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Testosterone levels in suicide attempters with bipolar disorder

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Abstract

Objective—The best known neurobehavioral effects of testosterone are on sexual function and aggression. However, testosterone and other androgens may be involved in the pathophysiology of mood disorders and suicidal behavior. This is the first study to examine whether there is a relation between testosterone levels and clinical parameters in bipolar suicide attempters.

Methods—Patients with a DSM-IV diagnosis of a bipolar disorder (16 males and 51 females), in a depressive or mixed episode with at least one past suicide attempt were enrolled. Demographic and clinical parameters, including lifetime suicidal behavior, were assessed and recorded. Plasma testosterone was assayed using a double antibody radioimmunoassay procedure.

Results—The number of major depressive episodes, the maximum lethality of suicide attempts, and the testosterone levels were higher in men compared to women. Current suicidal ideation scores were higher in women compared to men. Controlling for sex, we found that testosterone levels positively correlated with the number of manic episodes and the number of suicide attempts.

Conclusion—Our findings are consistent with previous observations of the association between testosterone levels and parameters of mood and behavior. This study suggests that testosterone levels may be related to the course of bipolar disorder and suicidal behavior. Further studies of the role of testosterone in the neurobiology of mood disorders and suicidal behavior are merited.

Keywords

testosterone; bipolar disorder; depression; suicide; smoking

Introduction

In addition to its gonadal functions, testosterone has many central nervous system effects (Rubinow and Schmidt, 1996; Schmidt and Rubinow, 1997; Zarrouf et al., 2009; Ebinger et al., 2009). Testosterone can influence neuronal function through binding to intracellular receptors, through modulation of ligand-gated ion channels, and through binding to

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neurotransmitter receptors. It is also involved in modeling the developing brain and influences the continuous process of neuronal adaptation to new environmental demands.

The best known neurobehavioural effects of testosterone are on sexual function and aggression (Rubinow and Schmidt, 1996; Ebinger et al., 2009). However, testosterone and other androgens might be involved in the pathophysiology of mood disorders and suicidal behavior.

Depressed men have lower plasma or serum testosterone levels (Barrett-Connor et al., 1999; Schweiger et al., 1999; Almeida et al., 2004; Ebinger et al., 2009) although this association is not observed consistently (Levitt and Joffe, 1988; O'Connor et al., 2004; Ebinger et al., 2009). Hypogonadal men frequently show depressive symptoms, and testosterone replacement may improve these symptoms (Wang et al., 1996; Pope et al., 2003). Testosterone and other androgens might have antidepressant properties (Altschule and Tillotson, 1948; Itil et al., 1984; Pope et al., 2003; Amiaz and Seidman, 2008; Zarrouf et al., 2009). For example, it has been shown that testosterone gel may produce antidepressant effects in depressed men with low testosterone levels (Pope et al., 2003).

The data on the relationship of testosterone to suicidal behavior have been less consistent. Some studies reported low plasma testosterone levels after suicide attempts (Tripodianakis et al., 2007; Markianos et al., 2009). However, a study of male veterans with posttraumatic stress disorder showed that in this patient population, serum levels of testosterone were not associated with a history of suicide attempt (Butterfield et al., 2005). A recent study reported that there was no difference in testosterone levels between male suicide attempters and healthy controls (Perez-Rodriguez et al., 2011).

We have performed an exploratory study to examine whether there is a relationship between testosterone levels and suicidal behavior and related clinical parameters in bipolar disorder.

Methods

Subjects

Participants were recruited through a combination of emergency department referrals, referrals from other outpatient services, and self-referral in response to advertisements. All participants provided written informed consent as approved by the New York State Psychiatric Institute Institutional Review Board. To be included, patients had to have a DSM-IV diagnosis of a bipolar disorder based on the Structured Clinical Interview for DSM-IV; be in a depressive or mixed episode; have at least one past suicide attempt; and be 18 to 75 years of age. Exclusion criteria were lack of capacity to provide informed consent; pregnancy or lactation; active medical problems, including substance abuse problems requiring detoxification. Forty five subjects had bipolar I disorder, and 22 subjects suffered from bipolar II disorder. Ten female participants were taking oral contraceptives.

Clinical evaluation

Axis I and II pathology was assessed at baseline with the Structured Clinical Interview for DSM-IV Axis I and II Disorders. Current severity of depression was assessed by the Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960). Lifetime aggression and impulsivity were assessed with the Aggression History Scale (Brown-Goodwin, revised; Brown and Goodwin, 1986) and the Barratt Impulsivity Scale, respectively (Barratt, 1965). Hostility (lifetime) was rated with the Buss-Durkee Hostility Inventory (Buss and Durkee, 1957). The Scale for Suicide Ideation (SSI) was used to measure the severity of suicidal ideation (Beck et al., 1979), and hopelessness during the previous week was measured with the Beck Hopelessness Scale (BHS) (Beck et al., 1974). A lifetime history of all suicide

attempts, including number of attempts and the method of the attempt, was recorded on the Columbia Suicide History Form (Oquendo et al., 2003). A suicide attempt was defined as a self-destructive act that was committed with some intent to end one's life. The Medical Lethality Rating Scale was used to measure the degree of medical damage caused by each suicide attempt (Beck et al., 1975). The scale was scored from 0 to 8 (0=no medical damage, 8=death), with anchor points for different suicide attempt methods. The degree of suicide intent for the worst attempt was rated with the Suicide Intent Scale (Beck et al., 1974). Interviewers were Masters or PhD-level psychologists. Inter-rater reliability was good to excellent (ICC 0.71 – 0.97).

Testosterone assay

Plasma testosterone was assayed using a double antibody ^{125}I radioimmunoassay procedure (MP BIOMEDICALS Costa Mesa, California). All assays were run in duplicate with an eight point standard curve encompassing 0.1–10ng/ml. Three quality control low, medium and high levels were run with each batch assay. Inter and intra assay coefficient of variation were < 8% and <10% respectively.

Statistical analyses

Demographic and clinical features of male and female patients were compared using t-test (for continuous variables) and chi-square test (for categorical variables). Differences in testosterone levels between smokers and non-smokers were tested controlling for sex and using linear regression analysis. Pearson's correlations were used to test the relation between testosterone levels and clinical parameters. Partial correlation analysis was employed to control for sex. The SPSS 19 statistical program was used to perform statistical analyses.

Results

Demographic and clinical characteristics of study participants are presented in Table 1. Sixteen men and 51 women were recruited into the study. As expected, testosterone levels were significantly higher in males compared with females. The number of major depressive episodes and the maximum lethality of suicide attempts were significantly higher in men compared to women, yet current suicide ideation scores were significantly higher in women compared to men. There were no other sex-related differences in the sample.

Controlling for sex, we found that testosterone levels positively correlated with the number of manic episodes and the number of suicide attempts (Table 2). We have not observed a correlation between testosterone levels and aggression scale scores.

Discussion

Demographic and clinical characteristics of the sample

The higher number of major depressive episodes in male participants is likely to be a sampling issue. In fact, most studies of patients with bipolar disorder found no consistent sex differences in number of depressive episodes across sexes (Baldassano et al., 2005; Diflorio and Jones, 2010; Grant et al., 2005; Hendrick et al., 2000; Kessing, 2004; Kawa et al., 2005; Robb et al., 1998). To the contrary, several reports suggest that bipolar women are more likely than men to show a predominance of depressive polarity (Angst, 1978; Roy-Byrne et al., 1985; Nivoli et al., 2011). However, it is possible that this observation regarding polarity does not apply to bipolar suicide attempters who represent a very specific patient population. It is worth noting that there is a trend towards older age among male participants in the study. This difference, however, is not statistically or clinically significant

and does not explain the significantly higher number of major depressive episodes in males compared to females in our study (Table 1).

In our study, male subjects made more medically damaging suicide attempts than females, which is consistent with a recent report that suicide attempts are more often violent amongst bipolar men than among women with bipolar illness (Nivoli et al., 2011). This finding is also consistent with observations that males take their own lives at nearly four times the rate of females and comprise approximately 80% of all suicides, even though female suicide attempt rates are estimated to be three to four times higher than men's (Moscicki et al., 1994; Cannetto and Lester, 1995; Callanan and Davis, in press). One of the primary reasons given for the substantial sex gap in suicide rates is the difference in suicide methods used by males and females. In general, men are more likely to use methods that ensure high lethality than are women, which is consistent with our observation that the maximum lethality of suicide attempts was significantly higher in men compared to women in our sample.

Demographic factors and testosterone

As expected, testosterone levels were significantly higher in males than in females. The mean testosterone level in males in our sample was nine times higher than females, a ratio consistent with the literature (Mooradian et al., 1987; Molina, 2006).

Number of manic episodes

We have observed that testosterone levels correlate with the number of manic episodes. This has never been reported on before. This finding may be related to the observation that anabolic steroid users, who consume high doses of testosterone and related androgens, sometimes develop manic or hypomanic symptoms during androgen use and depressive symptoms during androgen withdrawal (Pope and Katz, 1988; Pope and Katz, 1994). A study of the effects of supraphysiologic doses of testosterone on mood in healthy men aged 20 to 50 years showed that 16% of study participants became hypomanic (Pope et al., 2000). Two other studies of the effects of testosterone on healthy men showed that some study subjects developed symptoms of mania (Su et al., 1993; Yates et al., 1999). A case of mania in a patient taking testosterone as replacement therapy following bilateral orchidectomy, a selective serotonin reuptake inhibitor and St John's Wort has been described (Barbenel et al., 2004). A case of testosterone patch-induced mania in a patient with a history of bipolar II disorder has also been reported (Weiss et al., 1999). These observations suggest that there is a relation between testosterone blood levels and mania.

Number of suicide attempts

We found that the number of suicide attempts in bipolar suicide attempters correlate with testosterone levels. Some (Tripodianakis et al., 2007; Markianos et al., 2009) but not all (Butterfield et al., 2005; Perez-Rodriguez et al., 2011) studies find relationships between testosterone and suicidal behavior.

Tripodianakis et al. (2007) compared testosterone levels in males admitted to hospital wards after a suicide attempt with testosterone levels in healthy males in the same age range. Blood samples from suicide attempters were drawn during the first days of hospitalization. The authors found that attempters had significantly lower testosterone levels compared to control, and that the attempters who used violent methods had lower testosterone levels compared to the non-violent attempter subgroup. Markianos et al. (2009) examined testosterone levels in a group of male psychiatric patients who had attempted suicide by jumping, compared with a group of male subjects who were hospitalized after accidentally falling from a high height, and in healthy controls. Both accident and suicide attempt groups had lower testosterone levels compared to the control group, and there was a trend towards

lower testosterone levels in suicide attempters compared to the accident group. However, a recent study found no difference with regard to plasma testosterone levels between male suicide attempters and male controls (Perez-Rodriguez et al., 2011). In that study, blood samples were taken within 24 hours after the attempt. A study which investigated associations between neuroactive steroids and suicidality in military veterans with posttraumatic stress disorder found no association between testosterone levels and a history of a suicide attempt in the last six months (Butterfield et al., 2005). The discrepancies between the results of the studies of the relation between testosterone and suicidal behavior could be related to variations in sample selection criteria, psychiatric diagnoses, differences in time intervals between suicide attempts and blood sampling, smoking status and potentially other factors. Also, the control and patient groups were often poorly matched. No prior studies have looked at the relation between testosterone levels and the number of suicide attempts.

A significant number of studies suggest that testosterone is associated with aggression. It has been shown that violent individuals have higher plasma (Ehrenkranz et al., 1974; Mattsson et al., 1980), saliva (Soler et al., 2000) and CSF testosterone (Virkkunen et al., 1994) levels compared to non-violent controls. For example, in a study of impulsive offenders with alcoholism and antisocial personality disorder, higher levels of CSF testosterone were observed compared to healthy volunteers (Virkkunen et al., 1994). The authors suggested that high CSF testosterone levels may be associated with aggressiveness or interpersonal violence. In the same paper, the authors reviewed the literature on the relation of testosterone to aggression in humans, and proposed that both a repetitive pattern of aggressive behavior starting early in life, and a repetitive pattern of aggressiveness under the influence of alcohol are associated with elevated levels of testosterone. It has also been demonstrated that adolescent males with high plasma testosterone levels are more irritable and more likely to respond aggressively to provocation and threats than subjects with lower testosterone concentrations (Olweus et al., 1980; Olweus et al., 1988). Also, individuals receiving testosterone are more likely to have an aggressive response to perceived threats than subjects receiving placebo (Pope and Katz, 1990; Su et al., 1993; Pope et al., 2000).

Some authors have postulated that there are substantial similarities between aggression against the self and aggression against others, based on the clinical and epidemiological findings that some suicide attempters may share personality traits with violent criminals (Engstrom et al., 1999). We have also observed an association between aggression and suicidal behavior (Oquendo et al., 2004; Sher et al., 2005). For example, we have demonstrated that high aggression predicts suicidal acts (Oquendo et al., 2004). We have also shown that the higher prevalence of suicide attempters among depressed patients with a history of alcoholism compared to depressed patients without a history of alcoholism was related to higher aggression scores in the group with alcoholism (Sher et al., 2005).

Some studies, however, did not find an association between testosterone and aggression (Archer et al., 1991; Zitzmann and Nieschlag, 2001) which is consistent with our observation in this study that testosterone levels do not correlate with aggression scores. It has been suggested that the connection between testosterone and aggression is probably only of importance to athletes who supplement their testosterone levels to very high levels (Zitzmann, 2006).

Strengths and limitations

A strength of this study is that we have examined the relation between testosterone levels and clinical features in an unique patient population: suicide attempters with bipolar disorder. This is the first study of testosterone levels in this patient population. Another strength of this investigation is that the sample was very well characterized using multiple

psychometric scales. A limitation of the study is that we did not have a bipolar nonattempter or healthy volunteer control group for comparison and the sample size is modest. In addition, due to the exploratory nature of the study, results should be interpreted with caution. Overall, the study design is not adequate to definitely conclude that testosterone is a correlate of suicidal behavior.

Conclusion

This study suggests that testosterone levels may be related to the course of bipolar disorders and suicidal behavior. It is possible that a) testosterone levels influence the pathophysiology of bipolar illness and suicidal behavior; b) the presence of bipolar disorder and suicidal behavior affects testosterone levels; c) certain factors (e.g., genetics or smoking) affect both testosterone levels and the course of bipolar disorder and suicidal behavior; and d) there is a complex interplay of different factors which is most likely. Future research should focus on the role of testosterone in the pathophysiology of depression not only suicidal behavior taking into account that depressive disorders are associated with suicidal behavior. Whether testosterone has antidepressant properties thereby reducing suicidal behavior in patients with depression is unknown. It may also be important to examine the role of testosterone in the pathophysiology of manic states.

Our findings are consistent with some previous observations of the association between testosterone levels and parameters of mood and behavior. This study suggests that testosterone levels may be related to the course of bipolar disorders and suicidal behavior. Further studies of the role of testosterone in the neurobiology of mood disorders and suicidal behavior are merited.

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References

Almeida OP, Waterreus A, Spry N, Flicker L, Martins RN. One year follow-up study of the association between chemical castration, sex hormones, beta-amyloid, memory and depression in men. Psychoneuroendocrinology. 2004; 29(8):1071–81. [PubMed: 15219659]

Altschule MD, Tillotson KJ. The use of testosterone in the treatment of depressions. New England Journal of Medicine. 1948; 239(27):1036–8. [PubMed: 18103557]

Amiaz R, Seidman SN. Testosterone and depression in men. Current Opinion in Endocrinology, Diabetes and Obesity. 2008; 15(3):278–83.

Angst J. The course of affective disorders. II. Typology of bipolar manic-depressive illness. Archiv für Psychiatrie und Nervenkrankheiten. 1978; 226:65–73. [PubMed: 708228]

Archer J. The influence of testosterone on human aggression. British Journal of Psychology. 1991; 82 (Pt 1):1–28. [PubMed: 2029601]

Baldassano CF, Marangell LB, Gyulai L, Ghaemi SN, Joffe H, Kim DR, et al. Gender differences in bipolar disorder: Retrospective data from the first 500 STEP-BD participants. Bipolar Disorders. 2005; 7:465–470. [PubMed: 16176440]

Barbenel DM, Yusufi B, O'Shea D, Bench CJ. Mania in a patient receiving testosterone replacement postorchidectomy taking St John's wort and sertraline. Journal of Psychopharmacology. 2000; 14(1):84–6. [PubMed: 10757260]

Barratt ES. Factor analysis of some psychometric measures of impulsiveness and anxiety. Psychological Reports. 1965; 16:547–554. [PubMed: 14285869]

Barrett-Connor E, Von Mühlen DG, Kritz-Silverstein D. Bioavailable testosterone and depressed mood in older men: the Rancho Bernardo Study. Journal of Clinical Endocrinology and Metabolism. 1999; 84(2):573–7. [PubMed: 10022418]

Beck AT, Beck R, Kovacs M. Classification of suicidal behaviors: I. Quantifying intent and medical lethality. American Journal of Psychiatry. 1975; 132:285–287. [PubMed: 1115273]

Beck AT, Kovacs M, Weissman A. Assessment of suicidal intention: the Scale for Suicide Ideation. Journal of Consulting and Clinical Psychology. 1979; 47:343–352. [PubMed: 469082]

Beck RW, Morris JB, Beck AT. Cross-validation of the Suicidal Intent Scale. Psychological Reports. 1974; 34:445–446. [PubMed: 4820501]

Beck AT, Weissman A, Lester D, Trexler L. The measurement of pessimism: the hopelessness scale. Journal of Consulting and Clinical Psychology. 1974; 42:861–865. [PubMed: 4436473]

Briggs MH. Cigarette smoking and infertility in men. Medical Journal of Austria. 1973; 1(12):616–7.

Brown GL, Goodwin FK. Human aggression and suicide. Suicide and Life Threatening Behavior. 1986; 16:223–243. [PubMed: 2428140]

Buss AH, Durkee A. An inventory for assessing different kinds of hostility. Journal of Consulting Psychology. 1957; 21(4):343–9. [PubMed: 13463189]

Butterfield MI, Stechuchak KM, Connor KM, Davidson JR, Wang C, MacKuen CL, Pearlstein AM, Marx CE. Neuroactive steroids and suicidality in posttraumatic stress disorder. American Journal of Psychiatry. 2005; 162(2):380–2. [PubMed: 15677605]

Callanan VJ, Davis MS. Gender differences in suicide methods. Social Psychiatry and Psychiatric Epidemiology. in press.

Canetto SS, Lester D. Gender and the primary prevention of suicide mortality. Suicide and Life Threatening Behavior. 1995; 25(1):58–69. [PubMed: 7631375]

Chaudhury SR, Grunebaum MF, Galfalvy HC, Burke AK, Sher L, Parsey RV, Everett B, Mann JJ, Oquendo MA. Does first episode polarity predict risk for suicide attempt in bipolar disorder? Journal of Affective Disorders. 2007; 104(1–3):245–50. [PubMed: 17434597]

Diflorio A, Jones I. Is sex important? Gender differences in bipolar disorder. International Review of Psychiatry. 2010; 22(5):437–52. [PubMed: 21047158]

Ebinger M, Sievers C, Ivan D, Schneider HJ, Stalla GK. Is there a neuroendocrinological rationale for testosterone as a therapeutic option in depression? Journal of Psychopharmacology. 2009; 23(7): 841–53. [PubMed: 18562400]

Ehrenkranz J, Bliss E, Sheard MH. Plasma testosterone: correlation with aggressive behavior and social dominance in man. Psychosomatic Medicine. 1974; 36(6):469–75. [PubMed: 4431855]

Engström G, Persson B, Levander S. Temperament traits in male suicide attempters and violent offenders. European Psychiatry. 1999; 14(5):278–83. [PubMed: 10572358]

Fink G, Sumner B, Rosie R, Wilson H, McQueen J. Androgen actions on central serotonin neurotransmission: relevance for mood, mental state and memory. Behavioural and Brain Research. 1999; 105(1):53–68.

Grant BF, Stinson FS, Hasin DS, Dawson DA, Chou SP, Ruan WJ, Huang B. Prevalence, correlates, and comorbidity of bipolar I disorder and axis I and II disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. Journal of Clinical Psychiatry. 2005; 66:1205–1215. [PubMed: 16259532]

Hamilton M. A rating scale for depression. Journal of Neurology, Neurosurgery and Psychiatry. 1960; 23:56–62.

Hendrick V, Altshuler LL, Gitlin MJ, Delrahim S, Hammen C. Gender and bipolar illness. Journal of Clinical Psychiatry. 2000; 61:393–396. [PubMed: 10847318]

Hernandez-Rauda R, Aldegunde M. Effects of acute 17alpha-methyltestosterone, acute 17beta-estradiol, and chronic 17alpha-methyltestosterone on dopamine, norepinephrine and serotonin levels in the pituitary, hypothalamus and telencephalon of rainbow trout (Oncorhynchus mykiss). Journal of Comparative Physiology B. 2002; 172(8):659–67.

Itil TM, Michael ST, Shapiro DM, Itil KZ. The effects of mesterolone, a male sex hormone in depressed patients (a double blind controlled study). Methods and Findings in Experimental and Clinical Pharmacology. 1984; 6(6):331–7. [PubMed: 6431212]

Kapoor D, Malkin CJ, Channer KS, Jones TH. Androgens, insulin resistance and vascular disease in men. Clinical Endocrinology (Oxford). 2005; 63(3):239–50. [PubMed: 16117808]

Kawa I, Carter JD, Joyce PR, Doughty CJ, Frampton CM, Wells JE, Walsh AE, Olds RJ. Gender differences in bipolar disorder: age of onset, course, comorbidity, and symptom presentation. Bipolar Disorders. 2005; 7(2):119–25. [PubMed: 15762852]

Kessing LV. Gender differences in the phenomenology of bipolar disorder. Bipolar Disorders. 2004; 6(5):421–5. [PubMed: 15383135]

Levitt AJ, Joffe RT. Total and free testosterone in depressed men. Acta Psychiatrica Scandinavica. 1988; 77(3):346–8. [PubMed: 3394537]

Markianos M, Tripodianakis J, Istikoglou C, Rouvali O, Christopoulos M, Papageorgopoulos P, Seretis A. Suicide attempt by jumping: a study of gonadal axis hormones in male suicide attempters versus men who fell by accident. Psychiatry Research. 2009; 170(1):82–5. [PubMed: 19781790]

Mattsson A, Schalling D, Olweus D, Löw H, Svensson J. Plasma testosterone, aggressive behavior, and personality dimensions in young male delinquents. Journal of American Academy of Child Psychiatry. 1980; 19(3):476–90.

Molina, PE. Endocrine Physiology. Blacklick, OH: McGraw-Hill Medical Publishing Division; 2006. p. 181-206.

Mooradian AD, Morley JE, Korenman SG. Biological actions of androgens. Endocrinology Reviews. 1987; 8(1):1–28.

Mościcki EK. Gender differences in completed and attempted suicides. Annals of Epidemiology. 1994; 4(2):152–8. [PubMed: 8205283]

Nivoli AM, Pacchiarotti I, Rosa AR, Popovic D, Murru A, Valenti M, Bonnin CM, Grande I, Sanchez-Moreno J, Vieta E, Colom F. Gender differences in a cohort study of 604 bipolar patients: the role of predominant polarity. Journal of Affective Disorders. 2011; 133(3):443–9. [PubMed: 21620480]

O'Connor DB, Archer J, Wu FC. Effects of testosterone on mood, aggression, and sexual behavior in young men: a double-blind, placebo-controlled, cross-over study. Journal of Clinical Endocrinology and Metabolism. 2004; 89(6):2837–45. [PubMed: 15181066]

Olweus D, Mattsson A, Schalling D, Löw H. Circulating testosterone levels and aggression in adolescent males: a causal analysis. Psychosomatic Medicine. 1988; 50(3):261–72. [PubMed: 3387509]

Olweus D, Mattsson A, Schalling D, Löw H. Testosterone, aggression, physical, and personality dimensions in normal adolescent males. Psychosomatic Medicine. 1980; 42(2):253–69. [PubMed: 7454920]

Oquendo MA, Galfalvy H, Russo S, Ellis SP, Grunebaum MF, Burke A, Mann JJ. Prospective study of clinical predictors of suicidal acts after a major depressive episode in patients with major depressive disorder or bipolar disorder. American Journal of Psychiatry. 2004; 161(8):1433–41. [PubMed: 15285970]

Oquendo, MA.; Halberstam, B.; Mann, JJ. Risk factors for suicidal behavior: utility and limitations of research instruments. In: First, MB., editor. Standardized Evaluation in Clinical Practice. Washington, DC: APPI Press; 2003. p. 22

Oquendo MA, Mann JJ. The biology of impulsivity and suicidality. Psychiatric Clinics of North America. 2000; 23(1):11–25. [PubMed: 10729928]

Perez-Rodriguez MM, Lopez-Castroman J, Martinez-Vigo M, et al. Lack of association between testosterone and suicide attempts. Neuropsychobiology. 2011; 63(2):125–30. [PubMed: 21196783]

Pope HG Jr, Cohane GH, Kanayama G, Siegel AJ, Hudson JI. Testosterone gel supplementation for men with refractory depression: a randomized, placebo-controlled trial. American Journal of Psychiatry. 2003; 160(1):105–11. [PubMed: 12505808]

Pope HG Jr, Katz DL. Affective and psychotic symptoms associated with anabolic steroid use. American Journal of Psychiatry. 1988; 145(4):487–90. [PubMed: 3279830]

Pope HG Jr, Katz DL. Homicide and near-homicide by anabolic steroid users. Journal of Clinical Psychiatry. 1990; 51(1):28–31. [PubMed: 2295588]

Pope HG Jr, Katz DL. Psychiatric and medical effects of anabolic-androgenic steroid use. A controlled study of 160 athletes. Archives of General Psychiatry. 1994; 51(5):375–82. [PubMed: 8179461]

Pope HG Jr, Kouri EM, Hudson JI. Effects of supraphysiologic doses of testosterone on mood and aggression in normal men: a randomized controlled trial. Archives of General Psychiatry. 2000; 57(2):133–40. [PubMed: 10665615]

Robb JC, Young LT, Cooke RG, Joffe RT. Gender differences in patients with bipolar disorder influence outcome in the medical outcomes survey (SF-20) subscale scores. Journal of Affective Disorders. 1998; 49:189–193. [PubMed: 9629948]

Roy-Byrne P, Post RM, Uhde TW, Porcu T, Davis D. The longitudinal course of recurrent affective illness: Life chart data from research patients at the NIMH. Acta Psychiatrica Scandinavica, Suppl. 1985; 317:1–34.

Rubinow DR, Schmidt PJ. Androgens, brain, and behavior. American Journal of Psychiatry. 1996; 153(8):974–84. [PubMed: 8678193]

Schmidt PJ, Rubinow DR. Neuroregulatory role of gonadal steroids in humans. Psychopharmacology Bulletin. 1997; 33(2):219–20. [PubMed: 9230633]

Schweiger U, Deuschle M, Weber B, Körner A, Lammers CH, Schmider J, Gotthardt U, Heuser I. Testosterone, gonadotropin, and cortisol secretion in male patients with major depression. Psychosomatic Medicine. 1999; 61(3):292–6. [PubMed: 10367608]

Shaarawy M, Mahmoud KZ. Endocrine profile and semen characteristics in male smokers. Fertility and Sterility. 1982; 38(2):255–7. [PubMed: 6809501]

Sher L, Oquendo MA, Galfalvy HC, et al. The relationship of aggression to suicidal behavior in depressed patients with a history of alcoholism. Addictive Behavior. 2005; 30(6):1144–1153.

Soler H, Vinayak P, Quadagno D. Biosocial aspects of domestic violence. Psychoneuroendocrinology. 2000; 25(7):721–39. [PubMed: 10938451]

Su TP, Pagliaro M, Schmidt PJ, Pickar D, Wolkowitz O, Rubinow DR. Neuropsychiatric effects of anabolic steroids in male normal volunteers. Journal of the American Medical Association. 1993; 269(21):2760–4. [PubMed: 8492402]

Swaab DF, Bao AM, Lucassen PJ. The stress system in the human brain in depression and neurodegeneration. Ageing Research Reviews. 2005; 4(2):141–94. [PubMed: 15996533]

Thase ME. Newer medications for complicated depression. Journal of Clinical Psychiatry. 2009; 70(9):e33. [PubMed: 19818239]

Tripodianakis J, Markianos M, Rouvali O, Istikoglou C. Gonadal axis hormones in psychiatric male patients after a suicide attempt. European Archives of Psychiatry and Clinical Neuroscience. 2007; 257(3):135–9. [PubMed: 17131219]

van Heeringen K. The neurobiology of suicide and suicidality. Canadian Journal of Psychiatry. 2003; 48(5):292–300.

Virkkunen M, Rawlings R, Tokola R, Poland RE, Guidotti A, Nemeroff C, Bissette G, Kalogeras K, Karonen SL, Linnoila M. CSF biochemistries, glucose metabolism, and diurnal activity rhythms in alcoholic, violent offenders, fire setters, and healthy volunteers. Archives of General Psychiatry. 1994; 51(1):20–7. [PubMed: 7506515]

Wang C, Alexander G, Berman N, Salehian B, Davidson T, McDonald V, Steiner B, Hull L, Callegari C, Swerdloff RS. Testosterone replacement therapy improves mood in hypogonadal men--a clinical research center study. Journal of Clinical Endocrinology and Metabolism. 1996; 81(10): 3578–83. [PubMed: 8855804]

Weiss EL, Bowers MB Jr, Mazure CM. Testosterone-patch-induced psychotic mania. American Journal of Psychiatry. 1999; 156(6):969. [PubMed: 10360145]

Yates WR, Perry PJ, MacIndoe J, Holman T, Ellingrod V. Psychosexual effects of three doses of testosterone cycling in normal men. Biological Psychiatry. 1999; 45(3):254–60. [PubMed: 10023498]

Zarrouf FA, Artz S, Griffith J, Sirbu C, Kommor M. Testosterone and depression: systematic review and meta-analysis. Journal of Psychiatric Practice. 2009; 15(4):289–305. [PubMed: 19625884]

Zitzmann M. Testosterone and the brain. Aging Male. 2006; 9(4):195–9. [PubMed: 17178554]

Zitzmann M, Nieschlag E. Testosterone levels in healthy men and the relation to behavioural and physical characteristics: facts and constructs. European Journal of Endocrinology. 2001; 144(3): 183–97. [PubMed: 11248735]

Table 1

Demographic and clinical features of bipolar suicide attempters

Variable Name	All subjects (n=67)		Males (n=16)		Femalesv (n=51)		Analysis: comparison of males and females		
	Mean or (N)	SD or (%)	Mean or (N)	SD or (%)	Mean or (N)	SD or (%)	df	t/2	p
Demographic features									
Age (yrs)	34.5	9.9	38.6	9.9	33.2	9.6	65	2.0	0.05
Marital status (married)	(15)	(19.7)	(6)	(40)	(9)	(17.6)	1	3.3	0.09
Education (total years)	14.6	2.16	15.4	1.5	14.4	2.3	64	0.1	0.14
Clinical features									
Hamilton Depression Rating Scale (HDRS)	19.24	6.3	17.1	6.3	19.9	6.2	64	1.6	0.11
Brown-Goodwin Aggression History Scale	23.7	7.0	25.7	7.2	23.1	6.8	61	1.3	0.21
Barrat Impulsivity Scale (BIS)	68.2	17.7	72.5	16.3	66.9	18.0	57	1.0	0.32
Buss Durkee Hostility Scale	44.2	12.5	44.2	13.0	44.2	12.6	55	−0.2	0.98
Beck Hopelessness Scale (BHI)	11.7	5.7	11.8	4.8	11.7	5.9	55	<0.01	0.99
Age at first major depressive episode	15.4	7.5	14.7	6.2	15.6	7.8	56	−0.4	0.70
Age at first manic episode	19.1	7.2	15.2	4.0	20.1	7.6	39	−1.9	0.07
Age at first psychiatric hospitalization	25.9	9.8	23.9	10.0	26.6	9.8	41	−.08	0.42
Number of depressive episodes	10.4	6.8	15.3	6.4	9.0	6.3	55	3.9	<0.001
Number of manic episodes	7.2	7.5	10.0	8.9	6.5	7.0	57	1.1	0.26
Number of psychiatric hospitalizations	3.6	4.7	3.5	4.7	3.7	4.8	55	−.01	0.9
Number of suicide attempts	2.9	1.9	2.7	1.6	3.0	2.0	65	−0.5	0.6
Maximum lethality of suicide attempts	2.9	1.6	3.7	2.1	2.7	1.4	63	2.2	0.03
Beck Suicidal Ideation Scale	10.7	8.6	4.6	5.6	12.4	8.5	47	−2.9	0.006
Reasons for Living Scale	141.5	43.3	126.3	35.9	146.1	44.6	54	−1.5	0.15
Smoking status (%smokers)	(26)	(38.8)	(8)	(50)	(18)	(35.3)	1	1.1	0.38
Testosterone level	1.4	2.1	4.5	1.8	0.5	0.9	62	11.5	<0.001

Table 2

Correlations of testosterone levels with demographic and clinical features of bipolar suicide attempters

Variable Name	Correlations			Correlations controlled for sex		
	r	p	N	r	p	N
Demographic features						
Age (yrs)	0.12	0.34	67	−0.15	0.24	64
Education (total years)	0.01	0.96	66	−0.28	0.02	63
Clinical features						
Hamilton Depression Rating Scale (HDRS)	−0.13	0.30	66	0.06	0.63	63
Brown-Goodwin Aggression History Scale	0.25	0.05	63	0.20	0.12	60
Barrat Impulsivity Scale (BIS)	0.22	0.09	59	0.20	0.13	56
Buss Durkee Hostility Scale	0.002	0.99	57	0.01	0.96	54
Beck Hopelessness Scale (BHI)	0.03	0.84	57	0.05	0.74	54
Age at first major depressive episode	−0.12	0.39	58	−0.15	0.26	55
Age at first manic episode	−0.31	0.049	41	−0.13	0.44	38
Age at first psychiatric hospitalization	−0.23	0.13	43	−0.28	0.07	40
Number of depressive episodes	0.41	0.002	57	0.15	0.28	54
Number of manic episodes	0.31	0.016	59	0.32	0.02	56
Number of psychiatric hospitalizations	0.04	0.96	57	0.27	0.84	54
Number of suicide attempts	0.14	0.26	67	0.35	0.004	64
Maximum lethality of suicide attempts	0.3	0.009	65	0.20	0.12	62
Beck Suicidal Ideation Scale	−.03	0.016	49	0.002	0.99	46
Reasons for Living Scale	−0.26	0.049	56	−0.23	0.09	53