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Gastrin Enhances Autophagy-iysosome Pathway and Ubiquitin-proteasome System Activity to Break down Mutant Huntington

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Introduction

Epilepsy is a chronic neurological disorder characterized by recurrent and unprovoked seizures, which arise from abnormal electrical activity in the brain. It affects around 1-2% of the global population, making it one of the most prevalent neurological disorders worldwide. Seizures in epilepsy can vary in intensity and presentation, from subtle "minor" seizures to more severe "major" seizures (like tonic-clonic or focal seizures). The unpredictability and severity of seizures can have a profound impact on a patient's quality of life, often leading to social, cognitive, and psychological consequences. The most common treatment for epilepsy is Antiepileptic Drugs (AEDs); however, a significant proportion of individuals with epilepsy, approximately 30%, do not achieve full seizure control with pharmacological interventions. These patients are categorized as having "pharmacoresistant" or "drug-resistant" epilepsy. This represents a major challenge in clinical neurology, as individuals with drug-resistant epilepsy often suffer from frequent, debilitating seizures and may be at increased risk for other health complications, such as cognitive decline, depression, and even mortality [1].

Description

Vagus nerve stimulation is a form of neuromodulator therapy that works by delivering electrical impulses to the vagus nerve, one of the primary parasympathetic nerves in the body. The vagus nerve has widespread connections to several brain regions, including those involved in regulating mood, arousal, and seizure activity. The exact mechanism through which VNS reduces seizures is not fully understood, but it is believed to modulate neuronal excitability and neurotransmitter release in areas such as the brainstem, thalamus, and cortex, which play key roles in seizure generation and propagation [2]. The VNS system consists of two main components: the pulse generator (a small device implanted under the skin, typically in the chest area) and the lead, which is a wire attached to the pulse generator that is connected to the vagus nerve in the neck. The device is programmed to send regular electrical pulses to the vagus nerve, with the frequency and intensity of the stimulation adjusted according to the needs of the patient. In addition to the regular stimulation, patients can also use a handheld magnet to trigger the device during an impending seizure, providing acute intervention to potentially abort the seizure or reduce its severity [3].

VNS has been shown to reduce seizure frequency in many patients with drug-resistant epilepsy. Clinical trials and long-term studies have demonstrated that VNS therapy can result in a 30-50% reduction in seizure frequency for some individuals. However, the response to VNS is not uniform, with some patients experiencing significant benefits, while others show minimal to no improvement. As a result, understanding which patients are most likely to benefit from VNS, as well as the factors that influence its effectiveness, remains a critical area of ongoing research [4].

Differential Effects on Major vs. Minor Seizures the question of whether VNS has different levels of effectiveness in treating major versus minor seizures is of particular interest. Some clinical observations suggest that VNS may be more effective in reducing major seizures, such as generalized tonic-clonic seizures, than in controlling more subtle or less disruptive minor seizures. A study by Tecoma et al. (2001) reported that patients with major seizures, particularly generalized seizures, experienced a greater reduction in seizure frequency with VNS compared to those with minor seizures. This could be due to the difference in the neurophysiological mechanisms underlying the two types of seizures, with major seizures typically involving more widespread and synchronized neuronal firing across brain regions. On the other hand, some studies indicate that VNS can also be beneficial for patients with minor seizures, though the degree of benefit may be less pronounced. For instance, patients with absence seizures or simple partial seizures may experience fewer seizure episodes or a reduction in seizure duration when treated with VNS, but these effects may not be as dramatic as those seen in patients with major seizures. This disparity could be due to differences in the brain circuits involved in the generation of minor versus major seizures, as well as the more localized nature of many minor seizures compared to the widespread activity seen in major seizures [5].

Conclusion

Vagus Nerve Stimulation (VNS) represents an important advancement in the treatment of pharmacoresistant epilepsy, offering an alternative to traditional antiepileptic drugs for individuals who do not achieve adequate seizure control through medication alone. While the device has shown effectiveness in reducing both major and minor seizures in many patients, the degree of improvement varies widely, with some patients experiencing significant reductions in seizure frequency and others showing minimal benefit. VNS appears to be more effective in reducing major seizures, such as generalized tonic-clonic seizures, but it can also provide meaningful improvements for those with minor seizures, such as absence or focal seizures, particularly when these are frequent and disruptive. In addition to its effects on seizure frequency, VNS has been associated with improvements in quality of life, including better mood, cognition, and social functioning. However, the long-term benefits and challenges of VNS, including its variable response and potential side effects, highlight the need for individualized treatment strategies. Future research should focus on optimizing patient selection criteria, refining stimulation parameters, and exploring combination therapies to enhance the overall effectiveness of VNS, particularly for patients with diverse seizure types and underlying epilepsy syndromes.

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Conflict of Interest

There are no conflicts of interest by author.

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