In Reply:

We thank Numan *et al.* for their interest and comments on our recent publication in Anesthesiology.[1] The authors raise two concerns related to the methodology of our study. First, they point out that coherence, which was used to calculate functional cortical connectivity, may be affected by volume conduction. Spectral coherence is a widely used parameter-free feature in electroencephalogram studies and in brain functional connectivity analysis, and it measures the stability and reliability of phase differences between two sequences. We agree that in the analysis of a small number of electroencephalogram time samples, coherence estimates may detect spurious synchrony because of volume conduction or noise at the single subject level. However, in our study, the effect of volume conduction and noise was reduced for a number of reasons. First, we used the Welch modified periodogram averaging method to estimate the coherence from relatively long intervals of electroencephalogram recordings (88 s), followed by averaging across each frequency band. This procedure translates to an increased reliability and stability in coherence estimates, which reduces the effect of noise and random synchrony. More importantly, our analysis and conclusions were not based on an absolute value of localized coherence for each subject; rather, we used a baseline-corrected crossover design and performed a groupwise comparison between the two conditions (placebo *vs.* remifentanil) with subjectwise averaging. If we assume that for each subject, the effect of volume conduction holds between two consecutive experimental conditions, doing an analysis of differences between conditions would eliminate the effect of volume conduction. In our study, this approach resulted in a number of differences between baseline and remifentanil treatment, whereas there were no differences in the placebo arm. Taken together, we consider our findings to reflect significant changes in functional cortical connectivity specific to remifentanil administration, whereas the effect of spurious electroencephalogram fluctuations and volume conduction were cancelled out.

Besides coherence, a number of measures of functional connectivity have been proposed, including the phase lag index as suggested by Numan and coworkers.[2,3] We agree that each of these measures have their own properties and therefore provide complimentary information on the brain networks and could be considered in future studies.[4]

Second, Numan *et al.* suggest normalizing the network measures obtained from graph theoretical analysis (using the corresponding graph measures on a simulated random matched graph with the same number of nodes and edges as the original graph). We disagree with this suggestion because the functional connectivity graph we constructed using coherence was a fully connected undirected graph. Therefore, when performing a comparison of differences between two conditions (based on the same graph structure), such normalization will have no effect on the final result and conclusions.

Competing Interests

The authors declare no competing interests.

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49 Mathoura Road: To Grow Up, You Have to Leave Home

To the Editor:

I would like to congratulate Edwards and Waisel[1] on their excellent article about the failed experiment at 49 Mathoura Road and to comment on the editorial by Schwartz and Schroeder,[2] which accompanies it. I cannot attest to Geoffrey Kaye's character or to his affability, but there are other factors to be considered. Earlier in his career, Kaye had enough charisma to edit the first textbook on anesthesia in Australia. Published in 1932, this was a collaboration between seven physicians, with an interest in anesthesia, and one surgeon.[3] It was an amazing achievement for the 29-yr-old Kaye. Equally admirable is his role in the founding of the Australian Society of Anaesthetists (ASA); he was one of the seven founding members, its first treasurer, and the person largely responsible for the organization in its fledgling years.

Unfortunately, the commencement of the war coincided with those early years of the ASA and brought the developments to a sudden halt. Kaye returned from the war re-energized and determined to make the ASA a success; 49 Mathoura Road was a part of his new vision for the organization. But time and geography were against him. Those who had returned fell into two groups: (1) those who discovered that too much had changed in their absence and felt their skills were insufficient to continue in anesthetic practice and (2) those who were just starting out and had families and careers to consider. Neither of these groups

This letter was sent to the author of the Special Article referenced above, who declined to respond.