

## Psychiatric Briefs

### Interpersonal Dysfunction in Depressed Women: Impairments Independent of Depressive Symptoms

Hammen C, Brennan PA

**Background:** In this study, the extent of interpersonal dysfunction in depressed women was examined, and their degree of independence of current depressive episodes or symptoms was explored. **Method:** Using a variety of indices of interpersonal behavior and beliefs, 812 community-dwelling women who were formerly, currently, or never depressed were compared. The spouses and adolescent children of these women, as well as raters, also provided information. The study controlled for current depressive mood and sociodemographic factors that could affect social functioning. **Results:** Formerly depressed but not currently depressed women showed significantly more impairment than never-depressed women on nearly all measures of interpersonal dysfunction, a finding consistent with hypotheses that interpersonal difficulties are not merely consequences of depressive symptoms. Women who had formerly been depressed were less likely to be stably married, had less marital satisfaction, were more likely to experience spouse coercion and physical injury, had more problematic relationships with children and extended family members as well as friends, reported more stressful life events that had interpersonal and conflict content, and had greater insecurity in their beliefs about other people. The spouses and boyfriends of these women reported more problems as well, and they were more likely to have diagnosable disorders. No between-group differences were found, however, in children's perceptions of warmth or hostility on the part of the mothers. **Limitations:** Conclusions about the causal direction of the relationship between depressive symptoms and interpersonal difficulties are precluded by the cross-sectional design of this study. Clinical depression is usually followed by subthreshold symptoms not identified by standard diagnostic instruments; these symptoms are difficult to distinguish from preceding or co-occurring interpersonal problems. **Conclusions:** Interpersonal difficulties are a stable feature of depression. They pose a great challenge to treatment, and they may reflect an underlying susceptibility to both the onset and recurrence of depression.

(*J Affect Disord* 2002;72:145–156)

### Sexual Function and Behavior in Social Phobia

Bodinger L, Hermesh H, Aizenberg D, et al.

**Background:** Social phobia is a type of performance and interpersonal anxiety disorder and as such may be associated with sexual dysfunction and avoidance. The aim of the present study was to evaluate sexual function and behavior in patients

with social phobia compared with mentally healthy subjects. **Method:** Eighty subjects participated in the study: 40 consecutive, drug-free outpatients with social phobia (DSM-IV) attending an anxiety disorders clinic between November 1997 and April 1999 and 40 mentally normal controls. The Structured Clinical Interview for DSM-IV Axis I Disorders and the Liebowitz Social Anxiety Scale were used to quantitatively and qualitatively assess sexual function and behavior. **Results:** Men with social phobia reported mainly moderate impairment in arousal, orgasm, sexual enjoyment, and subjective satisfaction domains. Women with social phobia reported severe impairment in desire, arousal, sexual activity, and subjective satisfaction. In addition, compared with controls, men with social phobia reported significantly more frequent paid sex ( $p < .05$ ), and women with social phobia reported a significant paucity of sexual partners ( $p < .05$ ). **Conclusion:** Patients with social phobia exhibit a wide range of sexual dysfunctions. Men have mainly performance problems, and women have a more pervasive disorder. Patients of both genders show difficulties in sexual interaction. It is important that clinicians be aware of this aspect of social phobia and initiate open discussions of sexual problems with patients.

(*J Clin Psychiatry* 2002;63:874–879)

### The Grief Experiences and Needs of Bereaved Relatives and Friends of Older People Dying Through Suicide: A Descriptive and Case-Control Study

Harwood D, Hawton K, Hope T, et al.

**Background:** The grief experiences of those bereaved through the suicide of older persons are largely unknown. Legal procedures surrounding the death are a possible source of distress. In addition, research suggests that feelings of guilt, as well as a sense of stigma, shame, or rejection, are more common in relatives bereaved through suicide than in individuals bereaved through other modes of death. **Method:** In a cohort of 85 friends and relatives of older individuals ( $\geq 60$  years) who committed suicide, problems encountered during legal procedures following the death and grief experiences were examined. In addition, the study included a case-control comparison of the bereavement reactions of a subgroup of these individuals ( $N = 46$ ) and a control group of individuals bereaved through the natural death of an older person. Interviews were carried out 6 to 21 months after the death; these included a semistructured assessment of problems following the death, the Grief Experience Questionnaire (GEQ), and the Montgomery-Asberg Depression Rating Scale. **Results:** Among those bereaved through suicide, 36 (42.4%) reported problems related to dealings with the coroner's office, and 33 (38.8%) reported stress due to media

reporting of the inquest. Although individuals bereaved through suicide had depression scores similar to those of individuals in the control group, the former group had higher scores on the GEQ subscales measuring stigmatization, shame, sense of rejection, and "unique reactions." **Limitations:** This study had a low participation rate of potential subjects, especially for the control group. There were differences between the study and control groups in proportions of different kinships to the deceased. **Conclusions:** Relatives bereaved through suicide frequently experience distress related to media reporting of coroner's inquests and to inquest procedures. These relatives often experience stigma, shame, and a sense of rejection; counseling of these individuals, therefore, should address these themes.

(*J Affect Disord* 2002;72:185-194)

### Is Response to Prophylactic Lithium a Familial Trait?

Grof P, Duffy A, Cavazzoni P, et al.

**Background:** Selecting a drug according to the treatment response in a relative has been widely accepted advice in the management of mood disorders. However, this recommendation has not been adequately substantiated in the literature. We tested the hypothesis that response to long-term lithium treatment is a familial trait. **Method:** We compared response to long-term lithium treatment in bipolar relatives of bipolar lithium responders and bipolar controls. Twenty-four relatives with bipolar disorder (as determined using the Schedule for Affective Disorders and Schizophrenia-Lifetime version [SADS-L] and Research Diagnostic Criteria [RDC]) were identified in families of 106 patients with lithium-responsive bipolar disorder. A consecutive series of 40 lithium-treated patients in a bipolar clinic (meeting RDC and DSM-IV criteria for bipolar disorder) served as a comparison group. Lithium response was evaluated on a rating scale reflecting the quality and quantity of available data. **Results:** The prevalence of unequivocal response among the relatives was 67%, as compared with the response rate of 35% in the comparison group ( $\chi^2 = 6.04$ ,  $df = 1$ ,  $p = .014$ ). **Conclusion:** This highly significant difference in response between relatives and the control group supports the view that the response to lithium prophylaxis clusters in families.

(*J Clin Psychiatry* 2002;63:942-947)

### Nicotine Replacement to Reduce Cigarette Consumption in Smokers Who Are Unwilling to Quit: A Randomized Trial

Etter J-F, Laszlo E, Zellweger J-P, et al.

This study assessed whether the administration of nicotine replacement therapy in a real-life situation could lower the rate of cigarette consumption in smokers who had no current plan to quit. Study participants, selected from the general population, were daily smokers of more than 20 cigarettes per day who did not intend to quit smoking in the next 6 months. Participants were randomly assigned to 1 of 3 groups for a study period of 6 months: nicotine treatment (with a choice of a 15-mg nicotine

patch, a 4-mg nicotine gum, a 10-mg nicotine inhaler, or a combination of the 3;  $N = 265$ ), matching placebo products ( $N = 269$ ), or no intervention ( $N = 389$ ). Products were sent by mail to participants; participant education consisted solely of a booklet. At 6 months, a total of 879 (95%) of the 923 participants were followed up. In all groups, the mean baseline consumption was 30 cigarettes per day. Cigarette consumption was down after 6 months in all 3 groups with a median decrease of 10 cigarettes per day in the nicotine group, 7.5 cigarettes per day in the placebo group, and 2.5 cigarettes per day for controls ( $p < .04$  for all pairwise comparisons). Rates of smoking cessation were low (2%-4%); no significant difference was found between groups. Those in the control group had a lower rate of quit attempts (21%) than those in the nicotine (28%,  $p = .04$ ) and placebo (27%,  $p = .08$ ) groups. In conclusion, although nicotine replacement therapy led to reductions in cigarette consumption and helped maintain these reductions over 6 months, a placebo effect was largely responsible for these reductions. No impact of nicotine treatment on smoking cessation was detected.

(*J Clin Psychopharmacol* 2002;22:487-495)

### Nefazodone Treatment of Pathological Gambling: A Prospective Open-Label Controlled Trial

Pallanti S, Rossi NB, Sood E, et al.

**Background:** Pathological gambling is a disabling and highly prevalent impulse-control disorder not otherwise specified (NOS). According to the hypothesis of abnormal serotonin function in the pathophysiology of poor impulse control and pathological gambling, we assessed the efficacy and tolerability of nefazodone, a 5-HT antagonist reported to be effective in other impulse-control disorders NOS, in the treatment of pathological gambling. **Method:** Fourteen outpatients who met DSM-IV criteria for pathological gambling were enrolled in a prospective 8-week open-label oral nefazodone trial. Nefazodone was initiated at 50 mg/day and titrated upward to a maximum of 500 mg/day based on patient's response and side effects, with a minimum daily dose of 100 mg. Improvement in gambling was assessed via the pathological gambling modifications of the Yale-Brown Obsessive Compulsive Scale (PG-YBOCS), the Clinical Global Impressions-Improvement scale (PG-CGI-I), and self-rated gambling scales. Response was defined a priori as both a 25% reduction in PG-YBOCS score and a score of 1 (very much improved) or 2 (much improved) on the PG-CGI-I scale. **Results:** Twelve subjects completed the study, and 2 subjects were early dropouts who did not receive the minimum required dose. Significant improvements were noted in all gambling outcome measures, as well as in depression and anxiety ratings (which did not significantly correlate with gambling reduction). Nine (75%) of 12 patients were rated as responders according to a priori criteria. Side effects (dry mouth and sedation) of moderate severity occurred in 4 subjects. **Conclusion:** These preliminary results suggest that nefazodone may be effective in reducing symptoms of pathological gambling and is well tolerated.

(*J Clin Psychiatry* 2002;63:1034-1039)

### Risk Factors for Falls During Treatment of Late-Life Depression

Joo JH, Lenze EJ, Mulsant BH, et al.

**Background:** Prior studies have found that antidepressant medications are associated with an increased risk of falling in elderly persons. However, little is known about the prevention of falls during treatment for depression in elderly persons. This study evaluated the time course and potential risk factors for falls in a treatment protocol for late-life depression to identify specific at-risk periods and risk factors for falls in this population. **Method:** One hundred four subjects aged 69 years and over were treated in a protocolized manner using paroxetine and interpersonal psychotherapy. Those who did not respond received augmentation therapy with bupropion, nortriptyline, or lithium. Subjects were assessed at baseline and weekly during treatment; demographic and clinical characteristics of those who experienced a fall during treatment were compared with those who did not fall. Cox proportional hazards models were used to define risk factors for falls in univariate and multivariate models. **Results:** During a mean of 21 weeks of treatment, 40 subjects (38%) fell. About half (53%) of the subjects fell during the first 6 weeks of treatment. In the multivariate model, memory impairment and orthostatic changes in blood pressure during treatment were risk factors for falling. Additionally, augmentation with bupropion appeared to be a risk factor for falls in univariate analysis, but this result is preliminary due to the small number of subjects who took bupropion. **Conclusion:** Increased monitoring for falls is warranted during the acute treatment of late-life depression. When treating such patients, clinicians should be especially watchful of those with memory impairments or those who develop orthostatic blood pressure changes; orthostatic blood pressure should be measured throughout acute treatment. Additionally, augmenting paroxetine with bupropion may also increase the risk of falls, and this medication combination should be used with caution in elderly patients.

(*J Clin Psychiatry* 2002;63:936–941)

### Impact of Work Therapy on Health Status Among Homeless, Substance-Dependent Veterans: A Randomized Controlled Trial

Kashner TM, Rosenheck R, Campinell AB, et al.

**Background:** The health outcomes of clinician-supervised, performance-based, abstinence-contingent work therapy programs on homeless individuals with addictive disorders are largely unknown. In this study, the effect of the U.S. Department of Veterans Affairs compensated work therapy program (CWT) on nonvocational outcomes was assessed. CWT, which included mandatory urine screenings and adherence to addiction treatment schedules, provided employment opportunities—including wages, hours, and responsibilities—in the form of jobs created from contracts competitively obtained from the private sector by the Department of Veterans Affairs. **Method:** Substance-dependent, homeless veterans (N = 142) from 4 Department of Veterans Affairs medical centers were randomly

assigned to either the intervention (CWT) group or control group. Individuals from both groups received assessments at baseline and at 3-month intervals for 1 year. Access to comprehensive rehabilitation, addictions, psychiatric, and medical services was made available to both groups. Both the immediate effects of CWT and the differences over time between groups in outcome were determined. **Results:** Patients in the CWT program, compared with those in the control group, had a greater likelihood of (1) initiating outpatient treatment for addictions, (2) experiencing fewer problems related to drug and alcohol use, (3) reporting fewer physical symptoms related to substance use, (4) avoiding additional loss of physical functioning, and (5) having fewer episodes of incarceration and homelessness. The study found no effect on psychiatric outcomes. **Conclusion:** Nonvocational outcomes of addiction treatment for homeless individuals can be enhanced by work therapy; however, the long-term gains of such therapy are not yet known.

(*Arch Gen Psychiatry* 2002;59:938–944)

### The Impact of Treatment-Resistant Depression on Health Care Utilization and Costs

Crown WH, Finkelstein S, Berndt ER, et al.

**Background:** Approximately 50% of patients diagnosed with major depressive disorder will experience a recurrent or chronic course of illness for which long-term treatment is recommended. Moreover, at least 20% of patients diagnosed with depression do not respond satisfactorily to several traditional antidepressant medication treatment trials. Very little is known about the health care costs of patients with treatment-resistant depression. **Method:** Based on medical claims data (MarketScan Research Database, The MEDSTAT Group, Cambridge, Mass.) from January 1, 1995, to June 30, 2000, a naturalistic, retrospective analysis was conducted to study the characteristics and health care utilization of patients with treatment-resistant depression. All patients having an *International Classification of Diseases*, Ninth Revision (ICD-9), diagnosis code for unipolar or bipolar depression with specified antidepressant dosing and treatment durations were initially selected. Patients were then classified as “treatment resistant” if either they switched from or augmented initial antidepressant medication with other antidepressants at least twice (outpatient treatment-resistant group) or they switched from or augmented their initial antidepressant medication and also had a claim for either a depression-related hospitalization or suicide attempt (hospitalized treatment-resistant group). Those meeting the initial medication and diagnosis selection criteria but not meeting the treatment-resistance criteria constituted the comparison group. Members of the comparison group had comparatively stable antidepressant medication use patterns, consistent with an acceptable response to treatment. Patients were followed for a minimum of 9 months. Resource utilization was calculated from index date to last available claims data point and then annualized. **Results:** Treatment-resistant patients were more likely to be diagnosed with bipolar disorder or concurrent substance abuse or anxiety disorders than the comparison group

( $p < .001$ ). Treatment-resistant patients were at least twice as likely to be hospitalized (general medical and depression related) and had at least 12% more outpatient visits ( $p < .02$ ). Treatment resistance was also associated with use of 1.4 to 3 times more psychotropic medications (including antidepressants) ( $p < .001$ ). Patients in the hospitalized treatment-resistant group had over 6 times the mean total medical costs of non-treatment-resistant depressed patients (\$42,344 vs. \$6512) ( $p < .001$ ) and their total depression-related costs were 19 times greater than those of patients in the comparison group (\$28,001 vs. \$1455) ( $p < .001$ ). **Conclusion:** Treatment-resistant depression is costly and associated with extensive use of depression-related and general medical services. These findings underscore the need for early identification and effective long-term maintenance treatment for treatment-resistant depression.

(*J Clin Psychiatry* 2002;63:963–971)

### Are There Differences Between Women's and Men's Antidepressant Responses?

Quitkin FM, Stewart JW, McGrath PJ, et al.

**Objective:** In order to ascertain whether patients' sex affected the outcome of antidepressant treatment, this study examined a large data set. **Method:** In a retrospective analysis, data for 1746 patients aged 18 to 65 years who had received tricyclic antidepressants, monoamine oxidase inhibitors (MAOIs), fluoxetine, or placebo were examined to determine if antidepressant response differed between men and women. Results for female patients younger or older than 50, 52, 54, and 56 years of age were compared to examine the effect of menopausal status in the absence of data on the menopausal status of individual patients. **Results:** Response rates to tricyclic antidepressants and fluoxetine were equivalent for men and women both younger and older than 50 years of age, although women had a statistically better response to MAOIs. The placebo response was equivalent across all groups. **Conclusions:** In depressed adult patients up to 65 years of age, neither sex nor menopausal status may be relevant in antidepressant treatment. The statistically superior response by women to MAOIs may not be clinically relevant.

(*Am J Psychiatry* 2002;159:1848–1854)

### Efficacy and Safety of Hydroxyzine in the Treatment of Generalized Anxiety Disorder: A 3-Month Double-Blind Study

Llorca P-M, Spadone C, Sol O, et al.

**Background:** The prevalence of generalized anxiety disorder (GAD) represents an important public health issue. Hydroxyzine, an antagonist of histamine receptors, showed both efficacy and safety in previous short-term double-blind studies over placebo in this pathology. The aim of the current study was to confirm those positive results over a 3-month period in adult outpatients. **Method:** This multicenter, parallel (hydroxyzine [50 mg/day]; bromazepam [6 mg/day]), randomized, double-

blind, placebo-controlled trial included 2 weeks of single-blind run-in placebo, 12 weeks of double-blind randomized treatment, and 4 weeks of single-blind run-out placebo. Three hundred thirty-four of 369 selected outpatients with a diagnosis of GAD according to DSM-IV criteria and a Hamilton Rating Scale for Anxiety (HAM-A) total score  $\geq 20$  were randomized before entering the double-blind period. The primary outcome criterion was the change in the HAM-A score from baseline to 12 weeks of double-blind treatment with hydroxyzine compared with placebo. **Results:** In the intent-to-treat analysis, the mean  $\pm$  SD change in HAM-A scores from baseline to endpoint was  $-12.16 \pm 7.74$  for hydroxyzine and  $-9.64 \pm 7.74$  for placebo ( $p = .019$ ). Results at endpoint for percentage of responders ( $p = .003$ ) and remission rates ( $p = .028$ ), Clinical Global Impressions-Severity scale score ( $p = .001$ ), maintenance of efficacy ( $p = .022$ ), and Hospital Anxiety and Depression scale score on day 84 ( $p = .008$ ) also confirmed the efficacy of hydroxyzine over placebo. The study showed no statistically significant difference between hydroxyzine and bromazepam. Except for drowsiness, which was more frequent with bromazepam, safety results were comparable in the 3 groups. **Conclusion:** Hydroxyzine showed both efficacy and safety in the treatment of GAD and appears to be an effective alternative treatment to benzodiazepine prescription.

(*J Clin Psychiatry* 2002;63:1020–1027)

### Adult Psychosis, Common Childhood Infections, and Neurological Soft Signs in a National Birth Cohort

Leask SJ, Done DJ, Crow TJ

**Background and Aims:** Neurologic "soft signs" (e.g., coordination/balance, left-handedness) that precede adult-onset schizophrenia appear to have a neurodevelopmental origin. Early childhood infectious illness is a putative etiologic factor for adult-onset schizophrenia. This study sought to investigate whether neurologic soft signs and common infectious illnesses in childhood are associated with adult-onset psychosis. **Method:** Data from the U.K. National Child Development Study, a longitudinal sample of the general population, were used to calculate odds ratios for clinical diagnoses of common childhood viral illnesses and later adult psychotic illness, childhood epilepsy, and a variety of neurologic soft signs. **Results:** Neither the number of soft signs nor any particular adult outcome was related to the number of illnesses per individual. Schizophrenia, affective psychosis, and epilepsy, although not associated with common childhood illness, were associated with neurologic soft signs and with a higher (though small) frequency of previous meningitis and tuberculosis. **Conclusions:** Neurologic soft signs are not caused by infectious illness, but they do appear to be markers of disordered neurodevelopment in schizophrenia. In addition, an association appears to exist between childhood meningitis or tuberculosis and a small proportion of cases of epilepsy, affective psychosis, and schizophrenia.

(*Br J Psychiatry* 2002;181:387–392)

### Psychological Intervention and Antidepressant Treatment in Smoking Cessation

Hall SM, Humfleet GL, Reus VI, et al.

**Background:** Efficacy in the treatment of tobacco dependence has been shown with the use of the antidepressants bupropion sustained release and nortriptyline. However, whether psychological intervention increases the efficacy of these antidepressants is not known. In this study, both drugs were compared with placebo, and the efficacy of the 2 drugs and placebo with and without psychological intervention was examined. **Method:** This randomized trial employed a 2 (medical management vs. psychological intervention) by 3 (bupropion vs. nortriptyline vs. placebo) design and included 220 cigarette smokers. Biologically verified abstinence from cigarette smoking at weeks 12, 24, 36, and 52 was the outcome measure. **Results:** Compared with medical management alone, psychological interven-

tion led to higher 7-day point-prevalence rates of biologically verified abstinence. In addition, both bupropion and nortriptyline showed greater efficacy than placebo in measures of point-prevalence abstinence. However, the drugs did not differ from each other or from placebo on rates of 1-year continuous abstinence. No difference on rates of 1-year continuous abstinence was found between psychological intervention and medical management alone. **Conclusions:** In producing abstinence in cigarette smokers, both bupropion and nortriptyline show efficacy, and psychological intervention shows greater efficacy than simple medical management alone. However, the efficacy of both drugs and of psychological intervention is limited in producing sustained abstinence. In addition, the combination of psychological intervention and antidepressant drug treatment may not be more effective than antidepressant treatment alone.

(*Arch Gen Psychiatry* 2002;59:930-936)

© 2002 Physicians Postgraduate Press, Inc.  
One personal copy may be printed