cause of space limitations, we were unable to include several key aspects of clinical care. As educators as well as clinicians, we consistently remind those who we teach about the importance of close communication with school personnel regarding the functioning of our patients, wherever they may be on the spectrum of risk to others. In hindsight, including content that stressed the importance of close communication between the clinician and school personnel could have strengthened our article. We agree that the use of a systematic assessment of violence risk is essential. However, it is our opinion that a reductionistic tendency of systems to rely on only one approach of risk assessment—as we have frequently seen in our own clinical practices—often does not lead to optimal placements for young, school-age patients.

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Genetic Markers Within Glutamate Receptors Associated With Antidepressant Treatment-Emergent Suicidal Ideation

TO THE EDITOR: Although treatment with antidepressants is associated with a significant reduction in suicides (1), some patients develop treatment-emergent suicidal ideation following treatment initiation (2), which has led to a black-box warning by the Food and Drug Administration. Recently, the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study sample demonstrated associations of genetic polymorphisms within kainate and alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA)-glutamate receptors GRIK2 and GRIA3 with treatment-emergent suicidal ideation (3). To replicate these findings, we investigated associations between treatment-emergent suicidal ideation and single nucleotide polymorphisms (SNPs) within these two genes in 397 depressed inpatients from the Munich Antidepressant Response Signature (MARS) project.

Suicidal ideation was rated by item 3 (suicide) on the Hamilton Depression Rating Scale (HAM-D) and assessed weekly until discharge, and treatment-emergent suicidal ideation was defined as the onset of suicidal ideation following admission (a score of 0 on item 3 of the HAM-D at admission). The nontreatment-emergent suicidal ideation comparison groups were 1) all individuals without an increase in suicidality, independent of baseline suicidality, and 2) a subgroup of these patients who had a score of 0 on item 3 of the HAM-D throughout treatment.

We genotyped 112 SNPs in GRIK2 and 17 SNPs in GRIA3 using Illumina 300k and 100K BeadChips. Permutation-based allelic and genotypic association tests were applied for SNPs in the GRIK2 gene, and only an allelic test was applied for SNPs in the GRIA3 gene (X chromosomal).

The biomarker rs4825476 within the GRIA3 gene, which was associated with treatment-emergent suicidal ideation in the STAR*D study, was significantly associated with treatment-emergent suicidal ideation in the Munich Antidepressant Response Signature study but with a different risk allele. In the STAR*D study, the SNP within GRIK2 (rs2518224) did not show significant associations in our study sample. However, 15 SNPs in this gene showed nominally significant associations. The genotype distribution of the three best SNPs in the GRIK2 gene and the most significant SNP in both gene GRIA3 and gene GRIK2 that were identified in the STAR*D study is detailed in the table in the data supplement accompanying the online version of this article. Overall, significance was stronger when comparisons were made with the smaller but more strictly defined nontreatment-emergent suicidal ideation group.

Although our results cannot be considered a direct replication of the findings in the STAR*D study, they nevertheless support the involvement of genes GRIA3 and GRIK2 in treatment-emergent suicidal ideation. Permutation-based p values make it less likely that our results were confounded by spurious associations. Within GRIK2, we observed several associations with SNPs, which spanned the gene with negligible linkage disequilibrium. Furthermore, the two best SNPs found in the GRIK2 gene ranked below the top 1,000 (on positions 525 and 693) when all 408,801 SNPs were tested. Finally, using a stricter definition for nontreatment-emergent suicidal ideation, we observed an increase in the strength of association, although power declined.

The divergences found between our study and the STAR*D study may be the result of a series of differences in factors such as study design, outpatient sample versus inpatient sample, citalopram treatment versus the physician's choice of treatment, and population structure. In addition, the rare risk genotype of rs2518224 (GRIK2), which was strongly associated with treatment-emergent suicidal ideation in the STAR*D study sample, was not present in our treatment-emergent suicidal ideation group. Thus, our sample was not sufficiently powered to detect this effect. However, because of the lack of a placebo group in both studies, treatment-emergent suicidal ideation cannot be directly attributed to antidepressant treatment.

Although preliminary, our study supports the theory that there is a relationship between treatment-emergent suicidal ideation and the glutamate system (4, 5). Further large-trial placebo controlled studies on this association are needed in order to establish genetic biomarkers for early identification of patients who are at risk for treatment-emergent suicidal ideation.

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Drs. Binder, Holsboer, Müller-Myhsok, and Uhr are the inventors of FKBP5, a novel target for antidepressant therapy (international publication number: WO 2005/054500) and polymorphisms in ABCB1 associated with a lack of clinical response to medicaments (international application number: PCT/EP2005/005194). Dr. Binder has received grant support from Pfizer and GlaxoSmithKline. Dr. Holsboer is a founder of and shareholder with Affectis. Dr. Müller-Myhsok has served as a consultant to Affectis. Drs. Menke, Lucae, Kloiber, Horstmann, Bettecken, Ripke, and Ising report no competing interests.

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Addictive Potential of Quetiapine

TO THE EDITOR: The feigning of symptoms in order to gain access to addictive substances is a veritable cliché in urgent care settings. However, malingering psychotic symptoms in order to secure antipsychotic medication is unusual and counterintuitive. The preclinical *sine qua non* of antipsychotic efficacy has been the ability of a compound to ablate or at least attenuate reward learning in animal models. These compounds are notoriously "dysphorogenic," devoid of abuse potential, and subjectively noxious to the degree that medication adherence is one of the preeminent challenges of treatment. The newer "atypical" antipsychotic compounds have generally improved on this subjective intolerability, which has led to the steadily expanding use of these compounds in nonpsychotic patient populations, targeting extrapsychotic symptom clusters such as anxiety, mood variability, and even pedestrian insomnia. We present a case report of an individual who demonstrated classic drug seeking behavior, compulsive drug use, and diversion for resale of the atypical antipsychotic compound quetiapine.

"Mr. A" was a 29-year-old divorced, unemployed, Caucasian man, with an unclear medical history, who presented himself as a walk-in to our acute psychiatric treatment unit with a medication refill request. He reported that he had been diagnosed with schizophrenia (for which he was being treated with quetiapine [600 mg nightly]) and the local police were disturbing his sleep by "electronically monitoring" his testicles. He received his "usual" dose of quetiapine and then slept soundly. On examination the following morning, Mr. A had become cagey about the details of his somatic preoccupation and, although still somnolent, he lacked evidence for either a thought or mood disturbance. His urine toxicology screen was negative. The profundity of his sedation prompted a pharmacy review, which revealed that he had been receiving different and excessive amounts of quetiapine from several sources during the past few months. Upon confrontation, he admitted to both the excessive use and sale ($3.00 per 100 mg tablet) of quetiapine.

Quetiapine has come to dominate the atypical antipsychotic market, primarily through its use in the technically "off label" circumstances described previously. The modestly sedating toxic profile and perceived absence of abuse liability of the drug have prompted many clinicians to use it in place of traditional benzodiazepines for anxiety and insomnia. There is currently an accumulating body of anecdotal evidence (1–3) regarding the type of patient described in our case report, which questions both the accuracy of perceptions about the use of quetiapine and the wisdom of treatment practices. If the current misuse of the compound continues or expands, then the abuse "signal" will predictably become more evident and could ultimately prompt federal regulators to declare quetiapine a controlled substance. Should such an unfortunate eventuality come to pass, we will be able to confidently lay the blame at the feet of our collective prescriptive imprudence.

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Delirium Associated With Lamotrigine and Fluoxetine Treatment

TO THE EDITOR: The anticonvulsant lamotrigine has been increasingly utilized as a mood stabilizer after receiving approval by the Food and Drug Administration for the treatment of bipolar I disorder. Although there have been relatively few reports of toxicity, we report a case of delirium with lamotrigine use, which highlights the importance of cautious dose increase and attention to potential drug interactions.

"Ms. A" was a 35-year-old married, employed, Caucasian woman who had been treated for depression with fluoxetine (40 mg) over the past 5 years. She had no history of confusion, psychosis, or suicidality. Two months prior to admission to our intensive care unit, her psychiatrist added lamotrigine to her medication regimen to treat a mood instability characterized as a bipolar spectrum disorder, although she did not have bipolar I disorder. Her lamotrigine had been increased from 200 mg to 400 mg