Toward specifying the nature of the relationship between expressed emotion and schizophrenic relapse: the utility of curvilinear models

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Abstract
Although expressed emotion (EE) has been demonstrated to be associated with the course of schizophrenia, the nature of this relationship is unclear. This study proposes that testing for curvilinear relationships can identify the specific nature of the relationships between EE indices and relapse. The utility of curvilinear models was explored through a reanalysis of data from a prior study of EE among Mexican-Americans (Karno et al., 1987). The results suggest that the relationship between the EE index of emotional overinvolvement (EOI) and relapse is curvilinear and that high levels of EOI may exert a toxic effect on course of illness whereas medium levels of EOI may be protective. The relationship between the EE index of warmth and relapse is also curvilinear and high levels of warmth appear to exert a protective effect on the course of illness. The role of culture is explored in explaining the specific manner in which EE relates to relapse among Mexican-Americans. Copyright © 2006 John Wiley & Sons, Ltd.

Key words: expressed emotion, schizophrenia, curvilinear models, Mexican-Americans

It is clear from past research that family factors may influence the course of schizophrenia. For instance, numerous studies have found that expressed emotion (EE) is associated with the occurrence of future schizophrenic relapses (Butzlaff and Hooley, 1998). More specifically, these studies have revealed that individuals with schizophrenia who return to familial environments characterized by high levels of criticism, emotional overinvolvement (EOI), or hostility are more likely to experience a relapse than individuals who return to familial environments in which the presence of these variables is low. The success of this line of research has not only led EE to become one of the most studied psychosocial constructs in psychiatric research (Jenkins and Karno, 1992), but has also influenced the development of several treatment programs for schizophrenia (for example, Leff et al., 1982; Falloon et al., 1985; Hogarty et al., 1986; McFarlane, 2002).

In contrast to past studies, which have emphasized an examination of the global construct of EE (families are considered either high or low in expressed emotion), recent studies have demonstrated the utility of
exploring the relationship between individual EE indices and relapse (for example, Bertrand et al., 1992; Ivancović et al., 1994; King and Dixon, 1999; Marom et al., 2002). In particular, examining the relationships between individual EE indices and relapse has been especially useful in revealing how socio-cultural factors may influence the recovery process from schizophrenia. For example, López et al. (2004) found that family warmth, one of the original EE indices that is oftentimes overlooked, is negatively related to relapse for Mexican-Americans, whereas there is no significant relationship between warmth and clinical outcome among Caucasians. López et al. suggested that low levels of warmth might be associated with an increased risk of schizophrenic relapse for Mexican-Americans in that close family ties are highly valued among this largely Spanish-speaking and immigrant group of families.

An additional consideration in exploring the relationship between EE indices and schizophrenic relapse is the nature of these relationships. Although many studies of expressed emotion have emphasized the toxicity of high levels of negative family factors (such as EOI), it is equally plausible that exposure to caregivers who display low levels of a given negative family factor may exert a protective effect on the course of schizophrenia (Teague et al., 1989). For example, several studies have demonstrated that exposure to relatives who display low levels of criticism, hostility, and EOI is associated with decreased autonomic arousal among individuals with schizophrenia (Tarrier et al., 1979; Sturgeon et al., 1981). As increased autonomic activity has been hypothesized to play a critical role in triggering a schizophrenic relapse (Nuechterlein and Dawson, 1984), these results suggest that exposure to caregivers who display low levels of certain family factors can exert a protective effect on the course of schizophrenia. A similar uncertainty exists with regard to the relationship between positive family factors and relapse. For example, it is unclear whether the negative relationship between warmth and relapse among Mexican-Americans stems from the protectiveness of high levels of familial warmth, the toxicity of low levels of familial warmth, or both.

Consideration of the statistical models underlying tests of the association between EE indices and relapse may help discern the specific nature of the relationship between specific family factors and outcome. In particular, testing for the existence of curvilinear relationships may provide information with regard to the specific nature of a given family factor-outcome relationship (see Cortina, 1993 and Ganzach, 1997 for other applications of curvilinear statistical models).

Curvilinear models offer unique insight into the nature of statistical associations in that they can identify ranges within these associations in which strong modulation may occur. More specifically, linear models treat every one-unit change in the independent variable as associated with an equal change in the dependent variable. (Although logistic statistical models are not linear, this ‘assumption of linearity’ is still present in logistic regression. More specifically, we make interpretations of logistic models based on the logit of the predicted probabilities for these models. By default, these logits are linear. However, curvilinear forms of these logits can be constructed.) For example, a linear model would indicate that increases from 1 to 2 critical comments and 5 to 6 critical comments would be associated with equal increases in an individual’s risk of relapse. Analysis of curvilinear relationships allows researchers to examine whether certain levels of an EE index may exert a greater influence on the occurrence of a relapse than others. For instance, using the previous hypothetical example of criticism, a curvilinear model may allow a researcher to see that there is little change in the risk of relapse between one unit changes in the 0–5 range of critical comments, whereas there is a dramatic and ever-increasing rise in the risk of relapse beginning when one moves from 5 to 6 critical comments and continuing to the high end of the distribution of critical comments. If the risk of relapse associated with criticism scores of 0–5 respectively were consistent with the typical course of illness (the average risk of relapse in general), this pattern of modulation in the relationship between criticism and relapse would suggest that the presence of high levels of criticism is toxic, whereas the presence of low levels of criticism exerts relatively little influence over the course of illness. Of course the opposite pattern is also possible, suggesting that lower levels of criticism are protective and that high levels of criticism exert little influence over the course of illness. These two hypothetical relationships are depicted in Figure 1 along with the typical linear model used to describe the relationship between critical comments and relapse.

Thus, the overall objective of the current study is to explore the utility of curvilinear statistical models in discerning the specific nature of the relationship
between a given family factor and the course of schizophrenia. In particular, we tested for the existence of curvilinear relationships between three EE indices (emotional overinvolvement, warmth, and critical comments) and relapse among Mexican-Americans. Although EOI has been shown to be predictive of relapse (King and Dixon, 1999), to date studies of EE among Mexican-Americans have not evaluated the specific role of emotional overinvolvement in shaping the course of schizophrenia. Past research has indicated that warmth is predictive of relapse among Mexican-Americans (López et al., 2004). The index of critical comments has often appeared to play the predominant role in the EE-relapse association (Kavanagh, 1992).

We did not carry out analyses with the two EE indices of hostility and positive remarks. Hostility overlaps greatly with criticism and is actually an unordered categorical measure. To date we know of no evidence that the index of positive remarks is associated with outcome in schizophrenia. (In fact, there was not a statistically significant relationship between positive remarks and relapse in this sample: $\beta = -0.16$; 95% confidence interval; $\beta: -0.43 \sim -0.08$; exact p = 0.21.)

Finally, we discuss the theoretical implications of our findings with regard to our understanding of how cultural factors may influence the relationships between specific family factors and the course of schizophrenia among Mexican-Americans.

**Figure 1.** Examples of potential relationships between critical comments and relapse.
Method

Participants

The data analysed in this study were originally collected as part of a prior study of EE (Karno et al., 1987). Participants in this study were 44 Mexican-American individuals with schizophrenia, recruited from several inpatient facilities in southern California, and their respective key relative. The initial diagnosis of schizophrenia was based on reports of symptomatology elicited through the Present State Examination (PSE) (Wing et al., 1974). These reports were then compared to the DSM-III (American Psychiatric Association, 1980) criteria for schizophrenia to determine if a diagnosis of schizophrenia was warranted. The PSE has been shown to have high levels of interrater reliability at the item, syndrome, and diagnostic level (Wing et al., 1967; Kendell et al., 1968; Cooper et al., 1972).

Measures

Expressed emotion

Key relatives’ scores for the EE indices of EOI, warmth and critical comments were assessed through the Camberwell Family Interview (CFI) (Brown and Rutter, 1966) immediately upon their admission to the study. The CFI is a 1–2-hour semistructured interview that assesses key relatives’ experience of caring for and interacting with their ill relative over the past 3 months. This measure is considered to be the ‘gold standard’ for assessing EE (Van Humbeeck et al., 2002).

Given that the definition of EOI may vary across cultures (Jenkins and Karno, 1992), in the collection of data for the Karno et al. (1987) study, scores for EOI were adjusted in order to be congruent with the expression of EOI among Mexican-Americans. Descriptions of this adjustment can be found in Jenkins (1992).

In cases in which two key relatives were interviewed for one individual with schizophrenia, only one relative was included in the analysis. If one relative was high in EE (six or more critical comments, a score of 4 to 5 on EOI, or any amount of hostility) and the other was low in EE, the high EE relative was selected for analysis. If both relatives had a similar EE status (both relatives were high in EE or both relatives were low in EE), one relative was randomly selected for inclusion in the analyses.

Assessment of schizophrenic relapse

Participants were tracked for nine months following their admission to the study to assess if a relapse had occurred. Information from monthly contacts with key relatives was also used to consider whether a symptomatic exacerbation had taken place. If there was any indication that an exacerbation had occurred, the PSE, Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962) and Psychiatric Assessment Scale (PAS) (Krawiecka et al., 1977) were administered to the individual with schizophrenia. The PSE was used to elicit symptomatology and the PAS and BPRS were used to obtain a continuous measure of psychotic symptomatology. Independent raters placed participants into one of three categories based on their scores on the PSE, PAS and BPRS as well as information gathered from monthly telephone calls and participants’ medical records (relapse, no relapse, non-remitting symptoms). Participants in the non-remitting symptoms category were excluded from the analyses as it was difficult to assess whether a change occurred in their symptoms over the course of the study. All clinical coders established adequate levels of interrater reliability with pre-existing ratings of training interviews at both the item and diagnostic levels and were blind to the EE status of an ill individual’s key relative (Pearson correlations > 0.80). There were 17 participants in the relapse category and 27 participants in the no relapse category.

Statistical analyses

In order to investigate the nature of relationship between EOI and relapse, we tested for the existence of curvilinear relationships. First, linear models were fitted to the data using an exact logistic regression to determine whether there was a relationship between a specific EE index and relapse. Linear models were specifically used in this identification task in that they can identify the existence of a meaningful relationship even when the relationship is not linear (Hosmer and Lemeshow, 2000). If this analysis suggested that there was a meaningful relationship between an index and relapse, the nature of this relationship was explored by testing whether this relationship may be curvilinear. To test for curvilinear relationships, we first visually inspected the risk of relapse across different levels of a specific EE index to assess whether a specific curvilinear model (for example quadratic or cubic) may fit the data. Then, the particular curvilinear model was tested. If the curvilinear model was then found to be a statis-
cally significant predictor of relapse, it was compared to a linear model with regard to their respective accuracy in predicting relapse. If the curvilinear model was found to better describe the relationship between an individual index and relapse than the linear model, inferences could be made regarding the nature of the relationship based on the shape of the curve. In each of these analyses, exact logistic regressions were conducted, as opposed to asymptotic logistic regressions, due to the small sample size.

To evaluate how the risk of relapse at individual values of EOI, warmth, and critical comments may differ from the typical course of schizophrenia, the average risk of relapse while participating in an EE study was computed based on the results of 25 past studies of EE described by Butzlaff and Hooley (1998). This statistic was calculated by dividing the total number of participants who experienced a relapse by the total number of participants enrolled in these studies (38.35%). Although data from the Karno et al. (1987) study were reported by Butzlaff and Hooley, these data were not included in this calculation. If the previous analyses indicate that there was a meaningful relationship between a specific EE index and relapse, the risk of relapse at different levels of the specific index was compared to the average risk of relapse in past EE studies.

**Results**

*Emotional overinvolvement and relapse*

The possibility of a linear or curvilinear relationship between the numerical EOI variable and relapse was first assessed. Sample sizes for each respective EOI score are listed in Table 1. To determine what specific type of relationship (if any) may exist between EOI and relapse, the percentage of participants who suffered a relapse at each respective EOI score was graphed (Figure 2). When interpreting this plot, note that only one case was present at EOI = 5 and at EOI = 0; thus, the corresponding points should not be overinterpreted visually.

There was a near statistically significant linear relationship between EOI and relapse ($\beta = 0.58$; 95% confidence interval; $\beta$: $-0.07 - 1.30$; exact $p = 0.08$). However, the shape of the line in Figure 2 suggests that the relationship between EOI and relapse may be curved and may better be modelled by a quadratic curve. Thus, a new quadratic EOI variable was created by centring EOI scores and then squaring them. Centring the data involves subtracting the mean EOI score for all participants from each individual EOI score. This process helps to avoid the calculation of misleading regression coefficients and reduces multicollinearity (Kraemer and Blasey, 2004). Additionally, prior to squaring the centred linear EOI data, 0.61 was subtracted from each data point in order to facilitate computation by statistical software. When this new centred quadratic EOI term was entered into a logistic regression along with the centred linear EOI term, the centred quadratic term was found to be a statistically significant predictor of relapse ($\beta = 0.59$; 95% confidence interval; $\beta$: $0.02 - 1.30$; exact $p = 0.04$), and the centred linear EOI term remained a statistically significant predictor of relapse ($\beta = 1.19$; 95% confidence interval; $\beta$: $0.18 - 2.54$; exact $p = 0.01$). The quadratic model ($y = a + bx + cx^2$) accurately differentiated between participants who suffered a relapse and those who did not (exact likelihood ratio = 9.57; exact $p = 0.01$).

A goodness-of-fit test comparing the respective log likelihood for each exact model found that the quadratic

### Table 1. Sample sizes for respective EOI, warmth, and critical comments scores

<table>
<thead>
<tr>
<th>EOI</th>
<th>Number of participants</th>
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<tbody>
<tr>
<td>0</td>
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<tr>
<td>1</td>
<td>6</td>
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<tr>
<td>2</td>
<td>21</td>
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<td>4</td>
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<td>5</td>
<td>1</td>
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<table>
<thead>
<tr>
<th>Warmth</th>
<th>Number of participants</th>
</tr>
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<tbody>
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<td>0</td>
</tr>
<tr>
<td>1</td>
<td>4</td>
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<tr>
<td>2</td>
<td>10</td>
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<td>4</td>
<td>5</td>
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<td>5</td>
<td>12</td>
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<table>
<thead>
<tr>
<th>Critical comments</th>
<th>Number of participants</th>
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<td>0–2</td>
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<td>9–11</td>
<td>2</td>
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<td>12–14</td>
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model was superior to the linear model \((y = a + bx)\) in predicting relapse \(\chi^2 (1, N = 44) = 5.86, p = 0.02\). The percentage of participants suffering a relapse predicted by this quadratic model is displayed in Figure 2 along with percentages predicted by the linear model and the actual percentages of participants suffering a relapse. As shown in this figure, the quadratic model was the more accurate predictor of relapse at five of the six respective EOI scores. Given the previously noted warning about interpreting the model at EOI \(= 0\) and EOI \(= 5\), the relationship between EOI and relapse is modelled by a J-shaped curve (the risk of relapse is lowest at medium levels of EOI and increases at an increasing rate at the high end of the distribution). For all cases, the standardized residuals ranged from \(-1.90\) to 1.85, and scores for an analogue of Cook’s D ranged from \(<0.01\) to 0.49. (Standardized residuals and the analogue for Cook’s D were calculated based on the predictions of a maximum likelihood logistic regression using maximum likelihood.) This indicates that there were no outliers in the data set, nor were the regression coefficients overly influenced by any individual datum point (Hosmer and Lemeshow, 2000; Tabachnick and Fidell, 2001).

Using the F-test alternative for Fisher’s exact test derived by Overall and Starbuck (1983), there was a near significant difference between the risk of relapse at EOI \(= 4\) (71.40%) and the average risk of relapse in past EE studies \((F (6, 10) = 2.67; p = 0.08)\). The risk of relapse at EOI \(= 2\) (19%) was significantly lower than the average risk of relapse in past EE studies \((F (10, 34) = 2.10; p = 0.05)\). There was no difference between the risk of relapse at all other values of EOI and the average risk of relapse in past EE studies (all \(p\)-values = ns).

**Warmth**

The relationship between warmth and relapse was evaluated. The percentage of participants suffering a relapse at individual levels of warmth is described in Figure 3. The sample size for each level of warmth is listed in Table 1. (One participant in the Karno et al. (1987) study was not rated on warmth. Thus, for this subsection, there were only 43 participants.)

There was a statistically significant linear relationship between warmth and relapse \((\beta = -0.77; 95\% \text{ confidence interval}; \beta: -1.41 - -0.22; \text{exact } p < 0.01)\). However, Figure 3 suggests that this relationship may be best described by a curvilinear model in which the risk of relapse decreases at an increasing rate as warmth increases. Thus, a quadratic warmth term was created by centring the warmth scores and then squaring them. When both variables were entered into an exact logistic regression, scores for an analogue of Cook’s D ranged from \(<0.01\) to 0.74, and the standardized residuals ranged from \(-1.20\) to 3.09. (Standardized residuals and the analogue for Cook’s D were calculated based on the predictions of a maximum likelihood logistic regression using maximum likelihood.) As standardized residuals of 3.09 or greater may be considered outliers (Hosmer and Lemeshow, 2000), the data were reanalysed excluding this one datum point. For this reanalysis, a new quadratic warmth term was created by centring the

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**Figure 2.** Actual versus predicted percentages of participants suffering a relapse at different levels of EOI.
warmth scores (excluding the one outlier) and squaring them. Prior to squaring the centred linear warmth data, 0.74 was subtracted from each data point to facilitate computation by statistical software. There was a statistically significant linear relationship between warmth and relapse ($\beta = -0.75$; 95% confidence interval; $\beta: -1.45 - -0.17$; exact $p < 0.01$). When both the linear and quadratic variables were entered into a logistic regression, the quadratic term was not a statistically significant predictor of relapse ($\beta = -0.44$; 95% confidence interval; $\beta: -1.14 - 0.09$; exact $p = 0.12$), whereas the linear term remained a statistically significant predictor of relapse ($\beta = -1.76$; 95% confidence interval; $\beta: -4.13 - -0.28$; exact $p < 0.01$). The quadratic model ($y = a + bx + cx^2$) accurately differentiated between those participants who suffered a relapse and those who did not (exact likelihood ratio = 12.02; exact $p < 0.01$). A comparison of the respective log likelihood for each exact model suggests that the quadratic model is a superior predictor of relapse than the linear model ($y = a + bx$) ($\chi^2 (1, N = 42) = 3.47, p = .06$). The percentage of participants suffering a relapse predicted by this quadratic model is displayed in Figure 3 along with percentages predicted by the linear model and the actual percentages of participants suffering a relapse. As shown in this figure, the quadratic model was the more accurate predictor of relapse at three of the five respective warmth scores. The shape of the quadratic model suggests that the relationship between warmth and relapse is modelled by a J-shaped curve (there is relatively little modulation in the risk of relapse in the low range of warmth scores, whereas the risk of relapse decreases at an increasing rate at the high end of the distribution).

Using the $F$-test derived by Overall and Starbuck (1983), the risk of relapse at warmth = 5 (8.30%) was found to be significantly lower than the average risk of relapse in past EE studies ($F (4, 22) = 3.40; p = .03$). There was no difference between the risk of relapse at all other values of warmth and the average risk of relapse in past EE studies (all $p$-values = ns).

Critical comments

The relationship between critical comments and relapse was investigated. The percentage of participants suffering a relapse at individual levels of critical comments is described in Figure 4. The sample size for each level of critical comments is listed in Table 1.
There was no statistically significant relationship between critical comments and relapse ($\beta = 0.09; 95\%$ confidence interval; $\beta: -0.10 - 0.30; \text{exact } p = 0.37$). Likewise, no curvilinear relationship between critical comments and relapse is apparent in Figure 4. A quadratic model ($y = a + bx + cx^2$) was evaluated as this model could uncover either the toxic or protective relationship described in Figure 1. A quadratic critical comments variable was created by centring the linear critical comments variable and squaring it. Prior to squaring the centred linear critical comments data, 0.16 was subtracted from each data point in order to facilitate computation by statistical software. When both variables were entered into a logistic regression, neither the linear ($\beta = 0.18; 95\%$ confidence interval; $\beta: -0.07-0.46; \text{exact } p = 0.18$) nor the quadratic term ($\beta = -0.03; 95\%$ confidence interval; $\beta: -0.09-0.02; \text{exact } p = 0.21$) was found to be a statistically significant predictor of relapse. Likewise, the quadratic model ($y = a + bx + cx^2$) did not accurately differentiate between participants who suffered a relapse and participants who did not ($\text{exact likelihood ratio} = 2.75; \text{exact } p = 0.30$).

Discussion

The present results indicate that testing for curvilinear relationships between specific EE indices and schizophrenic relapse can help us to understand better the specific nature of how individual family factors are related to the course of schizophrenia. With regard to emotional overinvolvement, the pattern of results suggests that the high end of emotional overinvolvement may be toxic in that changes within this range are associated with the greatest relative increase in the risk of relapse. This is consistent with past interpretations of findings regarding the influence of emotional overinvolvement on the course of schizophrenia. What are novel in the present study are the findings that both a medium level of emotional overinvolvement and a high level of warmth are associated with a lower likelihood of relapse than what has been observed in past EE-schizophrenia studies. Our analyses, unlike those using chi-square or linear models of logistic regression, point out that both aspects of families (medium EOI and high family warmth) are likely to be protective against future relapse. There is no evidence suggesting that specific ranges of critical comment scores may exert a protective or toxic effect on the course of schizophrenia.

Learning that, for Mexican-Americans, high levels of emotional overinvolvement are toxic and high levels of warmth and medium levels of EOI are protective provides additional information with regard to our theoretical understanding of how sociocultural factors influence the course of schizophrenia for Mexican-Americans. Together, these findings demonstrate that family connections are most important. This is consistent with evidence noted by López et al. (2004) that Mexican-American family members spend considerably more time with their ill relatives in a given week than Caucasians, and other research pointing out the collectivistic or interdependent functioning of some Mexican-American families (for example Rauff et al., 2000). The results regarding the toxicity of high levels of emotional overinvolvement, however, suggest that maintaining one’s sense of autonomy or independence may also be an important factor in recovery from schizophrenia for Mexican-Americans. Thus, it may be that for this largely immigrant Mexican-American sample, there is an ongoing tension between close family ties and high EOI, whereby increases in family ties are helpful only up to the point that they violate the boundaries of one’s self (Jenkins, 1992). Although interdependence may be valued (and beneficial), too much interdependence can be problematic (Jenkins, 1992). The implication for family treatment concerns how to help caregivers maintain that fine balance between caring for their loved ones without becoming overinvolved in the recovery process. This family dynamic is different than the emphasis present in existing family treatments to reduce family negativity (see, for example, Falloon et al., 1985).

The findings obtained through this study may also explain an apparent paradox noted by López et al. (2004) with regard to the relationship between EE and the course of schizophrenia for Mexican-Americans. While the global measure of EE (high EE versus low EE) predicts relapse for Mexican-Americans (Karno et al., 1987; Kopelowicz et al., 2006), the EE index of criticism by itself does not (Kopelowicz et al., 2002; López et al., 2004). This is noteworthy in that the index of criticism has often been thought to play the predominant role in the EE-relapse association (Kavanagh, 1992). The results of the current study suggest that the relationship between EE and relapse for Mexican-Americans may largely be a function of the toxicity of high levels of EOI. In fact, when the curvilinear EOI model ($y = a + bx + cx^2$) is entered into a logistic regression with the global measure of EE, the quadratic EOI term remains a near statistically signifi-
cant predictor of relapse ($\beta = -0.51; 95\%$ confidence interval; $\beta: -0.05 - 1.22; exact p = 0.08$) whereas the global measure of EE ($\beta = 0.71; 95\%$ confidence interval; $\beta: -1.15 - 2.53; exact p = 0.59$) and the linear EOI term ($\beta = 0.93; 95\%$ confidence interval; $\beta: -0.18 - 2.38; exact p = 0.13$) are not statistically significant predictors of relapse.

It is important to note that this study suffered from several limitations, most notably, a small sample size. Consequently, we were limited in our ability to draw conclusions from certain ranges of data. For example, despite the fact that Figure 2 would suggest that low levels of EOI may be toxic, we cannot safely make this inference due to the fact that there was only one caregiving relative who received a score of 0 on EOI. Had the ill individual associated with this caregiving relative not suffered a relapse, Figure 2 would look very different. As such, further investigation of the generalizability of our findings is needed. Future studies applying this methodology to larger samples would be able to address this.

Altogether, the findings raise questions about the assumptions contained within past statistical models used to test the relationship between expressed emotion and relapse. This study also suggests that through the application of curvilinear models, researchers may be able to investigate the specific nature of the relationship between EE indices and schizophrenic relapse. By specifying the particular way in which a given family factor and relapse are related (toxic, protective, or both), we can shed further light on the family mechanisms associated with the course of illness (Jenkins and Karno, 1992). A greater understanding of such mechanisms has the potential to inform the development and improvement of family interventions for schizophrenia.

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