

Early vagus nerve stimulator implantation as a main predictor of positive outcome in pediatric patients with epileptic encephalopathy

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- The only significant factor predicting favorable outcome was time to VNS implantation, with the best outcome achieved when VNS implantation was performed within 3 years of seizure onset.
- VNS implantation within 5 years of seizure onset was associated with a more favorable overall response rate- 83.3% at 1 year of follow-up and 100% at 5 years, compared to unfavorable results for implants performed after 5 years (response rate - 9.5% at 1 year and 0% at 5 years of follow-up).
- VNS implantation between 3 and 5 years after epilepsy onset in this population also evidenced an improved QOL at last follow-up visit.

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- Intervention in early life during brain maturation would be expected to help prevent the encephalopathic effects of epilepsy and likely establishment of aberrant circuits
- This concept would lead to effects that are most evident in very young children who have greater brain plasticity, and for the epileptic encephalopathies, for which, by definition *“the epileptic activity itself may contribute to severe cognitive and behavioral impairments that worsen over time above and beyond what might be expected from the underlying pathology alone”*.
- VNS treatment causes a robust reorganization of functional brain networks towards a more efficient (i.e. more integrated) network structure. These changes are related to clinical improvement which supports the hypothesis that VNS mechanism of action is closely related to widespread reorganization of brain networks.

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- In conclusion, we speculate that earlier VNS implantation most likely supports a widespread reorganization of the brain networks and impedes the establishment of aberrant circuits linked to the encephalopathic state.
- All of these changes related to early VNS implantation may also influence complex processes determining drug resistance and the semiological variability of seizures in epileptic encephalopathies.
- The hypothesis of large-scale reorganization of brain networks may also explain why VNS also improves cognitive and behavioural functions.
- Seizure frequency reduction during the critical period of maturation would be expected to reduce, if not prevent, long-lasting changes in neuronal network formation, leading to clinical improvement and improved QOL. This would be expected to reduce caregiver burnout and favors a more positive patient-caregiver interaction.