Letters to the Editor

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FATIGUE AS A CORE SYMPTOM OF INSOMNIA

Dear Editor:

I found the article by Drs. Targum and Fava, "Fatigue as a Residual Symptom of Depression" [*Innov Clin Neurosci* 2011;8(10):40–43], to be quite interesting. Dr. Targum's questions to Dr. Fava, a specialist of psychopharmacology, were so didactic that it made this article sufficient to bridge the gap between research and practice. Nevertheless, I believe the article lacked sufficient discussion regarding several important elements, even though I understand that the article was limited to discussing fatigue related to major depressive disorder (MDD).

My dissatisfaction with the article is mainly due to the lack of explanation for another important aspect related to MDD: comorbid insomnia. Dr. Fava himself has already stressed such correlates elsewhere.[1,2] For example, he previously states that whether insomnia is a precursor, symptom, residual symptom, or side effect of depression or its treatment, clinicians must give serious attention and attempt to resolve sleep disturbances.[1] Based on this viewpoint, I feel some additional comments and questions should be addressed in order to elaborate on the current discussion by Drs. Targum and Fava.

Patients with MDD commonly experience insomnia complaints, including difficulty falling asleep, difficulty maintaining sleep, awakening early, and experiencing nonrestorative sleep. Previous epidemiological studies have estimated insomnia complaints to occur in up to 90 percent of patients with MDD.[2] Moreover, insomnia is among the most common residual symptom of MDD, and pharmacotherapy with selective serotonin reuptake inhibitors (SSRIs) and other antidepressants can cause insomnia, as the authors suggested.[1,2]

As Dr. Fava mentioned in a recent article,[2] it is true that a paradigm shift in treating insomnia and coexisting psychiatric disorders has occurred. Proposed criteria for insomnia in the forthcoming *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (*DSM-V*) reflects the research recommendations by United States National Institutes of Health (NIH), which has been widely adopted in the field of clinical sleep science.[3] The new terminology *insomnia disorder* signifies a 24-hour disease, implying both nighttime insomnia symptoms and the daytime impairment related to it. Therefore, based on this new "insomnia" definition, *fatigue* itself can be regarded as a core symptom of insomnia. Rather than treating insomnia as a symptom of MDD, the current empirically supported literature now recommends that each condition be treated independently. Importantly, Dr. Fava also suggests that insomnia and insomnia-related daytime symptoms respond differently from and independently of depression symptoms. I agree with his remarks that MDD and insomnia represent at least two different dimensions of a single disorder, if not two separate disorders.

Although clinicians often use depressive symptoms, such as fatigue, to characterize the daytime consequences of insomnia, strictly speaking, the criteria overlap between insomnia and MDD has only been restricted to the symptoms of insomnia itself.[4] In recent literature, while daytime sleepiness, hypersomnia, and fatigue are common symptoms of depression, such symptoms can occur independently or they may occur secondarily to insomnia comorbidity or the side effects of antidepressant medication themselves. Thus, while Drs. Targum and Fava stress the importance of recognizing, differentiating, and treating fatigue in patients with MDD, we need to take into account both aspects of insomnia and depression equally.[5]

I am also concerned that, in their current article, Drs. Targum and Fava only comment on new medications that may soon be available for the treatment as residual fatigue. I wonder if their conclusion might mislead the readers into having too much optimism for the development of new evaluation tools and novel pharmacological agents in the next few years. Further research studying on whether insomnia is a modifiable risk factor in depression treatment would be valuable, since effective antidepressant treatment surely affects sleep in some way.[1,4] We psychiatrists and mental health professionals should have empathy for such individuals manifesting fatigue in the current 24/7 society.

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With regards,

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Author Response

Dr. Targum and I appreciate the comments from Dr. Abe. We do agree with Dr. Abe that fatigue can be secondary to insomnia and, in fact, in the paper that Dr. Abe references by Fava et al [*J Clin Psychiatry.* 2011;72:914–928], zolpidem augmentation of SSRI treatment of MDD with insomnia did not lead to a significantly greater improvement in depressive symptoms than SSRI plus placebo treatment, although both insomnia and daytime fatigue did improve significantly. The findings of this study by Fava et al do suggest the potential independence of insomnia from MDD itself, despite the fact that insomnia is one of the common key symptoms of MDD.

With regards,

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ILLICIT DRUG USE IN TEENAGERS AND YOUNG ADULTS

Dear Editor:

I found the review article by Ali et al, "Early Detection of Illicit Drug Use in Teenagers" [*Innov Clin Neurosci.* 2011;8(12):25–34], to be quite informative and interesting. This article discussed in broad terms the risk factors and warning signs regarding illicit drug use in this subpopulation. I would like to add some additional comments to what the authors reviewed in their article.

First, I would like to mention a long-term epidemiology study, "Monitoring the Future," which surveyed the trend of legal and illicit drug use in American adolescents, college students, and adults for more than 30 years. The authors of this study mention that one of the main factors that plays a role in the comeback of certain illicit drugs after their popularity fades is "generational forgetting," which occurs when there is a decreased perceived risk of certain substances.[1]

Second, I would like to emphasize the importance that clinicians become aware of the increased production of alcoholic beverages, sold as energy drinks, with high caffeine content. These beverages are popular among teenagers and young adults, and their use has resulted in legal, ethical, and health concerns among this population.[2]

One beverage that recently received a lot of attention is "Four Loko," which contains the four ingredients alcohol (6–12% by volume), caffeine, taurine, and guarana, hence the name "Four Loko." The combination of the constituents, especially the mixture of alcohol and the caffeine, poses a serious health concern. The caffeine content of the alcoholic beverage counteracts the perceived depressing effect of the alcohol. When the caffeine effect wears off, the person then experiences the full effect of the alcohol. The delayed perceived effect of drunkenness has been shown to lead to increased consumption of alcohol before the caffeine effects wear off.[2] This public health concern led the United States Food and Drug Administration (FDA) to issue warnings to the manufacturer, which subsequently led to the removal of the caffeine from the beverage by the manufacturing company.

I would also like to remind clinicians of the substance gamma hydroxybutyric acid (GHB), known on the streets as "liquid ecstasy." GHB is usually consumed as an alcohol beverage and its use is often seen in teenagers and young adults. GHB has several adverse effects of which the more serious are seizures, loss of consciousness, and respiratory depression, leading to death in some cases. GHB has been classified by the United States Drug

Enforcement Agency (DEA) as a "predatory drug," along with rohypnol and ketamine, and has been implicated in sexual assault cases. Like rohypnol and ketamine, GHB causes significant memory impairment, and often victims who have consumed the substance have no recollection of the assault.[3]

Another drug of which clinicians should be aware is one that has been prevalent among teens and young adults over the last few years in the United States, and even longer in Europe—synthetic cannabis. this produce was initially marketed as a smokeable herbal product. In March 2011, five chemicals contained in synthetic cannabis were placed on emergency scheduling for the next 12 months and designated as Schedule 1 drugs by the DEA. Synthetic cannabis has similar effects as natural cannabis, hence the street name "fake pot." It is also known as "K2 " and "Spice." One very concerning property of the substance is that it lacks an antipsychotic chemical similar to cannabidiol, which is found in natural cannabis. As a result, synthetic cannabis has an increased risk of causing psychotic symptoms in comparison to natural cannabis.[4,5]

As recommended by Ali et al, a comprehensive multidisciplinary approach involving parents, educators, community leaders, government agencies, and physicians, particularly primary health physicians, would be required to adequately address illicit substance use in teens and young adults. The need for continued research in this field is necessary, but monitoring changing trends in drug use cannot be overemphasized.

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HISTORIES OF RAGES AND DISRUPTIVE BEHAVIORS IN THE MEDICAL SETTING

Dear Editor:

Aggressive patient behaviors may manifest in a number of different ways. However, beyond studies examining verbal and/or physical threats to clinicians, we did not locate any studies in the PsycINFO or PubMed databases that report general disruptive behaviors in the medical setting as they relate to patients' past histories of rage (either rage reactions or road rage)—the focus of the present study.

Participants included men and women at least 18 years of age who were being seen for nonemergent medical care at an internal medicine outpatient clinic, in a mid-sized mid-western United States city, that is staffed predominantly by residents. We excluded individuals with obviously compromising medical, intellectual, cognitive, or psychiatric symptoms that would preclude the candidate's ability to successfully complete a survey.

During clinic hours, one of the authors (S.F.) solicited patients in the lobby of the outpatient clinic, assessed exclusion criteria, and invited candidates to participate by completing a four-page questionnaire. Participants were informed on the cover page of the questionnaire that completion of the survey was implied consent to participate. We asked participants about demographic information, explored histories of rage reactions ("Have you ever had any rage reactions?") and road rage ("Have you ever had any road rages?"), and, using an author-developed questionnaire, asked about 17 disruptive behaviors related to the medical setting. As examples, with yes/no response options, participants were asked, "In dealing with medical personnel (office staff, assistants, nurses, doctors), either in an inpatient or outpatient medical (nonpsychiatric) setting, have you ever..." with items such as, "Yelled or screamed at medical personnel," "Cussed at medical personnel," "Verbally threatened medical

TABLE 1. Scores on the measure of disruptive behaviors in the medical setting as a function of history of rages (N=396)

QUESTIONS	NO		YES		F	*P*<
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION		
Ever had rage reactions?	0.94	1.33	2.08	2.22	42.56	0.001
Ever had road rages?	1.1	1.48	2.32	2.21	25.69	0.001

TABLE 2. Rates of endorsement of specific disruptive behaviors in the medical setting as a function of history of rages (rage reactions and/or road rages) (N=396)

DISRUPTIVE BEHAVIOR	HISTORY OF RAGES		Chi²
	NO %	YES %	
Yelled or screamed at medical personnel	2.2	10.6	12.82
Cussed at medical personnel	0.4	6.2	13.43
Stormed out of an appointment with medical personnel	1.2	11.5	21.87
Refused to talk to medical personnel	1.8	8.8	10.6
Talked negatively about medical personnel to your family	33.9	61.1	24.18
Talked negatively about medical personnel to your friends	31.4	61.1	29.34

Note: $p<0.001$ for all chi² values in the table

personnel," and, "Threatened to hit or strike medical personnel." The Disruptive Behaviors Survey as it appeared to respondents is located at www.MindingtheMind.com/disruptivebehaviors.pdf.

At the outset, 441 individuals were approached and 401 agreed to participate, for a participation rate of 90.9 percent. Of these, 396 completed at least one of the questions about rages and the Disruptive Behaviors Survey; 64.4 percent were women and participants ranged in age from 18 to 92 years (mean [M]=53.50, standard deviation [SD]=16.25). Most were White/Caucasian (89.4%), with 6.6 percent African-American, 1.5 percent Asian, 1.5 percent Hispanic, 0.5 percent Native American, 0.3 percent Other, and 0.3 percent undesignated. With regard to educational attainment, all but 7.6 percent had at least graduated from high school and 26.3 percent had earned at least a bachelor's degree.

Most respondents denied rage reactions (70.8%) or road rages (87.3%). Male subjects were somewhat more likely than female subjects (35.6% vs. 25.8%) to report rage reactions ($chi^2=4.05$, $p<0.05$), but not road rage (14.2% vs. 11.8%, $chi^2=0.46$, $p<0.50$). Possible scores on the Disruptive Behaviors Survey ranged from 0 to 17, but actual scores ranged from 0 to 11 (M=1.26, SD=1.63). There was not a statistically significant difference in score as a function of respondent sex [$F(1,394)=0.04$, $p<0.85$].

Scores on the Disruptive Behaviors Survey are presented in Table 1 as a function of history of rages. Note that those with histories of either rage reactions or road rage reported approximately twice the number of different disruptive behaviors in the medical setting.

We also examined whether endorsement of specific disruptive behaviors varied as a function of self-reported history of rages, either rage reactions or road rage. Of the 17 disruptive behaviors, two were not endorsed by any of the respondents. To adjust for the fact that we performed 15 separate analyses, we performed a Bonferroni correction on the effective probability value used for determining statistical significance within this set of analyses ($p<0.05/15=p<0.003$). There were statistically significant differences with regard to rates of endorsement of six of the 15 disruptive behaviors (Table 2).

Findings indicate that two forms of emotional volatility, rage

reactions and road rages, are statistically significantly associated with the number of different disruptive behaviors in the medical setting, with six specific behaviors evidencing statistical significance: yelling/screaming and cursing at medical personnel; refusing to talk with medical personnel and/or storming out of an appointment; and talking negatively about medical personnel to family and friends. In contrast to other items, these latter items suggest that volatile patients may have a "bark" but perhaps not much of a bite. In addition, volatility in one area of life functioning appears to carry over into other areas of life functioning.

This study has a number of potential limitations, including the self-report nature of all data, the vicissitudes of recollection, and the possibility that despite anonymity, some participants may have been too embarrassed to acknowledge particular behaviors. However, this is a novel study, and the sample was consecutive and reasonably large. Findings indicate that physicians need to be alert when dealing with patients with known histories of rage reactions or road rage—that very volatility demonstrated in the patient's personal life may spill into the medical setting in a number of aggressive ways.

With regards,

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