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Functioning in Middle Aged and Older Patients With Schizophrenia and Depressive Symptoms: Relationship to Psychopathology

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Abstract

Background—Depressive symptoms are common in middle aged and older patients with schizophrenia. The authors hypothesized that worse functioning in these patients would be associated with worse psychopathology.

Methods—Outpatients with schizophrenia were ≥ 40 years old with subsyndromal depression and Hamilton Depression Rating Scale Scores of ≥ 8 . Exclusions were dementia, two months of either mania or major depression or 1 month active substance abuse/dependence. The authors administered performance based functional assessments, the Positive and Negative Syndrome Scale of Schizophrenia [PANSS], and Calgary Depression Rating Scale.

Results—PANSS (–) scores were negatively correlated with the UCSD Performance Skills Based Assessment, Social Skills Performance Assessment and Medication Management Ability Assessment total error (MMAA) scores. Digit symbol scores served as a moderator of the relationship between MMAA and PANSS (–) scores.

Conclusions—Negative symptoms were associated with functioning. The relationship between negative symptoms and medication errors seem to weaken in subjects with quicker processing speed.

Keywords

Schizophrenia; functioning; psychopathology; negative symptoms

Depressive symptoms commonly accompany middle aged and older patients with schizophrenia.¹ Jin et al.² showed that patients with schizophrenia and worse depression had lower scores on the Medical Outcomes Scale SF-36. However, when using the Direct Assessment of Functioning scale in a similar population, Patterson et al.³ demonstrated that depressive symptoms were not related to levels of functioning. No studies have investigated these relationships utilizing performance-based measures developed specifically for an older

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population of patients with schizophrenia.⁴ The use of these measures circumvent the need for informants and avoid potential response bias. Furthermore, they are proximal in nature, measure capacity and at the time of testing do not require that the skills are actually deployed in the real-world environment.⁴

We hypothesized that worse functioning, measured with performance-based scales developed for older patients with schizophrenia,⁴ would be associated with worse psychopathologic scores, i.e., scores assessing positive and negative symptoms as well as depressive symptoms. We also hypothesized that cognition would serve as a mediator of this relationship given the evidence that cognitive deficits are known to be associated with psychopathologic symptoms⁵ in patients with schizophrenia. In addition, investigators have demonstrated that later age of onset of schizophrenia is associated with better prognosis and functional status.⁵ Therefore, we also hypothesized that age of onset of illness would serve as a moderator of our hypothesized relationship between psychopathology and functioning.

METHODS

Outpatients ≥ 40 years of age with schizophrenia or schizoaffective disorder were described previously⁶ and were participating in an NIMH trial examining SSRI augmentation of antipsychotic treatment in patients with schizophrenia and subsyndromal depression. This report represents the analysis of the trial's baseline data. Subjects had at least two of nine items required for major depression and a baseline 17 item Hamilton Depression score ≥ 8 . Exclusions were major depression or mania within 2 months, active substance abuse/dependence for the past month and dementia.

Scales assessing psychopathology included the Positive and Negative Syndrome Scale for Schizophrenia (PANSS; 4) and the Calgary Depression Rating Scale (CDRS; 6). Functional scales included: 1) UCSD Performance-based Skills Assessment (UPSA; 4), 2) Social Skills Performance Assessment (SSPA; 4), 3) Medication Management Ability Assessment (MMAA; 4). The UPSA addresses everyday functioning, whereas the SSPA tests interpersonal relatedness. The MMAA tests abilities needed to organize a medication regimen similar to what an older outpatient with schizophrenia would be expected to manage. In addition, we administered the digit symbol subtest of the WAIS to assess cognition.⁷ Interrater reliability between the two sites was reported previously.⁶

Of a total of 143 patients recruited, 80% were men, 55% were white, and 65% had a diagnosis of schizophrenia (versus schizoaffective disorder). Forty-five percent were single, 41% were separated/divorced or widowed and 14% were married/cohabitating; 27% were living independently. The average age was 51.9 ± 6.7 years and average age of onset of illness was 26.5 ± 10 .

The two study sites differed with regards to age and living situation. The average age at the San Diego, CA, site was 50.2 ± 5.9 ($n = 81$) and that at the Cincinnati, OH, site was 54.3 ± 7.0 ($n = 61$; $F = 13.95$, $df = 1, 140$, $p = 0.001$). At the San Diego, CA, site, 18.5% ($n = 15$) lived alone while 38.7% at the Cincinnati, OH, site lived alone ($n = 24$; $\chi^2 = 7.21$, $df = 1$, $p = 0.007$).

Continuous variables were assessed for normality of distribution and for homogeneity of variance. The residuals of the regressions and the partial correlations were assessed for normality. Because of the multiple comparisons we performed, we tested our hypotheses with $\alpha = 0.01$.

Mediator and moderator analyses were performed using partial correlations and multiple regression methods based on Baron and Kenny⁸ with site as a covariate. A variable was

determined to be a mediator if it accounted for the relationship between the independent and dependent variables.⁸ The following needed to hold true: 1) the independent variable must affect the mediator when regressing the mediator on the independent variable, 2) the independent variable must be shown to affect the dependent variable when regressing the dependent variable on the independent variable, and 3) the mediator must affect the dependent variable when regressing the dependent variable on both independent variable and mediator. If all three are significant, then the effect of the independent variable on the dependent variable must be less in the third assessment relative to the second one.

A moderator variable is one that affects the direction and/or strength of the relation between an independent and a dependent variable. A moderator effect can be represented as an interaction between a focal independent variable and a factor that specifies the appropriate conditions for its operation.

RESULTS

Patients' psychopathologic and functional scores were as follows: CDRS: 6.6 ± 3.1 ; PANSS (+): 15.9 ± 5.7 ; PANSS General: 32.1 ± 8.0 ; PANSS (-): 15.2 ± 4.8 ; SSPA: 1.81 ± 0.38 ; MMAA total errors: 8.5 ± 6.1 ; UPSA: 76.6 ± 14.9 . Between the two sites, there were significant site differences for the following: PANSS (+) [San Diego, CA, 18.1 ± 5.5 ; Cincinnati, OH, 13.0 ± 4.5 ; $F = 35.78$, $df = 1,141$, $p < 0.001$], PANSS general: [San Diego, CA, 34.5 ± 87.9 ; Cincinnati, OH, 29.1 ± 7.0 ; $F = 17.98$, $df = 1,141$, $p < 0.001$], and SSPA: [San Diego, CA, 1.73 ± 0.37 ; Cincinnati, OH, 1.92 ± 0.35 ; $F = 9.11$, $df = 1,141$, $p = 0.003$].

For testing our hypothesis, we used partial correlations to adjust for site differences. There were significant partial correlations of PANSS (-) scores with UPSA, SSPA, and MMAA total error scores. In addition, PANSS (+) scores had significant negative associations with SSPA scores (see Table 1). We also tested whether the three functional scales which exhibited significant relationships with PANSS (-) scores, were correlated with each other; the partial correlations between the three scales were as follows: MMAA total error with SSPA: $r = -0.217$, $df = 1,140$, $p = 0.010$; MMAA total error with UPSA: $r = -0.381$, $df = 1,140$, $p < 0.001$; SSPA with UPSA: $r = 0.542$, $df = 1,140$, $p < 0.001$. Two way interactions of site and independent variables were investigated and found to be nonsignificant.

Next we assessed whether digit symbol was a mediator of the relationship between PANSS (-) scores and functioning. To investigate mediation criterion 1, we created a linear regression with PANSS (-) and site with digit symbol scores and determined that the partial correlation between PANSS (-) and digit symbol scores was $r = -0.207$ ($df = 1,138$, $p = 0.014$). Based on $\alpha = 0.01$, digit symbol score was not a significant mediator.

In testing the hypothesis that age of onset was a moderator, we tested for an interaction between PANSS (-) scores and age of onset for our functional measures. These were not significant at $\alpha = 0.01$: UPSA: $F = 4.86$, $df = 1,114$, $p = 0.030$; SSPA: $F = 6.043$, $df = 1,114$, $p = 0.015$; MMAA total errors: $F = 1.49$, $df = 1,114$, $p = 0.840$. The interaction between PANSS (-) scores and digit symbol was significant for MMAA total errors at $\alpha = 0.01$: $F = 7.23$, $df = 1, 136$, $p = 0.008$; subjects with higher digit symbol scores showed weaker positive relationships between PANSS (-) and MMAA total errors. For UPSA or for SSPA, the interaction between digit symbol and PANSS (-) scores was not significant; for UPSA: $F = 0.204$, $df = 1,136$, $p = 0.652$; for SSPA scores: $F = 0.873$, $df = 1,136$, $p = 0.352$.

CONCLUSIONS

In this well characterized sample, PANSS (-) scores exhibited significant negative associations with all three functional measures. In addition, PANSS (+) scores were

significantly associated with SSPA scores. Measuring performance is an important outcome measure in middle aged and older adults with schizophrenia and depressive symptoms; in patients with schizophrenia, Siegel et al.⁹ recently determined that basal level of functioning seems to be a reliable predictor of later functioning. Moreover, a higher level of functioning at follow-up was predicted by lower levels of positive, negative, and depressive symptoms at baseline.

Our assessment of cognitive status, the digit symbol subtest measures processing speed and has been shown to predict vocational impairments in patients with schizophrenia.⁹ Our data suggests that the relationship between negative symptoms and medication errors seems to weaken in subjects with quicker processing speed. Our studies are limited in using only the digit symbol score as our sole measure of cognition. Later age of onset of schizophrenia has been shown to be associated with better prognosis and functional status⁵ and we hypothesized that age of onset would serve as a moderator of the relationship between the psychopathologic measures and functional scores. However, our data did not support this premise.

There were several limitations to our study. The data were cross-sectional and longitudinal assessments would have allowed us to determine how stable these relationships were. In addition, we determined that there were significant correlations between the three functional measures which implied that they are not entirely independent of one another. Second, we had many patients with schizoaffective disorder. Some experts criticize the use of this diagnostic category because “it blurs the zones of rarity between schizophrenia, depression, and bipolar disorder” and it has even been suggested that it should be eliminated altogether.¹⁰ Although we felt confident in our ability to diagnose this syndrome, it is true that making the diagnosis of schizoaffective disorder in general can sometimes be challenging. For instance, patients and family members at times may have difficulty recalling the precise details of the history. In addition, patient records may be lacking critical information needed to verify the diagnosis.

An important next step of these findings would be to examine how treatment interventions affect the relationships we found. Such a study might help pinpoint rational and feasible targets for intervention that could improve functioning in this important group of patients.

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TABLE 1

Partial Correlations Between Psychopathology and Functioning Adjusting for Site

	PANSS (-)	PANNS General Psychopathology	PANSS (+)	CDRS
UPSA	-0.367 (<0.001)	-0.208 (0.013)	-0.148 (0.079)	0.038 (0.657)
SSPA	-0.416 (<0.001)	-0.131 (0.121)	-0.080 (0.346)	0.043 (0.613)
MMAA total error	0.256 (0.002)	0.029 (0.729)	0.049 (0.566)	-0.069 (0.416)

Notes: Each value represents the partial correlation coefficient; accompanying p value is in parenthesis. Degrees of freedom = 140 except for those involving CDRS which is 139. CDRS, Calgary Depression Rating Scale; PANSS, Positive and Negative Syndrome Scale; SSPA, Social Skills Performance Assessment; MMAA, Medication Management Ability Assessment; UPSA, UCSD Performance based Skills Assessment.