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LETTER TO THE EDITORS

Drug Free Schizophrenics and Stage IV Sleep

The excellent polysomnographic study in drug-naive paranoid schizophrenic patients by Lauer et al. (1997) needs comment. I am impressed with the authors' data, but disagree with some of their conclusions. It is not clear in their study of mentally normal controls and patients, which, if any, were tobacco smokers. Inasmuch as tobacco smoke is a cesspool of chemicals in addition to nicotine, the authors should clarify whether their subjects were truly "drug" free. This is especially important because Fowler *et al*. (1996) have shown that brain MAO_A and MAO_B activity is reduced in tobacco smokers. If the normal controls and the schizophrenic patients were tobacco smokers, they were not "drug" free. This issue has been discussed previously in relationship to whether schizophrenic patients have reduced platelet MAO activity (Domino 1996).

Obviously, Lauer et al. (1997) were concerned with the long term effects of neuroleptics and not tobacco. They conclude that "their results indicate that the commonly reported SWS (slow wave sleep) and REM (rapid eye movement) sleep changes in schizophrenia reflect the remnant of prior neuroleptic treatment, rather than the pathophysiology of the disorder itself". In their Figure 1, for absolute amount of Stage IV sleep there are 10 of 22 paranoid schizophrenics that have no Stage IV sleep (45.5%) compared to 2 of 20 normal controls (10%). It is unusual that 10% of the normal controls had no Stage IV sleep, suggesting incomplete adaptation to the sleep environment (first night effect). If one compares their findings with those we reported 30 years ago (Caldwell and Domino 1967a,b) in "neuroleptic free" chronic process schizophrenics, there are some amazing similarities in the percentages of patients with no Stage IV. We selected 25 male chronic process schizophrenic patients who were nonresponders to classic neuroleptics available in the 1960s. Therefore, it was ethical to stop all psychotropic medication except coffee drinking and tobacco smoking for at least 2 years. The subjects were also asked to stop drinking coffee and smoking tobacco 6 hours prior to all night EEG sleep recordings for 5 consecutive nights with the data of night 2 summarized. In spite of the fact that all of the schizophrenic patients had previous neuroleptic exposure for 2 years or longer, the mean of 15 of the patients for Stage IV sleep was greater than the mean for controls. Ten of the remaining schizophrenic patients had no Stage IV sleep (40%). Additional differences among the two groups of schizophrenic patients compared to normals were also noted (Caldwell and Domino 1967a). In contrast, 0 of 10 normal controls lacked Stage IV sleep (0%), as would be expected of mentally normal subjects. If mean Stage IV sleep of all of the schizophrenic patients was compared to the normal controls, there was a slight but statistically significant reduction. However, the difference in the process schizophrenics between Stage IV sleep present and absent was striking. The finding of Lauer et al. (1997) that 45.5% of their paranoid schizophrenics have no Stage IV sleep agrees with our early finding of no Stage IV in 40% of process schizophrenics. Furthermore, one should note the greater variance in Stage IV sleep in the patients in both of our studies. Our two studies also agree that there is no difference in total REM. One can conclude that their research using paranoid drug free schizophrenics confirms our early report that about 40% of chronic process schizophrenics have a dramatic deficit in Stage IV sleep. Furthermore, since both Stage IV present and Stage IV absent schizophrenic patients had no neuroleptic medication for two plus years prior to our sleep study, one cannot ascribe these sleep differences to previous neuroleptic medication exposure. Further research must pursue the reasons why 40-45.5% of schizophrenic patients have such a profound disturbance in Stage IV sleep unrelated to prior neuroleptic medication.

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NEUROPSYCHOPHARMACOLOGY 1998–VOL. 18, NO. 5

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

0893-133X/98/$19.00
PII S0893-133X(97)00129-2

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