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Central Neural Versus Peripheral Muscular Origin of Vagus Somatosensory – Evoked Potentials

Dear Editors,

On sensory stimulation of the auricular branch of the Vagus nerve (ABVN) evoked potentials are recordable at the scalp which we called Vagus somatosensory evoked potentials (VSEP; 1). In previous studies, we discussed as an alternative explanation to a central neural origin of these potentials an interference with the facial or trigeminal nerve and thus a muscular origin. However, we regarded the latter as unlikely because of the reasons outlined in Table 1. In addition, VSEP show the same wave shape pattern in case of stimulation with needle electrodes. This is opposite to what was found in trigeminus SEP: The large myogenic potential (4–6 ms after stimulation) disappear when needle electrodes are used for stimulation [2]. As a consequence of the view of ABVN stimulation as an access to vagal afferences, more and more scientific studies now use this easily available way of stimulation for therapeutic purpose in various neuropsychiatric, inflammatory and cardiac diseases. However, Leutzow et al. recently described the disappearance of VSEP under anesthesia with pharmacologically induced muscle paralysis [3]. How can we integrate these results?

The observation of Leutzow et al. is an interesting finding. Muscular contamination is a long known problem that may even occur in medianus-SEP, for example, and differentiation is not easy [4]. However, Leutzow's results must be interpreted carefully before definite conclusions can be drawn. First, there are methodological differences between their work and ours, as they used a different stimulation electrode and no automatic artefact rejection that may have facilitated muscular contribution to their potentials. Second, on the start of anesthesia with propofol the wave shape pattern changes and an early peak at 1 ms disappears which should not be neither in peripheral muscular nor in central neural potentials. Third, the possibility that propofol used for anesthesia peaks when cis-atracurium is added and than has additional effects cannot be excluded since there is no control with propofol alone. Fourth, cis-atracurium is metabolized to laudanosine which is known to cross the blood brain barrier with CNS stimulating effects leading to EEG changes and, thus, may affect central nervous system potentials [5]. Interestingly, scalp recorded evoked potentials with latencies around 3 ms upon classical cervical stimulation of the

Table 1
Observations supporting a central neural origin of Vagus somatosensory evoked potentials (VSEP).

- more effective stimulation of VSEP at the tragus than at any other site of the outer ear
- prolonged latencies and diminished amplitudes of VSEP upon application of local anesthesia in the stimulation zone at the tragus [1]
- ipsilateral amplitude reduction in a subject with clinically asymmetric affection of Parkinson's disease [1]
- latencies of the first VSEP component <3 ms whereas latencies for muscle sum potentials recordable upon trigeminal and facial nerve stimulation are considerably longer [10]
- ressemblance to neural scalp-recordable evoked potentials upon classical cervical stimulation of the main vagus branch that persist under neuromuscular bloc [6]
- prolonged VSEP latencies in Alzheimer's and Parkinson's disease with known brainstem pathology, but not in Vascular dementia and Major depression
- trend for longer P1 latency in subjects with MS with brainstem involvement as compared to the group without
- linear trend of prolongation in all three peaks in groups of healthy over mild cognitive impaired to demented elderly subjects
- BOLD signal in a region attributed to the Locus coeruleus, a central relais station of the main vagus afferences upon R. auricularis stimulation [9]

main vagus branch persist when muscle paralysis during anesthesia is done with vecuronium and rocuronium, respectively, and they resemble VSEP upon R. auricularis stimulation [6]. Fifth, Leutzow et al. proposed that ABVN stimulation could lead to direct motor responses excited by a surface spread to nearby facial or trigeminal motor fibres. If this assumption was true, our findings of prolonged latencies in neurodegenerative diseases (Table 1) would imply that not only vagus-associated brainstem fibres, but also other brain nerves are target of neurodegeneration as it has been shown for sensory vagal branches of the oesophagus in PD [7] and for the optic nerve and retina in AD [8]. However, surface spread to nearby trigeminal and facial fibres seems not probable because VSEP show reduced amplitudes and prolonged latencies when the stimulation zone is treated with local anesthetics and are optimal only when stimulation is done at the tragus and not when done at any other site of the outer ear (Table 1).

In summary, whereas at the moment numerous observations are arguing for a predominantly central neural origin of VSEP, Leutzow et al. correctly point out that a muscular contribution cannot be excluded. Still missing is an animal study directly measuring electrical brain stem activity during ABVN – stimulation as it has been performed for acoustic evoked potentials. Likewise as proposed by Leutzow et al., in addition to fMRI studies [9] further electrophysiological investigations including source localization in humans are warranted to better define the origin of the potentials that can be measured on stimulation of the tragus and which we called VSEP.

Conflict of interest: The authors declare that they have no conflict of interest.

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On the Origin of Scalp Responses – A Comment on the Letter of Polak et al.

To the Editor:

We read with interest the Letter to the Editor from Polak et al. entitled "Central neural versus peripheral muscular origin of vagus somatosensory – evoked potentials," where the authors advocate the brainstem origin of the scalp responses (SR) registered during electrical stimulation of the inner side of the tragus.

Previously, the same research group (Fallgatter et al., 2003) described these SR in healthy volunteers, which were called (analogously to brainstem auditory evoked potentials) the vagus somatosensory evoked potentials (VSEP) [1]. In the last decade this research group published the results of several human experimental and clinical studies, where the methodological and diagnostic aspects of the postulated VSEP were further examined.

In our recent publication we have reported that the VSEP disappear after neuromuscular block (NMB) with cis-atracurium in patients scheduled to non-cranial surgery [2]. Usually, the early auditory brainstem or somatosensory evoked potentials do not disappear under NMB; in the absence of the muscular artifacts under NMB the evoked potentials are getting even better [3]. Therefore, we