Clinical Neurophysiology 130 (2019) 197–198

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Letter to the Editor

Filtering and other methodological issues of auditory N100 gating studies

As shown in my recent meta-analysis, the deficit of patients with schizophrenia in auditory N100 gating is characterized by a reduced N100 amplitude to the initial stimulus, as compared to controls, whereas the N100 amplitudes to repeated stimuli show little variation between patients and controls (Rosburg, 2018). In their comment to this study, Hsieh and Liu (2019) draw attention to three important methodological aspects, when conducting research on N100 gating.

The first issue is the one of filtering. Hsieh and Liu argue that the used filter settings across studies included in the meta-analysis were diverse and they exemplify this diversity with the studies of Turetsky et al. (2008) and Neuhaus et al. (2014), who used offline filters of 1–50 Hz and 0.5–20 Hz, respectively, for the analysis of the N100. Even though these filter settings are diverse, both are widely in line with standards recommended by the International Federation of Clinical Neurophysiology (IFCN) for analyzing long-latency auditory event-related potentials (AEPs), including the N100 (Goodin et al., 1994). These standards suggest that the high-pass filter should on no account be higher than 0.3–1 Hz, whereas low-pass filters might range from 30 to 100 Hz. Practically, the low-pass filter might affect the reliability for determining the N100 peak latency, but has only minor impact on the N100 amplitude (for exemplary data see Fig. 1). Most of the studies included in the meta-analysis (Rosburg, 2018) used filter parameters, as recommended by the IFCN standards (Goodin et al., 1994), and only few studies, explicitly mentioned in the meta-analysis, did not.

Hsieh and Liu (2019) further suggest that the S1-S2 difference should be reported in addition to S1 and S2 amplitudes measures and S2/S1 gating ratio, as also previously recommended by de Wilde et al. (2007). I do not oppose this recommendation. Comprehensive descriptive statistics make later meta-analyses much more convenient and some researchers prefer this measure over the gating ratio, also because of its better test-retest-reliability (Fuerst et al., 2007; Rentzsch et al., 2008). However, with regard to statistical procedures for analyzing group differences in sensory gating, I recommend using a repeated measures analysis of variance (ANOVA) with Stimulus (S1 vs. S2) as within-subject factor and Group as between-subject factor. In such statistical designs, the significance of the Group × Stimulus interaction effect equals the significance of the group effect obtained by a univariate ANOVA on the S1-S2 differences. Thus, for interferential statistics, the analysis of the S1-S2 differences is not necessarily of additional value.

The third issue of Hsieh and Liu (2019) is the impact of low S1 amplitudes when calculating the S2/S1 ratio, which was also addressed in the meta-analysis (Rosburg, 2018). The exclusion of individuals with small S1 amplitudes might be helpful to avoid distortions when determining the gating ratio, as suggested. To put it simple, sensory gating cannot be reliably determined when there is no identifiable response to the initial stimulus. Indeed, as mentioned by Hsieh and Liu, some research groups discarded AEP deflections with S1 amplitudes below 0.5 μV (e.g. Boutros et al., 2004). In elaboration to this approach, Lightfoot (2016) recommended that not just the amplitude of the signal but also the noise level should be taken into account when one seeks to determine whether an N100-P200 complex is present or absent. However, the N100 component as the most prominent AEP component is

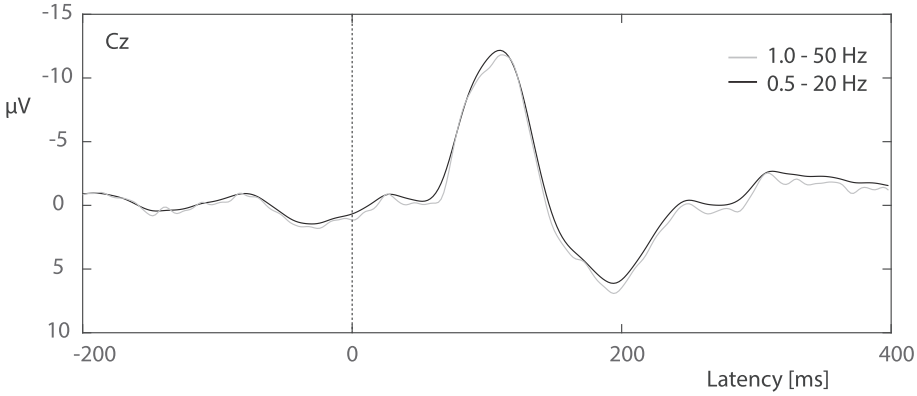

Fig. 1. The impact of filtering on the N100 of an individual (data from Rosburg et al., 2014): The stimulus onset is marked by the dotted vertical line. Data were filtered by 4th order zero phase shift Butterworth filters either from 0.5 to 20 Hz (black line) or from 1.0 to 50 Hz (grey line). The differential filtering results in some minor amplitude differences, which are primarily due to the differential high-pass filter.

https://doi.org/10.1016/j.clinph.2018.11.004

usually easy to identify: In the study of Neuhaus et al. (2014), 273 of the 288 participants had S1 N100 amplitudes larger than 1 μV. Thus, the issue of small S1 amplitudes requires some attention but does not represent a major obstacle in the study of N100 gating.

Overall, I greatly appreciated the comments of Hsieh and Liu (2019). The study of P50, N100, and P200 allows us to identify and to understand potential abnormalities of auditory perception in schizophrenia. Such deficits might contribute to impairments on higher cognitive levels, as reflected in other event-related potential components, such as the mismatch negativity or P3. Moreover, AEP alterations in schizophrenia might be related to genetic factors, brain structural deficits or changes in neurotransmission. Without doubt, we are still at an early stage of understanding the complete picture of such alterations. In order to evaluate and to understand AEP alterations, knowing potential methodological pitfalls of AEP recordings and data analysis is mandatory.

Conflict of interest statement

The author has no potential conflicts of interest to be disclosed.

Acknowledgements

The author greatly appreciated the assistance of Giulia Ammann and Gunnar Deuring in editing the letter.

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Available online 22 November 2018