

A Slightly Different Tune: The Multipart Harmony of Noisy Life Support

To the Editor:—I would like to bring to the attention of readers of ANESTHESIOLOGY some inaccuracies in the Editorial View “Noisy Mechanical Ventilation: Listen to the Melody” by Drs. Shimabukuro and Gropper.¹ This article provided an overview of the research published in the journal by Spieth *et al.*,² “Effects of different levels of pressure support variability in experimental lung injury.” As stated by the editorialists, “Using variability in breathing patterns is not a completely new concept. It was probably first elucidated by Suki *et al.*³ in *Nature* in 1998.” In fact such an approach, subsequently called biologically variable ventilation, was first elucidated in 1996 in work done in my laboratory by Lefevre *et al.*⁴ Careful reading of the article in *Nature* indicates that stochastic resonance was advanced as an explanation for the improvement in compliance and oxygenation with a noisy end-inspiratory pressure based on analysis of data from our publication. We have since extended these observations to more generally indicate where noisy ventilation will be efficacious and where it may be detrimental.⁵ This analysis is based on Jensen’s inequality—a mathematical proof stating that a variable input will enhance an output when a smoothly continuous curvilinear function is convex.⁶ In contrast, if the function describing a relationship is concave, the addition of noise can diminish output and potentially be detrimental. Noisy ventilation is especially advantageous with tidal volume protocols according to the Acute Respiratory Distress Syndrome Network trial because the volume-pressure curve is convex curvilinear in the range of low tidal volumes.⁷ The lone negative animal study examining noisy ventilation in an acute respiratory distress syndrome model may be a consequence of large tidal volumes administered over the concave region of the sigmoidal volume-pressure curve—the portion of the static compliance curve where it may be deleterious to provide positive pressure ventilation based on modeling using Jensen’s inequality.⁸

The editorial further raises the question of the use of noisy ventilation in normal lungs. My laboratory has examined the use of noisy ventilation in the experimental setting of baseline anesthesia without lung injury⁹ and during ventilation of the dependent lung during one-lung anesthesia (an article published in ANESTHESIOLOGY).¹⁰ Colleagues published, again in ANESTHESIOLOGY, the first clinical trial examining the application of variable ventilation during abdominal aneurysmectomy.¹¹ In each of these studies better gas exchange and respiratory mechanics were seen with noisy ventilation, as compared with conventional monotonous control mode ventilation, similar to the findings by Spieth *et al.*

I do concur with the editorialists that “The importance of variability, whether referring to the respiratory system or DNA, in biologic systems should not be underestimated.” Based on the nonlinear amplification of output in convex curvilinear systems as outlined above, we have shown that noisy perfusion can improve cerebral oxygenation,¹² diminish renal injury,¹³ and enhance delivery of cardioplegia¹⁴ during

cardiopulmonary bypass. These improvements are likely a consequence of better flow with noisy perfusion pressure over the convex curvilinear flow-pressure curve manifest by the microvasculature. An overview of some of these issues is discussed in a short review.¹⁵

I also concur that “the time is here to translate these studies to the bedside.” The article by Spieth *et al.* reinforces prior work by this European group, the group in Boston, and the group in Canada, all demonstrating the advantage of adding noise to life support systems.

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The above letter was sent to the authors of the referenced editorial. The authors did not feel that a response was required.—James C. Eisenach, M.D., Editor-in-Chief