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Methylene Blue for MDI

To the Editor:

The correspondence from Drs. Thomas and Callender (1985) regarding use of methylene blue in treatment of bipolar illness is of particular interest to me. In 1946, I wondered whether schizophrenia might be related to disturbance in redox potentials within neurons, a disturbance possibly correctable by oral administration of methylene blue. I wrote to Ralph W. Gerard, who responded that he had tried it without success and that another dye, which he named but I have forgotten, with a higher E_0^1 , might be useful. While I waited for Gerard's letter, I obtained permission from the VA (Dr. Daniel Blain) to try methylene blue 100 mg, t.i.d. Six psychiatric residents at the Northport facility each ordered the trial for 2 weeks on a patient of each. No patient exhibited a

favorable change. I must add that if further trial of methylene blue is contemplated, the product must be free of arsenic, an impurity usually present in consequence of synthesis of the dye.

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Sleep-Onset REM Period in Paranoid Schizophrenia

To the Editor:

A pathological sleep-onset rapid eye movement period (SOREMP) has been defined as any REM period occurring immediately after or within 15 min of the onset of sleep (Dement 1976). It has been reported in a number of conditions—narcolepsy (Dement 1976), primary depression (Patricia Koble et al. 1981), psychotic depression (Kupfer and Foster 1975), amphetamine withdrawal, disturbances of the sleep-wake cycle, and occasionally in normal individuals. There have been no reports of SOREMP in schizophrenia. We report a case of SOREMP in chronic paranoid schizophrenia; the patient was a nonresponder to treatment, and interestingly, the SOREMP persisted after treatment.

The patient was a 37-year-old black male who was admitted to the Clinical Studies Unit for Affective Disorders at the University of Michigan, after complaining of hearing voices of people he had known several years ago, a belief that objects from the environment were being incorporated into his body, and difficulty in concentrating. He further exhibited passive somatic delusions, thought insertion, and persecutory delusions. These symptoms had persisted for 3 years, and his highest level of adaptive functioning over the last 12 months was poor. He was diagnosed by several clinicians independently, using RDC/SADS and the DMS-III, as having chronic paranoid schizophrenia. His Brief Psychiatric Rating Scale (BPRS) score was consistently above 40, and he did not have any of the major symptoms and signs of depression. Furthermore, there were no clinical features indicative of narcolepsy (sleep attacks, cata-

plexy, sleep paralysis, or hypnagogic hallucinations), no apparent disturbance of his sleep-wakefulness cycle, and no jet lag. His physical exam and laboratory studies, which included (1) CBC, differential, (2) serum electrolytes, thyroid studies, B₁₂ and folate, (3) head CT, and (4) EEG with nasopharyngeal leads, were unremarkable. The patient underwent the 2-week drug-free washout period prior to his first sleep electroencephalogram (EEG) recording. The electrode placement and scoring were done according to the criteria established by Rechtschaffen and Kales (1968).

Sleep data obtained on the first and second nights of recording (pre-ECT) revealed zero REM latency on both nights (see Table 1). The patient was treated with thiothixene (40 mg/day) for over 3 weeks, followed by trifluoperazine (60 mg/day) for an adequate period of time. No clinical response was observed, and we consequently broke the research code for sleep EEG. The SOREMP was noted, and the prospect of delusional depression, though deemed unlikely, was entertained. A combination of trifluoperazine and desipramine (blood level of 208 ng/ml) for an adequate period of time, followed by a complete course of electroconvulsive therapy (ECT) (nine shock treatments), failed to bring about any significant clinical improvement (his BPRS score remained above 40). Sleep EEGs were repeated for 2 nights, 14 days after the last ECT, and the REM latency remained zero on both nights. A Multiple Sleep Latency Test (MSLT) was not performed, as the patient did not have any clinical features suggestive of narcolepsy.

Sleep-onset REM has not been reported in schizophrenia, though a variety of other REM irregularities have been noted. Some investigators (Jus et al. 1973) consider a decrease in REM latency to be one of the most consistent sleep pattern alterations in schizophrenia. It has also been suggested that a shortened REM latency in schizophrenia identifies a subgroup that require antidepressant treatment. Our patient neither had any clinical evidence of depression, nor did

he respond to any of the therapeutic interventions. The occurrence of persistent SOREMP in our patient may represent a distinct undefined pathophysiological process. We would like to suggest that SOREMP may occur in schizophrenia, as well as in other pathophysiological states for which it has been described, and furthermore, that this sleep EEG finding may indicate a poor treatment response. This question will require systematic assessment.

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Table 1.

Nights of sleep recording	HRSD scores	REM latency	Duration of first REM period in minutes	REM density	Percent REM sleep
Day 1 (pre-ECT)	9	0	8	1.1480	19.014
Day 2 (pre-ECT)	9	0	7	1.9320	24.104
Day 3 (14 days post-ECT)	3	0	3	1.3000	26.596
Day 4 (15 days post-ECT)	3	0	10	1.5780	19.453