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Sulfite intolerance: A cause of tinnitus?

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Abstract Tinnitus is a common disorder characterized by a ringing or buzzing in the ear, and is poorly understood. Recent studies have linked tinnitus with impairment of the nucleus accumbens, an area of the brain responsible for filtering sensory information. It is hypothesized that in individuals with sulfite intolerance, elevated serum sulfite levels inhibit enzymes related to the synthesis or activation of neurotransmitters active in the nucleus accumbens, resulting in tinnitus. Avoidance of sulfites in food and drugs may potentially bring relief to sulfite intolerant patients experiencing tinnitus, hyperacusis or other illnesses associated with decreased dopaminergic or serotonergic activity.

The nucleus accumbens is a collection of neurons within the forebrain that is known as the ''pleasure center''. It is involved in several functions ranging from motivation and reward to feeding and drug addiction. The nucleus accumbens is also a throttle point controlling the flow of sensory information reaching the cerebral cortex via the thalamus [1]. Similar to the way transistors regulate the flow of current in an electrical circuit, the nucleus accumbens regulates and prevents an overflow of sensory input from reaching our conscious mind [1].

In recent studies of people suffering from tinnitus, the subcallosal region including the nucleus accumbens was found to be smaller than normal [2]. It was hypothesized that in these patients, the impaired nucleus accumbens was unable to screen out unwanted sensory information including auditory noise, producing tinnitus [2].

This new elucidation of the development of tinnitus, opens the possibility that other causes of impairment to the nucleus accumbens could also result in the condition. The nucleus accumbens has both dopaminergic and serotonergic activity

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[2], and inhibition in the synthesis or metabolism of either of these neurotransmitters would theoretically decrease function. It is proposed that sulfites may play a role in this pathology.

Sulfites

Sulfites are inorganic salts that have antioxidant and preservative properties, and have a long history of use in foods as a preservative [3]. Though generally regarded as safe (GRAS), recent studies have revealed that a small subset of the population is sensitive to sulfites [3]. According to the Food and Drug Administration (FDA), this subset is approximately 1% of the population. Sulfite sensitivities may develop at any point in ones life [4].

The precise mechanisms of sensitivity responses to sulfites are not completely known, but several have been proposed including a deficiency or impairment of the mitochondrial enzyme: sulfite oxidase. Sulfite oxidase functions by converting sulfite to a harmless sulfate in the body [5]. When this enzyme function is impaired, serum sulfite levels may become elevated and persist chronically [9]. Sulfites are potent inhibitors of certain enzymes [6], and can have diverse effects on various biochemical pathways in the body [7—9].

It is hypothesized that sulfites, through several possible pathways, have an inhibitory effect on the nucleus accumbens resulting in tinnitus. Though other general neurotoxic mechanisms of sulfites are known [10], two specific pathways affecting dopaminergic and serotonergic activity are proposed, resulting from enzyme inhibition.

Reduction of dopaminergic activity in the nucleus accumbens

The synthesis of dopamine from tyrosine (Fig. 1.) involves a catalyzing enzyme known as tyrosine hydroxylase. Tyrosine hydroxylase is part of a family of enzymes known as tyrosinase, a multifunctional enzyme that exists widely in nature in slightly different forms [11].

Sulfites are known to effectively impair polyphenoloxidase (tyrosinase) when used in food production [5]. In vivo, a similar inhibition of tyrosine hydroxylase could inhibit the conversion of tryosine to dihydroxyphenylalanine in the synthesis of dopamine. The resulting reduction in dopaminergic activity could then impair function of various areas of the brain including the nucleus accumbens.

Reduction of serotonergic activity in the nucleus accumbens

The pineal gland is a small gland in the center of the brain responsible for a large range of regulating activities and produces melatonin and serotonin. A link between melatonin and serotonergic activity in the nucleus accumbens has been established in rat studies, showing specifically that melatonin affects serotonin synthesis and metabolism in several areas of the brain including the nucleus accumbens [12].

If a similar pathology exists in humans, it follows that any impairment of melatonin production in the pineal gland, could reduce serotonergic activity in the nucleus accumbens, and impair function.

Production of melatonin in the pineal gland happens in four steps, each step involves an enzyme catalyst (Fig. 2).

It is possible that sulfites may interfere with any of the four enzymes involved in the synthesis of melatonin from L-tryptophane. However, given the similarity in function of tryptophane hydroxylase and tyrosine hydroxylase, it is proposed that sulfites interfere specifically with tryptophane hydroxylase in the conversion of L-tryptophane to L-5-hydroxytryptophane. The resulting decrease in melatonin then leading to decreased serotonin synthesis and metabolism in the nucleus accumbens, resulting in tinnitus.

Link to hyperacusis?

As many as 40% of patients suffering from tinnitus also experience hyperacusis, an auditory condition characterized by an over-sensitivity to certain frequency ranges of sound. Patients with hyperacusis often perceive most sounds to be louder than those around them.

Given the nucleus accumbens role in the filtering and control of sensory information flow, it is likely that both conditions have a similar etiology. And, it is proposed that the coexistence of hyperacusis with tinnitus serves as an indicator that a patient's tinnitus includes an underlying neural component in the nucleus accumbens.

Link to other diseases?

Disturbances of dopamine and serotonin levels are already known to be correlated with other chronic illnesses, and whether sulfites play a role in their etiology is a question that may deserve further study.

Low dopamine levels have been found in patients with Alzheimer's disease, Parkinson's disease, depression and Attention-deficit/Hyperactivity Disorder (ADHD) [13]. Low serotonin levels have been linked to depression [14] and aggressive behavior [15—17]. And, altered serotonin synthesis has been found in autism [18].

Hypothyroidism may also be related to the etiology of tinnitus proposed herein, because of the generalized decrease in enzyme activity present in the illness, possibly affecting sulfite oxidase.

Recent research has shown that the thyroid state affects central dopaminergic and serotonergic activity in humans [19], though the mechanism has was not elucidated.

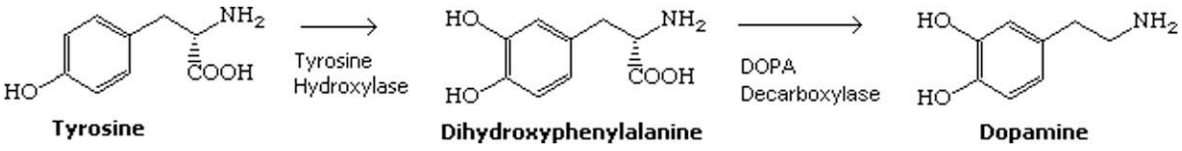

Figure 1 Synthesis of dopamine from tyrosine.