

Letter to the Editor

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In response to the Letter to the Editor by Dr. Andrew Francis and Dr. Adeeb Yacoub regarding the article “Catatonic variants, hyperthermic extrapyramidal reactions, and subtypes of neuroleptic malignant syndrome,” *Annals of Clinical Psychiatry* 2007;19:9–16.

AUTHOR’S REPLY:

As Dr. Francis and Dr. Yacoub point out, the finding that 5 of the 14 NMS episodes in the naturalistic study did not meet criteria for catatonia or respond to benzodiazepines is at variance with some studies, which show a close relationship between catatonia and NMS (1,2). Consistent with these studies, however, the remaining 9 episodes all had concurrent catatonia and most of them showed positive responses to benzodiazepines. The absence of catatonia in some NMS episodes and their lack of responses to benzodiazepines—an effective treatment for acute catatonia—cast doubt over the hypothesis that all NMS episodes are severe variants of catatonia and NMS and catatonia are one single entity. Dr. Francis and Dr. Yacoub rightly query if the NMS episodes were stringently assessed for catatonia and the poor responses to benzodiazepines were due to sub-optimal dosage of benzodiazepines. The diagnosis of catatonia, masked or overshadowed by NMS features, could be easily missed, and some NMS episodes may need high dosage of benzodiazepines for treatment (3).

The detection of catatonic signs requires a clinical examination beyond an ordinary psychiatric interview, preferably with the use of specific rating scales (4). The author examined all the patients with NMS in the study for catatonia during the course of NMS frequently (daily to several times daily) during weekdays and in some cases also on weekends. The Standard Examination for Catatonia proposed by Bush et al was used along with the Bush-Francis Catatonia Rating Scale (5) (published in 1996) in 9 episodes. Nursing observation with details documented provided further information. A number of diagnostic criteria, varying in diagnostic restrictiveness, were used, as there has been a lack of consensus as to what defines catatonia. In 5 episodes, catatonia was not diagnosed even with the least restrictive criteria.

If catatonia was masked by NMS features and its diagnosis missed in some NMS episodes, it was expected that these episodes and those with catatonia diagnosed would show similar responses to benzodiazepine. This was not the case. None of the 5 “non-catatonic” NMS episodes showed significant responses to benzodiazepines. All 14 episodes received both regular and PRN benzodiazepines, oral or/and parenteral (5 lorazepam, 5 lorazepam and clonazepam, 1 repeated intravenous diazepam, and 3 a mixture of lorazepam, clonazepam, and diazepam). The mean maximum daily dose of lorazepam or equivalent was 9.2mg (4–19; SD = 4.7). Those showing nil or partial responses received considerably higher doses (nil vs. partial vs. prompt responses: 12 mg (4–19; SD = 4.9) vs. 8 mg (6–10; SD = 1.4) vs. 4.3 mg (4–5; SD = 0.47). It was unlikely that the lack of response was a result of sub-optimal dosage of benzodiazepines. Of note, in a chart review study of 16 NMS episodes by Francis et al. (1) showing positive responses to benzodiazepines in all episodes, the mean dose of lorazepam or equivalent in the first 24 hours was 2.8 mg (1–6) and in the second 24 hours 2.9 mg (1–9).

The preliminary findings suggest that NMS may be subgrouped into catatonic and non-catatonic subtypes. The subtyping has potential clinical applications and pathophysiological implications. The validity of the proposed subtypes needs empirical examination with larger studies.

REFERENCES

1. Francis A, Chandragiri S, Rizvi S, Koch M, Petrides G. Is lorazepam a treatment for neuroleptic malignant syndrome? *CNS Spectrum*. 2000;5:54–57.
2. White DAC, Robins AH. An analysis of 17 catatonic patients diagnosed with neuroleptic malignant syndrome. *CNS Spectrum*. 2000;5:58–65.
3. Yacoub A, Francis A. Neuroleptic malignant syndrome induced by atypical neuroleptics and responsive to lorazepam. *Neuropsychiatr Dis Treat*. 2006;2:235–240.
4. Kirkhart R, Ahuja N, Lee JW, Ramirez J, Talbert R, Faiz K, Ungvari GS, Thomas C, Carroll BT. The detection and measurement of catatonia. *Psychiatry*. 2007;4:52–56.
5. Bush G, Fink M, Petrides G, Dowling F, Francis A. Catatonia I. Rating scale and standardized examination. *Acta Psychiatr Scand*. 1996; 93:129–136.

