country yielded similar results. As a follow-up, in a subsample reassessed 2 months later (109 individuals who provided their e-mail addresses), similar analyses examining predictors of posttraumatic stress symptoms (5) revealed a significant effect of Internet viewing that was mediated by peritraumatic reaction.

Limitations of this study include the convenience sample, the lack of an assessment of disruptive nocturnal behavior and posttraumatic stress symptoms before the event, an expectedly low level of symptoms, and the possible response bias. However, the results suggest that Internet coverage of a distant disaster may induce sleep disturbances and subclinical psychological symptoms of posttraumatic stress in the general population. Such effects, consistent with previous reports (6, 7) of posttraumatic stress disorder symptoms after trauma exposure, were mediated by peritraumatic reactions.

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## Conceptual Issues in Psychiatric Gene-Environment Interaction Research

TO THE EDITOR: In their critical review of candidate gene-by-environment (cG×E) interaction research, published in the October 2011 issue of the *Journal*, Duncan and Keller (1) raise several methodological issues that cast serious doubt on many published G×E findings. While informative in many respects, their virtually exclusive methodological perspective does not address an important conceptual issue that has emerged in recent years concerning cG×E interaction: putative risk alleles often operate as plasticity alleles (2). Duncan and Keller appear to maintain the tradition of viewing all G×E inquiry from a diathesis-stress perspective, which stipulates that individuals carrying risk alleles will be more likely to develop psychopathology in the face of adversity relative to individuals without risk alleles under the same conditions. However, as it turns out, ever more cG×E findings appear consistent with an alternative—and more evolutionarily plausible—conceptual framework: differential susceptibility. According to this theory, some individuals are, for genetic reasons, more responsive to both negative and positive environmental influences (3).

This theory raises the possibility that one reason cG×E findings often do not replicate is the misconceptualization of candidate genes as risk genes. If individuals carrying certain plasticity alleles are disproportionately susceptible to a wide range of developmental experiences and contextual exposures, not just adverse ones, then the failure to include propitious factors in cG×E research could increase false negative findings. Consider in this regard Kilpatrick and colleagues' study (4) of the role of the serotonin-transporter-linked polymorphic region (5-HTTLPR) in moderating the effect of hurricane exposure on posttraumatic stress disorder (PTSD). Had the investigators not been in a position to detect the disproportionate benefit that those hurricane-exposed individuals with short—putative "risk"—alleles accrued from high social support, then it seems likely that their G×E study would also have yielded null results. And this is because, as it turned out, it was only those especially susceptible to positive and negative environmental influences (i.e., short allele carriers) but exposed only to the latter—hurricane and low social support—who proved especially likely to develop PTSD.

Given that samples will usually vary in both environmental risk exposure and availability of protective resources and that candidate genes may be associated with elevated susceptibility to both, the failure to explicitly measure and include positive supportive aspects of the environment in cG×E studies may be one important reason why G×E findings fail to replicate. These practices, we contend, derive from the embracing of vulnerability-only rather than plasticity models.

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## Response to Pluess and Belsky Letter

TO THE EDITOR: We appreciate the opportunity to respond to Pluess and Belsky's interesting letter. We would like to make three main points. First, in contrast to Pluess and Belsky's contention, we do not view G×E inquiry exclusively from a diathesis-stress (as opposed to plasticity) perspective. Rather, in writing a review, the focus is necessarily on published studies, and the diathesis-stress perspective has been the dominant one in the candidate G×E (cG×E) literature. Second, we believe it unlikely that "one reason cG×E findings often do not replicate is the misconceptualization of candidate genes as risk genes." Such misconceptualizations would affect novel investigations and direct replication attempts in an identical manner, so that could not be a reason for the numerous failures to replicate cG×E findings. Third, Pluess and Belsky argue that including both risk and protective variables can lead to the correct identification of higher-order (e.g., three-way) interactions. We agree that this is theoretically possible. However, given that the central problems that were raised in our review—low power and likely high false discovery rate—are likely to be exacerbated in tests of higher-order interactions, we would urge caution before accepting novel reports of such findings. As argued in our original article, well-powered, direct replication attempts are crucial for understanding the legitimacy of novel candidate polymorphism findings. In a field with a poor record of subsequent empirical support for novel findings, such direct replications should be viewed as at least as scientifically important as the novel findings themselves.

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### Corrections

In the article "A Nationwide Cohort Study of Oral and Depot Antipsychotics After First Hospitalization for Schizophrenia," by Jari Tiihonen et al. (Am J Psychiatry 2011; 168:603–609), in the first sentence of the second paragraph of the Results section, the mean follow-up period of 2 years (5,221 person-years) reflects the potential time frame for discontinuation of medication. However, the actual mean follow-up time in the analysis of all-cause discontinuation was 0.5 years, and the number of person-years was 809, since follow-up for any given patient stopped after discontinuation of medication. The actual numbers of person-years for each antipsychotic are listed in Figure S1 in the online data supplement.

In the article "Treatment of Suicide Attempters With Bipolar Disorder: A Randomized Clinical Trial Comparing Lithium and Valproate in the Prevention of Suicidal Behavior," by Maria A. Oquendo et al. (Am J Psychiatry 2011; 168:1050–1056), in the Intervention subsection of the Method section, the units for the target blood level range for lithium were incorrectly reported. The correct range is 0.6–1.0 mEq/liter.