Correspondence

Antagonism of Diazepam by Physostigmine

To the Editor:—I read with interest the article by Bidwai et al.1 Although I commend the authors on their well-planned and well-executed study, I beg to differ regarding the purpose and the conclusions of their investigation.

Diazepam action is probably mediated through a facility of the GABA-ergic transmission2 and through specific receptor sites in the brain.3 Physostigmine, an inhibitor of acetylcholinesterase, acts through the cholinergic pathways, and if it antagonizes diazepam, it would probably be through a general arousal effect. This is not unexpected, since it has been found that the distribution of acetylcholinesterase neurons closely corresponds to the location of the reticular activating system.4 The drug arouses subjects from normal sleep5 and from stupor due to a variety of drugs and conditions. I suggest that the reversal of diazepam somnolence by physostigmine could have also been achieved by a wide variety of central nervous system stimulants, e.g., nikethamide, strychnine, and picrotoxin. The practice of using analeptics to counteract intoxication from general depressants and to hasten recovery from general anesthesia has been discredited by an understanding of the supportive care needed for the unconscious patient.

As is true with all central nervous system stimulants, the actions of physostigmine are dose-dependent and produce marked variability in responses among subjects. In one study, physostigmine, 1.5 to 2 mg, intravenously, produced increased speech, slowed thoughts, and mild sedation.6 It also impaired memory. A similar dose given to volunteers after diazepam did not counteract the memory deficit produced by diazepam, and the subjects felt more sedated than before receiving the physostigmine.7 However, physostigmine, 1 mg, given alone, enhanced the storage of information into long-term memory.8 It is possible that the actions of the drug may vary with the subject's baseline level of central cholinergic activity.

Finally, if one can avoid the use of a long-acting drug such as diazepam, whose average half-life is 31 hours, for an operation such as dilatation and curettage, the need to use a drug such as physostigmine is unlikely to occur.

M. M. Ghoneim, M.D.
Professor
Department of Anesthesia
University of Iowa
School of Medicine
Iowa City, Iowa 52242

REFERENCES


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In reply:—We would like to thank Dr. Ghoneim for his comments. We agree that the mechanisms by which physostigmine antagonizes the depressant actions of diazepam and other central nervous system depressants could be through a general arousal rather than through actions at specific receptor sites in the brain. It was neither possible nor was it the purpose of our study to define the mechanism by which physostigmine works, but simply to evaluate whether the drug is effective as an antagonist to CNS depression following diazepam–N2O anesthesia. The object of our study was not to advocate diaze-