Published in final edited form as:

Crit Care Med. 2015 December ; 43(12): e589–e590. doi:10.1097/CCM.0000000000001342.

Response to Hermus et al

Terrence E. Murphy, Ph.D.[†], Katy L.B. Araujo, M.P.H.[†], and Margaret A. Pisani, M.D., M.P.H.^{*}

[†]Department of Internal Medicine, Geriatrics Section, and the Program on Aging, Yale School of Medicine, New Haven, CT

^{*}Department of Internal Medicine, Pulmonary, Critical Care & Sleep Medicine, Yale School of Medicine, New Haven, CT

Keywords

hyper-active delirium; hypo-active delirium; haloperidol

We welcome the astute comments of Dr. Hermus and her Maastricht-based colleagues (1) concerning the paper by Pisani, Araujo, and Murphy published earlier this year in *Critical Care Medicine* (2). First and foremost, we see no substantive conflict between the major points raised by Hermus et al and the aforementioned article. We acknowledge that neither the CAM-ICU (3) nor the chart-based algorithm (4) discerned diagnoses of hypo- from those of hyper-active delirium, thereby yielding an outcome mix of both subtypes. We are also aware of the changes in clinical practice that have, in the ten plus years since our study data was collected (5), resulted in routinely lower dosages of haloperidol. We find no fault with their statement regarding the multiple factors that contribute to next day delirium and note that our estimated effect size for haloperidol was very small relative to those of such well recognized influences as cognitive impairment and intubation. Our citation of the Society for Critical Care Medicine guidelines (6) was deliberately neutral and intended to draw attention to the fact that our discipline's routine use of haloperidol is largely empirical, in contrast with the robust clinical trials that often justify the use of medications in other disciplines. In their closing statement Hermus et al conclude that the use of large doses of haloperidol among a case mix of hypo- and hyper-active delirium is very plausibly associated with positive diagnosis of next day delirium. In short, there is a great deal of consistency between the practice-based observations of Hermus et al and the model results reported in Pisani, Araujo, and Murphy (2).

What we most like about Hermus et al is their insistence that hypo- and hyper-active delirium are qualitatively distinct and likely require differential treatment. And while their assertion that low doses of haloperidol are efficacious for persons suffering from hyper-active delirium strikes us as pragmatic and compassionate, definitive studies have not yet resulted in a clinical consensus. Our study and their comments support the idea that better

Corresponding author: Terrence E. Murphy, Ph.D., Yale University School of Medicine, 300 George St, Suite 775, New Haven, CT 06511, Tel: (203) 737-2295; Fax: (203) 785-4823; terrence.murphy@yale.edu.

Copyright form disclosures:

Dr. Pisani disclosed that she does not have any potential conflicts of interest.

instruments are needed to diagnose delirium and to distinguish between hypo- and hyper-active delirium, as well as severity of ICU delirium. Like Hermus et al, we believe that the use of haloperidol to treat delirious patients must be carefully considered in terms of dosage and on patient symptoms such as the nature of their delirium, whether or not they are intubated, and severity of illness. Clinical trials randomizing delirious persons to treatment with haloperidol and placebo that examine outcomes based on motoric subtypes and intubation status are needed to provide more rigorous evaluation of the efficacy of haloperidol as a treatment for delirium.

Acknowledgments

Dr. Murphy and Ms. Araujo received support for this article from the National Institutes of Health (P30AG21342). All authors have disclosed they have no potential conflicts of interest.

References

1. Hermus IPM, Willems SJB, Bogmam ACCF, et al. "Delirium" Is No Delirium: on Type Specifying and Drug Response. *Crit Care Med*. 2015 in press.
2. Pisani MA, Araujo KL, Murphy TE. Association of cumulative dose of haloperidol with next-day delirium in older medical ICU patients. *Crit Care Med*. 2015; 43(5):996–1002. [PubMed: 25746748]
3. Ely EW, Margolin R, Francis J, et al. Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *Crit Care Med*. 2001; 29(7):1370–1379. [PubMed: 11445689]
4. Pisani MA, Araujo KL, Van Ness PH, et al. A research algorithm to improve detection of delirium in the intensive care unit. *Crit Care*. 2006; 10(4):R121. [PubMed: 16919169]
5. Pisani MA, Murphy TE, Van Ness PH, et al. Characteristics associated with delirium in older patients in a medical intensive care unit. *Arch Intern Med*. 2007; 167(15):1629–1634. [PubMed: 17698685]
6. Barr J, Fraser GL, Puntillo K, et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med*. 2013; 41(1):263–306. [PubMed: 23269131]