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### Authors

Estrada, Elena  
Hartz, Sarah M  
Tran, Jeffrey  
et al.

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## Nicotine dependence and psychosis in Bipolar disorder and Schizoaffective disorder, Bipolar Type

Elena Estrada<sup>a</sup>, Sarah Hartz<sup>b</sup>, Jeffrey Tran<sup>a</sup>, Donald Hilty<sup>a</sup>, GPCC, Pamela Sklar<sup>c</sup>, Jordan W. Smoller<sup>d</sup>, Carlos N. Pato<sup>a</sup>, and Michele T. Pato<sup>\*,a</sup>

<sup>a</sup>University of Southern California, Department of Psychiatry

<sup>b</sup>Washington University in St. Louis, Department of Psychiatry

<sup>c</sup>Mount Sinai Medical School, Department of Psychiatry

<sup>d</sup>Harvard University, Department of Psychiatry

### Abstract

**Objective**—Patients with Bipolar disorder smoke more than the general population. Smoking negatively impacts mortality and clinical course in Bipolar disorder patients. Prior studies have shown contradictory results regarding the impact of psychosis on smoking behavior in Bipolar disorder. We analyzed a large sample of Bipolar disorder and Schizoaffective disorder, Bipolar Type patients and predicted those with a history of psychosis would be more likely to be nicotine dependent.

**Methods**—Data from subjects and controls were collected from the Genomic Psychiatry Cohort (GPC). Subjects were diagnosed with Bipolar disorder without psychosis (N=610), Bipolar disorder with psychosis (N=1591), and Schizoaffective Disorder, Bipolar Type (N=1544). Participants were classified with or without nicotine dependence. Diagnostic groups were compared to controls (N=10065) using logistic regression.

**Results**—Among smokers (N=6157), those with Bipolar disorder had an increased risk of nicotine dependence (OR=2.5;  $p<0.0001$ ). Patients with Bipolar disorder with psychosis were more likely to be dependent than Bipolar disorder patients without psychosis (OR=1.3;  $p=0.03$ ). Schizoaffective disorder, Bipolar Type patients had more risk of nicotine dependence when compared to Bipolar disorder patients with or without psychosis (OR=1.2;  $p=0.02$ ).

**Conclusions**—Bipolar disorder patients experiencing more severity of psychosis have more risk of nicotine dependence.

### Keywords

smoking; severe mental illness; cigarettes

## Introduction

Smoking kills the mentally ill 13–30 years earlier than the general population (Colton and Manderscheid 2006) and has been identified as the single greatest modifiable risk factor for decreasing mortality in the mentally ill (Parks et al. 2006). Smoking also contributes to psychiatric morbidity in Bipolar disorder patients (Goldstein et al. 2008; Waxmonsky et al. 2005). Bipolar disorder patients who smoke experience worse outcomes in mania treatment (Berk et al. 2008), earlier age of first manic episode (Ostacher et al. 2006), and more lifetime suicide attempts (Goldstein et al. 2008) than Bipolar patients who do not smoke.

Severely mentally ill patients, including those with Bipolar disorder and Schizoaffective disorder, are eight times more likely than the general population to smoke cigarettes (Hartz et al. 2014). The impact of psychosis on smoking has been investigated in past with contradictory results. Waxmonsky et al 2005 found an association between history of psychosis with smoking severity in a large sample of Bipolar disorder patients (N=1904). Corvin et al 2001 found a similar association in a small sample of Bipolar disorder patients (N=92). However, Kreinin et al 2012 was not able to reproduce an association between smoking severity and psychosis in Bipolar disorder patients (N=102). Cassidy et al 2002 also failed to find the same association between psychosis severity and smoking in 67 Bipolar disorder patients.

We investigated the impact of psychosis on nicotine dependence in a large sample of patients with Bipolar disorder and Schizoaffective disorder, Bipolar type per the Diagnostic and Statistical Manual of Mental Disorders IV Text Revision (American Psychiatric Association. Task Force on DSM-IV. 1994). Furthermore, we separated patients with Bipolar disorder into those with and without psychosis. While multiple studies have shown that those with Bipolar disorder smoke more than those without mental illness (Hartz et al. 2014; Lasser et al. 2000; Parks et al. 2006) fewer studies have controlled for psychosis within their Bipolar disorder and Schizoaffective disorder, Bipolar type samples (Cassidy et al. 2002; Corvin et al. 2001; Kreinin et al. 2012; Vanable et al. 2003). Given that the DSM IV criteria for Bipolar disorder includes but does not require psychosis, a study that separates Bipolar disorder patients into those with and without psychosis can further demonstrate the relationship between smoking and psychosis in the severely mentally ill. We separated Bipolar disorder patients into those with and without a history of psychosis and further included a sample of Schizoaffective disorder, Bipolar type patients to analyze the effects of psychosis on smoking behavior. Controls were screened negative for mania and psychosis.

## Methods

### Diagnostic Instruments

Subjects were diagnosed using the Diagnostic Interview for Psychosis and Affective Disorders (DIPAD) which is an instrument based on the Diagnostic Interview for Genetic Studies (DIGS) (Nurnberger et al. 1994) and is consistent with the DSM-IV-TR. Nicotine dependence was defined using the CAGE questionnaire subtly modified for nicotine use (Kitchens 1994; Rustin 2000). Smokers were defined as individuals who endorsed smoking 100 cigarettes in their lifetime. Nicotine dependence was defined as smokers who had

difficult quitting, and who immediately smoke upon waking. This definition of nicotine dependence was compared with the database National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) and showed PPV=70% and NPV=79%.

### Sample and Analyses

Subjects and control data were attained from the Genomic Psychiatry Cohort (GPC) (Pato et al. 2013). Subjects were diagnosed with Bipolar disorder with psychosis (N=1591), Bipolar disorder without psychosis (N=610) or Schizoaffective disorder, Bipolar type (N=1544). Controls (N=10065) screened negative for mania and psychosis. Caucasians, African American, and Hispanic participants were included. Logistic regression analysis results were performed modeling the association between nicotine dependence and psychiatric diagnosis, adjusted for age, sex, race and ethnicity.

### Results

Table 2 shows logistic regression results for nicotine dependence among smokers (N=6,157) adjusted for age, sex, race, ethnicity. Odds ratio for having psychotic features is the additional risk of being a dependent smoker beyond the bipolar diagnosis. Odds ratio for schizoaffective disorder bipolar subtype is the additional risk of being a dependent smoker above both having bipolar disorder and having psychotic features. When comparing Bipolar disorder patients psychosis to those without psychosis, those with psychosis were found at higher risk for nicotine dependence (OR=1.3; p=0.03). Schizoaffective disorder, Bipolar type patients showed higher risk for nicotine dependence than Bipolar patients with or without psychosis (OR=1.2; p=0.02).

### Discussion

Patients with severe mental illness smoke to a greater extent than the general population (Hartz et al. 2014; Parks et al. 2006). Smoking is especially harmful to the clinical course of Bipolar disorder patients (Berk et al. 2008; Goldstein et al. 2008). Smoking effectively lowers circulating doses of psychotropic medication by inducing cytochrome P450 which complicates the treatment of Bipolar disorder (Desai, Seabolt and Jann 2001). Smoking has also been found to be associated with manic cycling, mixed episodes, and greater episode severity in Bipolar disorder patients (Waxmonsky et al. 2005).

This study demonstrated the impact of psychosis on risk of nicotine dependence. In smokers, Bipolar disorder diagnoses increased the risk of nicotine dependence (OR=2.5; p<0.0001). Within the Bipolar disorder sample, those patients with psychotic features were more likely to be nicotine dependent than Bipolar disorder patients without psychotic features (OR=1.3; p=0.03). Lastly, the Schizoaffective disorder, Bipolar type sample demonstrated more risk of nicotine dependence compared the Bipolar disorder sample with or without psychosis (OR=1.2; p=0.02). Our study shows that patients who are more severely psychotic are more likely to be nicotine dependent than those with less severe symptoms.

Schizoaffective disorder has been discussed as a sub type of Schizophrenia (DSM-I 1952; Williams and McGlashan 1987), a psychotic mood disorder (Lake and Hurwitz 2006), part

of the psychotic spectrum of diagnoses (Keshavan et al. 2011; Tamminga et al. 2013), or a separate diagnostic entity (Mitsuda 1965). Several studies have used clinical and demographic data to show Schizoaffective disorder patients fall between Bipolar and Schizophrenic patients on either ends of a psychosis spectrum (Mancuso et al. 2014; Pagel et al. 2013). This study investigates nicotine dependence in a sample of Schizoaffective disorder, Bipolar type and Bipolar patients with and without psychosis. Our findings support the theory of a psychosis spectrum by showing greater risk of nicotine dependence in patients experiencing a greater degree of psychosis.

Limitations of this study include an inability to quantify smoking severity or to assess withdrawal and tolerance. This study would have also benefited from the inclusion of Schizophrenic patients to further compare the association between psychosis and smoking across diagnostic groups. This is the largest study to date investigating psychosis and nicotine in Bipolar disorder patients and further includes a sample with and without psychotic features. We found that among the severely mentally ill, those with psychotic features demonstrated greater risk of nicotine dependence.

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## Appendix

The Genomic Psychiatry Cohort Consortium (GPCC) investigators are Helena Medeiros<sup>1</sup>, Janet L. Sobell<sup>1</sup>, Colony Abbott<sup>1</sup>, Maria Helena Azevedo<sup>2</sup>, Antonio Macedo<sup>2</sup>, Evelyn J. Bromet<sup>3</sup>, Peter F. Buckley<sup>4</sup>, Michael A. Escamilla<sup>5</sup>, Ayman H. Fanous<sup>6</sup>, Laura J. Fochtmann<sup>3</sup>, Douglas S. Lehrer<sup>8</sup>, Fabio Macciardi<sup>9</sup>, Dolores Malaspina<sup>10</sup>, Stephen R. Marder<sup>11</sup>, Christopher P. Morley<sup>13</sup>, Humberto Nicolini<sup>14</sup>, Diana O. Perkins<sup>15</sup>, Jeffrey J. Rakofsky<sup>7</sup>, Mark H. Rapaport<sup>7</sup>, Steven A. McCarroll<sup>12</sup>, Becky Kincaid<sup>7</sup>, James A. Knowles<sup>1</sup>, Marquis Vawter<sup>9</sup>. NESARC data were obtained from the NIAAA (<http://niaaa.census.gov>).

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<sup>1</sup>Department of Psychiatry and the Behavioral Sciences, Keck School of Medicine of the University of Southern California, Los Angeles, CA

<sup>2</sup>Department of Psychiatry, University of Coimbra, Coimbra, Portugal

<sup>3</sup>Department of Psychiatry and Behavioral Science, State University of New York, Stony Brook, NY

<sup>4</sup>Department of Psychiatry, Georgia Regents University Medical Center, Augusta, GA

<sup>5</sup>Department of Psychiatry, Texas Tech University Health Sciences Center, El Paso, TX

<sup>6</sup>Department of Psychiatry, Veterans Administration Medical Center, Washington, DC

<sup>8</sup>Department of Psychiatry, Wright State University, Dayton, OH

<sup>9</sup>Department of Psychiatry, University of California, Irvine, CA

<sup>10</sup>Department of Psychiatry, New York University, New York, NY

<sup>11</sup>Department of Psychiatry, University of California, Los Angeles, CA

<sup>13</sup>Departments of Family Medicine, Public Health & Preventive Medicine, and Psychiatry & Behavioral Sciences, State University of New York, Upstate Medical Center, Syracuse, NY

<sup>14</sup>Center for Genomic Sciences, Universidad Autónoma de la Ciudad de México, Mexico City, Mexico and Carracci Medical Group, Mexico City, MX

<sup>15</sup>Department of Psychiatry, University of North Carolina, Chapel Hill, NC

<sup>7</sup>Department of Psychiatry and Behavioral Science, Emory University, Atlanta, GA

<sup>12</sup>Department of Genetics, Harvard Medical School, Boston, MA; Stanley Center for Psychiatric Research, Broad Institute of MIT and Harvard, Cambridge, MA

**Table 1**

## Sample characteristics

	<b>Bipolar without psychosis</b>	<b>Bipolar with psychosis</b>	<b>Schizoaffective Disorder, Bipolar type</b>	<b>Controls</b>
N	610	1,591	1,544	10,065
% Female	61%	52%	42%	56%
Average Age (SD)	43 (14)	43 (13)	43 (11)	38 (15)
% Caucasian	68%	64%	55%	48%
% African American	15%	18%	25%	17%
% Hispanic	17%	18%	20%	35%
% Smokers *	72%	76%	84%	35%
% Nicotine dependent **	41%	48%	56%	12%

\* Smokers defined as individuals who have smoked 100 cigarettes lifetime

\*\* Nicotine dependence is defined as smokers who have difficulty quitting and smoke immediately upon waking

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**Table 2**

Logistic regression analysis for nicotine dependence among smokers, adjusted for age, sex, race and ethnicity. Age was positively associated with nicotine dependence ( $p=0.01$ ); no other covariates were statistically significant.

	Odds ratio	p-value
Bipolar disorder*	2.5	<0.0001
Psychotic Features**	1.3	0.03
Schizoaffective disorder, Bipolar type	1.2	0.02

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