ORIGINAL PAPER

# **Predictors of Community Functioning in Schizophrenia and Substance Use Disorder Patients**

Simon Zhornitsky · Ginette Aubin · Joelle Desfossés · Élie Rizkallah · Tania Pampoulova · Olivier Lipp · Jean-Pierre Chiasson · Emmanuel Stip · Stéphane Potvin

Received: 7 July 2011/Accepted: 2 July 2012/Published online: 31 July 2012 © Springer Science+Business Media, LLC 2012

Abstract Community functioning is a broad term that encompasses various 'real world' measures of disability among schizophrenia patients. It includes outcomes such as independent living, social competence and behavioural problems-all of which are priorities for treatment among schizophrenia patients, mental health care providers, and family members. An important goal for rehabilitation programs is to identify predictors of community functioning which, in turn, could be used as targets for intervention. The present case-control study examined socio-demographic and substance use disorder (SUD) variables as well as psychiatric, extrapyramidal, and cognitive symptoms as predictors of community functioning in schizophrenia patients with (DD patients; n = 31) and without comorbid SUDs (SCZ patients; n = 31), and non-psychosis substance abusers (SUD patients; n = 39). Psychiatric and extrapyramidal symptoms were evaluated with the Positive and Negative Syndrome Scale, the Calgary Depression Scale for Schizophrenia and the Extrapyramidal Symptoms Rating

S. Zhornitsky  $\cdot$  J. Desfossés  $\cdot$  T. Pampoulova  $\cdot$  O. Lipp  $\cdot$  E. Stip  $\cdot$  S. Potvin

Fernand-Seguin Research Centre, Department of Psychiatry, Faculty of Medicine, Université de Montréal, Montreal, QC, Canada

G. Aubin

Occupational Therapy Service, Centre Hospitalier de l'Université de Montréal, Montreal, QC, Canada

É. Rizkallah · T. Pampoulova · J.-P. Chiasson Clinique du Nouveau-Départ, Montréal, QC, Canada

S. Potvin (🖂)

Centre de recherché Fernand-Seguin, 7331 Hochelaga, Montreal, QC H1N 3V2, Canada e-mail: stephane.potvin@umontreal.ca Scale. Cognition was evaluated using the Cambridge Neuropsychological Test Automated Battery (speed of processing, explicit and working memory). In SCZ patients, community functioning was predicted by explicit memory performance. In DD patients, community functioning was predicted by substance abuse, depression and speed of processing. In SUD patients, community functioning was predicted by substance abuse, positive symptoms and education. Our results suggest that cognition should be among the top treatment priorities in SCZ patients, whereas the key treatment targets in DD patients should be substance abuse and depression. Future studies will need to replicate the current findings, using prospective research designs.

**Keywords** Community functioning · Schizophrenia · Substance use disorder · Memory · Depression

# Introduction

Community functioning is a broad term that encompasses various 'real world' measures of disability among schizophrenia patients living in the community (Barker et al. 1994). Components of community functioning such as independent living, social competence and behavioural problems are priorities for treatment among schizophrenia patients, mental health care providers and family members (Fischer et al. 2002). An important goal for rehabilitation programs is to identify predictors of community functioning which, in turn, could be used as targets for intervention (Prouteau et al. 2005; Aubin et al. 2009).

Previous studies have shown that cognition is the most reliable predictor of community functioning in schizophrenia patients (Green et al. 2000; Prouteau et al. 2004; Stip et al. 2007). Indeed, at least 70 % of schizophrenia patients have deficits in areas of cognition such as attention, executive function, and explicit and working memory, which are required to maintain adequate vocational, social and independent living skills (Palmer et al. 1997; Levaux et al. 2007; Tsang et al. 2010). Other predictors of community functioning such as psychiatric (mostly negative) symptoms and antipsychotic-induced side-effects (e.g. extrapyramidal symptoms, sedation) have also been documented, but their overall effect seems to be less prominent (Velligan et al. 1997; Green et al. 2000; Bozikas et al. 2006).

The lifetime prevalence of comorbid substance use disorder (SUD) in schizophrenia is nearly 50 % (Regier et al. 1990). In non-psychosis individuals, substance abuse can induce psychiatric and extrapyramidal symptoms (Zhornitsky et al. 2010). In schizophrenia patients, substance use has a negative impact on the course of the pathology. Compared to non-abusing patients, dual diagnosis (DD) schizophrenia patients are more frequently hospitalized, non-compliant with treatment, suicidal, impulsive and violent, homeless and unemployed, and they have more legal and health problems (Mueser et al. 1998; Negrete 2003). Moreover, there is evidence that DD patients have more psychiatric, extrapyramidal and cognitive symptoms, relative to nonabusing schizophrenia patients (Cooper et al. 1999; Potvin et al. 2006a; Maat et al. 2008). Previous studies have also demonstrated the deleterious effect of substance abuse/ dependence on community functioning in schizophrenia (Revheim and Medalia 2004).

Given the possibility for negative outcomes, there is a growing need to identify predictors of poor community functioning among DD patients. The present case-control study examined socio-demographic and SUD-related variables as well as psychiatric, extrapyramidal, and cognitive symptoms as predictors of community functioning in schizophrenia patients with (DD patients; n = 31) and without comorbid SUDs (SCZ patients; n = 31), and nonpsychosis substance abusers (SUD patients; n = 39). Importantly, this is the first study of its kind to study cognition as a predictor of community functioning in DD patients. Likewise, the inclusion of SUD patients undergoing the same evaluation is unique and crucial for parcelling out the effect of substance abuse on community functioning. The identification of predictors of community functioning may be helpful to improving disability outcomes in these vulnerable populations.

# Methods

Participants

Three groups of participants between 18 and 60 years of age were recruited, namely: (1) patients with

schizophrenia-spectrum disorders (schizophrenia, schizoaffective disorder, and schizophreniform disorder); (2) non-psychosis patients with substance use disorders; and (3) schizophrenia patients with comorbid SUDs. Patients were recruited by research staff at the Hospital Louis-H-Lafontaine and the Clinique Nouveau Depart. Psychiatric and SUD diagnoses were made by well-trained psychiatrists (LAB, OL, and ES) and physicians (JPC, TP), and were all based on DSM-IV criteria. Clinical and extrapyramidal assessments were made by a neurologist trained in schizophrenia and addiction medicine who was blind to the study objective (TP). Moreover, because this study was the first of its kind and its purpose was to characterize predictors of community functioning in a naturalistic fashion we did not match groups on sociodemographic characteristics. SUD diagnoses were complemented with urine drug screenings. Persons presenting with a major physical disability and/or cognitive deficits of organic origin were excluded. All participants signed a detailed consent form. The study was approved by the local ethics committee.

## **Clinical Assessments**

Speed of processing was assessed using the "Motor Screening" (MOT) task and explicit and working memory was assessed using the "Paired Associates Learning" (PAL) (total errors and total trials) and the "Spatial Working Memory" (SWM) (total errors and strategy) tasks of the Cambridge Neuropsychological Test Automated Battery (CANTAB) (Elliott et al. 1998; Potvin et al. 2005). Extrapyramidal symptoms (parkinsonism, dystonia, and dyskinesia) were evaluated with the Extrapyramidal Symptoms Rating Scale (ESRS) (Chouinard and Margolese 2005)—a scale that our group successfully used to measure neurological symptoms in DD, SCZ and SUD populations in the past (Zhornitsky et al. 2010). The positive, negative and depressive symptoms of schizophrenia were evaluated with the Positive and Negative Syndrome Scale (PANSS) (Kay et al. 1987) and the Calgary Depression Scale for Schizophrenia (CDSS) (Addington et al. 1992). The PANSS has been previously shown to differentiate between schizophrenia, substance-induced psychosis, and borderline personality disorder patients (Mauri et al. 2007; Lapworth et al. 2009). We chose the CDSS, because it has previously been shown to exhibit little overlap with negative symptoms in schizophrenia, and because it is less likely to overestimate depressive symptoms in dual-diagnosis schizophrenia, compared to other scales, as shown previously by our group (Rabany et al. 2011; Zhornitsky et al. 2011). SUD outcomes were evaluated with the Alcohol and Drug Use Scales (AUS and DUS) (Drake et al. 1990), and a DSM-IV adapted scale providing a measure of SUD severity for the last week (Potvin et al. 2006b).

Finally, community functioning was evaluated with the Multnomah Community Ability Scale (Barker et al. 1994), which includes four components, namely: "Interference with functioning", "Adjustment to living", "Social competence" and "Behavioral problems". Previous work from our group has shown the MCAS to be useful when examining the functional effects of cognitive deficits in schizo-phrenia (Prouteau et al. 2005).

## Statistical Analyses

Between-group differences for socio-demographic and clinical variables were examined using analyses of variance (ANOVA) (Chi-square tests for dichotomous variables). Multiple comparisons were performed using the Bonferroni correction. To identify the predictors of social functioning, stepwise linear regression analyses were performed, using socio-demographic data (age, gender and education level), psychiatric (positive, negative, and depressive symptoms), SUD variables (AUS and DUS scores, SUD severity) and extrapyramidal symptoms (parkinsonism, dystonia, and dyskinesia), and cognitive scores (MOT, PAL, and SWM) as regressors, and community functioning (MCAS total score) as the dependent variable. For all continuous variables, the Kolmogorov-Smirnov one-sample test for normality was applied. Root transformations were used in order to remove skews when appropriate. Stepwise regression generates consecutive models in which significant predictors are sorted according to the amount of variance they account for a given dependent variable. Stepwise regression analyses were separately applied in the SCZ, SUD and DD groups. Statistical analyses were performed using the Predictive Analytics SoftWare (PASW; version 18). The critical level of significance for rejecting the null hypothesis was set at 5 %. The significant baseline sociodemographic differences were included in the regression analyses.

#### Results

#### Socio-Demographic Variables

Baseline sociodemographic variables are shown in Table 1. The mean age of SCZ was significantly greater than the mean age of DD patients. In addition, there was a significantly greater ratio of males to females in the DD group compared to the SCZ and SUD group. Moreover, there was a higher prevalence of schizoaffective diagnoses among DD than among SCZ patients. Moreover, SUD patients had a significantly higher level of education. However, there were no significant differences in the type of substances used by DD and SUD patients. Likewise, there were no significant differences in the class of antipsychotic used by DD and SCZ patients.

# **Clinical Differences**

MCAS total score was significantly lower in DD patients (57.6 [8.8]; indicating poorer community functioning), compared to SUD (62.1 [5.9]) and SCZ patients (72.3 [4.9]), and significantly lower in SUD patients, compared to SCZ patients (p = 0.0001). After removing the behavioral cluster of the MCAS (which comprises a "substance abuse" item), DD patients still exhibited poorer community functioning, relative to the other two groups (p = 0.0001), but the difference between SUD and SCZ patients was no longer significant. However, SCZ patients (36.9 errors [41.9]) performed significantly poorer performance on the PAL, relative to DD (19.4 [20.7]) and SUD (16.9 [12.6]; p = 0.006) patients. SCZ patients (1183.1 ms [241.1]) also displayed poorer performance on the MOT, relative to SUD patients (1035.7 [379.5]; p = 0.017). In addition, DD patients (18.3 [4.6]) had significantly more positive symptoms than SUD patients (15.3 [5.1]; p = 0.02), as well as more depression, compared to the other two groups (DD: 7.3 [4.9]; SCZ: 2.0 [2.0]; SUD: 4.2 [4.8]; p = 0.0001). Finally, there were significant differences in

| Table 1 Baseline sociodemographic c | characteristics |
|-------------------------------------|-----------------|
|-------------------------------------|-----------------|

|   | DD (n = 31) | SCZ (n = 31) | SUD (n = 39) | Statistics (multiple comparisons) |
|---|-------------|--------------|--------------|-----------------------------------|
| Age (mean, SD)                            | 30.0 (9.8)  | 42.3 (10.4)  | 37.8 (11.9)  | p = 0.0001 (SCZ and SUD > DD)     |
| Gender (male:female)                      | 27:4        | 18:13        | 26:13        | p = 0.036                         |
| Diagnosis (SCZ:SA:SF)                     | 17:12:2     | 26:5:0       | -            | p = 0.034                         |
| Education (years)                         | 11.2 (2.3)  | 11.6 (3.0)   | 14.1 (2.4)   | p = 0.0001  (SUD > DD and SCZ)    |
| Substance type (ALC: CAN: STM)            | 15:18:9     | -            | 24:20:16     | p = n.s.                          |
| Antipsychotic type (ATP: TYP: BOTH: NONE) | 20:4:5:2    | 23:4:4:0     | -            | p = n.s.                          |

DD dual diagnosis group, SCZ schizophrenia group, SUD substance use disorder group, SD standard deviation, ALC alcohol, CAN cannabis, STM stimulants, ATP atypical antipsychotic, TYP typical antipsychotic, BOTH a mix of antipsychotic types, NONE drug-free

| Table 2 Predictors of   community functioning in SCZ,   SUD and DD patients   | Predictors of MCAS total score | $r^2$ | β      | Statistical significance |  |  |
|---|--------------------------------|-------|--------|--------------------------|--|--|
|   | SCZ patients                   |       |        |                          |  |  |
|   | Total PAL errors               | 0.186 | -0.824 | F = 6.2; p = 0.02        |  |  |
|   | SUD patients                   |       |        |                          |  |  |
|   | Model                          | 0.514 |        | F = 12.3; p = 0.0001     |  |  |
| MCAS Multnomah Community<br>Ability Scale, MOT motor<br>screening task, PAL Paired<br>Associated Learning, PANSS<br>Positive and Negative<br>Syndrome Scale, DD dual<br>diagnosis schizophrenia<br>patients, SUD non-psychosis<br>substance abusers, SCZ non-<br>abusing schizophrenia patients | Education level                |       | 1.016  | t = 3.4; p = 0.002       |  |  |
|   | SUD severity                   |       | -0.291 | t = -2.8; p = 0.008      |  |  |
|   | PANSS-positive symptoms        |       | -0.339 | t = -2.3; p = 0.026      |  |  |
|   | DD patients                    |       |        |                          |  |  |
|   | Model                          | 0.482 | _      | F = 7.4; p = 0.001       |  |  |
|   | Alcohol Use Scale              |       | 2.619  | t = -2.3; p = 0.029      |  |  |
|   | MOT latency                    |       | 0.010  | t = 3.0; p = 0.007       |  |  |
|   | Depressive symptoms            |       | -0.689 | t = -2.4; p = 0.025      |  |  |

SUD severity between SUD (29.9 [7.1]) and DD patients (21.7 [4.7]; p = 0.0001).

## **Regression Analyses**

In SCZ patients, the stepwise regression produced a model with one significant predictor of MCAS total score (PAL errors) which accounted for 18.6 % of the variance (Table 2). In SUD patients, the stepwise regression produced a model with three significant predictors of MCAS total score (education level, SUD severity and positive symptoms) that accounted for 51.4 % of the variance (Table 2). In DD patients, the stepwise regression produced a model with three significant predictors of MCAS total score (AUS scores, MOT latency and depression), which accounted for 48.2 % of the variance (Table 2). All of the above results remained significant when baseline sociodemographic values (age, gender, diagnosis, education) were entered into the regression analyses.

## Discussion

The present study compared community functioning and its predictors in DD, SCZ and SUD patients. We found that DD patients had significantly poorer community functioning, compared to SUD and SCZ patients, even though DD patients exhibited lower substance abuse severity than SUD patients. As such, this result is consistent with the literature showing that substance abuse significantly interferes with community functioning in schizophrenia, and it also suggests that DD patients are more vulnerable than SUD patients to the functional impairments resulting from substance abuse. In SCZ patients, explicit memory performance exclusively predicted community functioning and SCZ patients exhibited worse explicit memory performance than DD and SUD patients. These data are in accordance with previous studies which found that explicit memory is prominently impaired in SCZ patients and is associated with poor community functioning (Prouteau et al. 2005; Ritsner et al. 2006). Taken together, these results are consistent with the growing literature showing that cognitive functioning is relatively preserved in DD patients, relative to SCZ patients (Joyal et al. 2003; Carey et al. 2003; Potvin et al. 2005). By contrast, in DD patients, community functioning was predicted by substance abuse, depression and speed of processing and depressive symptoms were increased in DD patients, relative to the other groups, as repeatedly shown in the literature (Krausz et al. 1996; Cooper et al. 1999; Scheller-Gilkey et al. 2002). In addition, the finding that better speed of processing was associated with poorer community functioning may be related to increased impulsivity among DD patients (Schiffer et al. 2010) as well as the potentially stimulating effect of some drugs of abuse (Silver et al. 2002).

In SUD patients, community functioning was predicted by substance abuse, positive symptoms, and education. The latter result is unsurprising because SUD patients were significantly more educated, relative to the other two groups. Also noteworthy, a sub-analysis of our data revealed that the positive symptoms in SUD patients were not iatrogenic, but mostly related to excitement, hostility, and paranoia (data not shown). Such symptoms are commonly associated with substance abuse (Mauri et al. 2007; Lapworth et al. 2009). Moreover, analysis of socio-demographic variables revealed that these DD patients were more likely to be younger, male and schizoaffective/ depressive, as shown previously in the literature (Potvin et al. 2007; Wobrock et al. 2007; Koskinen et al. 2010), but these variables did not emerge as significant predictors of community functioning data in the regression models. Finally, it is important to note that extrapyramidal symptoms did not emerge as significant predictors of community functioning in any of the three groups.

The present study has both strengths and limitations. First, baseline differences between the groups may have confounded our results (age, gender, diagnosis, education). Nonetheless, we entered these variables into the regression model and they did not come out as significant (except for education in the SUD group). The study is also limited because we only administered three cognitive tests (MOT, PAL and SWM) to patients, and consequently, this may have led us to underestimate the impact of global cognition on community functioning in the three groups. Indeed, meta-analyses have revealed that functional outcome in schizophrenia is best predicted by immediate and delayed verbal memory, followed by card sorting (executive functioning) and attention (Green et al. 2000). Moreover, the present study not find a relationship between SWM and community functioning in SCZ or SUD patients, as has been previously reported in the literature (Saperstein et al. 2006; Mazhari et al. 2010; Grant et al. 2012). A recent meta-analysis (n = 2692) revealed a small significant relationship ( $\mu_p = 0.22$ ; p = 0.01) between community functioning and working memory (Fett et al. 2011). One reason for these differences may be the disparate nature of the scales(s) used to assess community functioning or heterogeneous nature of cognitive deficits in schizophrenia (Fioravanti et al. 2005).

Despite these limitations, however, this is the first study of its kind to compare the predictors of community functioning in substance abusers with and without schizophrenia and in non-abusing schizophrenia patients, and the first to consider cognition as a predictor of community functioning in DD patients. The results described here may have clinical implications as they suggest that clinicians have to target different clinical manifestations if they want to have an impact on the functioning of patients. More precisely, our results suggest that cognition should be among the top treatment priorities in SCZ patients (Prouteau and Doron 2008; Green et al. 2000), whereas the key treatment targets in DD patients should be substance abuse and depression. Future studies will need to replicate the current findings, using prospective research designs. Future studies should also measure additional variables such as problem solving skills for independent living, immediate and delayed verbal memory, and social reasoning, in order to get a more comprehensive picture of the predictors of community functioning.

Acknowledgments This study was funded by an academic partnership between AstraZeneca Pharmaceuticals and the Louis-H Lafontaine Hospital Foundation, and by a Catalyst grant from the Canadian Institute of Health Research. SP is holder of a Junior 1 Young Investigator Award from the Fonds de Recherche en Santé du Québec. ES is holder of the Eli Lilly Chair of schizophrenia from the University of Montreal.

#### References

- Addington, D., Addington, J., Maticka-Tyndale, E., & Joyce, J. (1992). Reliability and validity of a depression rating scale for schizophrenics. *Schizophrenia Research*, 6, 201–208.
- Aubin, G., Chapparo, C., Gélinas, I., Stip, E., & Rainville, C. (2009). Use of the perceive, recall, plan and perform system of task analysis for persons with schizophrenia: A preliminary study. *Australian Occupation Therapy Journal*, 56(3), 189–199.
- Barker, S., Barron, N., McFarland, B. H., & Bigelow, D. A. (1994). A community ability scale for chronically mentally ill consumers: Part I. Reliability and validity. *Community Mental Health Journal*, 30(4), 363–383.
- Bozikas, V. P., Kosmidis, M. H., Kafantari, A., Gamvrula, K., Vasiliadou, E., Petrikis, P., et al. (2006). Community dysfunction in schizophrenia: rate-limiting factors. *Progress in Neuropsychopharmacology and Biological Psychiatry*, 30(3), 463–470.
- Carey, K. B., Carey, M. P., & Simons, J. S. (2003). Correlates of substance use disorder among psychiatric outpatients: focus on cognition, social role functioning, and psychiatric status. *Journal* of Nervous and Mental Disease, 191, 300–308.
- Chouinard, G., & Margolese, H. C. (2005). Manual for the Extrapyramidal Symptom Rating Scale (ESRS). *Schizophrenia Research*, 76, 247–265.
- Cooper, L., Liberman, D., Tucker, D., Nuechterlein, K. H., Tsuang, J., & Barnett, H. L. (1999). Neurocognitive deficits in the dually diagnosed with schizophrenia and cocaine abuse. *Psychiatric Rehabilitation Skills*, *3*, 231–245.
- Drake, R. E., Osher, F. C., Noordsy, D. L., Hurlbut, S. C., Teague, G. B., & Beaudett, M. S. (1990). Diagnosis of alcohol use disorders in schizophrenia. *Schizophrenia Bulletin*, 16, 57–67.
- Elliott, R., McKenna, P. J., Robbins, T. W., & Sahakian, B. I. (1998). Specific neuropsychological deficits in schizophrenic patients with preserved intellectual function. *Cognitive Neuropsychiatry*, *3*, 45–70.
- Fett, A. K., Viechtbauer, W., Dominguez, M. D., Penn, D. L., van Os, J., & Krabbendam, L. (2011). The relationship between neurocognition and social cognition with functional outcomes in schizophrenia: a meta-analysis. *Neuroscience and Biobehavioral Reviews*, 35(3), 573–588.
- Fioravanti, M., Carlone, O., Vitale, B., Cinti, M. E., & Clare, L. (2005). A meta-analysis of cognitive deficits in adults with a diagnosis of schizophrenia. *Neuropsychology Review*, 15(2), 73–95.
- Fischer, E. P., Shumway, M., & Owen, R. R. (2002). Priorities of consumers, providers, and family members in the treatment of schizophrenia. *Psychiatric Services*, 53(6), 724–729.
- Grant, J. E., Chamberlain, S. R., Schreiber, L., & Odlaug, B. L. (2012). Neuropsychological deficits associated with cannabis use in young adults. *Drug Alcohol Dependence*, 121(1–2), 159–162.
- Green, M. F., Kern, R. S., Braff, D. L., & Mintz, J. (2000). Neurocognitive deficits and functional outcome in schizophrenia: are we measuring the "right stuff"? *Schizophrenia Bulletin*, 26(1), 119–136.
- Joyal, C. C., Hallé, P., Lapierre, D., & Hodgins, S. (2003). Drug abuse and/or dependence and better neuropsychological performance in patients with schizophrenia. *Schizophrenia Research*, 63, 297–299.
- Kay, S. R., Fiszbein, A., & Opler, L. A. (1987). The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizo-phrenia Bulletin*, 13, 261–276.
- Koskinen, J., Löhönen, J., Koponen, H., Isohanni, M., & Miettunen, J. (2010). Rate of cannabis use disorders in clinical samples of patients with schizophrenia: A meta-analysis. *Schizophrenia Bulletin*, 36(6), 1115–1130.

- Krausz, M., Mass, R., Haasen, C., & Gross, J. (1996). Psychopathology in patients with schizophrenia and substance abuse: A comparative clinical study. *Psychopathology*, 29, 95–103.
- Lapworth, K., Dawe, S., Davis, P., Kavanagh, D., Young, R., & Saunders, J. (2009). Impulsivity and positive psychotic symptoms influence hostility in methamphetamine users. *Addictive Behaviors*, 34(4), 380–385.
- Levaux, M. N., Potvin, S., Sepehry, A. A., Sablier, J., Mendrek, A., & Stip, E. (2007). Computerized assessment of cognition in schizophrenia: promises and pitfalls of CANTAB. *European Psychiatry*, 22(2), 104–115.
- Maat, A., Fouwels, A., & de Haan, L. (2008). Cocaine is a major risk factor for antipsychotic induced akathisia, parkinsonism and dyskinesia. *Psychopharmacology Bulletin*, 41(3), 5–10.
- Mauri, M. C., Volonteri, L. S., Fiorentini, A., Pirola, R., & Bareggi, S. R. (2007). Two weeks' quetiapine treatment for schizophrenia, drug-induced psychosis and borderline personality disorder: A naturalistic study with drug plasma levels. *Expert Opinion on Pharmacotherapy*, 8(14), 2207–2213.
- Mazhari, S., Badcock, J. C., Waters, F. A., Dragović, M., Badcock, D. R., & Jablensky, A. (2010). Impaired spatial working memory maintenance in schizophrenia involves both spatial coordinates and spatial reference frames. *Psychiatry Research*, 179(3), 253–258.
- Mueser, K. T., Drake, R. E., & Wallach, M. A. (1998). Dual diagnosis: A review of etiological theories. *Addictive Behaviors*, 23(6), 717–734.
- Negrete, J. C. (2003). Clinical aspects of substance abuse in persons with schizophrenia. *Canadian Journal of Psychiatry*, 48(1), 14–21.
- Palmer, B. W., Heaton, R. K., Paulsen, J. S., Kuck, J., Braff, D., Harris, M. J., et al. (1997). Is it possible to be schizophrenic yet neuropsychologically normal? *Neuropsychology*, 11(3), 437– 446.
- Potvin, S., Briand, C., Prouteau, A., Bouchard, R. H., Lipp, O., Lalonde, P., et al. (2005). CANTAB explicit memory is less impaired in addicted schizophrenia patients. *Brain and Cognition*, 59, 38–42.
- Potvin, S., Pampoulova, T., Mancini-Marië, A., Lipp, O., Bouchard, R. H., & Stip, E. (2006a). Increased extrapyramidal symptoms in patients with schizophrenia and a comorbid substance use disorder. *Journal of Neurology Neurosurgery and Psychiatry*, 77(6), 796–798.
- Potvin, S., Stip, E., Lipp, O., Mancini-Marië, A., Élie, R., Roy, M. A., et al. (2006b). Quetiapine in patients with comorbid schizophrenia-spectrum and substance use disorder: An open-label trial. *Current Medical Research and Opinion*, 22(7), 1277–1285.
- Potvin, S., Sepehry, A. A., Stip, E. (2007). Meta-analysis of depressive symptoms in dual-diagnosis schizophrenia. *Australian and New Zealand Journal of Psychiatry*, 41(10), 792–799.
- Prouteau, A., & Doron, J. (2008). Cognitive predictors of the community functioning dimensions in schizophrenia: State of the art and future directions. *Encephale*, 34(4), 360–368.
- Prouteau, A., Verdoux, H., Briand, C., Lesage, A., Lalonde, P., Nicole, L., et al. (2004). The crucial role of sustained attention in community functioning in outpatients with schizophrenia. *Psychiatry Research*, 129(2), 171–177.
- Prouteau, A., Verdoux, H., Briand, C., Lesage, A., Lalonde, P., Nicole, L., et al. (2005). Cognitive predictors of psychosocial functioning outcome in schizophrenia: A follow-up study of subjects participating in a rehabilitation program. *Schizophrenia Research*, 77(2–3), 343–353.

- Rabany, L., Weiser, M., Werbeloff, N., & Levkovitz, Y. (2011). Assessment of negative symptoms and depression in schizophrenia: revision of the SANS and how it relates to the PANSS and CDSS. *Schizophrenia Research*, 126(1–3), 226–230.
- Regier, D. A., Farmer, M. E., Rae, D. S., Locke, B. Z., Keith, S. J., Judd, L. L., et al. (1990). Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. JAMA, 264(19), 2511–2518.
- Revheim, N., & Medalia, A. (2004). Verbal memory, problemsolving skills and community status in schizophrenia. Schizophrenia Research, 68(2–3), 149–158.
- Ritsner, M. S., Blumenkrantz, H., Dubinsky, T., & Dwolatzky, T. (2006). The detection of neurocognitive decline in schizophrenia using the Mindstreams Computerized Cognitive Test Battery. *Schizophrenia Research*, 82(1), 39–49.
- Saperstein, A. M., Fuller, R. L., Avila, M. T., Adami, H., McMahon, R. P., Thaker, G. K., et al. (2006). Spatial working memory as a cognitive endophenotype of schizophrenia: assessing risk for pathophysiological dysfunction. *Schizophrenia Bulletin*, 32(3), 498–506.
- Scheller-Gilkey, G., Thomas, S. M., Woolwine, B. J., & Miller, A. H. (2002). Increased early life stress and depressive symptoms in patients with comorbid substance abuse and schizophrenia. *Schizophrenia Bulletin*, 28, 223–231.
- Schiffer, B., Müller, B. W., Scherbaum, N., Forsting, M., Wiltfang, J., Leygraf, N., et al. (2010). Impulsivity-related brain volume deficits in schizophrenia-addiction comorbidity. *Brain*, 133(10), 3093–3103.
- Silver, H., Shlomo, N., Hiemke, C., Rao, M. L., Ritsner, M., & Modai, I. (2002). Schizophrenic patients who smoke have a faster finger tapping rate than non-smokers. *European Neuro*psychopharmacology, 12(2), 141–144.
- Stip, E., Corbière, M., Boulay, L. J., Lesage, A., Lecomte, T., Leclerc, C., et al. (2007). Intrusion errors in explicit memory: Their differential relationship with clinical and social outcome in chronic schizophrenia. *Cognitive Neuropsychiatry*, 12(2), 112– 127.
- Tsang, H. W., Leung, A. Y., Chung, R. C., Bell, M., & Cheung, W. M. (2010). Review on vocational predictors: a systematic review of predictors of vocational outcomes among individuals with schizophrenia: an update since 1998. Australian and New Zeeland Journal of Psychiatry, 44(6), 495–504.
- Velligan, D. I., Mahurin, R. K., Diamond, P. L., Hazleton, B. C., Eckert, S. L., & Miller, A. L. (1997). The functional significance of symptomatology and cognitive function in schizophrenia. *Schizophrenia Research*, 25(1), 21–31.
- Wobrock, T., Sittinger, H., Behrendt, B., D'Amelio, R., Falkai, P., & Caspari, D. (2007). Comorbid substance abuse and neurocognitive function in recent-onset schizophrenia. *European Archives* of Psychiatry and Clinical Neuroscience, 257(4), 203–210.
- Zhornitsky, S., Stip, E., Pampoulova, T., Rizkallah, E., Lipp, O., Bentaleb, L. A., et al. (2010). Extrapyramidal symptoms in substance abusers with and without schizophrenia and in nonabusing patients with schizophrenia. *Movement Disorders*, 25(13), 2188–2194.
- Zhornitsky, S., Stip, E., Desfossés, J., Pampoulova, T., Rizkallah, E., Rompré, P. P., et al. (2011). Evolution of substance use, neurological and psychiatric symptoms in schizophrenia and substance use disorder patients: A 12-week, pilot, case-control trial with quetiapine. *Frontiers in Psychiatry*, 2, 22.