Causal model of insight and psychopathology based on the PANSS factors: 1-year cross-sectional and longitudinal revalidation

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This study presents results of a 1-year follow-up investigation of the causal model of insight in schizophrenia using a subsample of acute patients starting or switching to amisulpride included in an earlier study. Our causal model of insight based on the Positive and Negative Syndrome Scale factors, with the positive, negative, and autistic preoccupation factors designated as the primary predictors, and the activation factor as a mediating variable of insight, was examined for fitness at the stabilized stage (8 week) and at the chronic stage (1 year) using the structural equation modeling method. Results showed that the intercorrelations among the factors and regression coefficients toward insight changed in their magnitudes, but the validity of our hypothesized model of insight was still confirmed for both the stages with nearly perfect goodness-of-fitness indices. The fitness of the model was also confirmed for the longitudinal changes in the scores of insight and psychopathology. An alternative model, which included the anxiety/depressive factor as a second mediating variable between insight and the positive and negative factors, was also found to be valid for both the stages. A post-hoc causal model with anxiety/depressive factor showed tentative evidence favoring anxiety/depressive variable predicting insight than the other way around. *Int Clin Psychopharmacol* **24:189–198** © **2009 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Introduction

As 'insight' is an easily understood term in everyday common usage, research on insight in schizophrenia patients has favored a trend toward increasing complexity, both on the conceptual and methodological levels. For example, simple categorical approaches to insight based on the definition of 'presence of awareness' of impairment of intellectual functioning (Eskey, 1958) or emotional illness (Van Putten *et al.*, 1976) have largely been overshadowed by the conceptualization of insight as being continuous (McEvoy *et al.*, 1989) and multidimensional (Davis, 1990; Amador *et al.*, 1991, 1993; Mintz *et al.*, 2003). This may be because simple approaches have not yielded consistent results, especially in terms of the relationship between insight and psychopathology. In our earlier study (Hwang *et al.*, 2009), we suggested that such inconsistencies may be because of unrefined symptom categorization, such as the positive, negative, and general psychopathology subscales of the Positive and Negative Syndrome Scale (PANSS), and the lack of consideration for the complex interplay among the various symptom dimensions unaccountable by simple linear approaches, such as correlation and regression methods.

The utility of multidimensional approaches, such as the structural equation modeling (SEM) method, in depicting the complex interplay among the number of related variables and drawing causal links to insight has been shown in studies relating insight to paranoia, depression, and self-esteem (Drake *et al.*, 2004) and also to patient role perception and attitude toward treatment (Hayashi *et al.*, 2001). Nonetheless, SEM has never been applied to elucidate the possible multilevel causal relationship between specific symptom domains and insight. Accordingly, in our earlier study (Hwang *et al.*, 2009), we applied this method to construct and examine the fitness of a causal model of insight based on the five factors of the PANSS in acute-stage patients. Our model with the three primary 'upstream' predictors, that is, positive, negative, and autistic preoccupation factors (Dollfus and Petit, 1995; White *et al.*, 1997), and a 'downstream' mediating variable, that is, activation factor, showed near-perfect fitness superior to other alternative models. Specifically, we found activation factor to play the role of a partial mediator for positive and as a moderator for autistic preoccupation factor. In addition, the model that included anxiety/depressive as another 'downstream'

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mediating variable also had comparably superior fitness as a whole, but did not contribute to any substantial predictive power toward insight.

However, whether such a relationship between psychopathology and insight, as described by our model, is temporally stable is still in question. Studies have not only shown that symptoms vary in their temporal stability (Peralta and Cuesta, 2001; Ventura *et al.*, 2004), but also that the associations among them may undergo changes (Lançon *et al.*, 2001). Indeed, Peralta and Cuesta's (2001) comment that 'temporal relationship among symptoms, primary versus secondary distinction, and the confounding effects of the presence of certain symptoms over others, have not been sufficiently studied (p.280)' is still largely valid to date.

As the temporal stability of the relationship between insight and specific symptoms of schizophrenia has never been examined using the SEM, we sought to confirm our causal model of insight using the 1-year longitudinal data obtained from a subsample of acute patients starting or switching to amisulpride included in our earlier study. We hypothesized that the direction of their predictive relationships toward insight is likely to remain stable over time through different stages of illness, that is, 8-week acute stabilized stage and 1-year chronic stage, in spite of the plausible changes in the severity of, and relative associations among, the symptoms. The predicted changes in relative associations based on the findings of earlier longitudinal studies were as follows: first, the magnitude of correlations among the three primary predictive symptoms were hypothesized to remain stable or increase with time (Kulhara and Chandiramani, 1990; Mojtabai, 1999; Peralta *et al.*, 2001); second, in relation to insight, these primary symptoms in general would likely have similar or increased levels of predictive power toward insight, as significant correlations between mainly positive and negative factors and insight have been reported earlier (Mintz *et al.*, 2004); and third, the strength of associations between positive and anxiety/depressive factors should be increased (Emsley *et al.*, 1999). As for activation factor, we hypothesized that it would still serve as a mediator between the primary predictive factors and insight, but it was difficult to stipulate to what extent it may serve so because of lack of relevant empirical findings.

In addition, our model of insight not only allowed for the examination of the cross-sectional relationship between insight and psychopathology, but also of their longitudinal changes. Earlier studies have found longitudinal improvement in insight to be associated with decreased severity of some symptom domains (e.g. Smith *et al.*, 1997; Mintz *et al.*, 2004; Gharabawi *et al.*, 2006) or overall psychopathology (Weiler *et al.*, 2000) without a clear consensus on improvement in which symptoms would predict better insight. Such inconsistencies of results could be attributed to differences in samples and measures. In particular, some of these studies share the problem common to cross-sectional studies by failing to utilize more refined factor measures. Hence, in our study, our model was also applied to examine whether it could be used to delineate the longitudinal changes in insight in relation to the changes in psychopathology.

Finally, we also acknowledged the possibility that a significant causal relationship between anxiety/depression and insight may emerge (Smith *et al.*, 1998; Drake *et al.*, 2004; Lincoln *et al.*, 2007), which was not evidenced in baseline acute patients of our earlier study. If this is the case, it would allow us to conduct a post-hoc analysis to test the hypothesis that better insight predicts more severe anxiety and depression symptoms (Drake *et al.*, 2004; Karow and Pajonk, 2006) by the comparison of the models.

Methods

Patients

The individuals included in this follow-up study were 134 patients (64 male and 70 female) who participated in a 12-month, multicenter, open-label clinical trial of amisulpride treatment (Ahn *et al.*, 2009), which was one of the three studies included in our original study. These patients met the *Diagnostic and Statistical Manual of Mental Disorders* (fourth edition) criteria of either schizophrenia or schizophreniform disorder and were scheduled to start or switch to amisulpride from other antipsychotics because of the emergence of new or aggravated psychotic symptoms. All participants completed a written informed consent before enrollment to the study; the study was approved by the ethics committee of all the participating sites.

Data analysis

The purpose of this study was to examine whether the validity of our causal model of insight could be confirmed longitudinally. Accordingly, the five factors of the PANSS derived from the earlier study were applied directly to the models for the 8-week and 1-year cross-sectional data. As for the examination of how changes in psychopathology influence insight, changes in scores of the five factors and G12 between the follow-ups were obtained and analyzed for correlation to ascertain the usefulness of applying our model. Factor extraction and the rationales for the construction of our causal model of insight were detailed in our earlier study (Hwang *et al.*, 2009).

Our model includes positive, negative, and autistic preoccupation factors as the primary predictors of insight (G12) and activation factor as a mediator for the positive factor and a moderator for autistic preoccupation factor.

The same alternative models used in the earlier study with significant intercorrelations among the primary predictors of insight were applied to this study: (i) positive, negative, autistic preoccupation, and activation factors, all assigned as the main predictors of insight without any mediating variables; (ii) only positive, negative, and autistic preoccupation factors as the main predictors of insight without any mediating variables; (iii) positive, negative, and autistic preoccupation factors as the main predictors with activation (between positive and autistic preoccupation factors and insight) and anxiety/depressive factors (between positive, negative, and autistic preoccupation factors and insight) as two mediators; and finally (iv) positive, negative, and autistic preoccupation factors as the main predictors with anxiety/depressive as the only mediator.

The best-fit model was determined by the goodness-of-fit indices applied in the earlier study, which were derived from the maximum likelihood estimations. Such indices included nonsignificant χ^2 statistic, adjusted goodness-of-fit index (AGFI), comparative fit index (CFI), Tucker–Lewis Index (TLI), and the Root Mean Square Error of Approximation (RMSEA). The detailed descriptions of these indices are presented in the earlier study (Hwang *et al.*, 2009).

AMOS 5.0 (Amos Development Corporation, Spring House, Pennsylvania, USA) was used for performing SEM, and the SPSS 10.0 statistical package (SPSS Inc., Chicago, Illinois, USA) was used for all other analyses. A significance level of 0.05 was applied to all analyses.

Results

Demographic variables

At the baseline, 134 patients participated in a study to examine the efficacy and safety of starting or switching to amisulpride from earlier antipsychic medication. There were 64 male and 70 female patients with the mean age of 33.94 ± 9.29 years and the mean onset age of 26.16 ± 8.55 years. Their mean total PANSS score was 80.93 ± 17.39. This group of patients did not differ significantly from the other two groups included in our original study (Hwang *et al.*, 2009) in demographic variables, such as age, education, and sex distribution and clinical variables, such as age at onset and duration of illness.

At week 8, there were 35 cases lost to follow-up and the mean total PANSS score was 60.11 ± 15.71 for the remaining 99 patients (male = 47, female = 52). At 1-year follow-up, 70 patients (male = 34, female = 36) remained in the study with a mean total PANSS score of 55.43 ± 15.51. The demographic variables, such as sex distribution, age, and age at onset, were not significantly different between the completers and noncompleters. For both the follow-ups, age and dosage were not significantly related to G12 or the severity of the symptoms as measured by the PANSS total score and its subscales. Only age of onset was found to be significantly correlated with the positive subscale of the PANSS for both 8-week ($r = -0.254$, $P = 0.013$) and 1-year follow-ups ($r = -0.315$, $P = 0.009$), but it was not associated with insight. Finally, we also examined the fitness of our hypothesized model at baseline based on the sample of patients who failed to complete 1-year follow-up. As a result, our model was found to have an acceptable level of fitness ($\chi^2 = 1.575$, d.f. = 1, $P = 0.209$; AGFI = 0.853; CFI = 0.992; TLI = 0.916; RMSEA = 0.096, LO = 0.000, HI = 0.365) for this subgroup of patients as well.

Comparison of the good-of-fitness indices of the structural equation models of insight with 8-week and 1-year cross-sectional data

Presented in Table 1 are the goodness-of-fit indices of our hypothesized model of insight and the alternative models. Our hypothesized model indicated nearly perfect fit at the 8-week follow-up as indicated by the goodness-of-fit indices. Other models did not satisfy most criteria for goodness-of-fit, such as χ^2, AGFI, and RMSEA, except for the Alternative model 3, which showed superior indices of fitness comparable with our hypothesized model. For the 1-year follow-up, consistent with 8-week results, our hypothesized model satisfied all goodness-of-fit indices and this was also true for the Alternative model 3. All other models failed to satisfy almost all goodness-of-fit indices.

Construction of the structural equation models of insight with 8-week and 1-year cross-sectional

Presented in Fig. 1 are the constructed structural equation models of our hypothesized model and the Alternative model 3 for 8-week and 1-year follow-ups. The PANSS factors and Lack of Insight (G12) are connected with unidirectional (causal relationships) or bidirectional (correlation) paths. For the 8-week follow-up, the pattern and the degrees of intercorrelations among the PANSS factors were quite similar to those of the pooled data at the baseline (Hwang *et al.*, 2009). However, the amount of variance of G12 explained by our hypothesized model increased from 0.19 at the baseline to 0.34. Activation was found to play a partial mediating role for both positive and autistic preoccupation factors, as their standardized regression coefficient decreased from 0.23 to 0.14 and 0.24 to 0.16, respectively, when it was introduced as a mediator. In the Alternative model 3, anxiety/depressive factor presented a negative standardized coefficient toward the G12 and its inclusion into the hypothesized model had an effect of slightly increasing the positive standardized coefficients of the positive and negative factors. In essence, anxiety/depressive factor played a moderating role for the three primary symptoms, whereby increased level of anxiety

Table 1 Goodness-of-fit indices for the hypothesized model and the alternative models

Model	χ^2	d.f.	*P* value	AGFI	CFI	TLI	RMSEA	RMSEA LO	RMSEA HI
8 week									
Hypothesized model	**0.124**	**1**	**0.725**	**0.992**	**1.000**	**1.071**	**0.000**	**0.000**	**0.190**
Alternative model									
1[a,b]	0.000	0	0.000	0.363	1.000	0.000	0.354	0.302	0.409
2[a,c]	0.000	0	0.000	0.412	1.000	0.000	0.370	0.303	0.441
3[d]	**0.472**	**2**	**0.790**	**0.983**	**1.000**	**1.076**	**0.000**	**0.000**	**0.128**
4[a,e]	0.000	0	0.000	0.410	1.000	0.000	0.332	0.280	0.387
1 year									
Hypothesized model	**0.659**	**1**	**0.417**	**0.943**	**1.000**	**1.031**	**0.000**	**0.000**	**0.295**
Alternative model									
1[a,b]	0.000	0	0.000	0.293	1.000	0.000	0.400	0.337	0.465
2[a,c]	0.000	0	0.000	0.345	1.000	0.000	0.417	0.337	0.502
3[d]	**1.033**	**2**	**0.597**	**0.948**	**1.000**	**1.043**	**0.000**	**0.000**	**0.197**
4[a,e]	0.000	0	0.000	0.239	1.000	0.000	0.434	0.372	0.500

Indices of the models with superior fitness are set in 'bold'.
ACT, activation factor; A/D, anxiety/depressive factor; AGFI, adjusted goodness-of-fit index; AUT, autistic preoccupation factor; CFI, comparative fit index; NEG, negative factor; POS, positive factor; RMSEA, Root Mean Square Error of Approximation; RMSEA LO/RMSEA HI, low and high limits of the confidence interval for RMSEA; TLI, Tucker–Lewis Index.
[a]AGFI, TLI, and RMSEA values reported here are for independence model.
[b]POS, NEG, AUT, and ACT assigned as the main predictors of G12 without any mediating variables.
[c]Only POS, NEG, and AUT assigned as the main predictors of G12 without any mediating variables.
[d]POS, NEG, and AUT assigned as the main predictors with ACT (between POS and AUT factors and G12) and A/D (between POS, NEG, and AUT and G12) as two mediators.
[e]POS, NEG, and AUT assigned as the main predictors with A/D as the only mediator.

and depression caused by aggravation of symptoms would have an effect of decreasing lack of insight, or simply improving insight. However, as a whole, the addition of anxiety/depressive factor into our hypothesized model (i.e. the Alternative model 3) resulted in a mere 0.01 increase in the total variance of the G12 explained.

As for the 1-year follow-up, the pattern of intercorrelations between the PANSS factors were similar to that of the 8-week follow-up, but the magnitude of correlations among the factors increased, especially between autistic preoccupation and negative factors. Other changes over time were also evident in our hypothesized model, as the amount of variance of activation factor explained by autistic preoccupation and the positive factors somewhat increased. The weight of prediction from each of the primary predictive symptoms also changed from the 8-week follow-up. Specifically, autistic preoccupation factor now had little unique predictable power for G12 when activation factor was introduced, whereas the standardized regression coefficient of positive factor toward G12 dropped from 0.37 to 0.27. Hence, activation factor now played the role of a full mediator for autistic preoccupation factor and a partial mediator for positive factor. With the introduction of anxiety/depressive factor into the model (the Alternative model 3), the most notable difference from the 8-week follow-up was the increase in R^2 value of anxiety/depressive factor from 0.27 to 0.59 accounted by the three primary 'upstream' factors. In other words, the overall severity of the three primary symptoms accounted for more than half of anxiety and depression symptoms by the end of 1 year and the moderating role of anxiety/depressive factor was still maintained. Interestingly, the amount of variances of G12 explained by the models remained unchanged from that of the 8-week follow-up.

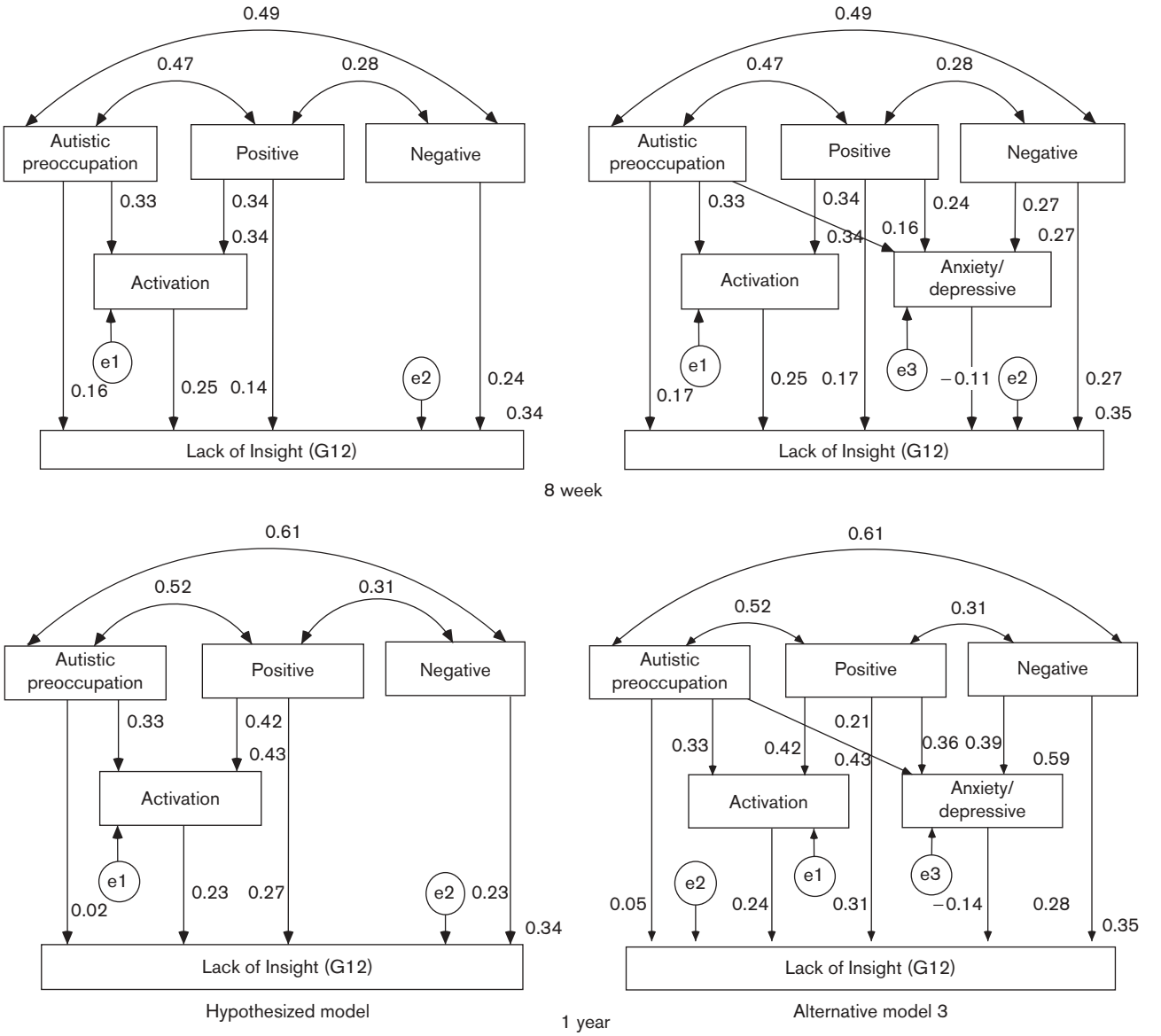
Relationship between longitudinal changes in psychopathology and insight

Presented in Table 2 is the result of correlation analysis for the changes in G12 and the PANSS factor scores during the stabilizing period (baseline to 8 weeks) and chronic period (8 weeks to 1 year). For the stabilizing period, improvement in all the five factors was significantly correlated with increased insight, but for the chronic period, improvement in negative factor only proved to be significantly correlated. Hence, we tested our hypothesized model and the alternative models of insight directly on the changes in scores during the stabilizing period only. As a result, both our hypothesized model ($\chi^2 = 0.178$, d.f. = 1, $P = 0.673$; AGFI = 0.989; CFI = 1.000; TLI = 1.058; RMSEA = 0.000, LO = 0.000, HI = 0.201) and the Alternative model 3 ($\chi^2 = 2.056$, d.f. = 2, $P = 0.358$; AGFI = 0.928; CFI = 1.000; TLI = 0.998; RMSEA = 0.017, LO = 0.000, HI = 0.202) were found to have superior fit. What was noteworthy, however, was that improvement in the primary symptoms of positive and negative factors strongly predicted improvement in insight, with only anxiety/depressive factor marginally serving as a mediator (Fig. 2).

The post-hoc causal model of anxiety/depression in relation to insight

The validity of the Alternative model 3 that includes anxiety/depressive factor as a predictor of insight at

Fig. 1



Constructed structural equation models for 8-week and 1-year follow-ups. The values associated with bidirectional arrows are correlation coefficients. The values associated with unidirectional arrows are standardized regression coefficients. The values at the corner of activation, anxiety/depressive, and Lack of Insight (G12) are R^2 values. 'e' denotes error variances.

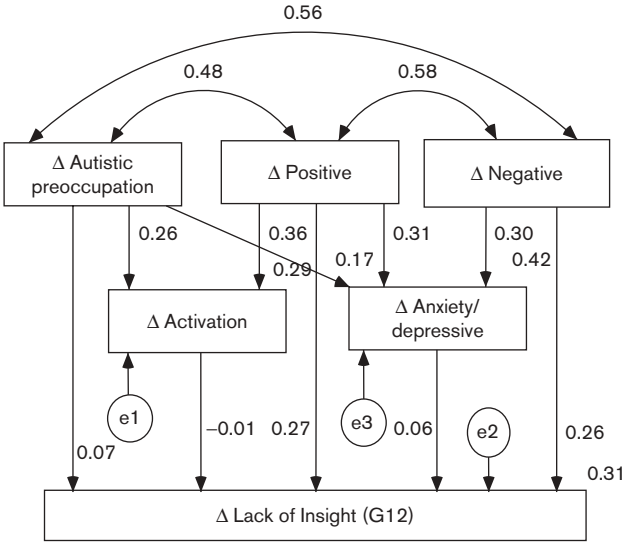
8-week and 1-year follow-ups allowed us to conduct a post-hoc analysis to examine the hypothesis that insight predicts symptoms of anxiety and depression. This was achieved by modifying the Alternative model 3 by designating anxiety/depressive factor as the dependent variable below G12 (Fig. 3). The post-hoc causal model of anxiety/depression satisfied all of goodness-of-fit indices for both 8-week ($\chi^2 = 0.871$, d.f. = 2, $P = 0.435$; AGFI = 0.969; CFI = 1.000; TLI = 1.056; RMSEA = 0.000, LO = 0.000, HI = 0.175) and 1-year ($\chi^2 = 1.287$, d.f. = 2, $P = 0.526$; AGFI = 0.936; CFI = 1.000; TLI = 1.032; RMSEA = 0.000, LO = 0.000, HI = 0.210) follow-ups. For the 8-week follow-up, the R^2 value of anxiety/depressive factor accounted by four predictors was 0.28, with the G12 yielding a standardized regression coefficient of −0.10. In comparison with the Alternative model 3 at 8-week follow-up, it can be noted that the R^2 value of anxiety/depressive factor increased only by 0.01. For the 1-year follow-up, the proportion of variance of anxiety/depressive factor accounted by four predictors was identical to that of the Alternative model 3, but the size of the standardized regression coefficient of G12 toward anxiety/depressive factor diminished to −0.07.

Table 2 Correlations between the changes in G12 and five PANSS factor scores for baseline to 8-week stabilizing period and 8-week to 1-year chronic period

	Stabilizing phase ($n=99$)		Chronic phase ($n=69$)	
	r	*P* value	*r*	*P* value
NEG	0.489	0.000	0.338	0.005
ACT	0.268	0.007	0.087	0.478
POS	0.489	0.000	0.192	0.117
AUT	0.374	0.000	0.044	0.722
A/D	0.393	0.000	−0.115	0.350

ACT, activation factor; A/D, anxiety/depressive; AUT, autistic preoccupation factor; NEG, negative factor; PANSS, Positive and Negative Syndrome Scale; POS, positive factor.

Fig. 2



Constructed structural equation model of the Alternative model 3 for changes (Δ) in insight and psychopathology during the stabilizing phase (baseline to 8 week). The values associated with bidirectional arrows are correlation coefficients. The values associated with unidirectional arrows are standardized regression coefficients. The values at the corner of Δ activation, Δ anxiety/depressive, and Δ Lack of Insight (G12) are R^2 values. 'e' denotes error variances.

In addition, we applied a post-hoc model to the changes in scores of insight and the five factors from baseline to 8-week follow-up (i.e. stabilizing phase) only. The model had a high level of fitness ($\chi^2 = 2.063$, d.f. = 2, $P = 0.357$; AGFI = 0.928; CFI = 1.000; TLI = 0.998; RMSEA = 0.018, LO = 0.000, HI = 0.202), but the regression coefficient from G12 to anxiety/depressive factor was 0.05, which was hardly different from 0.06 of its reverse.

Discussion

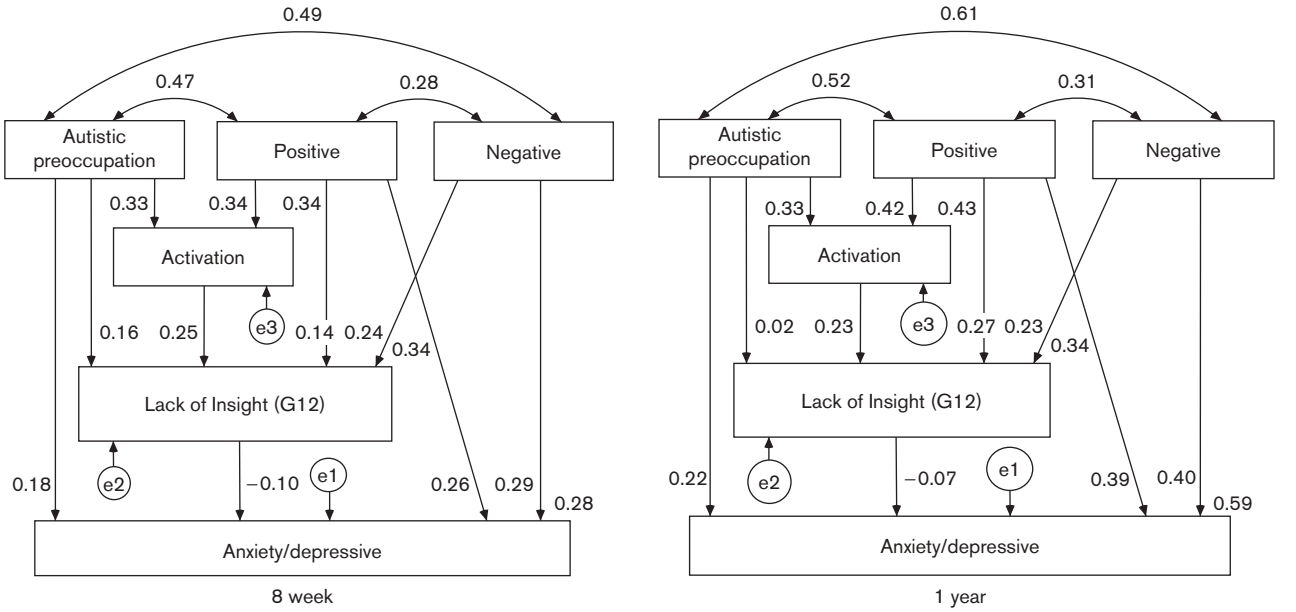
The results of this study further confirmed the validity of our causal model of insight initially constructed at baseline with the data from a pooled sample of acute schizophrenia patients. Despite the temporal changes in the magnitude of associations among symptoms and their respective predictive strength, our causal model of insight has proven to reliably capture the dynamics between psychopathology and insight in schizophrenia patients at both the stabilized (8-week) and chronic (1-year) stages. Hence, the overall results generally followed the directions of our initial hypotheses, but not without some exceptions that warranted further discussion.

Temporal changes in cross-sectional causal relationships between psychopathology and insight

As predicted, the magnitude of intercorrelations among the three primary predictive symptoms generally showed stability from the baseline to 8 weeks and then increased by 1-year follow-up. The most pronounced increase was the correlation between negative and autistic preoccupation factors, which was consistent with a body of research that closely links chronicity of negative symptoms with cognitive deterioration in schizophrenia patients. We had also predicted that the primary symptoms would show temporally stable or increasing predictive power toward insight. Accordingly, after controlling for activation factor, the standardized regression coefficient of negative factor toward G12 increased from 0.17 at the baseline to 0.27 at the 8-week follow-up and remained stable until 1-year follow-up. That of positive factor remained stable until the 8-week follow-up (0.16 at the baseline and 0.14 at the 8-week follow-up) and then increased by 1-year follow-up (0.27). Such results were in support of the earlier 1-year long-term studies (Mintz *et al.*, 2004; Gharabawi *et al.*, 2006) that found association between improvement in insight and severity of psychopathology. In contrast, however, standardized regression coefficient of autistic preoccupation factor toward G12 showed a pattern of gradual decline. This trend was not hypothesized initially, but was consistent with the positive short-term relationship found between disorganization factor and insight in patients with acute-stage or inpatient status (Smith *et al.*, 1998; Weiler *et al.*, 2000), and little or no long-term longitudinal association found between insight and cognitive functioning in chronic patients (David *et al.*, 1995; Cuesta *et al.*, 2006; Saeedi *et al.*, 2007). In contrast, a recent report by Monteiro *et al.* (2008) found awareness of symptoms to be significantly associated with disorganization factor, but not with neuropsychological tests, in chronic patients, hence future research should focus on identifying which aspects of cognitive functioning specifically relates to insight.

The mediating role of activation factor toward G12 has proven to be stable over time in our study for both autistic preoccupation and positive factors. Poor attention ($r = 0.339$, $P = 0.001$) and mannerism and posturing ($r = 0.298$, $P = 0.003$) items of autistic preoccupation factor were significantly correlated with G12 but not with activation factor at the 8-week follow-up. By 1-year follow-up, those items were no longer significantly correlated with G12 but with activation factor ($r = 0.245$, $P = 0.043$ for poor attention and $r = 0.382$, $P = 0.003$ for mannerism and posturing). Hence, poor

Fig. 3



Post-hoc structural equation models of anxiety/depression at 8-week and 1-year follow-ups. The values associated with bidirectional arrows are correlation coefficients. The values associated with unidirectional arrows are standardized regression coefficients. The values at the corner of activation, anxiety/depressive, and Lack of Insight (G12) are R^2 values. 'e' denotes error variances.

attention and inappropriate mannerism at the stabilized stage may have been evaluated by the raters as indicating residual cognitive impairment which, in part, adversely affected the ratings of insight, whereas in the chronic stage these same symptoms may have been interpreted as signs of psychomotor arousal related to activation symptoms. In case of positive factor, the introduction of activation factor as a mediating variable caused its standardized regression coefficient toward G12 to decrease for both 8-week and 1-year follow-ups. This result showed that the presence of psychotic symptoms not only contributed directly toward impaired insight, but also indirectly by causing elevation of activation symptoms. As activation factor consists of uncooperativeness, poor impulse control, excitement, hostility, and disturbance of volition, one could argue that the activation factor might be merely the reflection of the patients' hostility and suspiciousness toward the rater that may have negatively affected the ratings of insight. However, this is unlikely as the correlation between activation factor and G12 remained significant ($r = 0.27$, $P = 0.027$) even after delusion and suspiciousness items have been partialled out. Rather, it may be more reasonable to consider activation factor as reflecting a pathological agitation, or excitability. In fact, the composition of our activation factor was very similar to the mania-like excitement factor derived from the PANSS with a pool of acute manic bipolar patients by Lindenmayer *et al.* (2004). The presence of activation symptoms in both schizophrenia and bipolar patients may have been one of the reasons why Pini *et al.* (2001) found no significant difference in their levels of insight. As a number of studies have found links between severity of mood disorder and lack of insight (Ghaemi *et al.*, 2000; Ghaemi and Rosenquist, 2004; Varga *et al.*, 2007), treatment strategies that aim to decrease such activation symptoms in a variety of psychiatric illnesses that accompany agitated mood and excitability, such as mania, agitated depression, schizoaffective disorder, etc. may result in better compliance and treatment outcome because of increased insight. Such a strategy may include forming a better therapeutic alliance (Couture *et al.*, 2006), as well as applying appropriate psychosocial education and training and pharmacotherapy. The mediating role of the activation factor has been further discussed in the study by Hwang *et al.* (2009).

Our results evidenced the emergence of anxiety/depressive factor as a significant predictor of insight after the stabilizing phase, as both 8-week and 1-year alternative models that included it as a secondary predictor showed superior fitness. Along with Loza *et al.* (2003), who found greater expression of the depression factor after 8 weeks, such a result was in support of the long-term association between insight and anxiety and/or depression (Smith *et al.*, 1998; Drake *et al.*, 2004; Lincoln *et al.*, 2007). However, anxiety/depressive factor was apparently found to play a moderating role between the 'upstream' primary symptoms and insight; increased severity of the primary symptoms caused more severe anxiety/depressive

symptoms, and this, in turn, led to increased insight. More specifically, after the emergence of anxiety/depressive factor as a significant predictor or G12 at 8-week follow-up, the proportion of its variance explained by positive factor increased over time to the 1-year follow-up. As the result of a separate correlation analysis, positive factor showed significant correlations with only depression ($r = 0.221$, $P = 0.028$) and active social avoidance ($r = 0.513$, $P = 0.000$) of anxiety/depressive factor at 8-week follow-up. At 1-year follow-up, however, positive factor was significantly correlated with all items of anxiety/depressive factor (tension $r = 0.276$, $P = 0.022$; anxiety $r = 0.476$, $P = 0.000$; depression $r = 0.503$, $P = 0.000$; active social avoidance $r = 0.443$, $P = 0.000$). Such results were consistent with those studies that reported association between positive symptoms and depression (Sax *et al.*, 1996; Emsley *et al.*, 1999; Lançon *et al.*, 2001) and suggested that association found at the stabilizing stage may be related to postpsychotic depression, whereas that found at the later stage may be reflective of dysphoric mood rather than specific dimension of anxiety and depression (Norman and Malla, 1991) owing to chronicity of schizophrenia.

The standardized regression coefficients of negative and autistic preoccupation factors toward anxiety/depressive factor also increased over time. This is consistent with earlier studies where anxiety/depression symptoms were found to be significantly correlated with negative (Nkam *et al.*, 1997; Guillem *et al.*, 2005) and cognitive symptoms (Lancon *et al.*, 2000) in stabilized patients. As negative factor was significantly correlated with only tension ($r = 0.292$, $P = 0.003$) and active social avoidance ($r = 0.463$, $P = 0.000$) at 8 weeks and then became significantly correlated with all items of anxiety/depressive factor at 1 year (tension $r = 0.484$, $P = 0.000$; anxiety $r = 0.263$, $P = 0.029$; depression $r = 0.423$, $P = 0.000$; active social avoidance $r = 0.640$, $P = 0.000$), this may also relate to the diffusion of initial tension into overall dysphoric mood mentioned above. Finally, autistic preoccupation factor was significantly correlated with all items of anxiety/depressive factor at both 8-week and 1-year follow-ups, but the magnitude of correlations of all items increased over time. The above results concerning the differential moderating effect of anxiety/depressive factor for positive and negative factors point to the possibility that finer distinctions in conceptualization of dysphoria may be empirically useful for more accurate description of the relationships among symptoms in schizophrenia, as was shown by some researchers (e.g. Norman & Malla, 1991, Guillem *et al.*, 2005).

Longitudinal causal relationships between psychopathology and insight

Our correlation analysis of changes in G12 and factor scores revealed improvement in G12 score to be significantly correlated with improvement in all factor scores during the stabilizing phase and with only negative factor in chronic phase. Upon applying our model to the baseline data, however, only positive and negative factors were found to modestly predict G12, with little contribution from the autistic preoccupation factor. This result was comparable with those obtained from studies that examined the short-term stabilizing phase of acute patients upon their admission into psychiatric hospitals (Kemp and Lambert, 1995; Weiler *et al.*, 2000) or early psychosis program (Mintz *et al.*, 2004). In terms of the long-term chronic phase, the significant longitudinal relationship between changes in insight and psychopathology was limited only to negative symptoms in our study, but others have implicated positive symptoms (Mintz *et al.*, 2004) as well as disorganization and anxiety/depressive symptoms (Gharabawi *et al.*, 2006). Such differences may be explained partly by the differences in demographic and clinical features of the patients, for example, age, inclusion of inpatients, first-episode, etc., and types of treatment received, for example, amisulpride versus risperidone, pharmacotherapy-only versus pharmacotherapy with psychoeducation, etc.

Causal relationship between insight and anxiety/depressive factor: post-hoc analysis of cross-sectional and longitudinal models

Superior fitness of the Alternative model 3 allowed post-hoc cross-sectional analysis of a model that designated G12 as a mediating variable and anxiety/depressive factor as the dependent variable. As a result, we have found evidence to support the fact that, whereas bidirectional effect does exist, more severe anxiety and depressive symptoms predict better insight in chronic patients: 8-week data showed similar levels of predictability between anxiety/depressive factor and G12, but 1-year follow-up data revealed anxiety/depressive factor to be twice as predictive of insight than the other way around, albeit the standardized regression coefficient was relatively small. However, it should not be hastily concluded that higher levels of anxiety/depressive symptoms lead to better insight, as such a relationship emerged only after a significant decrease in overall pathology has occurred. It is sobering to note that, in a separate analysis of 1-year follow-up data, a significant positive correlation ($r = 0.363$, $P = 0.002$) between anxiety/depressive factor and G12 was found before partialling out positive, negative, and autistic preoccupation factors. Hence, the overall severity of psychopathology is likely to play a moderating role between anxiety/depressive symptoms and insight: at lower levels of psychopathology, increased dysphoric mood may lead to better self-evaluations through changes in attribution processes (Lincoln *et al.*, 2007), but at more severe levels of psychopathology, such processes might become impaired and severe dysphoric mood symptoms may not necessarily lead to a better insight.

In terms of longitudinal changes in anxiety/depressive factor and G12, Gharabawi *et al.* (2006) have reported that changes in insight scores over a 50-week period corresponded to the changes in anxiety/depressive symptoms, as well as social functioning. Our results, based on an 8-week stabilizing period, showed that influence between anxiety/depressive factor and G12 was bidirectional. A separate correlation analysis showed that increase in insight was specifically related to improvement in anxiety ($r = 386$, $P = 0.000$) and active social avoidance ($r = 0.334$, $P = 0.001$) of anxiety/depressive factor. Hence, it may be suggested that the long-term associations between insight and clinical measures found by Gharabawi *et al.* (2006) may be largely confined to the stabilized stage where patients who gain insight into their illness learn to cope with the social consequences of their illness. However, further research may be necessary to delineate the relationships between insight and various aspects of anxiety and coping responses to confirm this account.

Conclusion

Our causal model of insight has proven to reliably describe both cross-sectional and short-term longitudinal relationships between insight and psychopathology in schizophrenia, with superior fitness. However, this study also showed that the relationships between insight and psychopathology vary according to the phase of illness, which may partly explain inconsistent results from past studies. For example, we have evidenced the emergence of anxiety/depressive factor as a significant predictor of insight after a stabilizing period of only 8 weeks. In both clinical and research settings, the evaluation of insight should take into account such temporal differences in psychopathology. For example, the assessment of insight in stabilized or chronic patients should take into account the presence of anxiety or depressive symptoms, as in our alternative model, to avoid overestimation of lack of insight. For acute-stage patients, our original hypothesized model without anxiety/depressive factor should be more efficient for evaluating insight. Along the same lines, future studies on insight should benefit by applying more refined measures of psychopathology as well as a more homogenous group of patients, especially first-onset patients of schizophrenia. Finally, this study shares the same limitation of our earlier study, in that we applied the unidimensional measure of insight. As discussed in our earlier study, further research is necessary to verify if our model can be generalized to a multidimensional conceptualization of insight as well. In addition, as our sample was limited to those patients whose primary antipsychotic was amisulpride, which has been found to be effective on negative symptoms (Storosum *et al.*, 2002). Our model should also be applied to other patients on different antipsychotics, especially when validating the long-term relationship between changes in insight and negative symptoms. However, our separate analysis of the level of baseline psychopathology did not uncover any significant difference in negative symptom subscale score and negative factor score between amisulpride and the combined olanzapine groups, hence it cannot necessarily be concluded that negative symptoms *per se* were the primary target of treatment for the amisulpride group. Therefore, taken together with the fact that they also did not differ in the demographic variables, our results are not likely to have rested on the specific type or action of the medication. Nonetheless, the application of this model to other medications is encouraged for further validation and refinement.

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