Smoking and the course of anxiety and depression

Jamal, M.

CHAPTER 1

General Introduction

Background

Despite effective campaigns to reduce cigarette smoking, smoking remains a significant public health burden and one of the largest causes of death worldwide. It is estimated that in Europe and the Central Asia region, 122 million people smoke, with a higher prevalence in males (56 %) than in females (17 %)[1]. In the United States, 40 % of 45 million smokers attempt to quit each year; however, only 3 % are successful[2]. The detrimental effects of smoking on physical health are widely publicized and well-understood. Recently, there is growing interest to investigate its effects on mental health. This interest is instigated by the strong empirical association of smoking with psychiatric disorders. The prevalence of smoking is higher among psychiatric patients than in the general population[3,4]. In a study assessing rates of smoking and smoking cessation in adults, it was found that respondents with a current mental illness had the highest current and lifetime smoking rates and lowest quitting rates compared to those with remitted mental illness and those with no history of mental illness[4].

Smoking-Psychopathology Association Studies

Cross-sectional studies have indicated that smokers experience certain signs of depression such as sadness, hopelessness, or trouble sleeping more often than non-smokers[5,6]. Similarly, smokers are more likely to have higher rates of depressive symptoms than non-smokers[7,8]. Other studies have distinguished between current smokers, former smokers and never-smokers. In a report from the National Household Survey on Drug Abuse (NHSDA), current adolescent smokers had the highest odds of depressive symptoms, followed by former smokers, and then never-smokers[9]. Consistent with these findings in adolescents, studies in adults[10-14] and elderly[15] have also found significant differences among current smokers, former smokers and never-smokers in their symptoms of depression.

There seems to be a dose-response relationship between smoking and depression. Heavy smoking, as opposed to light smoking, is related to increased

severity of depressive symptoms[7, 10, 16, 17]. Similarly, the number of days smoked predicts depressive symptoms[8]. Many heavy smokers fulfill criteria for nicotine dependence. It is, therefore, not surprising that high levels of depressive symptoms are associated with nicotine dependence. In one study, it was found that as compared to non-dependent-, former, and never-smokers nicotine-dependent current smokers had higher scores on CES-D[18].

The smoking-anxiety association has received relatively little research attention. Regular smokers diagnosed with panic disorder have greater severity and intensity of anxiety symptoms than patients who do not smoke[19]. Similarly, heavy smokers have more severe anxiety symptoms than light smokers[20].

Depression and anxiety disorders often co-occur. In a large population-based survey of adults, depression was only marginally associated with smoking except in the presence of comorbid anxiety. Comorbid disorders had the strongest association with smoking, followed by anxiety, and then depression[21].

Cross-sectional studies have also shown that the prevalence of smoking in depressed individuals is higher than in the general population. Depressed individuals are more likely to have ever smoked, and they are less successful in their attempts to quit smoking than those with no history of major depression[22]. Individuals with depressed mood, a history of major depression, or both conditions have greater likelihood of ever smoking and smoking initiation than never-depressed[23] across all developmental stages. The prevalence of smoking seems to be related to the severity of depression[24, 25].

Studies that examine smoking prevalence in individuals with anxiety disorders usually focus on patients with panic disorder. Zvolensky et al.[26] put forward a theory suggesting that the association of smoking with anxiety disorders is specific to panic disorder and not generally to other anxiety disorders. To test this theory McCabe et al.[27] examined smoking behaviors across three anxiety disorders and found that smoking prevalence was higher in patients with panic disorder than in patients with social phobia or obsessive-

compulsive disorders. Moreover, patients with panic disorder were more likely to be heavy smokers.

Developmental Pathways to the Co-occurrence of Smoking and Psychopathology

Depression and Anxiety Preceding Smoking

The self-medication hypothesis posits that the motivation to continue to smoke is to alleviate depressive symptoms and so, depression is a predisposing factor in smoking initiation. This has been investigated in a number of longitudinal studies. For example, two six-wave longitudinal school-based studies found that depressive symptoms predicted later cigarette use[28, 29]. Another study found that adolescents with depressive symptoms were more likely to start smoking than those with no depressive symptoms[30]. These studies investigated the relation of smoking with depressive symptoms and not with a clinical diagnosis of depression, which also seems to be associated with smoking. For example, young people who met DSM-IV criteria for major depression were interviewed at 16, 18, and 21 years of age and were found to have elevated daily smoking rates and nicotine dependence[31].

Anxiety disorder as a predisposing factor in the onset of smoking has not been studied extensively. One population-based study found that non-smokers and non-dependent smokers with social fears had increased odds of subsequent nicotine dependence during a 4-year follow-up[32].

Few studies have assessed the role of both depressive and anxiety symptoms in smoking initiation. In a recent 10-year longitudinal school-based study, increasing severity of the symptoms of depression and anxiety in teenage was associated with an increased risk of nicotine dependence in young adulthood[33]. In a population-based study, it was found that pre-existing, currently active psychiatric disorders (unlike remitted disorders) including major depression and anxiety predicted subsequent onset of daily smoking and progression to nicotine dependence. Individuals with more than one pre-existing

disorder were at higher risk to starting smoking and progressing to nicotine dependence than individuals with one currently active psychiatric disorder[34].

Smoking Preceding Depression and Anxiety

The role of smoking as a vulnerability factor in the development of depression has been examined in significant epidemiological investigations and population-based surveys using longitudinal design. The question of whether adolescent cigarette smoking predicts the development of depressive symptoms was addressed in a longitudinal follow-up survey of adolescents who were not depressed at baseline. Cigarette smoking was found to be the stronger determinant of developing depressive symptoms. Moreover, a dose-response relationship was observed between smoking level and depressive symptoms [35]. In two large population-based studies on adolescents, smokers exhibited high depressive symptoms at follow-up than non-smokers[36, 37].

Smoking is associated not only with elevated depressive symptoms but also with an increased risk of clinical depression as assessed according to DSM criteria. In population-based, longitudinal studies on adults, a strong association was found between smoking and subsequent depression[38, 39]. Furthermore, total smoking years and number of cigarettes smoked per day were associated with increasing risk of major depression [38]. Another population-based prospective investigation revealed that pre-existing daily smoking predicted the onset of major depression, dysthymia, panic disorder, agoraphobia, alcohol- and drug-use disorders. Furthermore, independent of nicotine dependence, current smokers were more likely than former smokers to have subsequent onset of panic disorder, agoraphobia and substance use disorders[40].

Investigating the Bi-directionality of Smoking-Depression / Anxiety Association

Smoking and depression may mutually influence each other. A number of longitudinal studies have found a two-way temporal relation. For example, in adolescents, heavy and persistent smoking predicted increase in depressive

symptoms in a 1.5 year period after controlling for baseline depressive symptoms and other potential confounders; conversely, severe and persistent depressive symptoms predicted increases in smoking rates across the same time period after controlling for baseline smoking and other confounding variables[41]. In another longitudinal study it was found that never-smokers at follow-up (1 year later) had lower depressive symptoms at baseline than those who were current or former smokers at follow-up. Baseline never-smokers with high depressive symptoms had a higher likelihood of being a smoker one year later. The study also found that current smokers and former smokers developed high depressive symptoms over time than never-smokers. Moreover, baseline never-smokers who started smoking at follow-up had high depressive symptoms at both waves than baseline never-smokers and former smokers whose smoking status did not change at follow-up[42]. Consistently, history of major depression at baseline has increased the risk for progression to daily smoking and vice versa in a population-based study of young adults[43]. A history of major depression has increased the risk for progression to nicotine dependence. Similarly, a history of nicotine dependence was associated with first-incidence of major depression than no history of nicotine dependence in a prospective population-based study of young adults[44].

Several longitudinal studies that examined two-way smoking-depression temporal association found evidence for a uni-directional relation from smoking initiation to the development of depressive symptoms. For example, in one study, a one-way temporal relation was found; prior smoking was associated with a modest increased risk of subsequent depressed mood; however, prior depressed mood was not associated with a risk to starting smoking[45]. Similarly, in a large population-based study, it was found that at 1-year follow-up, current smoking was the strongest predictor of developing high levels of depressive symptoms; however, baseline high rates of depressive symptoms were not predictive of heavy smoking[46]. Similar uni-directional temporal relation from starting smoking to developing depressive symptoms[47, 48] or major depression[49] was observed in other studies.

Studies that investigated the directionality of smoking-anxiety association found a one-way temporal association from starting smoking to the onset or increasing risk of an anxiety disorder. No evidence for the reverse association, in which anxiety was a predisposing factor to start smoking, was found. Breslau and Klein[50] found that daily smoking was associated with an increased risk of the first onset of panic attack, and the risk was higher in current than in former smokers. However, prior panic attacks did not predict the onset of daily smoking[50]. A similar pattern of uni-directional association between smoking and panic disorders was reported in a school-based study[51]. Cigarette smoking may also be associated with an increased risk of other anxiety disorders. In a 3-wave community-based prospective investigation of adolescents, it was found that heavy smoking during adolescence was associated with an increased risk of generalized anxiety disorder, agoraphobia and panic disorder during early adulthood after controlling for demographics, anxiety and depression during adolescence, alcohol and drug use, and parental smoking. No association of smoking with obsessive-compulsive disorder or social anxiety was found. Anxiety disorders during adolescence were not associated with starting smoking in young adulthood[52]. Another study found that regular smokers and nicotine-dependent smokers at baseline had an increased risk for new onset of panic attacks and disorder and other anxiety disorders except for generalized anxiety disorder and obsessive-compulsive disorder at a 4-year follow-up period; however, after controlling for comorbid disorders including depression, anxiety and substance-use disorders, smoking or nicotine dependence increases the risk of only panic attacks and disorders. Pre-existing panic attacks or disorder was not associated with subsequent smoking initiation or the development of nicotine dependence[53].

Some studies investigated the temporal association of smoking with comorbid anxiety and depressive disorders. In a prospective population-based study, a bidirectional association between a mental disorder and smoking was found; starting smoking was associated with the subsequent first-ever incidence of generalized anxiety disorder and dysthymia, whereas generalized anxiety disorder was associated with subsequent onset of smoking[54]. In a 13-year

population-based study, nicotine-dependent young adults had elevated rates of anxiety and depression after controlling for history of mental health problems and other covariates. However, reduced mental health did not predict subsequent smoking initiation or the development of nicotine dependence[55].

Theories Explaining Smoking-Depression / Anxiety Association

Causal Theories

Two different causal hypotheses have been put forward to explain these co-occurring conditions: (i) depression and anxiety disorders instigate smoking initiation, or maintain smoking behavior as a means of self-medicating negative affect[17, 56, 57] which might be the result of neuropharmacological actions of nicotine in the brain leading to pleasure stimulation and the reduction of anxiety and tension[58]. This hypothesis is consistent with a finding that the level of monoamine oxidase B (which is inhibited or lowered by anti-depressants) is lower in the brains of smokers than in former smokers or non-smokers[59]; (ii) smoking initiation is temporally associated with the development of depression and anxiety disorders[60] probably because of the effect of nicotine on the neurotransmission systems that are implicated in depression and anxiety disorders[61]. Studies that have found a dose-response relationship between smoking and the symptom severity of depression or anxiety disorders[7, 8, 10, 16, 17, 20], relatively high rates and symptoms of depression and/ or anxiety in nicotine-dependent current smokers than non-dependent, former- or never-smokers[18, 44, 55, 62-66], higher rate of cigarette use and low mental health[67], or longitudinal uni-temporal association in either direction[28-40, 46-50, 52, 53, 55, 68] can further support these causal hypotheses.

Non-Causal Theories

Non-causal theories have been suggested when a bidirectional association between smoking/ nicotine dependence and the affective disorders was found[41, 44, 54, 69, 70]. These theories have gained support from a number of twin studies that proposed that these co-occurring conditions can both be explained by shared genetic[71-75] and environmental factors[71, 75-77] that increase both smoking as well as depression risks, independent of each other.

Shared Vulnerability Factors Explaining Smoking-Depression / Anxiety Association

As mentioned earlier, some longitudinal studies, that investigated the nature of the direction of smoking-psychopathology association, found a bi-directional temporal association in which smoking was associated with the onset of an affective disorder, and vice versa. These studies suggested the shared vulnerability hypothesis of smoking-psychopathology association, and conceptualized that common vulnerability factors might operate that reflect this association[44, 69]. This hypothesis has gained support from twin studies. In these studies evidence has been found for genetic and environmental factors accounting for the co-variation between depression and smoking. A prospective study on female twins tested both causal and non-causal models for evaluating smoking-major depression association. No direct causal relation in either direction was observed. However, controlling for the personal history of smoking and of major depression, a family history of major depression predicted smoking and a family history of smoking predicted major depression. Environmental factors also played some role which were mainly individual-specific and had little in common. Thus the study supported the non-causal model whereby the comorbidity was mainly due to genetic factors[72]. Another study examined the relationship between depression, smoking and nicotine dependence in male twins and explored genetic and environmental influences. Genetic factors predisposed to both depression and smoking and nicotine dependence. The odds of smoking in co-twins of depressed probands was greater than those in which neither of the twins had a lifetime history of depression. Moreover, the non-depressed co-twins of the depressed probands reported more withdrawal symptoms and depressed mood after quitting[74]. After controlling for familial factors, that is, by using discordant twin-pairs, smoking remained a gender-sensitive predictor of depressive symptoms, thus supporting the causal association. However, after controlling for genetic factors, that is, by using monozygotic and dizygotic twin-pairs, the persistent smokers and the quitters among the monozygotic twin-pairs were at higher risk for depression than among the dizygotic twin-pairs. The stronger association in men was modestly accounted for by underlying shared genes[73]. Similarly, the question of

whether major depression, smoking and nicotine dependence share a common genetic and /or environmental liability, and whether there is a difference between these different trajectories of smoking, was addressed in another study. A non-causal association was found, which, in males, was entirely accounted for by shared underlying genes, whereas in females, both genetic and environmental liabilities accounted for this comorbidity[71]. Inconsistent with these findings, McCaffery and colleagues found that the significant association of current and lifetime smoking with depressive symptoms in late-adult male twins[76] and adolescent male twins[75] was predominantly influenced by non-shared environmental factors while in adolescent female twins[75] both genetic and non-shared environmental factors accounted for the co-variation. A study investigating the genetic and environmental liability factors of smoking-panic association in female twin-pairs found that panic attacks and lifetime smoking had shared or familial environmental factors and no genetic liability factors in common[77].

Other Risk Factors

Other studies in general population and schools have found common risk factors that explain smoking-psychopathology association. For example, after controlling for the effects of demographic variables, comorbid depression, neuroticism, generalized anxiety disorder, and substance-use disorders, neuroticism was an independent predictor of the co-occurrence of smoking and panic attacks in adults[78]. A birth cohort was examined until the age of 16 years (N = 947), and it was found that significant associations between depressive symptoms and nicotine dependence were largely explained by common risk factors such as affiliation with deviant peers and lower self-esteem[63]. Another longitudinal investigation that followed students from teenage to young adulthood found that the association between smoking and panic attacks was no longer significant after adjusting for parental smoking and parental anxiety disorder[51]. Another risk factor explaining smoking-depression association was a history of conduct problems which was a predictor of both smoking and depression, and partially accounting for this association[43].

To explain conflicting findings in the literature regarding smoking-depression association, Johnson et al.[79] in a population-based sample of young adults tested Neale and Kendler's[80] etiological models of comorbidity for lifetime major depression and different smoking levels. The correlated liability model explained the comorbidity of depression with daily smoking, heavy smoking and nicotine dependence where familial liability explained the substantial amount of variance shared between depression and these levels of smoking; and in case of ever-smoking, it was associated with depression only when the smokers exceeded a higher threshold on the liability of smoking. Thus, depression is associated with regular (heavy) smoking, and ever-smokers would have depression only in case of heavy smoking.

Smoking-Depression / Anxiety Possible Linking Mechanisms

To date, the mechanisms underlying the association of smoking with depression and anxiety disorders have rarely been investigated.

BDNF Val^{66}Met Polymorphism

One possible mechanism linking smoking to an affective disorder may be BDNF Val^{66}Met polymorphism. The *BDNF gene* which, in humans, is located on chromosome 11, encodes the BDNF protein[81]. The single nucleotide polymorphism (SNP) rs6265 in BDNF gene results in an amino acid Valine-to-Methionine substitution at codon 66 (Val^{66}Met)[82].

The Val^{66}Met polymorphism in the brain-derived neurotrophic factor (BDNF) gene may be a plausible candidate gene polymorphism underlying smoking-depression/ anxiety association. An association of this polymorphism has been found with affective disorders[83-86], and to some extent, with smoking[87, 88] and other addictive behaviors[89, 90].

Several studies have supported the association of BDNF Val^{66}Met polymorphism with clinical major depression. For example, Met^{66} carriers were more often diagnosed with major depression than Val^{66}Val carriers[85]. Few studies that investigated the relationship of combination of gene markers including BDNF Val^{66}Met polymorphism with depression, found that haplotype analysis of the combination of markers including BDNF rs6265 produced significant associations with major depression[83, 84, 86]. With the exception of one study in a community sample of children and adolescents[91], no association of BDNF Val^{66}Met polymorphism has been found with anxiety disorders including generalized anxiety disorder and panic disorder[92-94].

Though not extensively, the polymorphism has also been investigated in relation to addictive behaviors. Heroin-dependent individuals were more often involved in drug-seeking behaviors and higher rates of cigarette use if they

carried the Met[66] allele of BDNF gene polymorphism as compared to those having Val[66]Val genotype[90]. Similarly, Met[66] carriers were more likely to be current and former smokers than never-smokers[87]; however, a following study failed to replicate these findings[88]. A recent study with healthy Chinese male participants reported that smokers with the Met[66] allele of the BDNF gene initiated smoking significantly earlier than the Val[66]Val carriers[95].

These studies indicate that BDNF Val[66]Met polymorphism may be involved in psychopathology and in addictive behaviors, however, there are some inconsistencies in findings, and the number of studies and sample size are small. Moreover, there is no study that has investigated smoking-psychopathology association taking into account the role of this polymorphism. It has been suggested that gene-environment interaction studies may be more useful to elucidate the underlying molecular mechanisms that may explain the association between different phenotypes[96]. We investigate the smoking-psychopathology association and examine the role of BDNF Val[66]Met polymorphism in this association.

Serum Brain-Derived Neurotrophic Factor

Another possible linking mechanism may be serum brain-derived neurotrophic factor (BDNF) which has been shown to be associated, both, with smoking and with depression and anxiety. BDNF is a small dimeric protein densely expressed in the central and the peripheral nervous system with high concentrations in the hippocampus and cerebral cortex[97, 98]. It is involved in the growth, development, survival, and function of neurons in the nervous system[99]. Animal studies have shown that stress decreases the expression of BDNF mRNA and protein in rat brain[100, 101]. Human postmortem studies have found reduced expression of BDNF mRNA and proteins in the brain of suicide victims diagnosed with different psychiatric disorders including depression, as compared to those with no psychiatric diagnosis[102].

Clinical studies have consistently reported the down regulation of serum BDNF expression with regard to depression. Various studies have shown that

depressed patients are characterized by lower serum BDNF levels than normal healthy controls[103-113] and that, the severe the depressive symptoms, the lower the serum BDNF levels[104, 109, 111, 114-118]. Two recent meta-analyses have confirmed these findings[119, 120].

Given that depression and anxiety disorders are highly comorbid, and may share similar pathophysiological factors[121-124], few studies have also investigated serum BDNF levels in patients with anxiety disorders. One study found lower baseline serum BDNF in patients with panic disorder as compared to normal controls[125]. A recent study reported gender-specific association of serum BDNF with anxiety: female patients diagnosed with anxiety had lower serum BDNF than female healthy participants, while no differences were found in male participants[126]. However, one study did not find significant difference in serum BDNF between patients with panic disorder and healthy participants[127]. Taken together, these preclinical and clinical studies adequately support the role of BDNF in the pathophysiology of depression and anxiety disorders.

There is also an evidence of an association of serum BDNF with smoking/ nicotine exposure, however, research in this area is sparse. An animal study has found that the expression of BDNF mRNA and protein in the hippocampus of neonatal piglets is significantly increased following nicotine infusion[128]. Few studies in humans have also investigated an association of serum BDNF with smoking and nicotine dependence. With the exception of a small Japanese study (N = 29; 16 smokers)[129], these studies have found that smoking was associated with increased serum BDNF levels[130, 131].

Given that smoking and nicotine dependence are highly associated with depression and anxiety disorders, there is reason to examine serum BDNF levels in relation to smoking/ nicotine dependence and depression/ anxiety. This issue has not been addressed before.

Attentional Control

Attentional bias in smokers to smoking-related cues has widely been documented, and it has been reported that smokers preferentially allocate their attention to such cues[132-151]. This attentional tendency has been thought to be important in maintaining drug-seeking behavior by enhancing the perception of drug-related cues in the environment, increasing drug-related cognitions for the cues and making it difficult to draw attention away from them; and because of the limited capacity of attention, the attentional resources left of competitive cues are depleted. The smoker may relapse to smoking after quitting because it is difficult for the addict to apply attentional resources to prevent relapse[152].

The ability of an individual to use executive functioning to selectively keep focus on task-relevant stimuli and to inhibit interference from distracting stimuli has been termed as attentional control[153]. In high-anxious individuals, inhibiting processing of task-irrelevant threatening stimuli seems to be difficult as compared to low-anxious individuals[154]. Similarly, low attentional control is associated with distracting effect of task-irrelevant threat-related emotional cues[155-157]. These findings suggest that anxiety is associated with impaired inhibition, and that better attentional control might help reducing anxiety by disengaging a person's attention from threat.

Attentional control might be another possible mechanism linking smoking with negative mood. There is no study investigating the role of attentional control in smoking-psychopathology association. However, it can be speculated that smokers with better attentional control might be able to disengage their attention from smoking-related cues in the environment, and thus may be able to control their smoking urges which might help improve their mood states.

Aims and Outlines of the Thesis

The main objective of this thesis is to enhance our understanding of the association of smoking with depression and anxiety disorders, and to find possible explanations of this association. We used data from Netherlands Study of Depression and Anxiety, or NESDA[158] to address our research questions regarding smoking-psychopathology association (chapter 2 to chapter 5). In chapter 6, we investigated the role of attentional control in attentional bias to smoking-related pictures. The data for this project were collected using the students of Leiden University.

1. Given that early-age nicotine exposure has adverse effects on brain and behavior (see for example, Slawecki et al.[159], Iniguez et al.[160], Thapar et al.[161]), chapter 2, retrospectively, examines the association of smoking age-onset with the onset of depression and/ or an anxiety disorder. The chapter is based on the data of those psychiatric patients who developed depression and / or an anxiety disorder after they started smoking.
2. In chapter 3, the severity and course of depressive and anxiety symptoms in never-smokers, former smokers, current smokers without nicotine dependence, and current smokers with nicotine dependence is investigated. The data of only those patients are used who had a current diagnosis (past 6 months) of an affective disorder. The chapter is based on baseline and 2-year follow-up NESDA data.
3. In chapter 4, the interaction between the BDNF gene Val^{66}Met polymorphism and smoking status with symptom severity of depression and anxiety disorders is investigated. The data is based on the same NESDA sample that was used in chapter 3, that is, patients with a current diagnosis of an affective disorder. The sample is stratified into never-smokers, former smokers, and current smokers with and without nicotine

dependence. This chapter is based on the baseline NESDA data.

4. Chapter 5 focuses on the association of serum BDNF with smoking or nicotine dependence in participants stratified according to their smoking status. The interaction of the BDNF gene Val^{66}Met polymorphism and smoking status with serum BDNF is also examined. The analyses were controlled for the diagnosis of an affective disorder, as well as other demographic and health variables.
5. In chapter 6, attentional bias across information processing phases, that is, the initial orienting and the maintenance phases of attention, and the role of attentional control in each of these phases is investigated using a dot-probe task with smoking-related and neutral pictures in smokers and non-smokers. Participants are students from Leiden university with age range from 18 to 35 years.
6. Finally, chapter 7 summarizes the main findings of the studies, discusses possible mechanisms, and provides clinical implications and future research directions.

References

1. Jha P, Chaloupka FJ, Corrao M, Jacob B. (2006). Reducing the burden of smoking world-wide: effectiveness of interventions and their coverage. *Drug and Alcohol Review, 25*(6): 597-609.
2. Dube SR, Asman K, Malarcher A, Carabollo R. (2009). Cigarette smoking among adults and trends in smoking cessation-United States, 2008 (Reprinted from MMWR, vol 58, pg 1227-1232, 2009). *Journal of the American Medical Association, 302*(24): 2651-2654.
3. Hughes J, Hatsukami D, Mitchell J, Dahlgren L. (1986). Prevalence of smoking among psychiatric outpatients. *American Journal of Psychiatry, 143*(8): 993-997.
4. Lasser K, Boyd JW, Woolhandler S, Himmelstein DU, McCormick D, Bor DH. (2000). Smoking and mental illness: a population-based prevalence study. *Journal of the American Medical Association, 284*(20): 2606-2610.
5. Pesa JA, Cowdery JE, Wang MQ, Fu Q. (1997). Self-reported depressive feelings and cigarette smoking among Mexican-American adolescents. *Journal of Alcohol and Drug Education, 43*(1): 63-75.
6. Wang MQ, Fitzhugh EC, Westerfield RC, Eddy JM. (1994). Predicting smoking status by symptoms of depression for united states adolescents. *Psychological Reports, 75*(2): 911-914.
7. Gulec M, Bakir B, Ozer M, Ucar M, Klc S, Hasde M. (2005). Association between cigarette smoking and depressive symptoms among military medical students in Turkey. *Psychiatry Research, 134*(3): 281-286.
8. Lee Ridner S, Staten RR, Danner FW. (2005). Smoking and depressive symptoms in a college population. *The Journal of School Nursing, 21*(4): 229-235.
9. Martini S, Wagner FA, Anthony JC. (2002). The association of tobacco smoking and depression in adolescence: evidence from the United States. *Substance Use and Misuse, 37*(14): 1853-1867.
10. Benjet C, Wagner FA, Borges GG, Medina-Mora ME. (2004). The relationship of tobacco smoking with depressive symptomatology in the Third Mexican National Addictions Survey. *Psychological Medicine, 34*(5): 881-888.
11. Luk JW, Tsoh JY. (2010). Moderation of gender on smoking and depression in Chinese Americans. *Addictive Behaviors, 35*(11): 1040-1043.
12. Perez-Stable EJ, Marin G, Marin BV, Katz MH. (1990). Depressive symptoms and cigarette smoking among Latinos in San-Francisco. *American Journal of Public Health, 80*(12): 1500-1502.
13. Son BK, Markovitz JH, Winders S, Smith D. (1997). Smoking, nicotine dependence, and depressive symptoms in the CARDIA study: effects of educational status. *American Journal of Epidemiology, 145*(2): 110-116.
14. Wiesbeck GA, Kuhl H-C, Yaldizli O, Wurst FM. (2008). Tobacco smoking and depression: results from the WHO/ISBRA study. *Neuropsychobiology, 57*(1-2): 26-31.
15. Lam TH, Li ZB, Ho SY, Chan WM, Ho KS, Li MP, Leung GM. (2004). Smoking and depressive symptoms in Chinese elderly in Hong Kong. *Acta Psychiatrica Scandinavica, 110*(3): 195-200.
16. Almeida OP, Pfaff JJ. (2005). Depression and smoking amongst older general practice patients. *Journal of Affective Disorders, 86*(2-3): 317-321.

17. Massak A, Graham K. (2008). Is the smoking-depression relationship confounded by alcohol consumption? an analysis by gender. *Nicotine and Tobacco Research, 10*(7): 1231-1243.
18. Brown C, Madden PAF, Palenchar DR, Cooper-Patrick L. (2000). The association between depressive symptoms and cigarette smoking in an urban primary care sample. *International Journal of Psychiatry in Medicine, 30*(1): 15-26.
19. Zvolensky MJ, Schmidt NB, McCreary BT. (2003). The impact of smoking on panic disorder: an initial investigation of a pathoplastic relationship. *Journal of Anxiety Disorders, 17*(4): 447-460.
20. Collins BN, Lepore SJ. (2009). Association between anxiety and smoking in a sample of urban black men. *Journal of Immigrant and Minority Health, 11*(1): 29-34.
21. Mykletun A, Overland S, Aaro LE, Liabo HM, Stewart R. (2008). Smoking in relation to anxiety and depression: evidence from a large population survey: the HUNT study. *European Psychiatry, 23*(2): 77-84.
22. Glassman AH, Helzer JE, Covey LS, Cottler LB, Stetner F, Tipp JE, Johnson J. (1990). Smoking, smoking cessation, and major depression. *Journal of the American Medical Association, 264*(12): 1546-1549.
23. Escobedo LG, Kirch DG, Anda RF. (1996). Depression and smoking initiation among US Latinos. *Addiction, 91*(1): 113-119.
24. Tanskanen AT, Viinamaki H, Koivumaa-Honkanen HT, Hintikka J, Jaaskelainen J, Lehtonen J. (1999). Smoking and depression among psychiatric patients. *Nordic Journal of Psychiatry, 53*(1): 45-48.
25. Anda RF, Williamson DF, Escobedo LG, Mast EE, Giovino GA, Remington PL. (1990). Depression and the dynamics of smoking. *The Journal of the American Medical Association, 264*(12): 1541-1545.
26. Zvolensky MJ, Schmidt NB, Stewart SH. (2003). Panic disorder and smoking. *Clinical Psychology: Science and Practice, 10*(1): 29-51.
27. McCabe RE, Chudzik SM, Antony MM, Young L, Swinson RP, Zolvensky MJ. (2004). Smoking behaviors across anxiety disorders. *Journal of Anxiety Disorders, 18*(1): 7-18.
28. Repetto PB, Caldwell CH, Zimmerman MA. (2005). A longitudinal study of the relationship between depressive symptoms and cigarette use among African American adolescents. *Health Psychology, 24*(2): 209-219.
29. Prinstein MJ, La Greca AM. (2009). Childhood depressive symptoms and adolescent cigarette use: a six-year longitudinal study controlling for peer relations correlates. *Health Psychology, 28*(3): 283-291.
30. Escobedo LG, Reddy M, Giovino GA. (1998). The relationship between depressive symptoms and cigarette smoking in US adolescents. *Addiction, 93*(3): 433-440.
31. Fergusson DM, Goodwin RD, Horwood LJ. (2003). Major depression and cigarette smoking: results of a 21-year longitudinal study. *Psychological Medicine, 33*(8): 1357-1367.
32. Sonntag H, Wittchen H-U, Hofler M, Kessler RC, Stein MB. (2000). Are social fears and DSM-IV social anxiety disorder associated with smoking and nicotine dependence in adolescents and young adults? *European Psychiatry, 15*(1): 67-74.
33. McKenzie M, Olsson CA, Jorm AF, Romaniuk H, Patton GC. (2010). Association of adolescent symptoms of depression and anxiety with daily smoking and nicotine dependence in young adulthood: findings from a 10-year longitudinal study. *Addiction, 105*(9): 1652-1659.
34. Breslau N, Novak SP, Kessler RC. (2004b). Psychiatric disorders and stages of smoking. *Biological Psychiatry, 55*(1): 69-76.

35. Choi WS, Patten CA, Gillin JC, Kaplan RM, Pierce JP. (1997). Cigarette smoking predicts development of depressive symptoms among US adolescents. *Annals of Behavioral Medicine, 19*(1): 42-50.
36. Duncan B, Rees DI. (2005). Effect of smoking on depressive symptomatology: a reexamination of data from the national longitudinal study of adolescent health. *American Journal of Epidemiology, 162*(5): 461-470.
37. Steuber TL, Danner F. (2006). Adolescent smoking and depression: which comes first? *Addictive Behaviors, 31*(1): 133-136.
38. Klungsoyr O, Nygard JF, Sorensen T, Sandanger I. (2006). Cigarette smoking and incidence of first depressive episode: an 11-year, population-based follow-up study. *American Journal of Epidemiology, 163*(5): 421-432.
39. Pasco JA, Williams LJ, Jacka FN, Ng F, Henry MJ, Nicholson GC, . . . Berk M. (2008). Tobacco smoking as a risk factor for major depressive disorder: population-based study. *British Journal of Psychiatry, 193*(4): 322-326.
40. Breslau N, Novak SP, Kessler RC. (2004a). Daily smoking and the subsequent onset of psychiatric disorders. *Psychological Medicine, 34*(02): 323-333.
41. Windle M, Windle RC. (2001). Depressive symptoms and cigarette smoking among middle adolescents: prospective associations and intrapersonal and interpersonal influences. *Journal of Consulting and Clinical Psychology, 69*(2): 215-226.
42. Lam TH, Stewart SM, Ho SY, Lai MK, Mak KH, Chau KV, . . . Salili F. (2005). Depressive symptoms and smoking among Hong Kong Chinese adolescents. *Addiction, 100*(7): 1003-1011.
43. Breslau N, Peterson EL, Schultz LR, Chilcoat HD, Andreski P. (1998). Major depression and stages of smoking: a longitudinal investigation. *Archives of General Psychiatry, 55*(2): 161-166.
44. Breslau N, Kilbey MM, Andreski P. (1993). Nicotine dependence and major depression: new evidence from a prospective investigation. *Archives of General Psychiatry, 50*(1): 31-35.
45. Wu LT, Anthony JC. (1999). Tobacco smoking and depressed mood in late childhood and early adolescence. *American Journal of Public Health, 89*(12): 1837-1840.
46. Goodman E, Capitman J. (2000). Depressive symptoms and cigarette smoking among teens. *Pediatrics, 106*(4): 748-755.
47. Brook JS, Schuster E, Zhang CS. (2004). Cigarette smoking and depressive symptoms: a longitudinal study of adolescents and young adults. *Psychological Reports, 95*(1): 159-166.
48. Kang E, Lee J. (2010). A longitudinal study on the causal association between smoking and depression. *Journal of Preventive Medicine and Public Health, 43*(3): 193-204.
49. Boden JM, Fergusson DM, Norwood LJ. (2010). Cigarette smoking and depression: tests of causal linkages using a longitudinal birth cohort. *British Journal of Psychiatry, 196*(6): 440-446.
50. Breslau N, Klein DF. (1999). Smoking and panic attacks: an epidemiologic investigation. *Archives of General Psychiatry, 56*(12): 1141-1147.
51. Goodwin RD, Lewinsohn PM, Seeley JR. (2005). Cigarette smoking and panic attacks among young adults in the community: the role of parental smoking and anxiety disorders. *Biological Psychiatry, 58*(9): 686-693.
52. Johnson JG, Cohen P, Pine DS, Klein DF, Kasen S, Brook JS. (2000). Association between cigarette smoking and anxiety disorders during adolescence and early adulthood. *Journal of the American Medical Association, 284*(18): 2348-2351.

53. Isensee B, Wittchen H-U, Stein MB, Hofler M, Lieb R. (2003). Smoking increases the risk of panic: findings from a prospective community study. *Archives of General Psychiatry, 60*(7): 692-700.
54. Cuijpers P, Smit F, ten Have M, de Graaf R. (2007). Smoking is associated with first-ever incidence of mental disorders: a prospective population-based study. *Addiction, 102*(8): 1303-1309.
55. Pedersen W, von Soest T. (2009). Smoking, nicotine dependence and mental health among young adults: a 13-year population-based longitudinal study. *Addiction, 104*(1): 129-137.
56. Glass RM. (1990). Blue mood, blackened lungs--depression and smoking. *Journal of the American Medical Association, 264*(12): 1583-1584.
57. Lerman C, Audrain J, Orleans CT, Boyd R, Gold K, Main D, Caporaso N. (1996). Investigation of mechanisms linking depressed mood to nicotine dependence. *Addictive Behaviors, 21*(1): 9-19.
58. Pomerleau OF, Pomerleau CS. (1984). Neuroregulators and the reinforcement of smoking: towards a biobehavioral explanation. *Neuroscience and Biobehavioral Reviews, 8*(4): 503-513.
59. Fowler JS, Volkow ND, Wang GJ, Pappas N, Logan J, MacGregor R, . . . Cilento R. (1996). Inhibition of monoamine oxidase B in the brains of smokers. *Nature, 379*(6567): 733-736.
60. Patton GC, Hibbert M, Rosier MJ, Carlin JB, Caust J, Bowes G. (1996). Is smoking associated with depression and anxiety in teenagers? *American Journal of Public Health, 86*(2): 225-230.
61. Newhouse PA, Hughes JR. (1991). The role of nicotine and nicotinic mechanisms in neuropsychiatric disease. *British Journal of Addiction, 86*(5): 521-526.
62. Breslau N, Kilbey MM, Andreski P. (1991). Nicotine dependence, major depression and anxiety in young adults. *Archives of General Psychiatry, 48*(12): 1069-1074.
63. Fergusson DM, Lynskey MT, Horwood LJ. (1996). Comorbidity between depressive disorders and nicotine dependence in a cohort of 16-year-olds. *Archives of General Psychiatry, 53*(11): 1043-1047.
64. John U, Meyer C, Rumpf HJ, Hapke U. (2004a). Depressive disorders are related to nicotine dependence in the population but do not necessarily hamper smoking cessation. *Journal of Clinical Psychiatry, 65*(2): 169-176.
65. John U, Meyer C, Rumpf HJ, Hapke U. (2004b). Smoking, nicotine dependence and psychiatric comorbidity: a population-based study including smoking cessation after three years. *Drug and Alcohol Dependence, 76*(3): 287-295.
66. Strong DR, Cameron A, Feuer S, Cohn A, Abrantes AM, Brown RA. (2010). Single versus recurrent depression history: differentiating risk factors among current US smokers. *Drug and Alcohol Dependence, 109*(1-3): 90-95.
67. Ismail K, Sloggett A, Stavola BD. (2000). Do common mental disorders increase cigarette smoking? results from five waves of a population-based panel cohort study. *American Journal of Epidemiology, 152*(7): 651-657.
68. Audrain-McGovern J, Rodriguez D, Kassel JD. (2009). Adolescent smoking and depression: evidence for self-medication and peer smoking mediation. *Addiction, 104*(10): 1743-1756.
69. Brown RA, Lewinsohn PM, Seeley JR, Wagner EF. (1996). Cigarette smoking, major depression, and other psychiatric disorders among adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry, 35*(12): 1602-1610.
70. Munafo MR, Hitsman B, Rende R, Metcalfe C, Niaura R. (2008). Effects of progression to cigarette smoking on depressed mood in adolescents: evidence from the National Longitudinal Study of Adolescent Health. *Addiction, 103*(1): 162-171.

71. Edwards AC, Maes HH, Pedersen NL, Kendler KS. (2011). A population-based twin study of the genetic and environmental relationship of major depression, regular tobacco use and nicotine dependence. *Psychological Medicine, 41*(2): 395-405.
72. Kendler KS, Neale MC, MacLean CJ, Heath AC, Eaves LJ, Kessler RC. (1993). Smoking and major depression: a causal analysis. *Archives of General Psychiatry, 50*(1): 36-43.
73. Korhonen T, Broms U, Varjonen J, Romanov K, Koskenvuo M, Kinnunen T, Kaprio J. (2007). Smoking behaviour as a predictor of depression among Finnish men and women: a prospective cohort study of adult twins. *Psychological Medicine, 37*(5): 705-715.
74. Lyons M, Hitsman B, Xian H, Panizzon MS, Jerskey BA, Santangelo S, . . . Tsuang MT. (2008). A twin study of smoking, nicotine dependence, and major depression in men. *Nicotine and Tobacco Research, 10*(1): 97-108.
75. McCaffery JM, Stanton C, Papandonatos GD, Lloyd-Richardson EE, Niaura R. (2008). Depressive symptoms and cigarette smoking in twins from the National Longitudinal Study of Adolescent Health. *Health Psychology, 27*(3): S207-S215.
76. McCaffery JM, Niaura R, Swan GE, Carmelli D. (2003). A study of depressive symptoms and smoking behavior in adult male twins from the NHLBI twin study. *Nicotine and Tobacco Research, 5*(1): 77-83.
77. Reichborn-Kjennerud T, Roysamb E, Tambs K, Torgersen S, Kringlen E, Magnus P, Harris JR. (2004). Genetic and environmental influences on the association between smoking and panic attacks in females: a population-based twin study. *Psychological Medicine, 34*(7): 1271-1277.
78. Goodwin R, Hamilton SP. (2002). Cigarette smoking and panic: the role of neuroticism. *American Journal of Psychiatry, 159*(7): 1208-1213.
79. Johnson EO, Rhee SH, Chase GA, Breslau N. (2004). Comorbidity of depression with levels of smoking: an exploration of the shared familial risk hypothesis. *Nicotine and Tobacco Research, 6*(6): 1029-1038.
80. Neale MC, Kendler KS. (1995). Models of comorbidity for multifactorial disorders. *American Journal of Human Genetics, 57*(4): 935-953.
81. Maisonpierre PC, Lebeau MM, Espinosa R, Ip NY, Belluscio L, Delamonte SM, . . . Yancopoulos GD. (1991). Human and rat brain-derived neurotrophic factor and neurotrophin-3: gene structures, distributions, and chromosomal localizations. *Genomics, 10*(3): 558-568.
82. Bath KG, Lee FS. (2006). Variant BDNF ($Val^{66}Met$) impact on brain structure and function. *Cognitive Affective and Behavioral Neuroscience, 6*(1): 79-85.
83. Anttila S, Huuhka K, Huuhka M, Rontu R, Hurme M, Leinonen E, Lehtima T. (2007). Interaction between 5-HT1A and BDNF genotypes increases the risk of treatment-resistant depression. *Journal of Neural Transmission, 114*(8): 1065-1068.
84. Schumacher J, Abou Jamra R, Becker T, Ohlraun S, Klopp N, Binder EB, . . . Cichon S. (2005). Evidence for a relationship between genetic variants at the brain-derived neurotrophic factor (BDNF) locus and major depression. *Biological Psychiatry, 58*(4): 307-314.
85. Verhagen M, Van der Meij A, Van Deurzen PAM, Janzing JGE, Arias-Vasquez A, Buitelaar JK, Franke B. (2010). Meta-analysis of the BDNF $Val^{66}Met$ polymorphism in major depressive disorder: effects of gender and ethnicity. *Molecular Psychiatry, 15*(3): 260-271.
86. Zhang K, Yang C, Xu Y, Sun N, Yang H, Liu J, . . . Shen Y. (2010). Genetic association of the interaction between the BDNF and GSK3B genes and major depressive disorder in a Chinese population. *Journal of Neural Transmission, 117*(3): 393-401.

87. Lang UE, Sander T, Lohoff FW, Hellweg R, Bajbouj M, Winterer G, Gallinat J. (2007). Association of the Met[66] allele of brain-derived neurotrophic factor (BDNF) with smoking. *Psychopharmacology, 190*(4): 433-439.
88. Montag C, Basten U, Stelzel C, Fiebach CJ, Reuter M. (2008). The BDNF Val[66]Met polymorphism and smoking. *Neuroscience Letters, 442*(1): 30-33.
89. Colzato LS, Van der Does AJW, Kouwenhoven C, Elzinga BM, Hommel B. (2011). BDNF Val[66]Met polymorphism is associated with higher anticipatory cortisol stress response, anxiety, and alcohol consumption in healthy adults. *Psychoneuroendocrinology, 36*(10): 1562-1569.
90. Greenwald MK, Steinmiller CL, Śliwerska E, Lundahl L, Burmeister M. (2013). BDNF Val[66]Met genotype is associated with drug-seeking phenotypes in heroin-dependent individuals: a pilot study. *Addiction Biology, 18*(5): 836-845.
91. Tocchetto A, Salum GA, Blaya C, Teche S, Isolan L, Bortoluzzi A, . . . Manfro GG. (2011). Evidence of association between Val[66]Met polymorphism at BDNF gene and anxiety disorders in a community sample of children and adolescents. *Neuroscience Letters, 502*(3): 197-200.
92. Lam P, Cheng CY, Hong CJ, Tsai SJ. (2004). Association study of a brain-derived neurotrophic factor (Val[66]Met) genetic polymorphism and panic disorder. *Neuropsychobiology, 49*(4): 178-181.
93. Otowa T, Shimada T, Kawamura Y, Liu X, Inoue K, Sugaya N, . . . Sasaki T. (2009). No association between the brain-derived neurotrophic factor gene and panic disorder in Japanese population. *Journal of Human Genetics, 54*(8): 437-439.
94. Surtees PG, Wainwright NWJ, Willis-Owen SAG, Sandhu MS, Luben R, Day NE, Flint J. (2007). No association between the BDNF Val[66]Met polymorphism and mood status in a non-clinical community sample of 7389 older adults. *Journal of Psychiatric Research, 41*(5): 404-409.
95. Zhang XY, Chen DC, Xiu MH, Luo X, Zuo L, Haile CN, . . . Kosten TR. (2012). BDNF Val[66]Met variant and smoking in a Chinese population. *Plos One, 7*(12): 1-5.
96. Duncan LE, Hutchison KE, Carey G, Craighead WE. (2009). Variation in brain-derived neurotrophic factor (BDNF) gene is associated with symptoms of depression. *Journal of Affective Disorders, 115*(1-2): 215-219.
97. Conner JM, Lauterborn JC, Yan Q, Gall CM, Varon S. (1997). Distribution of brain-derived neurotrophic factor (BDNF) protein and mRNA in the normal adult rat CNS: evidence for anterograde axonal transport. *Journal of Neuroscience, 17*(7): 2295-2313.
98. KatohSemba R, Takeuchi IK, Semba R, Kato K. (1997). Distribution of brain-derived neurotrophic factor in rats and its changes with development in the brain. *Journal of Neurochemistry, 69*(1): 34-42.
99. Huang EJ, Reichardt LF. (2001). Neurotrophins: roles in neuronal development and function. *Annual Review of Neuroscience, 24*: 677-736.
100. Roceri M, Hendriks W, Racagni G, Ellenbroek BA, Riva MA. (2002). Early maternal deprivation reduces the expression of BDNF and NMDA receptor subunits in rat hippocampus. *Molecular Psychiatry, 7*(6): 609-616.
101. Smith MA, Makino S, KvetŇAnskÝ R, Post RM. (1995). Effects of stress on neurotrophic factor expression in the rat brain. *Annals of the New York Academy of Sciences, 771*(1): 234-239.
102. Dwivedi Y, Rizavi HS, Conley RR, Roberts RC, Tamminga CA, Pandey GN. (2003). Altered gene expression of brain-derived neurotrophic factor and receptor tyrosine kinase B in postmortem brain of suicide subjects. *Archives of General Psychiatry, 60*(8): 804-815.
103. Bocchio-Chiavetto L, Bagnardi V, Zanardini R, Molteni R, Gabriela Nielsen M, Placentino A, . . . Gennarelli M. (2010). Serum and plasma BDNF levels in major

depression: a replication study and meta-analyses. *World Journal of Biological Psychiatry, 11*(6): 763-773.

104. Diniz BS, Teixeira AL, Talib LL, Mendonca VA, Gattaz WF, Forlenza OV. (2010). Serum brain-derived neurotrophic factor level is reduced in antidepressant-free patients with late-life depression. *World Journal of Biological Psychiatry, 11*(3): 550-555.
105. Duman RS, Monteggia LM. (2006). A neurotrophic model for stress-related mood disorders. *Biological Psychiatry, 59*(12): 1116-1127.
106. Hashimoto K. (2010). Brain-derived neurotrophic factor as a biomarker for mood disorders: an historical overview and future directions. *Psychiatry and Clinical Neurosciences, 64*(4): 341-357.
107. Hashimoto K, Shimizu E, Iyo M. (2004). Critical role of brain-derived neurotrophic factor in mood disorders. *Brain Research Reviews, 45*(2): 104-114.
108. Huang T-L, Lee C-T, Liu Y-L. (2008). Serum brain-derived neurotrophic factor levels in patients with major depression: effects of antidepressants. *Journal of Psychiatric Research, 42*(7): 521-525.
109. Karege F, Perret G, Bondolfi G, Schwald M, Bertschy G, Aubry JM. (2002). Decreased serum brain-derived neurotrophic factor levels in major depressed patients. *Psychiatry Research, 109*(2): 143-148.
110. Piccinni A, Marazziti D, Catena M, Domenici L, Del Debbio A, Bianchi C, . . . Dell'Osso L. (2008). Plasma and serum brain-derived neurotrophic factor depressed patients during 1 year of antidepressant (BDNF) in treatments. *Journal of Affective Disorders, 105*(1-3): 279-283.
111. Shimizu E, Hashimoto K, Okamura N, Koike K, Komatsu N, Kumakiri C, . . . Iyo M. (2003). Alterations of serum levels of brain-derived neurotrophic factor (BDNF) in depressed patients with or without antidepressants. *Biological Psychiatry, 54*(1): 70-75.
112. Sozeri-Varma G, Enli Y, Toker-Ugurlu T, Alacam H, Kalkan-Oguzhanoglu N. (2011). Decreased serum BDNF levels in major depressive patients. *Neurology Psychiatry and Brain Research, 17*(4): 84-88.
113. Umene-Nakano W, Yoshimura R, Ikenouchi-Sugita A, Hori H, Hayashi K, Ueda N, Nakamura J. (2009). Serum levels of brain-derived neurotrophic factor in comorbidity of depression and alcohol dependence. *Human Psychopharmacology: Clinical and Experimental, 24*(5): 409-413.
114. Aydemir O, Deveci A, Taneli F. (2005). The effect of chronic antidepressant treatment on serum brain-derived neurotrophic factor levels in depressed patients: a preliminary study. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 29*(2): 261-265.
115. Cunha ABM, Frey BN, Andreazza AC, Goi JD, Rosa AR, Goncalves CA, . . . Kapczinski F. (2006). Serum brain-derived neurotrophic factor is decreased in bipolar disorder during depressive and manic episodes. *Neuroscience Letters, 398*(3): 215-219.
116. Gervasoni N, Aubry JM, Bondolfi G, Osiek C, Schwald M, Bertschy G, Karege F. (2005). Partial normalization of serum brain-derived neurotrophic factor in remitted patients after a major depressive episode. *Neuropsychobiology, 51*(4): 234-238.
117. Gonul AS, Akdeniz F, Taneli F, Donat O, Eker C, Vahip S. (2005). Effect of treatment on serum brain-derived neurotrophic factor levels in depressed patients. *European Archives of Psychiatry and Clinical Neuroscience, 255*(6): 381-386.
118. Matrisciano F, Bonaccorso S, Ricciardi A, Scaccianoce S, Panaccione I, Wang L, . . . Shelton RC. (2008). Changes in BDNF serum levels in patients with major depression disorder (MDD) after 6 months treatment with sertraline, escitalopram, or venlafaxine. *Journal of Psychiatric Research, 43*(3): 247-254.

119. Brunoni AR, Lopes M, Fregni F. (2008). A systematic review and meta-analysis of clinical studies on major depression and BDNF levels: implications for the role of neuroplasticity in depression. *International Journal of Neuropsychopharmacology, 11*(8): 1169-1180.
120. Sen S, Duman R, Sanacora G. (2008). Serum brain-derived neurotrophic factor, depression, and antidepressant medications: meta-analyses and implications. *Biological Psychiatry, 64*(6): 527-532.
121. Baldwin D, Rudge S. (1995). The role of serotonin in depression and anxiety. *International Clinical Psychopharmacology, 9*: 41-45.
122. Kendler KS, Neale MC, Kessler RC, Heath AC, Eaves LJ. (1992). Major depression and generalized anxiety disorder: same genes, (partly) different environments. *Archives of General Psychiatry, 49*(9): 716-722.
123. Kendler KS, Walters EE, Neale MC, Kessler RC, Heath AC, Eaves LJ. (1995). The structure of the genetic and environmental risk factors for 6 major psychiatric disorders in women: phobia, generalized anxiety disorder, panic disorder, bulimia, major depression, and alcoholism. *Archives of General Psychiatry, 52*(5): 374-383.
124. Klaassen T, Klumperbeek J, Deutz NEP, Van Praag HM, Griez E. (1998). Effects of tryptophan depletion on anxiety and on panic provoked by carbon dioxide challenge. *Psychiatry Research, 77*(3): 167-174.
125. Ströhle A, Stoy M, Graetz B, Scheel M, Wittmann A, Gallinat J, . . . Hellweg R. (2010). Acute exercise ameliorates reduced brain-derived neurotrophic factor in patients with panic disorder. *Psychoneuroendocrinology, 35*(3): 364-368.
126. Molendijk ML, Bus BAA, Spinhoven P, Penninx BWJH, Prickaerts J, Voshaar RCO, Elzinga BM. (2012). Gender-specific associations of serum levels of brain-derived neurotrophic factor in anxiety. *World Journal of Biological Psychiatry, 13*(7): 535-543.
127. Kobayashi K, Shimizu E, Hashimoto K, Mitsumori M, Koike K, Okamura N, . . . Iyo M. (2005). Serum brain-derived neurotrophic factor (BDNF) levels in patients with panic disorder: as a biological predictor of response to group cognitive behavioral therapy. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 29*(5): 658-663.
128. Andresen JH, Loberg EM, Wright M, Goverud IL, Stray-Pedersen B, Saugstad OD. (2009). Nicotine affects the expression of brain-derived neurotrophic factor mRNA and protein in the hippocampus of hypoxic newborn piglets. *Journal of Perinatal Medicine, 37*(5): 553-560.
129. Umene-Nakano W, Yoshimura R, Yoshii C, Hoshuyama T, Hayashi K, Hori H, . . . Nakamura J. (2010). Varenicline does not increase serum BDNF levels in patients with nicotine dependence. *Human Psychopharmacology: Clinical and Experimental, 25*(3): 276-279.
130. Zhang XY, Xiu MH, Chen DC, Yang FD, Wu GY, Lu L, . . . Kosten TR. (2010). Nicotine dependence and serum BDNF levels in male patients with schizophrenia. *Psychopharmacology, 212*(3): 301-307.
131. Bus BAA, Molendijk ML, Penninx BJWH, Buitelaar JK, Kenis G, Prickaerts J, . . . Voshaar RCO. (2011). Determinants of serum brain-derived neurotrophic factor. *Psychoneuroendocrinology, 36*(2): 228-239.
132. Attwood AS, O'Sullivan H, Leonards U, Mackintosh B, Munafo MR. (2008). Attentional bias training and cue reactivity in cigarette smokers. *Addiction, 103*(11): 1875-1882.
133. Canamar CP, London E. (2012). Acute cigarette smoking reduces latencies on a smoking Stroop test. *Addictive Behaviors, 37*(5): 627-631.
134. Chanon VW, Sours CR, Boettiger CA. (2010). Attentional bias toward cigarette cues in active smokers. *Psychopharmacology, 212*(3): 309-320.

135. Drobes DJ, Elibero A, Evans DE. (2006). Attentional bias for smoking and affective stimuli: a Stroop task study. *Psychology of Addictive Behaviors, 20*(4): 490-495.
136. Janes AC, Pizzagalli DA, Richardt S, De B. Frederick B, Holmes AJ, Sousa J, . . . Kaufman MJ. (2010). Neural substrates of attentional bias for smoking-related cues: an fMRI study. *Neuropsychopharmacology, 35*(12): 2339-2345.
137. Johnsen BH, Thayer JF, Laberg JC, Asbjornsen AE. (1997). Attentional bias in active smokers, abstinent smokers, and nonsmokers. *Addictive Behaviors, 22*(6): 813-817.
138. Mogg K, Bradley BP. (2002). Selective processing of smoking-related cues in smokers: manipulation of deprivation level and comparison of three measures of processing bias. *Journal of Psychopharmacology, 16*(4): 385-392.
139. Mogg K, Bradley BP, Field M, De Houwer J. (2003). Eye movements to smoking-related pictures in smokers: relationship between attentional biases and implicit and explicit measures of stimulus valence. *Addiction, 98*(6): 825-836.
140. Rzetelny A, Gilbert DG, Hammersley J, Radtke R, Rabinovich NE, Small SL. (2008). Nicotine decreases attentional bias to negative-affect-related Stroop words among smokers. *Nicotine and Tobacco Research, 10*(6): 1029-1036.
141. Waters AJ, Feyerabend C. (2000). Determinants and effects of attentional bias in smokers. *Psychology of Addictive Behaviors, 14*(2): 111-120.
142. Waters AJ, Shiffman S, Bradley BP, Mogg K. (2003). Attentional shifts to smoking cues in smokers. *Addiction, 98*(10): 1409-1417.
143. Wertz JM, Sayette MA. (2001). Effects of smoking opportunity on attentional bias in smokers. *Psychology of Addictive Behaviors, 15*(3): 268-271.
144. Bradley BP, Field M, Healy H, Mogg K. (2008). Do the affective properties of smoking-related cues influence attentional and approach biases in cigarette smokers? *Journal of Psychopharmacology, 22*(7): 737-745.
145. Bradley BP, Mogg K, Wright T, Field M. (2003). Attentional bias in drug dependence: vigilance for cigarette-related cues in smokers. *Psychology of Addictive Behaviors, 17*(1): 66-72.
146. Ehrman RN, Robbins SJ, Bromwell MA, Lankford ME, Monterosso JR, O'Brien CP. (2002). Comparing attentional bias to smoking cues in current smokers, former smokers, and non-smokers using a dot-probe task. *Drug and Alcohol Dependence, 67*(2): 185-191.
147. Field M, Duka T, Tyler E, Schoenmakers T. (2009). Attentional bias modification in tobacco smokers. *Nicotine and Tobacco Research, 11*(7): 812-822.
148. Hogarth LC, Mogg K, Bradley BP, Duka T, Dickinson A. (2003). Attentional orienting towards smoking-related stimuli. *Behavioural Pharmacology, 14*(2): 153-160.
149. Kwak SM, Na DL, Kim G, Kim GS, Lee JH. (2007). Use of eye movement to measure smokers' attentional bias to smoking-related cues. *Cyberpsychology and Behavior, 10*(2): 299-304.
150. Mogg K, Field M, Bradley BP. (2005). Attentional and approach biases for smoking cues in smokers: an investigation of competing theoretical views of addiction. *Psychopharmacology, 180*(2): 333-341.
151. Waters AJ, Shiffman S, Sayette MA, Paty JA, Gwaltney CJ, Balabanis MH. (2003). Attentional bias predicts outcome in smoking cessation. *Health Psychology, 22*(4): 378-387.
152. Franken IHA. (2003). Drug craving and addiction: integrating psychological and neuropsychopharmacological approaches. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 27*(4): 563-579.
153. Miyake A, Friedman NP, Emerson MJ, Witzki AH, Howerter A, Wager TD. (2000). The unity and diversity of executive functions and their contributions to

complex "frontal lobe" tasks: a latent variable analysis. *Cognitive Psychology, 41*(1): 49-100.

154. Derakshan N, Ansari TL, Hansard M, Shoker L, Eysenck MW. (2009). Anxiety, inhibition, efficiency, and effectiveness: an investigation using the antisaccade task. *Experimental Psychology, 56*(1): 48-55.
155. Derryberry D, Reed MA. (2002). Anxiety-related attentional biases and their regulation by attentional control. *Journal of Abnormal Psychology, 111*(2): 225-236.
156. Peers PV, Lawrence AD. (2009). Attentional control of emotional distraction in rapid serial visual presentation. *Emotion, 9*(1): 140-145.
157. Reinholdt-Dunne ML, Mogg K, Bradley BP. (2009). Effects of anxiety and attention control on processing pictorial and linguistic emotional information. *Behaviour Research and Therapy, 47*(5): 410-417.
158. Penninx BWJH, Beekman ATF, Smit JH, Zitman FG, Nolen WA, Spinhoven P, . . . NESDA Research Consortium. (2008). The Netherlands Study of Depression and Anxiety (NESDA): rationale, objectives and methods. *International Journal of Methods in Psychiatric Research, 17*(3): 121-140.
159. Slawecki CJ, Gilder A, Roth J, Ehlers CL. (2003). Increased anxiety-like behavior in adult rats exposed to nicotine as adolescents. *Pharmacology Biochemistry and Behavior, 75*(2): 355-361.
160. Iniguez SD, Warren BL, Parise EM, Alcantara LF, Schuh B, Maffeo ML, . . . Bolanos-Guzman CA. (2009). Nicotine exposure during adolescence induces a depression-like state in adulthood. *Neuropsychopharmacology, 34*(6): 1609-1624.
161. Thapar A, Fowler T, Rice F, Scourfield J, Van den Bree M, Thomas H, . . . Hay D. (2003). Maternal smoking during pregnancy and attention deficit hyperactivity disorder symptoms in offspring. *American Journal of Psychiatry, 160*(11): 1985-1989.