Reinhardt, S., Schröder, H., & Maelicke, A. (1995). Nicotinic receptor function in the mammalian central nervous system. Annals of the New York Academy of Sciences, 757, 48–72. doi: 10.1111/j.1749-6632.1995.tb17464.x, PubMed: 7611705.

Andrea, S., & Torraoluiz, R. G. (2002). Britto: Neurotransmitter regulation of neural development: Acetylcholine and nicotinic receptors. Biomedical and medical sciences. An Acad. Bras. Science, 74(3).

Andrei B. Belousov, Bruce F. O'Hara and Janna V. Denisova. Acetylcholine becomes the major excitatory neurotransmitter in the hypothalamus in vitro in the absence of glutamate excitation (2001). Journal of Neuroscience 15 March 2001, 21 (6) 2015-2027;

Arie, O. V., Guillaume, S. C. G., Marieke, W. V., & Ronald, W. (2012). Effects of acetylcholine and noradrenalin on action potentials of isolated rabbit sinoatrial and atrial myocytes. Frontiers in Physiology

Armstrong, D. M., Saper, C. B., Levey, A. I., & Wainer, B..

Armstrong, D. M., Saper, C. B., Levey, A. I., Wainer, B. H., & Terry, R. D. (1983). Distribution of cholinergic neurons in rat brain: Demonstrated by the immunocytochemical localization of choline acetyltransferase. Journal of Comparative Neurology, 216(1), 53–68. doi: 10.1002/cne.902160106, PubMed: 6345598

Belousov, A. B., O'Hara, B. F., & Denisova, J. V. (March 15 2001). Acetylcholine becomes the major excitatory neurotransmitter in the hypothalamus in vitro in the absence of glutamate excitation. Journal of Neuroscience, 21(6), 2015–2027. doi: 10.1523/JNEUROSCI.21-06-02015.2001, PubMed: 11245685;

Blokland, A., Honig, W., & Raaijmakers, W. G. (1992). Effects of intra-hippocampal scopolamine injections in a repeated spatial acquisition task in the rat. Psychopharmacology, 109(3), 373–376. doi: 10.1007/BF02245886, PubMed: 1365638.

Boccia, M. M., Acosta, G. B., Blake, M. G., & Baratti, C. M. (2004). Memory consolidation and reconsolidation of an inhibitory avoidance response in mice: Effects of i.c.v. injections of hemicholinium-3. Neuroscience, 124(4), 735–741. doi: 10.1016/j.neuroscience.2004.01.001, PubMed: 15026114.

Boccia, M. M., Blake, M. G., Acosta, G. B., & Baratti, C. M. (2003). Atropine, an anticholinergic drug, impairs memory retrieval of a high consolidated avoidance response in mice. Neuroscience Letters, 345(2), 97–100. doi: 10.1016/S0304-3940(03)00493-2, PubMed: 12821180.

Boccia, M. M., Blake, M. G., Baratti, C. M., & McGaugh, J. L. (2009). Involvement of the basolateral amygdala in muscarinic cholinergic modulation of extinction memory consolidation. Neurobiology of Learning and Memory, 91(1), 93–97. doi: 10.1016/j.nlm.2008.07.012, PubMed: 18706510.

Christian, S., & Bruno, B. Physiology acetylcholine. StetPearls (2023).

Colebatch, H. J., & Halmagyi, D. F. (1963). Effect of vagotomy and vagal stimulation on lung mechanics and circulation. Journal of Applied Physiology, 18, 881–887. doi: 10.1152/jappl.1963.18.5.881, PubMed: 14063255.

Dani, J. A., & Bertrand, D. (2007). Nicotinic acetylcholine receptors and nicotinic cholinergic mechanisms of the central nervous system. Annual Review of Pharmacology and Toxicology, 47, 699–729. doi: 10.1146/annurev.pharmtox.47.120505.105214, PubMed: 17009926.

Del Arco, A., Segovia, G., Garrido, P., De Blas, M., & Mora, F. (2007b). Stress, prefrontal cortex and environmental enrichment: Studies on dopamine and acetylcholine release and working memory performance in rats. Behavioural Brain Research, 176(2), 267–273. doi: 10.1016/j.bbr.2006.10.006, PubMed: 17097747.

Duris, K., Manaenko, A., Suzuki, H., Rolland, W. B., Krafft, P. R., & Zhang, J. H. (2011). α7 nicotinic acetylcholine receptor agonist PNU-282987 attenuates early brain injury in a perforation model of subarachnoid hemorrhage in rats. Stroke, 42(12), 3530–3536. doi: 10.1161/STROKEAHA.111.619965, PubMed: 21960575.

Eglen, R. M. (2005). Muscarinic receptor subtype pharmacology and physiology. Progress in Medicinal Chemistry, 43, 105–136. doi: 10.1016/S0079-6468(05)43004-0, PubMed: 15850824.

Eglen, R. M. (2006). Muscarinic receptors sub-types in neuronal and non-neuronal cholinergic function. Autonomic and Autacoid Pharmacology, 26(3), 219–233. doi: 10.1111/j.1474-8673.2006.00368.x.

Elgueta, C., Vielma, A. H., Palacios, A. G., & Schmachtenberg, O. (2015). Acetylcholine induces GABA release onto tod bipolar cells through heteromeric nicotinic receptors expressed in A17 amacrine cells. Frontiers in Cellular Neuroscience, 9. doi: 10.3389/fncel.2015.00006.

Fine, A., Hoyle, C., Maclean, C. J., Levatte, T. L., Baker, H. F., & Ridley, R. M. (1997). Learning impairments following injection of a selective cholinergic immunotoxin, ME20.4 IgG-saporin, into the basal nucleus of Meynert in monkeys. Neuroscience, 81(2), 331–343. doi: 10.1016/S0306-4522(97)00208-X, PubMed: 9300425.

Francis, P. T. (2005). The interplay of neurotransmitters in Alzheimer's disease. CNS Spectrums, 10(11) (Suppl. 18), 6–9. doi: 10.1017/s1092852900014164, PubMed: 16273023.

Gotti, C., & Clementi, F. (2004). Neuronal nicotinic receptors: From structure to pathology. Progress in Neurobiology, 74(6), 363–396. doi: 10.1016/j.pneurobio.2004.09.006, PubMed: 15649582.

Grando, S. A., Kawashima, K., & Wessler, I. (2003). Introduction: The non-neuronal cholinergic system in humans. Life Sciences, 72(18–19), 2009–2012. doi: 10.1016/S0024-3205(03)00063-8, PubMed: 12628450.

Hansen, M. B. (2003). Neurohumoral control of gastrointestinal motility. Physiological Research, 52(1), 1–30. doi: 10.33549/physiolres.930255, PubMed: 12625803

Hasselmo, M. E. (December 2006). The role of acetylcholine in learning and memory. Current Opinion in Neurobiology, 16(6), 710–715. doi: 10.1016/j.conb.2006.09.002, PubMed: 17011181

Hasselmo, M. E., & Bower, J. M. (1993). Acetylcholine and memory. Trends in Neurosciences, 16(6), 218–222. doi: 10.1016/0166-2236(93)90159-J, PubMed: 7688162.

Herlenius, E., & Lagercrantz, H. (2004). Development of neurotransmitter systems during critical periods. Experimental Neurology, 190 (Suppl. 1), S8–S21. doi: 10.1016/j.expneurol.2004.03.027, PubMed: 15498537.

Himmelheber, A. M., Sarter, M., & Bruno, J. P. (2000). Increases in cortical acetylcholine release during sustained attention performance in rats. Brain Research. Cognitive Brain Research, 9(3), 313–325. doi: 10.1016/S0926-6410(00)00012-4, PubMed: 10808142.

Houser, C. R., Crawford, G. D., Barber, R. P., Salvaterra, P. M., & Vaughn, J. E. (1983). Organization and morphological characteristics of cholinergic neurons: An immunocytochemical study with a monoclonal antibody to choline acetyltransferase. Brain Research, 266(1), 97–119. doi: 10.1016/0006-8993(83)91312-4, PubMed: 6850348.

Hutchins, J. B., & Hollyfield, J. G. (1984). Autoradiographic identification of muscarinic receptors in human iris smooth muscle. Experimental Eye Research, 38(5), 515–521. doi: 10.1016/0014-4835(84)90129-5, PubMed: 6745327.

Iino, S., & Nojyo, Y. (2006). Muscarinic M2 acetylcholine receptor distribution in the guinea-pig gastrointestinal tract. Neuroscience, 138(2), 549–559. doi: 10.1016/j.neuroscience.2005.11.021, PubMed: 16387450.

Imperato, A., Puglisi-Allegra, S., Casolini, P., & Angelucci, L. (1991). Changes in brain dopamine and acetylcholine release during and following stress are independent of the pituitary-adrenocortical axis. Brain Research, 538(1), 111–117. doi: 10.1016/0006-8993(91)90384-8, PubMed: 2018923.

Jones, B. E. (2005). From waking to sleeping: Neuronal and chemical substrates. Trends in Pharmacological Sciences, 26(11), 578–586. doi: 10.1016/j.tips.2005.09.009, PubMed: 16183137.

Julian, R. D. (2000). Moiseiwitsch. The role of serotonin and neurotransmitters during craniofascial development. Critical Reviews in Oral Biology and Medicine, 11(2), 230–239

Kanazawa, H., Ieda, M., Kimura, K., Arai, T., Kawaguchi-Manabe, H., Matsuhashi, T., . . . Fukuda, K. (2010). Heart failure causes cholinergtransdifferentiation of cardiac sympathetic nerves via gp130-signaling cytokines in rodents. Journal of Clinical Investigation, 120(2), 408–421. doi: 10.1172/JCI39778, PubMed: 20051627

Kesler, B. S., & Canning, B. J. (1999). Regulation of baseline cholinergic tone in guinea-pig airway smooth muscle. Journal of Physiology, 518(3), 843–855. doi: 10.1111/j.1469-7793.1999.0843p.x, PubMed: 10420019.

Laplante, F., Stevenson, C. W., Gratton, A., Srivastava, L. K., & Quirion, R. (2004). Effects of neonatal ventral hippocampal lesion in rats on stress-induced acetylcholine release in the prefrontal cortex. Journal of Neurochemistry, 91(6), 1473–1482. doi: 10.1111/j.1471-4159.2004.02831.x, PubMed: 15584923.

Lara, A., Damasceno, D. D., Pires, R., Gros, R., Gomes, E. R., Gavioli, M., . . .Guatimosim, S. (2010). Dysautonomia due to reduced cholinergic neurotransmission causes cardiac remodeling and heart failure. Molecular and Cellular Biology, 30(7), 1746–1756. doi: 10.1128/MCB.00996-09, PubMed: 20123977

Lauder, J. M., & Schambra, U. B. (1999). Morphogenetic roles of acetylcholine. Environmental Health Perspectives, 107(1) (Suppl. 1), 65–69. doi: 10.1289/ehp.99107s165, PubMed: 10229708.

Levy, M. N. (1997). Neural control of cardiac function. Bailliere's Clinical Neurology, 6(2), 227–244. PubMed: 9483290.

Lightfoot, A. P., Kew, J. N. C., & Skidmore, J. (2008). Alpha7 nicotinic acetylcholine receptor agonists and positive allosteric modulators. Progress in Medicinal Chemistry, 46, 131–171. doi: 10.1016/S0079-6468(07)00003-3, PubMed: 18381125.

Lind, G. J., & Cavanagh, H. D. (1995). Identification and subcellular distribution of muscarinic acetylcholine receptor-related proteins in rabbit cornea and Chinese hamster ovaries. Investigative Ophthalmology and Visual Science, 36(8), 1492–1507. PubMed: 7601630.

Mahmoud, A. I., O'Meara, C. C., Gemberling, M., Zhao, L., Bryant, D. M., Zheng, R. (2015). Nerves regulate cardiomyocyte proliferation and heart regeneration. Developmental Cell, 34(4), 387–399. doi: 10.1016/j.devcel.2015.06.017, PubMed: 26256209.

Mark, G. P., Rada, P. V., & Shors, T. J. (1996). Inescapable stress enhances extracellular acetylcholine in the rat hippocampus and prefrontal cortex but not the nucleus accumbens or amygdala. Neuroscience, 74(3), 767–774. doi: 10.1016/0306-4522(96)00211-4, PubMed: 8884772.

Maurer, S. V., & Williams, C. L. (2017). The cholinergic system modulates memory and hippocampal plasticity via its interactions with non-neuronal cells. Frontiers in Immunology, 8, 1489. doi: 10.3389/fimmu.2017.01489, PubMed: 29167670.

Ming, C. L. C., Wang, X., & Gentle, C. Protective role of acdtylcholine and the cholinergic system in the injured heart. Isience (2024).

Miranda, M. I., & Bermúdez-Rattoni, F. (1999). Reversible inactivation of the nucleus basalis magnocellularis induces disruption of cortical acetylcholine release and acquisition, but not retrieval, of aversive memories. Proceedings of the National Academy

of Sciences of the United States of America, 96(11), 6478–6482. doi: 10.1073/pnas.96.11.6478, PubMed: 10339613.

Muir, J. L. (1997). Acetylcholine, aging, and Alzheimer's disease. Pharmacology, Biochemistry, and Behavior, 56(4), 687–696. doi: 10.1016/S0091-3057(96)00431-5, PubMed: 9130295.

Nachmansohn, D. (1955). The generation of bioelectric potentials. Circulation Research, 3(5), 429–433. doi: 10.1161/01.RES.3.5.429, PubMed: 13250708.

Newman, E. L., Gupta, K., & Climer, J. R. (2012). Monaghan, C.K. and Hasselmo, M.E.: Cholinergic modulation of cognitive processing: Insight drawn from computational model. Frontiers in Behavioral Neuroscience.

Parent, M. B., & Baxter, M. G. (2004). Septohippocampal acetylcholine: Involved in but not necessary for learning and memory? Learning and Memory, 11(1), 9–20. doi: 10.1101/lm.69104, PubMed: 14747512.

Pavlovsky, L., Bitan, Y., Shalev, H., Serlin, Y., & Friedman, A. (2012). Stress-induced altered cholinergic-glutamatergic interactions in the mouse hippocampus. Brain Research, 1472, 99–106. doi: 10.1016/j.brainres.2012.05.057, PubMed: 22796599.

Pérez, M. M., Pimentel, V. E., Fuzo, C. A., da Silva-Neto, P. V., Toro, D. M., Fraga-Silva, T. F. C., . . . ImmunoCOVID Brazilian Research Consortium (2022). Acetylcholine, fatty acids, and lipid mediators are linked to COVID-19 severity. Journal of Immunology, 209(2), 250–261. doi: 10.4049/jimmunol.2200079, PubMed: 35768148, Google Scholar

Picciotto, M. R., Higley, M. J., & Mineur, Y. S. (2012). Acetylcholine as a neuromodulator: Cholinergic signaling shapes nervous system function and behavior. Neuron, 76(1), 116–129. doi: 10.1016/j.neuron.2012.08.036, PubMed: 23040810.

Power, A. E., Vazdarjanova, A., & McGaugh, J. L. (2003). Muscarinic cholinergic influences in memory consolidation. Neurobiology of Learning and Memory, 80(3), 178–193. doi: 10.1016/S1074-7427(03)00086-8, PubMed: 14521862.

Rasmusson, D. D. (2000). The role of acetylcholine in cortical synaptic plasticity. Behavioural Brain Research, 115(2), 205–218. doi: 10.1016/S0166-4328(00)00259-X, PubMed: 11000421.

Ridley, R. M., Bowes, P. M., Baker, H. F., & Crow, T. J. (1984). An involvement of acetylcholine in object discrimination learning and memory in the marmoset. Neuropsychologia, 22(3), 253–263. doi: 10.1016/0028-3932(84)90073-3, PubMed: 6431311.

Robin, M., Frank, B., Sachse, E., Moreno-Galindo, G., Ricardo, A., Navarro-Polanco, M. T. F., & Gunnar, S. (2018). Modeling effects of voltage dependent properties of the cardiac muscarinic receptor on human sinus node function. PLOS Computational Biology, 14(10).

Ruan, Y., Patzak, A., Pfeiffer, N., & Gericke, A. (2021). Muscarinic acetylcholine receptors in the Retina- A therapeutic implication. International Journal of Molecular Sciences, 22(9), 4989. doi: 10.3390/ijms22094989, PubMed: 34066677.

Sastry, B. V., & Sadavongvivad, C. (1978). Cholinergic systems in non-nervous tissues. Pharmacological Reviews, 30(1), 65–132. doi: 10.1016/S0031-6997(25)06755-9, PubMed: 377313.

Segovia, G., del Arco, A., Garrido, P., De Blas, M., & Mora, F. (2008b). Environmental enrichment reduces the response to stress of the cholinergic system in the prefrontal cortex during aging. Neurochemistry International, 52(6), 1198–1203. doi: 10.1016/j.neuint.2007.12.007, PubMed: 18242778.

Severinghaus, J. W., & Stupfel, M. (1955). Respiratory dead space increase following atropine in man, and atropine, vagal or ganglionic blockade and hypothermia in dogs. Journal of Applied Physiology, 8(1), 81–87. doi: 10.1152/jappl.1955.8.1.81, PubMed: 13242494.

Shaw, S., Bencherif, M., & Marrero, M. B. (2002). Janus kinase 2, an early target of alpha 7 nicotinic acetylcholine receptor-mediated neuroprotection against a beta-(1–42) amyloid. Journal of Biological Chemistry, 277(47), 44920–44924. doi: 10.1074/jbc.M204610200, PubMed: 12244045.

Sheppard, D., Epstein, J., Holtzman, M. J., Nadel, J. A., & Boushey, H. A. (1982). Dose-dependent inhibition of cold air-induced bronchoconstriction by atropine. Journal of Applied Physiology: Respiratory, Environmental and Exercise Physiology, 53(1), 169–174. doi: 10.1152/jappl.1982.53.1.169, PubMed: 6749773.

Stillman, M. J., Shukitt-Hale, B., Coffey, B. P., Levy, A., & Lieberman, H. R. (1997). In vivo hippocampal acetylcholine release during exposure to acute stress. Stress, 1(4), 191–200. doi: 10.3109/10253899709013740, PubMed: 9787244.

Strang, C. E., Renna, J. M., Amthor, F. R., & Keyser, K. T. (2010). Muscarinic acetylcholine receptor localization and activation effects on ganglion response properties. Investigative Ophthalmology and Visual Science, 51(5), 2778–2789. doi: 10.1167/iovs.09-4771, PubMed: 20042645.

Suryanarayanan, A. (2014). In Encyclopedia of toxicology (3rd ed).

Takada-Takatori, Y., Kume, T., Sugimoto, M., Katsuki, H., Sugimoto, H., & Akaike, A. (2006). Acetylcholinesterase inhibitors used in treatment of Alzheimer's disease prevent glutamate neurotoxicity via nicotinic acetylcholine receptors and phosphatidylinositol 3-kinase cascade. Neuropharmacology, 51(3), 474–486. doi: 10.1016/j.neuropharm.2006.04.007, PubMed: 16762377.

Talita, H. F., Isabella, M. G., Flavia, R. S., & Fabiola, M. R. (2016). Alzheimeir's Disease: Targeting the cholinergic system. Current Neuropharmacology, 14(1), 101–115. doi: 10.2174/1570159X13666150716165726.

Wanke, E., & Ferroni, A. (1988). Modulation of neuronal excitability of acetylcholine (pp. 277–286).

Wilcock, G. K., Esiri, M. M., Bowen, D. M., & Smith, C. C. (1982). Alzheimer's disease. Correlation of cortical choline acetyltransferase activity with the severity of dementia and histological abnormalities. Journal of the Neurological Sciences, 57(2–3), 407–417. doi: 10.1016/0022-510X(82)90045-4, PubMed: 7161627.

Winters, B. D., & Bussey, T. J. (2005). Removal of cholinergic input to perirhinal cortex disrupts object recognition but not spatial working memory in the rat. European Journal of Neuroscience, 21(8), 2263–2270. doi: 10.1111/j.1460-9568.2005.04055.x, PubMed: 15869523.

Woolf, N. J. (1991). Cholinergic systems in mammalian brain and spinal cord. Progress in Neurobiology, 37(6), 475–524. doi: 10.1016/0301-0082(91)90006-M, PubMed: 1763188.

Woolf, N. J., & Butcher, L. L. (2011). Cholinergic systems mediate action from movement to higher consciousness. Behavioural Brain Research, 221(2), 488–498. doi: 10.1016/j.bbr.2009.12.046, PubMed: 20060422.

Zimmerman, G., & Soreq, H. (2006). Readthrough acetylcholinesterase: A multifaceted inducer of stress reactions. Journal of Molecular Neuroscience, 30(1–2), 197–200. doi: 10.1385/JMN:30:1:197, PubMed: 17192675.

Cite this article: Anju C. Acetylcholine: The Master Messenger of the Nervous System. Asian J Biol Life Sci. 2026;15(1):9-14.