Response to Spencer et al. Letter

TO THE EDITOR: We read with interest the letter by Spencer et al., who argue against the medication status definitions in our study (1). This is a good point, as meta-analyses are usually biased by the surrounding basic literature retrieved. In this sense, the authors are right that there is some uncertainty in the definition of the clinical status of ADHD patients and previous exposure to treatments. We accept this and explicitly acknowledge such a limitation in our work. However, Spencer et al. raise a number of critical points that are not supported by evidence. For example, they argue that the Volkow et al. study did not enroll drug-naive subjects. This is explicitly contradicted in the method section of the Volkow et al. article: "We studied 53 never-medicated ADHD patients" (2). We feel the Volkow et al. study provides the best description of inclusion and exclusion criteria for ADHD subjects, as it fully characterizes the clinical status of the sample:

> To minimize confounding from prior drug exposures or comorbidity, participants were excluded if they had a prior history of substance abuse (other than nicotine) or with positive urine drug screen results, prior or current treatment with psychotropic medications (including stimulants), psychiatric comorbidities (axis I or II diagnosis other than ADHD), neurological disease, medical conditions that may alter cerebral function (ie, cardiovascular, endocrinological, oncological, or autoimmune diseases), or head trauma with loss of consciousness (>30 minutes). These rigorous exclusion criteria contributed to the length of the study (from 2001 to 2009).

Contrary to what Spencer et al. argue, we believe this high-quality study should be taken as model for future studies in such a population. Another good description of medication status is given by Jucaite et al. (3): "Nine of the 12 boys were drug naive (in other words, they had not previously been treated with any psychostimulants)." With respect to this study, Spencer et al. are incorrect when interpreting an elevated mean dopamine transporter binding in ADHD as compared with control subjects: both Table 1 and Figure 3 indicate no statistically significant between-group differences. Conversely, the sample selection of la Fougère et al. (4) is poorly described, and in fact there is no mention at all that the subjects were "drug-naive" or "never treated," as Spencer et al. speculate. The criticisms the authors raise are thus not corroborated by the literature. However, we take this opportunity to fully highlight the true methodological limitations of our study: it had a small sample size; the causality of the regression findings could not be tested in cross-sectional designs; the study had limited statistical power for meta-regression analysis; and it used an artificial comparison across several radiotracers, each with differential dopamine transporter sensitivity. We acknowledge that because of these limitations the results of our study should be considered preliminary and subject to verification in well-designed large-scale longitudinal investigations of drug naive ADHD subjects.

References

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The author's disclosures accompany the original article.

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