BEST JOURNAL 20(1): 46 - 51
Date received: 11/01/2023
Date accepted: 26/04/2023

INHIBITORY TRANSMISSION OF HISTAMINE IN INSECTS ANTENNAL LOBE- A REVIEW

Suleiman, K and Maigari, A. K*
Department of Biological Sciences, Faculty of Life Sciences, College of Natural and Pharmaceutical Sciences, Bayero University, Kano, PMB 3011, Kano State-Nigeria
*akmaigari.bio@buk.edu.ng; GSM: +2348036028452

ABSTRACT
Antennal lobe is an insects' analogue to specific spatio – temporal activity patterns of the olfactory bulb of vertebrates, where the first synaptic processing of the olfactory input from the antennae occurs. It is involved in the processing of odours to shape afferent odour response. Fundamental components of the olfactory network in the antennal lobe include the local interneurons (LI) and the projection (output) neurons. Majority of LI in most insects are non-gamma – Amino butyric acid (GABA), histamine been one of the possible candidates. This is because, histamine - like immunoreactivity is found in a number of interneurons in the central nervous system of various insects and, this uneven distribution of histamine in the brain suggests that it is a neuro transmitter. A brief description on the chemical composition of histamine, its formation and precursors, physiology, neurophysiology and presumed transmission were carefully enunciated. The review underscores the significance of inhibitory transmission of histamine in the insect antennal lobe.

Keywords: Antennae, Histamine, Insects, Neurons, Olfactory

INTRODUCTION

The reactions by which complex molecules interact with one another and by which they are synthesized and degraded accounts for the extra – ordinary attributes of all that is recognized as living. For instance, odours are represented by specific spatio temporal activity in the Olfactory Bulb (OB) of vertebrates, or its insect analogue, the Antennal Lobe.

Antennal lobe (AL) is the primary olfactory brain area in insects. It is deutocerebral neutrophil in the insects' brain which receives the input from which the olfactory receptor neurons is expressed. Both the AL and OB, consist of different neuron types, which modulate and optimize the afferent input in a complex network. It has been shown that intrinsic inhibitory circuits within the AL and OB network of branched and interconnected pathways shape temporal and spatial aspects of the odour evoked patterns to improve odour detection and discrimination (Sachse *et al.*, 2006).

Although Gamma-Aminobutyric Acid (GABA) has been identified as a constituent of the inhibitory network of insects, many studies have shown that not all interneurons are GABA (Sasche *et al.*, 2006). For instance, histamine (an amine) produced from decarboxylation reaction of histidine, proved to be powerful vasodepressor sustenance (Murray *et al.*, 2000). Histamine is also a neurotransmitter in arthropod photo receptors (Carol *et al.*, 1995; Stewart, 1999). Invertebrates lack metabotropic histamine receptors, thus histaminergic neurotransmission is mediated through inotropic histamine receptors, further elucidated the idea of an inhibitory effect by histamine – gated chloride channels (Sachse *et al.*, 2006).

In *Drosophila melanogaster*, histamine is reported to be a major mechanosensory transmitter candidate of the adult nervous system (Buchner *et al.*, 1993).

However, the hypothesized histamine functions as a neurotransmitter in the photoreceptors of insects, whose biochemical measurements were correlated well with the immunohistochemical data of histamine, revealed that brain of cockroach consists of widespread distribution of histamine containing somata and fibres (Sachse *et al.*, 2006). A similar outcome has long been reported by Esslen and Kaissling (1976) in the honey bee specific inhibitory network, which enhances overlapping glomerular response profiles and is picrotoxin insensitive. The researchers argued that, since picrotoxin blocks chloride channels, the second network is either constituted by metabotropic GABA receptors or a different transmitter system altogether (Sachse *et al.*, 2006). Therefore, the likely transmitter could be histamine.

Histamine led to a strong and reversible reduction of the odour evoked responses of both the input and the output neurons (Christensen *et al.*, 1993). The Projection Neurons (PN) responses were more sensitive to histamine than the compound responses, suggesting different histaminergic input to Receptor Neurons (RN). However, little is known about the synaptic interactions among the olfactory neurons involved in odour processing in insects, despite the experimental advantages offered by histamine as an inhibitory transmitter in insects' antennal lobe (Sachse *et al.*, 2006). Thus, the principal objective of this write-up is to accentuate the role play by histamine in the inhibitory transmission of insect antennal lobe.

The Antennal Lobe

Antennal lobe (AL) of insects is the functional analogue of the olfactory lobe (OB) in mammals, which is the first central neuropil where information from the olfactory receptor neurons (RNs) is processed (Sachse *et al.*, 2006). Insects' olfactory pathway starts at the antennae (Keller and Vosshall, 2004) from where the sensory neurons on the antenna to the antennal lobe. The antennal lobe is composed of densely packed neutrophils, termed glomeruli (Laurent, 2002), where the sensory neurons synapse with the two other kinds of neurons, the projection neurons and the local neurons (Laurent, 2002).

Stopper *et al.* (2003) brought to life the picture of the antennal lobe in Drosophila where 43 glomeruli are found. The projection neurons project to higher brain centres such as the mushroom body and lateral horn of the protocerebrum. The local neurons, which are primarily inhibitory, have their neutritis restricted to the antennal lobe. In Drosophila, each olfactory sensory neuron generally receives information from a single glomerulus. The interaction between the olfactory receptor neurons, local neurons and projection neurons reformats the inflammation input from the sensory neurons into a spatio – temporal code before it is sent to higher centres (Vosshal *et al*., 2001; Turin, 2002).

Histamine: An Overview

Histamine (C5H9N3), 2-(1H-imidazol-5-yl)ethanamine, is an arakylamino compound belonging to the class of imidazoles that is 1H-imidazole substituted at position C-4 by a 2-aminoethyl group (National Centre for Biotechnology Information, NCBI 2023). Histamine, with a molecular weight of 111.15 kg/mol, is a conjugate base of histaminium that plays roles both as metabolite and a neurotransmitter (NCBI, 2023).

Bites in insects are accompanied by release of a toxin into the victim and causes the release of histamine, which acts to increase the permeability of the capillary walls to large molecules. Histamine is the irritating ingredients present in the venome of many species of wasps and bees (Gaire *et al.*, 2022). The rate of filtration is of histamine greatly increased, resulting in swelling around the bite (Stewart, 1999).

At the cellular level, these compounds cause cell lysis, hydrolysis of connective tissue, induced allergic reactions and depressed blood pressure. Andrew and Craig (2001) affirm that the central chemical involved in itching is histamine, a molecule released by mast cells in the skin. Histamine is chemically classified as an amine, an organic molecule based on the structure of ammonia (NH_3) (Gaire *et al.*, 2022). The chemical histamine is an example of a local chemical mediator (Carol *et al.*, 1995) which are substances secreted by cells that are not part of specialized endocrine organs and in most cases are rapidly taken up or destroyed such that they affect only cells in their immediate neighbourhood. Normally they do not enter the blood in significant amount (Carol *et al.*, 1995).

Histamine mediates the allergic response such as anaphylaxis, which is a severe, immediate, and often fatal response to exposure to a previously encountered antigen (Gaire *et al.*, 2022). It is released by mast cells and signals nearby capillaries to dilate and leak, allowing more blood to reach the site. It also binds to local nerve endings on specific receptors. An itch caused by histamine is transmitted to the brain by a different neural pathway (Andrew and Craig, 2001). As with pain, histamine – induced itch travels via the spinothalamic tract, but in fibres specific itch, it is found that the venom from ant (*Mymecia gulosa*) contains histamine – like activity (Andrew and Craig, 2001). Studies show that bugs produce potentially dangerous amounts of histamine (Gaire *et al*., 2022)

In humans, histidine can be considered as a semi – essential amino acid (Frisell, 2006). It is a dietary requirement for the young animal but can be synthesized at a rate adequate to maintain nitrogen balance in the adult. In most cells histidine undergoes an enzymatic decarboxylation to form histamine, a powerful vasodilator (Murray *et al.* 2000; Andrew and Craig, 2001; Frisell, 2006). This amine is liberated in traumatic shock and is localized in areas of inflammation. Decarboxylation of histidine forms histamine, a reaction catalysed by a broad – specificity of aromatic L – amino acid decarboxylase which also catalyses decarboxylation of dopa, 5 – hydroxytryptophan, phenyl alanine, tyrosine and tryptophan (Murray *et al.*, 2000). A different enzyme, histidine decarboxylase, present in mast cells, also catalyses, the decarboxylation of histidine (Murray *et al.*, 2000; Frisell, 2006).

Histamine as an Inhibitory Transmitter in Insects Antennal lobe

Histamine is a biologically active substance found in a great variety of living organisms (Gaire *et al.*, 2022). The role of histamine as a neurotransmitter has been well studied in both vertebrates and invertebrates (Scaros *et al.*, 2020), including insects antennal lobe, reflecting species differences. Using immunohistochemical techniques, Buchner *et al.* (1993) noted that, most or all mechanosensory neurons of imaginable hair sensilla in *Drosophila melanogaster*, selectively bind antibodies directed against histamine.

Histamine is distributed widely throughout animal Kingdom, certain plants, bacteria and insects (Gaire *et al.*, 2022). Histamine levels were measured with high pressure liquid chromatography, and the most intense immunolabelling was seen in the retinal photo receptors and in the first optic ganglion, as well as the laminar where the short visual fibres make synaptic connections with the monopolar neurons. In the honey bee, 95% of the sensory cells located on the antenna are olfactory neurons (Sachse, 2006) which convey the olfactory information to two categories of AL neurons namely 4000 local interneurons (LNs) and 800 projection neurons (PNs) as revealed by Wilson and Laurent (2005).

LNs branch exclusively within the AL, whereas PNs relay the olfactory information to higher order brain centres. Almost all synaptic contacts between the sensory neurons, LNs and PNs are strictly located in areas of high synaptic density, the olfactory glomeruli (Sachse *et al.*, 2006). Each of the 156 olfactory glomeruli represents an identifiable morphological and functional subunit, arranged in a single layer around the honey bee AL (Sachse *et al.*, 2006). Honey bees have anatomically and functionally distinct classes of olfactory LNs similar to the olfactory system of lobsters and moths (Christein *et al.*, 1993). The majority of them are heterogeneous LNs, have high density of dendrite branches in one particular glomerulus and sparser branches distributed across other glomeruli (Christein *et al.*, 1993).

Homogenous LNs distribute their branches more homogeneously over the whole AL. It is inconceivable that these different LN types are involved in functionally distinct inhibitory networks to shape the odour responses of olfactory PNs. Indeed, in vertebrates (Yokoi *et al.*, 1995) and lobsters (Christein *et al*., 1993), dual inhibitory pathways at the first synaptic level have been well characterized. In lobsters, the existence of both GABA and histaminergic inhibitory pathways have been reported (Christein *et al.*, 1993), whereas in vertebrates both pathways are mediated by the inhibitory transmitter GABA (Yokoi *et al*., 1995).

Sachse *et al*. (2006) carried out analysis of the effect of histamine application to honey bee antennal lobe, recording two different processing levels. The study measures odour evoked responses of a compound signal mainly reflecting afferent input to the AL, and of PNs which represents the AL output, during histamine application. The results show that applying histamine to the honeybee brain led to a strong and reversible reduction of both the compound and the PN odour responsive while spontaneous activity of PNs was totally abolished due to histamine. These findings corroborate with electrophysiological recordings of lobster olfactory neurons, which reported that histamine application suppressed both spontaneous and odour evoked activity in OSNs as well as electrically induced responses in olfactory PNs.

Sachse *et al*. (2006) uses an *in vivo* preparation of whole animal with an intact blood – brain barrier and succinctly opined that, it is likely that blood brain barrier has only a very limited permeability to histamine. Sachse *et al*. (2006) further reported that, higher concentrations of histamine are needed to silence the compound signal than PNs. However, because the two signals were measured with different staining methods and different dyes, the observed shift could be due to a shift in recording sensitivity, rather than in the underlying physiology. Diffusion barriers may also differ since the two preparations differ. Also, along the pathway from OSNs to PNs there are multiple occurrences of histaminergic channels. While the PN signal is been affected only by some, this may reduce the effect because of the resulting small numbers of synapses or because different populations of histaminergic receptors may have different affinities. The fact that histamine abolishes responses in the compound signal suggested that there is direct histaminergic input onto OSN synaptic terminals such as those found in lobsters (Christein *et al.*, 1993). Cultured honeybee antennal lobe neurons (LN and PNs) did not show any histamine induced currents (Sachse *et al*., 2006) further supporting the idea that OSN terminals expresses these reports.

In the Calypteran flies, *Musca* and *Calliphora*, it was observed that no comparable immunoreactivity associated with either hair sensilla or nerves entering the central nervous system (Sachse *et al.*, 2006) which was found to be in conformity with the earlier studies on *Calliphora* (Buchner *et al.*, 1993). Thus, histamine may be said to be a neurotransmitter of insect photoreceptors, besides the already establishes role of GABA.

CONCLUSION AND RECOMMENDATIONS

Histamine is a neurotransmitter in arthropod photoreceptors as it binds to local nerve endings on specific receptors. Although some researchers attempted to demonstrate the role played by histamine in inhibitory transmission, it is evident that histaminergic antennal lobe is not ubiquitous to insects. However, considering the enormous inotropic histamine receptors in invertebrates, one would not but agree with many assertions that GABA and histamine may be constituents of a multifaceted system of inhibitory transmitter in antennal lobe. Therefore, further researches are needed to characterize histaminergic neurons in the antennal lobe of insects. The review also recommends more pharmacological researches with histamine antagonists to help in elucidating the clear role played by histamine in the insects' olfactory system.

REFERENCES

Andrew, D. and Craig, A.D. (2001). Spinothalamic lamina I neurons selectively sensitive toHistamine central neural pathway for itch. *Nature Neuroscience,* **4** (1): 9 – 10.

Buchner, E., Buchner, S., Burg, M. G. Hofbauer, A., Pak, W. L. and Pollak, I. (1913). Histamine is a major mechanosensory neurotransmitter candidate in *Drosophilamelanogaster*. *Cell Tissue Research,* 273(**1**): 119 – 125.

Carol, H., Fadden, M.C. and Keeton, W.T. (1995). *Biology: An Exploration of life*. W W Norton and Comp. Inc., USA. 25: 527.

Christensen, T.A., Waldrop, B.R., Harrow, I.D. and Hildebrand, J.G. (1993). Local interneurons and information processing in the olfactory Glomeruli of the moth *Manduca sexta. Journal of Comparative Physiology,* **173**: 385 – 399.

Esslen, J. and Kaissling, K.E. (1976). Number and distribution of sensilla on antennal flagellum of honey bee. *APIS Zoomorphologie,* **83**: 227 – 251.

Frisell, W. R. (2006). *Biochemistry*. Macmillan Plc. **8**: 206 – 483.

Ignell, R. (2001). Monoamines and neuropeptides in antennal lobe: Interneurons of the desert locust. Lund University, Sweden, **306** (1): 143 – 156.

Keller, A. and Vosshal, L.B. (2004). A Psychophysical test of the vibration Theory of olfaction. *Nature Neuroscience,* **7**: 337 – 338.

Laurent, G. (2002). Olfaction network dynamics and the coding of Multidimensional signals. *Nature Reviews Neuroscience* **3**: 884 – 895.

Murray, R.K., Granner, D.K., Mayers, PA and Rodwell, V.W. (2000). Herper's Biochemistry 25th Edition, Appleton and Lange, USA, 4:29, 33:349, 55: 6 71.

National Centre for Biotechnology Information, NCBI (2023). Pub Chem Compound Summary for CID 774, Histamine. Retrieved April 26, 2023 from https://pubchem.ncbi.nlm.nih.gov/compound/Histamine.

Sachse, S., Peele, P., Silbering, A.F., Guhmann, M. and Glizia, C.G. (2006). Role of Histamine as a putative transmitter in the honey bee antennal lobe. *Frontiers inZoology*, **3**: 22 – 37.

Gaire, S., Principato, S., Schal, C. and DeVries, Z. C. (2022). Histamine Excretion by the common bed bug (Hemiptera: Cimidae). *Journal of Medical Entomology*, 59(**6**): 1898 – 1904.

Stewart, M. (1999). Animal Physiology: Biology forms and Functions. Hodder and S Stoughton, 1: 4, 5: 138 – 281.

Stopper, M., Jyaraman, V. and Laurent, G. (2003). Intensity versus identity coding in an olfactory system. *Neuron*, **39**: 991 – 1004.

Turin, L. (2002). A Method for the calculation of odour character from molecular structure.*Journal of Theoretical Biology*, **216**: 367 – 385.

Vosshal, L.B., Marin, E.C., Stocker, R.F. and Luo, L (**2001**). An olfactory sensory map in the fly brain. *Cell*, **102** (2): 147 – 159.

Wilson, R. and Laurent, I. G. (2005). Role of GB Aergic inhibition in shaping odour evoked spatiotemporal patterns in the Drosophila antennal lobe. *Journal of Neuroscience*, **25**: 9069 – 9079.

Yokoi, M., Mori, K. and Nakanishi, S. (1995). Refinement of odour molecule tuning bydendrodendritic synaptic inhibition in the olfactory bulb. *Proceedings of the NationalAcademy of Science, USA*, **92**: 3371 – 3375.