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Panic Symptoms, Cigarette Smoking and Drinking in Adolescent Female Twins

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Introduction

- **In adults, cigarette (Breslau & Klein, 1999; Goodwin & Hamilton, 2002) and alcohol use (Merikangas et al., 1998) are significantly associated with panic disorder symptoms, even after adjusting for other anxiety disorders.**
- **In adolescents, cigarette smoking is associated with panic symptoms, even after controlling for other anxiety disorders (Johnson et al., 2000).**

Introduction

- **Twin studies find substantial genetic influences on smoking and drinking (Heath, Madden, and Martin, 1998; Heath and Madden, 1995) with heritability estimates as high as 40-80 percent.**
- **There is evidence from family studies (Horwath et al., 1995; Fyer et al., 1996) and twin studies (Kendler et al., 1993; Scherrer et al., 2000) that panic disorder runs in families, and this is at least in part due to genetic factors in adults.**
- **Molecular genetics studies have found a polymorphic duplication on human chromosome 15 (15q24-26; DUP25) that is highly associated with panic disorder (Gratacos et al., 2001).**

Introduction

- **Drinking, smoking, other substance use, and other comorbid psychopathologies have an age of onset that predates the development of panic disorder.**
 - **Associations between drinking and smoking and panic disorder may be due to causative effects of drinking and smoking on panic symptoms**
 - **E.g. Klein’s “suffocation-false alarm hypothesis model”, or**
 - **Drinking, Smoking and Panic may share some common etiologies (environmental and genetic)**
 - **They may be related through some third unmeasured factor**
- **Examination of familial effects on panic and unique associations between panic and cigarette and alcohol use remains unexplored in adolescents.**

Aims

- The aim of the proposed research is to examine the extent to which:
 - 1) There are familial effects on panic severity in adolescent girls
 - 2) Smoking and Drinking-related problems are uniquely associated with panic symptoms, after adjusting for familial influences on panic, other substance use, personality, and major depression, conduct disorder and social phobia

Sample

- **Twins from the Missouri Adolescent Female Twin Study (MOAFTS) were ascertained from Missouri State birth records**
 - **Interview and mailed-questionnaire-data from a survey conducted in 1995-1997 of adolescent female twins (N=1422 individuals)**
 - **Age Range: 16-23**

Lifetime Panic Severity

(outcome measure)

– Panic severity: four level variable:

- 1) never had an attack
- 2) uncued anxiety attack (“came out of the blue”)
- 3) DSM-IV diagnostic uncued panic attacks
- 4) DSM-IV Panic Disorder

Lifetime Smoking Behavior

- **Ever smoking:** reports having tried cigarettes
- **Regular smoking :** reports smoking weekly for three weeks or more
- **Subclinical Nicotine Dependence:** reports 2 or more DSM-IV nicotine dependence items

Lifetime Drinking Behavior

- **Ever drinking:** reports having a full drink of alcohol
- **Regular drinking :** reports drinking at least one drink every month for 6 months or more
- **Subclinical Alcohol Dependence:** reports 2 or more DSM-IV alcohol dependence items

Lifetime Marijuana Use Behavior

- **Ever smoked:** reports having tried marijuana
- **Regular use:** reports have used marijuana 40 or more times
- **Subclinical Marijuana Dependence:** reports 2 or more DSM-IV marijuana dependence items

Other Drugs and Psychopathology

- **Lifetime Experimentation with other drugs**
 - **Stimulants**
 - **Opiates**
 - **Sedatives**
 - **Hallucinogens**
 - **Inhalants**
 - **Cocaine**
- **Lifetime History of DSM-IV Major Depression, Conduct Disorder, and Social Phobia**

Self-Report Personality Measures

Junior Eysenck Personality Inventory

(JEPI, Eysenck, 1965)

- **Extraversion:** sociable, lively, active, assertive, sensation-seeking
- **Neuroticism:** anxious, depressed, guilt feelings, low self-esteem
- **Social Non-conformity:** (“lie” scale): honest, blatant

Statistical Analysis

Multinomial Logistic Regression

- **PHENOTYPIC ANALYSES:**
 - **Dependent Variable:** Panic Severity (4 levels)
 - **Independent Variables:** smoking and drinking variables, other drugs, major depression, conduct disorder, social phobia and personality
- **GENETIC ANALYSES:**
 - **Dependent Variable:** panic status of respondent
 - **Independent Variables:** cotwin's panic status, covariates, smoking and drinking variables of the respondent

Outcome Variable	Prevalence % (n=1422)
Anxiety Attack	8.7
Panic Attack	1.6
Panic Disorder	1.9

Predictor Variables	Prevalence % (n=1422)
Ever Smoked Cigarettes	64.3
Regular Cigarette Smoking	32.7
Subclinical Nicotine Dependence	28.5
Ever Drinking Alcohol	76.4
Regular Alcohol Drinking	39.4
Subclinical Alcohol Dependence	25.5
Ever Used Marijuana	36.4
Regular Marijuana Use	7.8
Subclinical Marijuana Dependence	1.8
Ever Used Stimulants	5.5
Ever Used Opiates	3.5
Ever Used Sedatives	2.6
Ever Used Hallucinogens	7.9
Ever Used Inhalants	2.2
Ever Used Cocaine	4.2
History of Major Depression	21.5
History of Conduct Disorder	2.8
History of Social Phobia	17.1

Phenotypic Associations with Panic Severity

Odds Ratios (and 95% Confidence Interval) with never having a panic attack as the comparison group
-only significant effects shown, after controlling for age

Unadjusted	Anxiety Attacks	Panic Attacks	Panic Disorder
Ever smoking	2.1 (1.3-3.5)	n.s.	n.s.
Regular Smoking	n.s.	n.s.	4.1 (1.6-10.7)
Subclinical Nicotine Dependence	1.8 (1.3-2.7)	n.s.	6.2 (2.4-16.5)
Subclinical Alcohol Dependence	1.8 (1.2-2.9)	n.s.	n.s.
Subclinical Marijuana Dependence	n.s.	7.3 (1.7-32.0)	n.s.
Stimulant Use	3.1 (1.6-5.9)	n.s.	n.s.
Opiate Use	3.9 (1.8-8.4)	n.s.	n.s.
Sedative Use	3.0 (1.2-7.5)	4.9 (1.0-23.1)	6.4 (1.3-30.8)
Major Depression	2.6 (1.7-4.1)	6.5 (2.5-16.8)	24.8 (8.1-76.2)
Conduct Disorder	2.7 (1.04-7.2)	n.s.	n.s.
Social Phobia	2.0 (1.3-3.2)	3.1 (1.2-7.9)	4.7 (1.9-11.6)
Neuroticism	1.4 (1.2-1.7)	n.s.	1.8 (1.1-3.2)

Phenotypic Associations with Panic Severity

Odds Ratios (and 95% Confidence Interval) with never having a panic attack as the comparison group
-only significant effects shown, after controlling for age

Adjusted	Anxiety Attacks	Panic Attacks	Panic Disorder
Subclinical Nicotine Dependence	n.s.	n.s.	9.98 (2.5-39.2)
Major Depression	2.0 (1.2-3.3)	5.9 (1.8-18.8)	15.0 (3.3-67.6)
Social Phobia	1.9 (1.1-3.2)	n.s.	n.s.
Neuroticism	1.3 (1.1-1.6)	n.s.	n.s.

Residual Associations with Panic Severity

Odds Ratios (and 95% Confidence Interval) with never having a panic attack as the comparison group
 -only significant effects shown, after controlling for age and zygosity

Unadjusted	Anxiety Attacks	Panic Attacks	Panic Disorder
Cotwin's anxiety attack	8.7 (5.2-14.5)	8.7 (5.2-14.5)	n.s.
Cotwin's panic attack	n.s.	8.7 (5.2-14.5)	n.s.
Cotwin's panic disorder	n.s.	n.s.	8.7 (5.2-14.5)
Adjusted			
Cotwin's anxiety attack	6.8 (3.8-12.4)	6.8 (3.8-12.4)	n.s.
Cotwin's panic attack	n.s.	6.8 (3.8-12.4)	n.s.
Cotwin's panic disorder			6.8 (3.8-12.4)
Subclinical Nicotine Dependence	n.s.	n.s.	8.1 (2.2-30.0)
Major Depression	n.s.	4.9 (1.5-15.9)	18.4 (1.1-300.8)
Social Phobia	2.3 (1.3-4.0)	n.s.	n.s.
Neuroticism	1.3 (1.07-1.6)	n.s.	n.s.

Discussion

- Results confirm that panic severity runs in families in adolescent girls.
- Even after accounting for familial effects on panic severity, major depression, social phobia and neuroticism, nicotine dependence remained as a significant risk factor for panic disorder.
 - However, at the same time, nicotine dependence did not significantly reduce familial effects on panic, suggesting that it does not mediate those familial effects
- Relative to alcohol or other psychoactive substances, the relationship between nicotine dependence and panic disorder appears particularly strong.

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