

Editor's Notes

Hypergraphia and Droperidol—A Case Study

By Stephen Jackson, M.D., Editor

Writing editorials can be challenging. You must have something of interest and value to say, and then communicate that to your readers, always hopeful that you did a good enough job so that they will not pass by your column in the next issue. Since July, yours truly also has been responsible for the “President’s Page” for my (Santa Clara) County Medical Association’s *monthly* bulletin. As there is *no* editor, my column is the *de facto* editorial, which, by the very nature of a county medical society, must be of interest to members across *all* specialties. One might ponder how one goes about attempting to generate editorials of even meager value on such a frequent basis?

Writing has to be a fulfilling and stimulating activity for an editor. After all, my editorship does command the semblance of a bully pulpit, although admittedly one that must reside within the boundaries of politically, socially and even legally correct constraints, as well as within the restraints of scientific credibility.

The majority of my time wearing an editor’s hat is spent as a “hunter-gatherer” of information across a broad range of physician-relevant issues, seeking articles that are likely to be of interest and value to CSA members (both personally and professionally), and then orchestrating, editing and proofing the material into an understandable and reader-friendly product.

As is wont with other writers, I do experience periods of frenzied inspiration and exuberant creative production, yet I also occasionally do plunge into the depths of writer’s block and the throes of procrastination. Surprisingly, there has been little disciplined inquiry into such matters of the mind, as scientists consider literary creativity (the production of novel and valuable things) to be intangible, subjective, and, for that matter, scientifically unapproachable. However, “the times— they are a changin’.” Alice Flaherty, M.D., a neurologist, has written a book advocating for the scientific study of creative writing, which, to date, is largely

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based on functional magnetic resonance imaging, a technology that is thought to enable identification of patterns of brain activity that are at the seat of creativity.¹ Dr. Flaherty examined the roles played by the temporal lobes and limbic system in the desire to write, the former enabling humans to understand the meaning of words, the latter serving as the seat of emotion, inspiration and drive. The interaction of these two structures “underlies the importance of emotion **and** drive to creativity.” In fact, it may even be that drive weighs in more heavily than talent in the production of creative works.

The most striking form of productive (even excessive) writing is that of *hypergraphia*, an overwhelming desire to write. “Darwinians” have proffered that the most creative people are also the most productive, their proclivity to generate and filter a multitude of ideas permitting them to discard many lesser ideas while on the road toward identifying the better ones (the “survivors”). Indeed, hypergraphics are more likely to be motivated by a powerful and conscious internal drive rather than by external forces and influences.

A hypergraphic state may well have catalyzed the remainder of this editorial, one prompted by my “limbic” reactions to a series of what I believe to be inappropriate intrusions into my practice of anesthesia by governmental and quasi-governmental institutions. These included the “locked carts” safety issue, JCAHO’s terrorization (well, perhaps harassment is a kinder descriptive) of anesthesiology departments, and *especially*, the “black box” status mandated by the Food and Drug Administration (FDA) for droperidol.² Indeed, for me, the droperidol issue has become particularly hypergraphia-genic (an editor even can invent words with some degree of impunity).

Three decades ago droperidol was approved by the FDA for use as a tranquilizer in doses *greater* than 2.5 mg. Unexplainedly, lower doses, those *less* than 2.5 mg, always have remained an “off label” use! Unexpectedly in late 2001, the FDA declared droperidol to be a risk for causing *torsades de point*, polymorphic ventricular tachycardia and cardiac death. Despite more than thirty worldwide years of hundreds of millions of patients receiving droperidol uneventfully from a cardiac standpoint, the FDA’s epiphany led to a “black box” warning status for adverse sequelae related to droperidol’s property of causing prolongation of the QT interval. The FDA had several cases of severe cardiac complications in its database, and this allegedly was supplemented by a miniscule number of published case reports, *none of which involved the low doses typically deployed for the prevention/treatment of postoperative nausea and vomiting (PONV)*! Eight other structurally unrelated drugs also have been removed from the market, or had their availability severely restricted, because of this rare form of toxicity.³

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The low dose's "black box" status is scientifically unfounded.⁴ This condemnation is particularly outrageous in light of our specialty's preoccupation with prevention of PONV. There is, in fact, a well-established role for droperidol in the prevention of PONV,⁵ and although never one of my preferred anti-PONV drugs, it has fulfilled a therapeutic niche in many practices.

Despite a scientifically credible rebuttal by highly respected anesthesiologists, the FDA determined that there is insufficient data to demonstrate the safety of even *low dose* droperidol, and it demanded appropriate clinical data upon which it might base a reversal of its decision. Realistically, there is minimal likelihood of this happening. Droperidol's manufacturer has limited financial resources, the drug is inexpensive (limited profitability), and the 5-hydroxytryptamine₃ (5-HT₃) receptor antagonist "competitors" would not take any resurgence of droperidol lightly. Even more damaging, the FDA's determinations have created a legal risk for its use. Indeed, the same institutional pharmacies that have railed against the use of more costly PONV drugs have been quick to expunge droperidol from our drug carts and formularies.

Laying aside the legal shackles, the question arises as to whether anesthesiologists have an *ethical* obligation to use droperidol when, based on an extensive scientific literature and clinical experience of safety, we believe it to be medically indicated? The ASA's ethical imperative is that of "placing our patient's interests foremost, faithfully caring for the patient."⁶ Do we as a specialty have an ethical obligation to continue to advocate for droperidol's appropriate use, to demand or facilitate appropriate scientific study? Would such a study, if it were proposed, pass ethical muster with institutional review boards in light of the FDA's pronouncement?⁷

Perhaps you now can understand why droperidol indirectly induced a state of hypergraphia in this editor. But, don't report it to the FDA. Let's keep it on the Q.T.

¹ Flaherty, Alice. *The Midnight Disease—The Drive to Write, Writer's Block and the Creative Brain*. Houghton Mifflin, 2004.

² Cullen, B. Drug Shortages and Droperidol. *ASA Newsletter*. 2004;68(5): 2, 12.

³ Roden D. Drug-Induced Prolongation of the QT Interval. *NEJM*. 2004;350: 1013-1022.

⁴ White P. Prevention of Postoperative Nausea and Vomiting—A Multimodal Solution to a Persistent Problem. *NEJM*. 2004;350: 2511-2512.

⁵ Apfel C, Korttila K, Abdalla M, et al. A Factorial Trial of Six Interventions for the Prevention of Postoperative Nausea and Vomiting. *NEJM*. 2004;350: 2441-2451.

⁶ Guidelines for the Ethical Practice of Anesthesiology. American Society of Anesthesiologists Standards, Guidelines and Statements. October 2003, p. 1-2.

⁷ Nicholson R. Research Ethics. In *Ethics in Anaesthesia and Intensive Care* (H Draper, W Scott, Eds). Butterworth Heinemann. 2003, p. 107-118.