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```In response: No evidence of thalamic metabolic abnormality associated with continuous spike-and-wave during sleep

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Response to Trotta et al.

To the Editors,

We thank Trotta et al for their critique and appreciate their efforts to evaluate thalamic metabolism quantitatively in their cohort of patients with continuous spike-and-wave in sleep (CSWS) using F-18-fluorodeoxyglucose positron emission tomography (FDG-PET). Although their findings are in contrast with our results, it is noteworthy that their methodology remains fairly distinct.[1] Even in our cohort, not everybody had thalamic abnormality; with thalamic abnormalities ranging from hypo- to hypermetabolism, as well as 'increased asymmetry only' with thalamic FDG uptake in the apparently normal range. This emphasizes the complexity of the issue, with thalamic metabolism perhaps getting modulated by various clinical factors which may confound the results of small sample-size studies with non-homogeneous patient population. Furthermore, a voxel-based analysis may not be the most appropriate approach to evaluate the aforementioned variability in thalamic FDG uptake due to possible averaging of the uptake values at the group level. Results of individual region-of-interest analysis with subsequent analytical approach, as employed in our study, might have been more comparable with our findings.

We would like to highlight that several authors have reported structural thalamic abnormalities in patients with CSWS and that this relationship has been recognized for over a decade.[2,3,4] This association of a structural thalamic abnormality (visible on MRI, not requiring statistical processing) and CSWS cannot be completely discounted. Similarly, in our patient group with CSWS and normal MRI, *a priori* qualitative analysis of glucose uptake on FDG-PET (by visual analysis) revealed thalamic abnormalities in 6/23 patients (patients # 2, 6, 8, 10, 11, 15). Despite the differences in the quantitative methods between Trotta et al and our group, it is hard to ignore this obvious pattern of abnormalities visible to the naked eye. Therefore, we do not concur with their conclusion that metabolic thalamic abnormalities are *not* associated with CSWS, although we do believe that this needs further exploration to fully explain and understand it.

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While studies on functional thalamic abnormalities in patients with CSWS are being investigated, various clinical and genetic factors may impact the development and pathophysiology of CSWS and thalamic abnormalities. Indeed, a standardized methodology with larger patient population would be the way to go forward. Of course, given the rarity of this condition, this may be accomplished only by collaborative work of clinicians and scientists with expertise and interest in CSWS and anatomical/functional neuroimaging.

We acknowledge that thalamic abnormalities are seen in patients with epilepsy without CSWS; however, the proportion of patients who had thalamic abnormalities in our study far exceeds the expected proportion otherwise.[5] Thus, there appears to be a more specific role of thalamic metabolic abnormalities in patients with CSWS. We concur with their comment that the cortex is likely to be the primary generator of the epileptic discharges in CSWS patients and do not believe otherwise, but we disagree that the thalamus is merely a propagation node. Our hypothesis is that an abnormal thalamus leads to aberrant thalamocortical interactions, which in turn leads to CSWS, although this remains to be further validated.

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None.

Disclosures:

None of the authors has any conflict of interest to disclose.

Ethical Publication Statement:

The authors confirm that they have read the journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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