Risk of overestimating loss of cerebral autoregulation—author’s reply

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Editor—We read with great interest the correspondence from Claudia Niño and colleagues about our paper ‘Impact of impaired cerebral blood flow autoregulation on electroencephalogram signals in adults undergoing propofol anaesthesia: a pilot study’.1 Their main concern is that the number of patients with impaired cerebral autoregulation (CA) may have been overestimated. They point to a possible difference in prevalence of comorbidities between the preserved CA group (CA+, mean flow index, Mxa < 0.3) and the impaired CA group (CA−, Mxa ≥ 0.3). They also question the accuracy of the Mxa score. Finally, they note that cerebral blood flow velocity (Vm) values seem low in our study, compared with those that can be found in the literature.

The authors first questioned the possible difference in age, ASA score, hypertension, and diabetes between the CA+ and CA− groups. This is a very relevant point because these variables are potential confounding factors. In our cohort, as shown in Figure 3 of the article, age did not differ significantly between the two groups (P = 0.132). Similarly, neither the incidence of hypertension nor diabetes differed significantly (P = 0.264 and P = 0.112, respectively). These P-values were not shown as they were non-significant and outside the scope of our hypotheses. Yet, our analysis does not exclude the potential difference in age, hypertension, or diabetes that may be found between CA+ and CA− patients in the general population. In our cohort, the ASA score differed between the two groups (P = 0.033), so we adjusted for it in our multivariable analysis.

Niño and colleagues make an interesting point regarding the high intrinsic variability in the Mxa distribution. This is a fascinating and technical topic directly related to signal processing methods. We used the methodology described by Czosnyka and colleagues.2 In their first descriptions in the 1990s, the sampling time window varied between 5 and 10 s.3 In the last decade, the consensual value for the duration of the time window has been set at 10 s, while the number of windows to calculate the correlation coefficient has been determined to be 30.4–6 These parameters allow filtering out physiological events unrelated to CA.7 In addition, the interpretation of Mxa relies on the fact that it is a Pearson correlation coefficient ‘r’. Therefore, its significance depends on its value and the number of samples considered (or degree of freedom, df). For example, if we consider non-overlapping windows of 10 s collected over 5 min we obtain 30 samples. Consequently, for a null hypothesis r ≤ 0 (and an a level of 0.05) we can say that a positive linear relationship exists from an Mxa of r ≥ 0.306, and below this correlation scores become more and more variable (see Fig. 1). These observations motivated us to dichotomise the Mxa using a cut-off of 0.3, a value that echoes several retrospective studies where Mxa was used to improve outcome after head injury.8

Regarding the admissible CA accuracy in clinical practice, there is unfortunately no consensus on this in the literature. However, correlation-based indices are defined in the literature as the best method for assessing static autoregulation.5 This is particularly true for the pressure reactivity index (Prx), which is based on ICP and MAP. Therefore, Mxa, the noninvasive equivalent of Prx, currently appears to be the best approach to assess intraoperative brain perfusion during steady states.

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Niño and colleagues highlight the low Vm values we found in the middle cerebral artery among our patients and suggest that this may lead to impaired CA. The decrease in Vm during propofol-based general anaesthesia depends on several factors. First, as the authors mentioned in their correspondence, Vm is proportional to MAP only when CA is impaired. Thus, more than the value itself, it is the observation of such a linear relationship that characterises impaired CA, and thus low Vm.

Indeed, Vm values also depend on the measurement devices used (here Athys Doppler using a robotic probe) and on the insonation angle. In our case, the analogic signal was passed to a Phillips monitor which could lead to the addition of a systematic bias. Although this does not impact Mxa values (absolute values of the variables for Pearson correlation do not impact the result), this observation calls for future clarification.

In conclusion, in our study, we showed that alpha-band frequency is significantly slower among CA− patients, independent of identified confounding factors (ASA and norepinephrine) and with no significant effect from age, hypertension, or diabetes. CA was assessed using Mxa, the most reliable deployable strategy in the operating theatre, which has been widely studied. However, we agree with Niño and colleagues that a larger study is needed to validate our results. Nevertheless, the concerns presented, especially the large number of altered CA cases, do not affect our main objective, which was to clarify the relationship between CA and intraoperative EEG.

**Declarations of interest**
The authors declare that they have no conflicts of interest.

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**References**
