

support the multi-site expansion hypothesis whereby "general anaesthesia results from the expansion of differing sites which vary in their physical properties."¹ There is, however, another explanation for these data which seems to have been overlooked, namely that anaesthesia and analgesia are different phenomena.^{2,3} For this reason these two entirely different conditions could be mediated by dissimilar means.^{3,4} It is therefore conceivable that whilst the underlying mechanism for anaesthesia is a non-specific membrane effect, that for analgesia involves stereo-specific occupation of receptors by specific pharmacological agents.⁴

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- 3 *Gillman MA*. Analgesic (subanesthetic) nitrous oxide interacts with the endogenous opioid system: a review of the evidence. *Life Sci* 1986; 39: 1209-21.
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REPLY

In his thoughtful letter, Dr. Gillman has proposed "another explanation" for the data presented in my recent article.¹ I believe his remarks are most appropriate; however, his hypothesis should be considered complementary to, and not inconsistent with, my conclusions. I postulated that "multiple effects of general anaesthetics may be mediated at different loci," possibly through the mechanism suggested by the multi-site expansion hypothesis.² This approach suggests that "general anaesthesia can be produced by the expansion of more than one molecular site with different physical properties." This is not incompatible with the idea that different mechanisms also may be involved. Indeed, Halsey and co-workers² have stated that their data provide evidence that effects of different agents "are unlikely to involve common molecular interaction."

In conclusion, my data suggest only "that analgesia may result from anaesthetic action at a site different from that responsible for altered consciousness." This certainly does not preclude the possibility that the mechanisms responsible for the production of analgesia and narcosis also differ. Since I made no attempt to study any specific mechanisms, I have not made firm proposals regarding the physical or chemical factors responsible for these differences.

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