ELSEVIER

RESPONSE

Response to Mitul Mehta's Letter

When interpreting the results of psychopharmacological studies it is important to recognize alternative explanations accounting for observed differences. Indeed, before recommendations may be made to expose patients to any clinical treatment conclusive evidence of a benefit should be provided. Thus, we appreciate the opportunity to present additional information about our study and results.

As Dr. Mehta points out, the baseline performance of the schizophrenic patients treated with risperidone and guanfacine versus those treated with risperidone and placebo was not equivalent. Dr. Mehta therefore argues that drug-placebo differences observed in this study might be accounted for by baseline dependent effects such as "regression to the mean." While this is always a possibility when baseline differences are present, this phenomenon is due to random retest variance. The improvement of the guanfacine patients may, superficially, appear consistent with regression to the mean. If there was random variance, however, the untreated groups would be expected to regress to the mean as well, manifesting deterioration. What is not apparent from the presentation of the data is that two of the patients in the placebo group could not complete the entire endpoint testing session. This fact alone accounted for the apparent deterioration in performance of the placebo group, undermining the argument that random retest variance accounts for performance improvement.

Dr. Mehta questions the test-retest reliability of the spatial working memory test as another alternative source of the observed change. This argument is based upon the observed worsening of the placebo group at the endpoint testing session. In response, Pearson correlations of the baseline and endpoint scores on the 5 and 15 s delay conditions of the spatial working memory test for the placebo group demonstrated coefficients of $-.67$ and $-.64$ respectively. We interpret this as fairly good retest reliability for the spatial working memory test in these patients, especially considering the small sample size.

Dr. Mehta's additional explanation of a ceiling or floor effect leading to is equally unlikely to the observed change. Each condition of the spatial working memory test has a potential score ranging from 0 to 24. The baseline performance of both the placebo and guanfacine groups were not close to either the minimum or maximum scores for this test, meaning that there was ample room for improvement or deterioration of performance for both groups. Healthy individuals perform this test much better than the performance of guanfacine treated patients at endpoint, meaning that there is ample room for improvement above and beyond the changes seen.

The results of our study revealed a modest improvement on spatial working memory and attention related to treatment with guanfacine and risperidone in patients with schizophrenia. Given that these results were the product of post hoc analyses of subgroups we did not initially intend to study, these analyses were underpowered. We explained in our original report that these results were preliminary and limited. We did not expect readers to make definitive conclusions about a positive cognitive enhancement effect of guanfacine. Rigorous discussions of pilot data are unnecessary and premature, according to our own estimation, given the inherent limitations of pilot data. Instead, our findings were presented in order to encourage further research designed to make more definitive determinations of a treatment's potential beneficial effect.

Joseph Friedman, M.D.,
Phillip Harvey, Ph.D.,
and Kenneth Davis, M.D.

From the Department of Psychiatry, Mount Sinai Hospital, New York, NY

Address correspondence to: D. J.I. Friedman, Mount Sinai Hospital, Department of Psychiatry Box 1230, One Gustave L. Levy Place, New York, NY 10029. Tel.: (631) 761-3607; Fax: (631) 761-2718; E-mail: jfredma@mail.idt.net

Received January 10, 2002; accepted February 27, 2002.

Online publication: 4/23/02 at www.acnp.org/citations/Npp042302290.

Published by Elsevier Science Inc.
655 Avenue of the Americas, New York, NY 10010

0893-133X/02/$–see front matter
PII S0893-133X(02)00360-3