sion began earlier in childhood, he was becoming progressively more dangerous in his community because of his increasing size and the increasingly frequent and indiscriminate nature of his assaultive behavior. Previously, numerous medications were prescribed for Alex, including stimulants, selective serotonin reuptake inhibitors, tricyclic antidepressants, buspirone, and secretin. Of note, Alex had never received any antipsychotic medications.

Risperidone was begun at 0.5 mg/day in our clinic and was increased gradually because of ongoing episodes of aggression and impulsivity. Alex's dose eventually reached 3 mg/day after 16 months of treatment. Shortly thereafter, Alex's behavior improved dramatically, with decreased aggression, less hyperactivity, improved language functioning, and increased sociability.

By the 23rd month of treatment, Alex began to develop a "jerking" of his trunk and abdomen. He and his mother reported that he was moving and writhing his shoulders and trunk throughout the day. Upon examination, Alex had periodic choreic movements of his shoulders and trunk. No oral, lingual, or buccal movements were seen or reported. A neurological examination revealed no other abnormalities. Trials of anticholinergic agents and vitamin E proved to be of little to no benefit. When risperidone was reduced to 2 mg/day, Alex's behavior deteriorated dramatically, so his dose was returned to 3 mg/day. Subsequently, Alex also experienced dyskinetic movements in the oculomotor muscles.

After numerous discussions with Alex and his parents about the risks and benefits of risperidone, Alex continues to take risperidone at 3 mg/day, along with benztropine, 2 mg b.i.d., and a vitamin E supplement. He continues to benefit behaviorally from the drug regimen.

This report presents the emergence of tardive dyskinesia secondary to risperidone in an individual with autism who had previously been naive to antipsychotics. This case demonstrates the effectiveness of risperidone in treating the disruptive behaviors of autism. The use of atypical antipsychotics to ameliorate the maladaptive behaviors associated with autism is likely to increase, given the absence of treatments that robustly address its core symptoms. The case points to the need for a careful discussion of the potential risks and benefits of risperidone, the identification of specific target symptoms, and education regarding the time course of treatment. The risk of tardive dyskinesia should be discussed explicitly. There should also be thorough discussions about pharmacological and nonpharmacological interventions that may need to be exhausted before considering the use of antipsychotic medications.

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Can Interpersonal Loss Precipitate Panic Disorder?

TO THE EDITOR: A central aspect of the DSM-IV diagnosis of panic disorder is that the symptoms appear to come "out of the blue." Nonetheless, there is a substantial literature documenting psychosocial stressors precipitating panic disorder (for example, references 1 and 2) and, specifically, anxiety disorders in bereavement (3). No investigator to date, to our knowledge, has examined the frequency of events involving interpersonal loss (through death or relationship disruption) that immediately preceded the onset of panic disorder.

We examined the frequency of interpersonal loss events immediately preceding the onset of panic disorder (within 6 weeks) in two groups of patients with panic disorder, both of whom participated in the evaluation of efficacy of panic-focused psychodynamic psychotherapy at Weill Medical College of Cornell University (4).

We examined the onset of panic in 51 patients, 21 of whom had participated in an open trial of panic-focused psychodynamic psychotherapy (5) and 30 of whom had been treated in an ongoing randomized, controlled clinical trial, as rated on the Anxiety Disorders Interview Schedule for DSM-IV: Lifetime Version (6). All patients met DSM-IV criteria for panic disorder with or without agoraphobia.

Twenty-four (47%) of our patients experienced an onset of panic disorder within 6 weeks after a significant interpersonal loss. Without a control group, it is not clear whether a similar rate of interpersonal loss would be found for patients in other diagnostic groups.

Panic disorder has heretofore not been conceptualized in the psychiatric literature as an outcome of loss or a form of complicated bereavement. It will be important to determine whether other groups of panic patients experience panic onset after loss with the same high frequency. It remains to be determined whether the history of interpersonal loss in panic onset may function to moderate the outcome of specific treatment interventions (7).

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Sertraline and the Cheshire Cat in Geriatric Depression

TO THE EDITOR: The study by Lon S. Schneider, M.D., and associates (1) on the treatment of geriatric depression with sertraline does not rank among the glories of clinical research. It does raise questions about corporate influence and Orwellian "newspeak" in reporting clinical trials.

The study is remarkable first for its size, determined a priori by a power analysis. The aim was to achieve power sufficient to detect a mean difference of 2 points in change scores on the 17-item Hamilton Depression Rating Scale. With a projected pooled standard deviation of 8 points, this difference would represent an effect size of only 0.25. Based on past trials, a group of 700 patients was deemed necessary. The group finally enrolled numbered 747, a stunning instance of excess to answer the straightforward question of whether sertraline is superior to placebo, especially considering the low bar that the drug was asked to clear. The study has all the hallmarks of an "experimercial," a cost-is-no-object exercise driven by a corporate sponsor to create positive publicity for its product in a market niche.

The authors concluded that sertraline is superior to placebo. The difference in mean Hamilton depression scale change score in the key intent-to-treat group was 0.8 points, less than half the stated goal. This clinically trivial difference achieved statistical significance by virtue of the gargantuan group size and because the pooled variance was less than the authors had assumed in the preliminary power analysis. "Statistically significant" differences on other dimensional primary outcome measures were likewise clinically trivial. Somewhat more encouraging data were obtained for the "completer" group, but with 131 fewer patients, that group was not representative of the drug's performance in clinical settings. Completer data are no longer accepted as evidence of efficacy.

In the intent-to-treat group, the authors further reported a "statistically significant" advantage for sertraline in a categorical measure of response, defined as a 50% reduction of Hamilton depression scale score (35% response rate for sertraline and 26% for placebo). This difference is also clinically trivial. It translates to a number needed to treat of 11. This means that clinicians would have to use sertraline 11 times to obtain one response that would not have occurred anyway with placebo (2). In an earlier time, when antidepressant drugs first were developed, the drug-placebo difference in response rates averaged 30%–35% (3, 4), based on a number needed to treat of about three. Clearly, as reflected in this trial and elsewhere, there has been much "dumbing down" of expectations for antidepressant efficacy in recent years.

And where, by the way, are the data on remission? There is currently wide agreement that remission is the optimal indicator of antidepressant efficacy (5). The authors withheld remission data. When challenged, they will doubtless use the procedural rationalization that remission was not specified a priori as an outcome measure. The question must be, why not? By this fig leaf they conceal clinically relevant data that would probably reflect poorly on the putative efficacy of sertraline. This technique allows the authors to present their results with the best "spin." Thus does the corporate mandate to put lipstick on the pig prevail over the academic duty to communicate independent analyses of the data (6–8). The *Journal* is complicit in this scientific failure.

The authors also failed to emphasize in the abstract (where most readers would notice it) that none of the functional or quality-of-life outcome measures favored sertraline over placebo. Something has changed in our conceptual paradigm when a drug can be described as "effective" for depression, but the patients do not confirm that their lives are any better with respect to vitality, social functioning, emotional role functioning, or mental health. Like the Cheshire cat's smile, the only evidence that sertraline was there is the disembodied p value, grinning in statistical space, with no connection to clinical reality. That is not quite what Percy Bridgman had in mind when he introduced operationalism in science. Lewis Carroll, on the other hand, would have appreciated the irony.

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Dr. Schneider and Colleagues Reply

TO THE EDITOR: Dr. Carroll's essential complaint seems to be that there was no reason to perform this trial but to "create positive publicity" for "niche" marketing. He elaborates with sarcasm and hyperbole that 1) statistical significance was achieved as a product of an excessively large group size; 2) the