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Correspondence

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Letter to the Editor

Context dependency of major depression

A recent paper (Kendler *et al*. 2010) in the Journal sought to determine whether the diagnosis of major depression (MD) can be made independent of the psychosocial context in which it occurs. The authors argue that if MD following severe life events represents an understandable or non-pathological depressive reaction, those afflicted should be characterized by a reduced frequency of exposure to known MD liability factors such as family history, history of sexual abuse, neuroticism, etc. This prediction is described as arising from a 'context-dependent' theory of aetiology which is juxtaposed in the paper against a 'context-independent' theory. In the paper, the context-dependent hypothesis is rejected because a comparable frequency of liability factors is observed in depressed respondents across a range of adversity levels. The paper examines an important aspect of context dependency; the possibility that depressive reactions following psychosocial adversity may be misclassified as MD because diagnostic criteria are fulfilled when there is actually not an occurrence of 'real' MD. This hypothesis is rejected in the paper. However, this conceptualization of the role of psychosocial adversity as a potential cause of false-positive diagnostic ratings does not fully incorporate the potential importance of psychosocial context to the diagnosis of MD.

One view of MD aetiology is that the condition is characterized by an exaggerated reactivity to environmental stressors resulting from genetic or epigenetic influences or longstanding effects of stressful events during psychological development. This view of MD aetiology suggests that afflicted persons will more often respond to minor life events as if those were more severe events. However, it does not necessarily follow that the frequency of exposure to liability factors would be lower in persons with MD triggered by more pronounced adversity. An exaggerated reactivity to minor life events may manifest as a multiplicative interaction between liability factors and stressful life events on MD risk (Kendler *et al*. 1995). In a multiplicative scenario, the relative risk associated with the combined exposure equals the product of the individual relative risks, suggesting that liability factors magnify the effects of life events. If liability factors and stressful life events are distributed independently in the population the frequency of exposure to the liability factors in depressed respondents will depend on the frequency of those factors in the population and on their relative risks, but these frequencies are not expected to differ between MD cases exposed or not exposed to stressful life events.

Many arguments can be made in support of Kendler *et al*.'s position that the diagnosis of MD should be context-independent, e.g. the advantages of empirical diagnostic definitions in remaining free from theory-laden clinical judgements. Furthermore, a role for psychosocial context in the aetiology of MD does not necessarily convey sufficient clinical utility to warrant its inclusion in diagnostic criteria, especially since some of the data presented in this paper indicate that it may not have strong predictive value for prognosis. However, the data presented in the paper are consistent with a multiplicative risk model, a model that implies important context dependency of MD.

Declaration of Interest

Dr Patten is a Senior Health Scholar with Alberta Innovates, Health Solutions. He has received consulting fees from Servier Canada.

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PROFESSOR SCOTT B. PATTEN
Department of Community Health Sciences, University of Calgary, 3rd Floor TRW, 3280 Hospital Drive NW, Calgary, Canada T2N 4Z6
(Email: patten@ucalgary.ca)

The authors reply

I would like to thank Dr Patten for his interest in our article and his thoughtful and informed comments. Short letters like these are not always the best format in which to discuss the methodologic subtleties he

raises but I will try to respond to his central concern. Stressful life events (SLEs) have been convincingly shown to have a strong main effect on risk for major depression (MD) (e.g. Brown & Harris, 1978; Kendler *et al*. 1998). Good evidence has also suggested that those at high genetic risk for MD are more sensitive to the depressogenic effects of SLEs – what Dr Patten refers to correctly as a multiplicative model (Kendler *et al*. 1993, 2004). However, at least in our sample, these interactions are typically fan-shaped, so at every level of adversity, those at higher risk to MD have a greater chance of developing MD than those at lower risk, and at every level of genetic risk, those exposed to adversity have higher rates of MD than those not exposed (Kendler *et al*. 1993, 2004). Given this pattern of findings, I would defend the basic prediction of this paper. That is, we predicted that if a context-dependent theory of MD is correct, subjects with MD selected for recent exposures to high levels of adversity should, on average, have lower levels of liability factors than subjects with MD selected for exposure to no or minimal levels of stress. I do not deny that some cases might fit the pattern suggested by Dr Patten – individuals with high levels of liability who react to minor adversity to develop a MD. Similarly, some individuals would have quite high levels of liability and the association of the onset of MD with adversity could be a largely chance phenomenon. But, we would argue that such cases should be the exception. Given the kinds of effects we have seen for stress and MD (strong main effects with a fan-shaped interaction), I would still argue that the 'stress-induced' cases would have to be over-represented in our high stress group (LTCT = 3 or 4) and under-represented in our low stress group (LTCT levels 0 an 1). If these stress-induced cases were just average people – with no predisposition to disorder – we should see that reflected in our liability indicators. We see little evidence for this hypothesis.

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KENNETH S. KENDLER, M.D.
Virginia Institute of Psychiatric and Behavioral Genetics, and Departments of Psychiatry, and Human and Molecular Genetics, Virginia Commonwealth University School of Medicine, Richmond, VA, USA
(Email: kendler@vcu.edu)

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