

Tobacco Dependence in Psychiatric Disorder

Altaweel M.

Abstract:

Rates of dependence in psychotic population appears to be high, and it has been estimated that patients with mental illness consume 44.3% of all cigarettes in the United States. The present study aimed at studying how can psychiatric disorders (schizophrenia, bipolar disorder, and substance abuse) affect the dependence of nicotine. The study included 95 patients from the outpatient clinic in Kuwait psychological medicine hospital, (39 schizophrenic, 36 bipolar disorder and 30 substance abuse), in addition to similar number of healthy controls. Both patients and control were assessed for nicotine dependence using DSM IV criteria, as well as Fagerstrom test for nicotine dependence. 25 schizophrenic patients showed nicotine dependence, compared to 6 control subjects while 23 patients out of 30 bipolar compared to only 6 controls, and 24 substance abuse patients out of 30 showed positive nicotine dependence compared to only 8 controls. Higher rates of nicotine dependence are observed in various psychiatric disorder patients.

Introduction

Large population-based studies in the United States report the current rate of smoking to be approximately 22% to 28% (CDC, 2004; Grant et al., 2004). Smokers with current psychiatric disorders have significantly higher rates of smoking (41% on average), and it has been estimated that patients with mental illness consume 44.3% of all cigarettes in the United States (Lasser et al., 2000).

Data from the National Co morbidity Survey revealed that whereas the population prevalence of current smoking among those with no mental illness was 22.5%, some 41% of those reporting a mental illness were current smokers. People with mental illnesses also consumed more cigarettes -- current smokers without mental illnesses had a mean peak consumption of 22.6 cigarettes per day, compared with 26.2 by those with a mental illness. Furthermore, those with a diagnosable psychiatric disorder consume an estimated 34% to 44% of all cigarettes smoked in the United States.

Rates of dependence in psychotic populations also appear to be high (Dalack et al., 1998; Kalman et al., in press). Smokers with comorbid psychiatric or substance use disorders are less likely to attempt quitting (Lasser et al., 2000) and have higher risk of developing smoking-related illnesses (Hurt et al., 1996; Lichtermann et al., 2001).

There have been several hypotheses to explain the high rates of smoking among people with psychiatric and substance use disorders. One hypothesis is that genetic factors influence vulnerability to both smoking and these disorders (Kendler et al., 1993). Two, certain environmental factors (e.g., stress, poverty) are associated with increased smoking and the onset of symptoms of psychiatric disorders. Three, people with psychiatric or substance use disorders use smoking as a way to self-medicate clinical symptoms, side effects of psychiatric medication or cognitive deficits (Chambers et al., 2001; Sacco et al., 2004).

Nicotine stimulates the release of several neurotransmitter systems, including dopamine, norepinephrine, 5-hydroxytryptamine (5-HT), glutamate, γ -aminobutyric acid (GABA) and endogenous opioid peptides, and acts as an agonist on presynaptic nicotinic acetylcholine receptors (nAChRs), which are stimulated endogenously by acetylcholine (Picciotto, 2003). Although chronic exposure of agonists typically produces receptor downregulation, chronic nicotine administration causes a paradoxical upregulation of nAChRs through rapid desensitization followed by receptor inactivation (Gentry and Lukas, 2002). After a short period of abstinence (e.g., overnight), nAChRs are resensitized and once again responsive to nicotine. This may explain why many smokers tend to report the first cigarette of the morning as their most satisfying.

The dopamine reward system is associated with addiction to drugs of abuse, including nicotine (Volkow et al., 2002). Nicotine is thought to be reinforced by stimulating nAChRs in the ventral tegmental area of the midbrain that project to the nucleus accumbens, an important limbic area thought to be involved in drug reinforcement and reward. Further, these neurons project to the prefrontal cortex, which is thought to directly influence cognitive states, such as arousal and cognitive functioning.

Background:

Although rates of cigarette smoking have been found to be higher in schizophrenic and depressed patients than in the general population, data regarding rates of bipolar patients are limited. This study further examines the relationship between bipolar disorder and smoking and compares the rate

of smoking in bipolar disorder patients with rates in schizophrenic patients and in the general population

Aim of the Work

To study whether psychiatric disorders (Schizophrenia, Bipolar disorders, and substance abuse disorder) affects the dependence of nicotine or not, and how can different types inside a single disorder differs as regards the rate of abuse of nicotine

Methods

Assessment of 95 patients taken from the out patient clinic in the Kuwait psychiatric hospital, randomly chosen as every other one coming to the clinic in a period of 3 weeks. Complete psychiatric and substance use evaluations was done using DSM-IV semistructured interview. Substance abuse was excluded from the sample exception the substance abuse group, where any other axis I psychiatric disorder was excluded. Thirty nine patient was diagnosed with schizophrenia according to DSM-IV and only 34 agreed to continue the interview. Out of 36 patient diagnosed with bipolar disorder only 30 patient went on the rest of the interview, and all 30 substance abuse subject diagnosed with DSM-IV criteria continued the interview. Nicotine dependence was determined by daily smoking of 10 to 40 cigarettes according to DSM-IV resulting in tolerance to smoking effect and in the presence of withdrawal symptoms after cessation of smoking. Also, assessment of smoking behaviors did include self-report of cigarette and other tobacco use over the past 30 days and surrogate measures of smoking such as plasma nicotine levels (levels >15 ng/ml are considered dependence) (Benowitz et al., 2002).

Level of nicotine dependence was assessed through the Fagerstrom Test for Nicotine Dependence and the presence of nicotine withdrawal symptoms (e.g., irritability, cravings, headache, and fatigue) upon smoking abstinence.

Controls were chosen from patients family members matching nearly same age and sex, as family members has same socio-economic and educational status.

All control groups did undergo the general health questionnaire. (The Arabic version revised by Okasha et al 1989, where the cut off point was changed and raised to 7 for the middle east.) to exclude any psychiatric disorder. Only those who did score under 7 was taken as controls. 70 control patients were interviewed as regard nicotine dependence using Fagerstrom test and as regard substance abuse using the DSM-IV criteria.

Results

Out of 34 patients with the diagnosis of schizophrenia, 25 showed nicotine dependence. The different types of schizophrenia were nearly equal with no significant difference among them as regard nicotine dependence. Out of 25 controls taken from schizophrenic families, only 6 showed nicotine dependence. (Table 1).

Among 30 patients with the diagnosis of bipolar disorder, 23 showed positive nicotine dependence, and the number was more in the currently depressed subjects than those with the diagnosis of mania at the current interview. Only 5 out of the 23 normal controls taken from the bipolar patients families showed nicotine dependence. (Table 2).

Twenty four out of the 30 patients with the diagnosis of substance abuse mostly poly

substance use disorder (showed positive nicotine dependence). Out of 22 normal control subjects from families of substance abuse patients only 8 showed positive nicotine dependence (Table 3).

It was shown clearly in table 4 that patients with disorganized schizophrenia had the greatest number of dependence with 13 patients out of 25 patient nicotine dependent schizophrenics, followed by paranoid type schizophrenia with 9 patients and only 3 male patients with undifferentiated schizophrenia showing nicotine dependence. Male / female difference was very apparent in both disorganized and undifferentiated schizophrenics. Again table 2 made it clear for bipolar patients that the currently depressed 16 patients was the leading in nicotine dependence with a clear difference than those with a current manic episode 9 patients.

Table 5 showed the relation of symptomatology to nicotine dependence severity, and it was found that negative symptoms, and anxious mood to be the most leading association with nicotine dependence. As 9 patients out of 25 schizophrenics showed negative symptoms and 11 out of the 25 nicotine dependent schizophrenics had anxious mood according to DSM IV diagnostic criteria, and depression followed anxiety in its relation to nicotine dependence. However, Vulnerability to Extra pyramidal symptoms was highly related to nicotine dependence and to the severity of smoking as it showed that 17 out of 25 nicotine dependent schizophrenics are vulnerable to extrapyramidal symptoms in response to antipsychotic medication.

Table 1: number of positive nicotine dependent subjects among both schizophrenic and control groups.

		Control	Cases	Total
schiz-case	Non Smokers	19	9	28
	Smokers	6	25	31
Total		25	34	59
Pearson Chi-Square		Value	Exact Sig. (1-sided)	
		14.174(b)	.000	

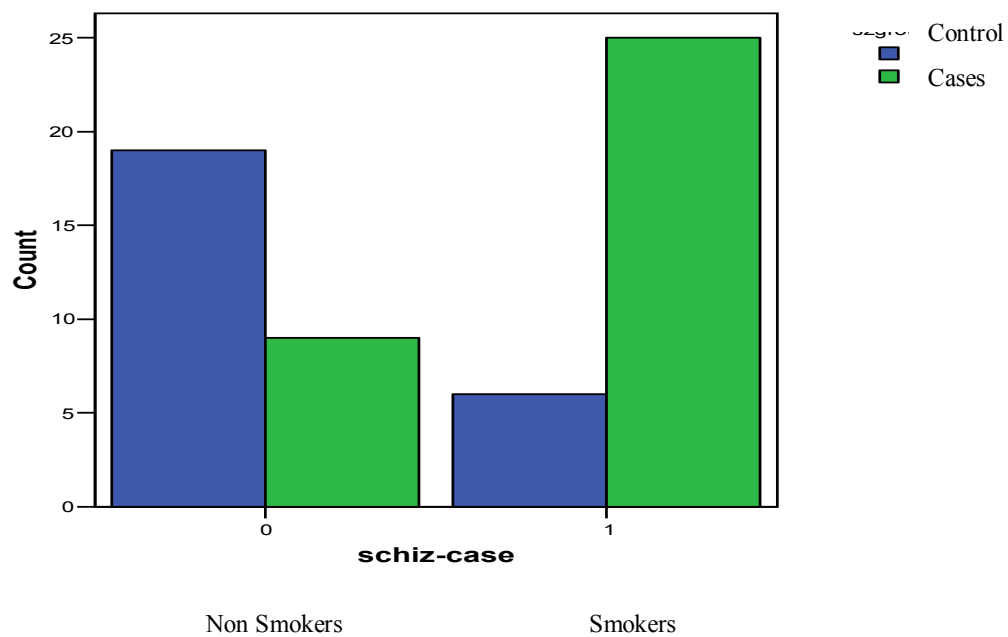
Bar Chart

Table 2: number of positive nicotine dependent subjects among both bipolar and control groups.

		Control	Cases	Total
bip-case	Non Smokers	17	7	24
	Smokers	6	23	29
Total		23	30	53
Pearson Chi-Square		Value	Exact Sig. (1-sided)	
		13.442(b)	.000	

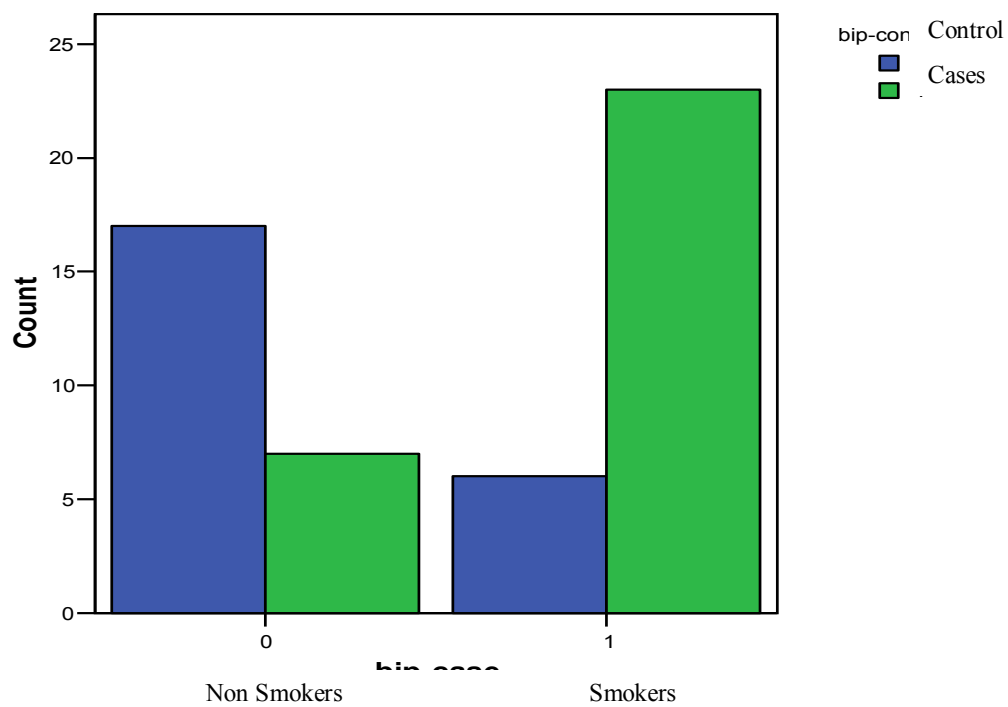
Bar Chart

Table 3: number of positive nicotine dependent subjects among both Substance abuse and control groups.

		Control	Cases	Total
subst-case	Non Smokers	14	6	20
	Smokers	8	24	32
Total		22	30	52
Pearson Chi-Square		Value	Exact Sig. (1-sided)	
		10.211(b)	.002	

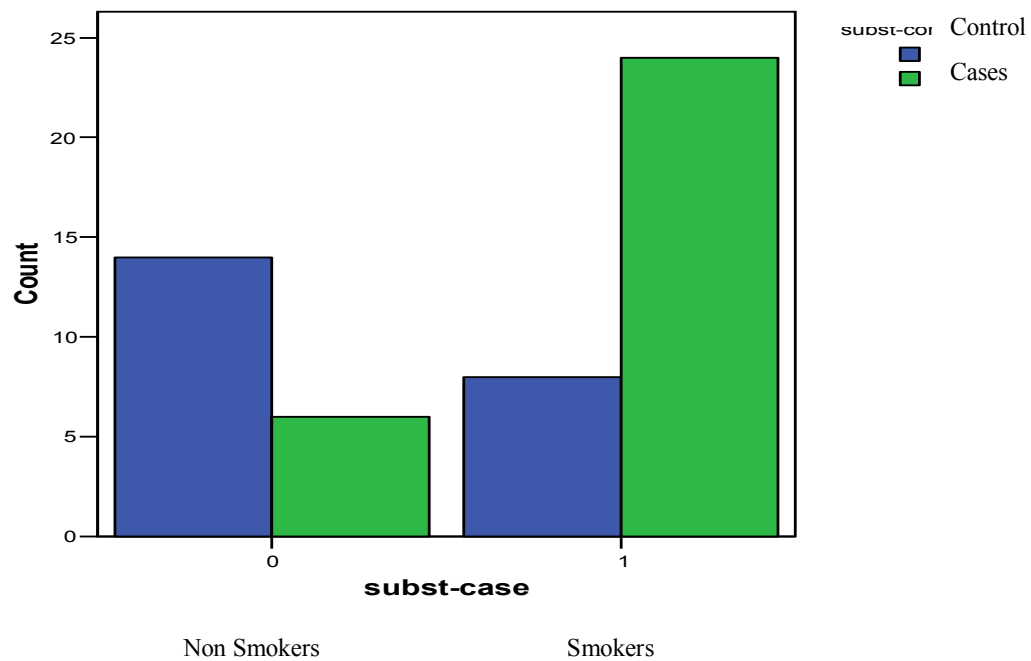
Bar Chart

Table 4: Nicotine dependence in subtypes of schizophrenia and bipolar disorder.

		Schizophrenia					Total
Type	Disorganized		Undifferentiated		Paranoid		
Gender	Male	Female	Male	Female	Male	Female	
No.	8/32%	5/20%	3/12%	0/0%	4/16%	5/20%	25
Total	13		3		9		
		Bipolar disorder					
Type	Current Manic			Current Depression			
No.	5/22%	3/10%		11/48%		4/20%	23
Total	9			16			

Table 5 Description of variables in 25 patients with schizophrenia, according to their nicotine dependence status: non-smokers (NS), mildly dependent smokers (MDS) and highly dependent smokers (HDS)

Variable	25 patients	7 NS	10 MDS	8 HDS
Presence of symptoms				
Negative	9 (37%)	3	3	3
Positive	7 (30%)	2	2	3
Disorganised	3 (14%)	1	1	1
Excited	4 (20%)	1	1	2
Anxious	11 (47%)	3	4	4
Depressive	7 (31%)	3	2	2
Vulnerability to extrapyramidal symptoms	17 (69%)	5	5	7
Presence of akathisia	3 (14%)	1	1	1

NS = non smokers, MDS = mild smokers, HDS = Heady smokers, D.F = degree of freedom

Discussion

In our results (Table 1), among 34 schizophrenic patients 25 showed positive nicotine dependence as opposed to control, who showed only 6 positives. This opposed difference between patients and controls did

record its highest values in the bipolar population (Table 2), whereas among 30 patient studied with bipolar disorder studied 23 showed positive nicotine dependence compared to only 6 among 21 controls showed positive dependence. Substance

abuse (Table 3) did not show great difference to schizophrenia where 19 out of 30 patients with substance abuse showed positive results opposed to 8 among controls.

This results was nearly comparable to the highest smoking prevalence found for people with bipolar (68.8%), psychotic (49.4%) and substance use disorders (49.0%) by Lasser et al., 2000.

Female in present study showed clear difference than male in dependence of nicotine, being less in number in both patients and controls and this goes with the cultural difference between male and female, and also showed the tight supervision and disapproval of smoking among females from families. Still there was clear difference between female patients and female controls.

Nicotine administration has been shown to improve neurocognitive deficits in schizophrenia (Sacco et al., 2005), attention-deficit/hyperactivity disorder (Conners et al., 1996; Levin et al., 1996) and Alzheimer's disease (Potter et al., 1999). And this can explain the high prevalence of nicotine dependence and suggests a potentially critical role for nAChR stimulation in mediating cognitive dysfunction in these specific disorders (Sacco et al., 2004). Interestingly these effects are not consistently observed in healthy smoking controls. A series of studies have shown that an auditory gating measure (P50) deficit associated with schizophrenia is mediated by nicotine and smoking (Leonard et al., 2002), and that these effects are related to activation of one form of nAChR ($\alpha 7$ nAChR [CHNRA7]) and that the expression of this receptor appears to be dysregulated (Leonard et al., 2002). Potential Explanations for the

Association between Smoking and Schizophrenia

The causes of the very high prevalence of cigarette smoking in individuals with serious mental illnesses are complex and multifactorial. Most of the literature examining reasons for the association between smoking and schizophrenia focuses on the neurobiologic effects of nicotine, such as its interactions with dopaminergic circuits. Consuming nicotine may ameliorate some of the negative symptoms of schizophrenia, such as amotivation, anhedonia, and social isolation and this could explain our finding recorded in (Table 5) that showed that 9 out of 25 nicotine dependant schizophrenic subjects did show negative symptoms and it came as the second cluster of symptoms to increase nicotine dependence among our patient sample. Nicotine also may improve auditory gating impairments in persons with schizophrenia, which in turn may enhance attention, sensory processing, and the ability to interact with their environments. Again psychological factors may influence use of nicotine among patients

When we studied the rate of nicotine dependence among the subtypes of schizophrenia (disorganized, and paranoid) and bipolar disorder (either manic or depressive episodes) in table 4. Disorganised schizophrenia showed the highest rates of dependence among the schizophrenic population with 13 patients out of 25 and this in a part can be explained by the increased cognitive deficit symptomatology and flattening of affect among disorganized compared to other types. While the currently depressed patients showed a higher rate of dependence than those with current mania. As there was 16 currently depressed bipolar patients

(70%) compared to 7 patients with current manic episode. A relationship between nicotine dependence and depression has been seen in both epidemiological and clinical samples done by Brown et al 1993. Going also with our results as shown in table 4, Huges et al 1996 found that a clinical sample of depressed outpatients were twice as likely to smoke as the general population. Again individuals in a study by Covey et al 1993 with a lifetime history of depression were more likely to have smoked in their life time (76%) versus 52% in non depressed, the finding was more significant among male smokers. also in(Table 5) it was clear that depression was the third cluster of symptoms that caused cigarette smoking among schizophrenia, the thing that goes with Glassman A H- 1993 who noticed that persistant depressive symptoms in schizophrenia may influence the prevalence of smoking.

Although some research has reported that smoking cessation can lead to a reemergence of depressive symptoms (Covey et al., 1997; Glassman et al., 1993), other studies have questioned this relationship (Thorsteinsson et al., 2001). However, a past history of major depression does not appear to influence tobacco treatment outcomes (Hayford et al., 1999).

It is undoubtedly expected for substance abuse disorder population to show high prevalence of nicotine dependence, and to show an equal rate among males and females, in our study, female substance use patients were quite few, and there was no explanation why female patients seek less psychiatric help.

The development of effective strategies for promoting smoking cessation in schizophrenia is of great importance given the high rates of smoking and cessation

failure in this patient group. The nicotine transdermal patch (NTP) is associated with smoking cessation rates of 27% to 42% in smokers with schizophrenia (Chou et al., 2004). Further, use of the nicotine nasal spray, which produces higher plasma levels of nicotine, is associated with reduction of withdrawal and craving, and smoking cessation in smokers with schizophrenia (Williams et al., 2004) and it may help in recovery of cognitive dysfunction, hence putting hope in recovery of schizophrenia.

Although cigarette smoking may partially ameliorate specific psychiatric symptoms (such as negative symptoms) and cognitive measures,¹ the general "self-medication" hypothesis (improvement in negative, cognitive, or depressive symptoms and reduction of antipsychotic side effects) has not been supported by all studies.(Dalak et al 1998) The higher prevalence of smoking found among individuals (before the onset of their illness) who later develop schizophrenia may further indicate that impaired nicotinic neurotransmission is involved in the pathophysiology of schizophrenia.

We suggest that an association exists between smoking and psychotic symptomatology, and not with the categorical diagnosis of either schizophrenia or bipolar affective disorder.

Appendix

Fagerstrom test for Nicotine dependence

1. Are you evaluating a person who smokes cigarettes for how severe a nicotine dependence the person has? (Y or N)
2. number of minutes after the person wakes up before s/he smoke the first cigarette

3. number of cigarettes smoked by the person daily
4. Is it difficult for the person to refrain from smoking in places where smoking is forbidden? (Y or N)
5. Is the first cigarette of the day the one cigarette that the person would most hate to give up? (Y or N)
6. Does the person smoke more frequently during the first hours after waking than during the rest of the day? (Y or N)
7. Does the person smoke even when so ill that s/he must stay in bed most of the day? (Y or N)

References

- Benowitz NL, Jacob P III, Ahijevich K et al. (2002):** Biochemical verification of tobacco use and cessation. Report from the SRNT Subcommittee on Biochemical Verification. *Nicotine Tob Res* 4(2):149-159 [see comment].
- Brown RA, Kahler CW, Niaura R et al. (2001):** Cognitive-behavioral treatment for depression in smoking cessation. *J Consult Clin Psychol* 69(3):471-480.
- Chambers RA, Krystal JH, Self DW (2001),** A neurobiological basis for substance abuse comorbidity in schizophrenia. *Biol Psychiatry* 50(2):71-83.
- Chou KR, Chen R, Lee JF et al. (2004),** The effectiveness of nicotine-patch therapy for smoking cessation in patients with schizophrenia. *Int J Nurs Stud* 41(3):321-330.
- Conners CK, Levin ED, Sparrow E et al. (1996),** Nicotine and attention in adult attention deficit hyperactivity disorder (ADHD). *Psychopharmacol Bull* 32(1):67-73.
- Covey LS, Glassman AH, Stetner F (1997),** Major depression following smoking cessation. *Am J Psychiatry* 154(2):263-265.
- Dalack GW, Healy DJ, Meador-Woodruff JH (1998),** Nicotine dependence and schizophrenia: clinical phenomenon and laboratory findings. *Am J Psychiatry* 155(11):1490-1501.
- Gentry CL, Lukas RJ (2002),** Regulation of nicotinic acetylcholine receptor numbers and function by chronic nicotine exposure. *Curr Drugs Targets CNS Neurol Disord* 1(4):359-385.
- Glassman AH, Covey LS, Dalack GW et al. (1993),** Smoking cessation, clonidine, and vulnerability to nicotine among dependent smokers. *Clin Pharmacol Ther* 54(6):670-679.
- Glassman A H (1993):** Cigarette smoking implication for psychiatric illness. *Am. j .psychiatry* 150:546-553-Grant BF, Hasin DS, Chou P et al. (2004), Nicotine dependence and psychiatric disorders in the United States. *Arch Gen Psychiatry* 61(11):1107-1115.
- Hayford KE, Patten CA, Rummans TA et al. (1999),** Efficacy of bupropion for smoking cessation in smokers with a former history of major depression or alcoholism. *Br J Psychiatry* 174:173-178 [see comment].
- Hughes JR (1996):** The future of smoking cessation therapy in the United States. *Addiction* 91(12):1797-1802.
- Kendler KS, Neale MC, MacLean CJ et al. (1993):** Smoking and major depression: a causal analysis. *Arch Gen Psychiatry* 50(1):36-43.
- Lasser K, Boyd JW, Woolhandler S et al. (2000):** Smoking and mental illness: a population-based prevalence study. *JAMA* 284(20):2606-2610.

Leonard S, Gault J, Hopkins J et al. (2002): Promoter variants in the alpha-7 nicotinic acetylcholine receptor subunit gene are associated with an inhibitory deficit found in schizophrenia. *Arch Gen Psychiatry* 59(12):1085-1096.

Levin ED, Conners CK, Sparrow E et al. (1996): Nicotine effects on adults with attention-deficit hyperactivity disorder. *Psychopharmacology* 123(1):55-63.

Lichtermann D, Ekelund E, Pukkala E et al. (2001), Incidence of cancer among persons with schizophrenia and their relatives. *Arch Gen Psychiatry* 58(6):573-578 [see comment].

Picciotto MR (2003), Nicotine as a modulator of behavior: beyond the inverted U. *Trends Pharmacol Sci* 24(9):493-499.

Potter A, Corwin J, Lang J et al. (1999), Acute effects of the selective cholinergic channel activator (nicotinic agonist) ABT-418 in Alzheimer's disease. *Psychopharmacology (Berl)* 142(4):334-342.

Sacco KA, Bannon KL, George TP (2004), Nicotinic receptor mechanisms and cognition in normal states and neuropsychiatric disorders. *J Psychopharmacol* 18(4):457-474.

Sacco KA, Termine A, Seyal AA et al. (2005), Effects of cigarette smoking function on spatial working memory and

attentional function in schizophrenia: involvement of nicotinic receptor mechanisms. *Arch Gen Psychiatry* 62(6):649-659.

Thorsteinsson HS, Gillin JC, Patten CA et al. (2001), The effects of transdermal nicotine therapy for smoking cessation on depressive symptoms in patients with major depression. *Neuropsychopharmacology* 24(4):350-358.

Volkow ND, Fowler JS, Wang GJ (2002), Role of dopamine in drug reinforcement and addiction in humans: results from imaging studies. *Behav Pharmacol* 13(5-6):355-366 [comment].

Williams JM, Ziedonis DM, Foulds J (2004), A case series of nicotine nasal spray in the treatment of tobacco dependence among patients with schizophrenia. *Psychiatr Serv* 55(9):1064-1066.

Authors:

Altaweel M.

Lecturer of Psychiatry
Faculty of Medicine
Cairo University

Address of Correspondence:

Altaweel M.

Lecturer of Psychiatry
Faculty of Medicine
Cairo University

û P ψ Ÿ H H QH
 é ° é
 û (é) û û
 (ð) ()
 . é
 é