Abstracts

Panic and Social Anxiety Disorder

Given space limitations and varying reprint permission policies, not all of the influential publications the editors considered reprinting in this issue could be included. This section contains abstracts from additional articles the editors deemed well worth reviewing.

Combination of Psychotherapy and Benzodiazepines Versus Either Therapy Alone for Panic Disorder: A Systematic Review
Watanabe N, Churchill R, Furukawa TA.
BMC Psychiatry. 2007 May 14; 7:18.

Background: The efficacy of combined psychotherapy and benzodiazepine treatment for panic disorder is still unclear despite its widespread use. The present systematic review aims to examine its efficacy compared with either monotherapy alone. **Methods:** All randomised trials comparing combined psychotherapy and benzodiazepine for panic disorder with either therapy alone were identified by comprehensive electronic search on the Cochrane Registers, by checking references of relevant studies and of other reviews, and by contacting experts in the field. Two reviewers independently checked eligibility of trials, assessed quality of trials and extracted data from eligible trials using a standardized data extraction form. Our primary outcome was "response" defined by global judgement. Authors of the original trials were contacted for further unpublished data. Meta-analyses were undertaken synthesizing data from all relevant trials. **Results:** Only two studies, which compared the combination with behaviour (exposure) therapy, met our eligibility criteria. Both studies had a 16-week intervention. Unpublished data were retrieved for one study. The relative risk for response for the combination was 1.25 (95% CI: 0.78 to 2.03) during acute phase treatment, 0.78 (0.45 to 1.35) at the end of treatment, and 0.62 (0.36 to 1.07) at 6–12 months follow-up. Some secondary outcomes hinted at superiority of the combination during acute phase treatment. One study was identified comparing the combination to benzodiazepine. The relative risk for response was 1.57 (0.83 to 2.98), 3.39 (1.03 to 11.21, statistically significant) and 2.31 (0.79 to 6.74) respectively. The superiority of the combination was observed on secondary outcomes at all the time points. No sub-group analyses were conducted due to the limited number of included trials. **Conclusion:** Unlike some narrative reviews in the literature, our systematic search established the paucity of high quality evidence for or against the combined psychotherapy plus benzodiazepine therapy for panic disorder. Based on limited available published and unpublished data, however, the combined therapy is probably to be recommended over benzodiazepine alone for panic disorder with agoraphobia. The combination might be superior to behaviour therapy alone during the acute phase, but afterwards this trend may be reversed. We know little from these trials about their adverse effects.

Intensive Group Cognitive Treatment and Individual Cognitive Therapy vs. Treatment As Usual in Social Phobia: A Randomized Controlled Trial
Mörtberg E, Clark DM, Sundin O, Aberg Wistedt A.
Acta Psychiatr Scand. 2007 Feb; 115(2):142–54.

To compare the effects of an intensive group cognitive treatment (IGCT) to individual cognitive therapy (ICT) and treatment as usual (TAU) in social phobia (DSM-IV). **Method:** Hundred patients were randomized to: IGCT involving 16 group sessions spread over three weeks; ICT involving 16 shorter weekly sessions in 4 months and; TAU involving an indicated selective serotonin reuptake inhibitor (SSRI) with therapy sessions as required for 1 year. The main outcome measure was a Social Phobia Composite that combined several standardized self-report measures. Diagnostic assessment was repeated at 1-year follow-up. **Results:** Significant improvements were observed with all treatments. ICT was superior to IGCT and TAU, which did not differ in overall effectiveness. **Conclusion:** The study confirms

and extends previously reported findings that ICT is more effective than group cognitive treatment and treatment with SSRIs. IGCT lasts only 3 weeks, and is as effective as more protracted TAU.

Remote Treatment of Panic Disorder: A Randomized Trial of Internet-Based Cognitive Behavior Therapy Supplemented with Telephone Calls
Carlbring P, Bohman S, Brunt S, Buhrman M, Westling BE, Ekselius L, Andersson G.
American Journal of Psychiatry 2006 Dec; 163(12):2119–25.

Objective: This study evaluated a 10-week Internet-based bibliotherapy self-help program with short weekly telephone calls for people suffering from panic disorder with or without agoraphobia. **Method:** After the authors confirmed the diagnosis by administering the Structured Clinical Interview for DSM-IV by telephone, 60 participants were randomly assigned to either a wait-listed control group or a multimodal treatment package based on cognitive behavior therapy plus minimal therapist contact via e-mail. A 10-minute telephone call was made each week to support each participant. Total mean time spent on each participant during the 10 weeks was 3.9 hours. The participants were required to send in homework assignments before receiving the next treatment module. **Results:** Analyses were conducted on an intention-to-treat basis, which included all randomly assigned participants. From pretreatment to posttreatment, all treated participants improved significantly on all measured dimensions (bodily interpretations, maladaptive cognitions, avoidance, general anxiety and depression levels, and quality of life). Treatment gains on self-report measures were maintained at the 9-month follow-up. A blind telephone interview after the end of treatment revealed that 77% of the treated patients no longer fulfilled the criteria for panic disorder, whereas all of the wait-listed subjects still suffered from it. **Conclusions:** This study provides evidence to support the use of treatment distributed via the Internet with the addition of short weekly telephone calls to treat panic disorder. Replication should be made to compare self-help and telephone treatment based on cognitive behavior methods with nonspecific interventions.

Etiology and Neurobiology of Social Anxiety Disorder
Sanjay J. Mathew, M.D., and Stephanie Ho, M.D.
Journal of Clinical Psychiatry 2006;67[suppl 12]:9–13

Social anxiety disorder (SAD) is influenced by multiple genetic and environmental factors. Imaging genomics combines genotyping with neuroradiological techniques, such as functional MRI (fMRI) and positron emission tomography (PET), to investigate samples relevant to psychiatric pathophysiology. Neuroanatomical areas implicated in SAD include the amygdala, prefrontal cortex, hippocampus, and striatum. Recent investigations have suggested that allelic polymorphisms may play a role in the disorder; 2 candidate genes, the serotonin transporter (*SLC6A4*) and catechol-*O*-methyl transferase (*COMT*), are described. The biology of extinction learning is relevant to the rapeutic approaches that aim to augment existing psychotherapies. In the future, novel uses of imaging genomics integrated with rational, biologically informed treatments will offer a more refined understanding of this complex and disabling disorder.

Treatment-Resistant Anxiety Disorders
Bystritsky A.
Mol Psychiatry 2006 Sep; 11(9):805–14. Epub 2006 Jul 18.

Several epidemiological studies confirmed that Anxiety Disorders as a group are the most prevalent psychiatric conditions in the United States. The importance of these conditions is underlined by the fact that they cause significant disability, poor quality of life, alcohol and drug abuse. Anxiety disorders are treatable conditions and respond to the front-line interventions such as serotonin reuptake inhibitors and cognitive behavioral therapy. However, only about 60% of patients respond to those treatments to any significant degree. Many still have residual symptoms or stay treatment refractory. The group of anxiety patients that is resistant to the treatment has been shown to have very poor quality of life and have highest rate of suicidal attempts than any other disorders. Many biological, treatment specific and social factors are affecting treatment resistance. In this paper, we are attempting to review reasons for the treat-

ment resistance. In addition, we would like to review current strategies that could be helpful in reducing treatment resistance and aiding people chronically suffering from these severe and disabling conditions.

One-Year Follow-up of Pharmacotherapy-Resistant Patients with Panic Disorder Treated with Cognitive-Behavior Therapy: Outcome and Predictors of Remission
Heldt E, Gus Manfro G, Kipper L, Blaya C, Isolan L, Otto MW.
Behav Res Ther. 2006 May; 44(5):657–65. Epub 2005 Jul 20.

Non-response to pharmacotherapy for panic disorder (PD) is a well-documented problem. However, little information exists to guide next-step strategies for these non-responders. In addition to pharmacologic augmentation strategies, several studies support the efficacy of cognitive-behavior therapy (CBT) for these patients, although data on long-term outcomes has been lacking. In this study, we provide one-year outcomes on a sample of 63 patients who completed group CBT for PD after failing to respond adequately to previous pharmacotherapy. Sustained significant benefit was found for all dimensional outcome scores, and nearly two-thirds of the sample met remission criteria. This occurred with reductions in medication use over the follow-up period. Negative predictors of remission status included comorbid dysthymia, social phobia, and generalized anxiety disorder. These results provide additional evidence for the efficacy of CBT for medication non-responders with PD.

The Epidemiology of Panic Attacks, Panic Disorder, and Agoraphobia in the National Comorbidity Survey Replication
Kessler RC, Chiu WT, Jin R, Ruscio AM, Shear K, Walters EE.
Archives of General Psychiatry 2006 Apr; 63(4):415–24.

Context: Only limited information exists about the epidemiology of DSM-IV panic attacks (PAs) and panic disorder (PD). **Objective:** To present nationally representative data about the epidemiology of PAs and PD with or without agoraphobia (AG) on the basis of the US National Comorbidity Survey Replication findings. **Design and Setting:** Nationally representative face-to-face household survey conducted using the fully structured World Health Organization Composite International Diagnostic Interview. **Participants:** English-speaking respondents (N=9282) 18 years or older. **Main Outcome Measures:** Respondents who met DSM-IV lifetime criteria for PAs and PD with and without AG. **Results:** Lifetime prevalence estimates are 22.7% for isolated panic without AG (PA only), 0.8% for PA with AG without PD (PA-AG), 3.7% for PD without AG (PD only), and 1.1% for PD with AG (PD-AG). Persistence, lifetime number of attacks, and number of years with attacks increase monotonically across these 4 subgroups. All 4 subgroups are significantly comorbid with other lifetime DSM-IV disorders, with the highest odds for PD-AG and the lowest for PA only. Scores on the Panic Disorder Severity Scale are also highest for PD-AG (86.3% moderate or severe) and lowest for PA only (6.7% moderate or severe). Agoraphobia is associated with substantial severity, impairment, and comorbidity. Lifetime treatment is high (from 96.1% for PD-AG to 61.1% for PA only), but 12-month treatment meeting published treatment guidelines is low (from 54.9% for PD-AG to 18.2% for PA only). **Conclusion:** Although the major societal burden of panic is caused by PD and PA-AG, isolated PAs also have high prevalence and meaningful role impairment.

Augmentation of Exposure Therapy with D-Cycloserine for Social Anxiety Disorder
Hofmann SG, Meuret AE, Smits JA, Simon NM, Pollack MH, Eisenmenger K, Shiekh M, Otto MW.
Archives of General Psychiatry 2006 Mar; 63(3):298–304.

Context: Social anxiety disorder (SAD) is common and debilitating. Although exposure therapy is one of the most effective forms of psychotherapy for this disorder, many patients remain symptomatic. Fear reduction in exposure therapy is similar to extinction learning, and early clinical data with specific phobias suggest that the treatment effects of exposure therapy for SAD may be enhanced with d-cycloserine, an agonist at the glutamatergic N-methyl-d-aspartate receptor. **Objective:** To determine whether short-term treatment with 50 mg of d-cycloserine enhances the efficacy of exposure therapy for SAD. **Design:**

Randomized, double-blind, placebo-controlled augmentation trial examining the combination of d-cycloserine or pill placebo with exposure therapy for SAD. **Setting:** Patients were self-referred from the general community to 1 of 3 research clinics. **Participants:** Twenty-seven participants meeting DSM-IV criteria for SAD with significant public speaking anxiety. **Interventions:** Following a diagnostic interview and pretreatment assessment, participants received 5 therapy sessions delivered in either an individual or group therapy format. The first session provided an introduction to the treatment model and was followed by 4 sessions emphasizing exposure to increasingly challenging public speech situations with videotaped feedback of performances. One hour prior to each session, participants received single doses of d-cycloserine or placebo. **Main Outcome Measures:** Symptoms were assessed by patient self-report and by clinicians blind to the randomization condition before treatment, after treatment, and 1 month after the last session. **Results:** Participants receiving d-cycloserine in addition to exposure therapy reported significantly less social anxiety compared with patients receiving exposure therapy plus placebo. Controlled effect sizes were in the medium to large range. **Conclusion:** The pilot data provide preliminary support for the use of short-term dosing of d-cycloserine as an adjunctive intervention to exposure therapy for SAD.

Aging and Panic Disorder: Phenomenology, Comorbidity, and Risk Factors
Sheikh JI, Swales PJ, Carlson EB, Lindley SE.
American Journal of Geriatric Psychiatry 2004 Jan-Feb; 12(1):102–9.

Objective: The authors compared young and older adults with panic disorder (PD) to investigate differences in panic-associated phenomenology, psychiatric comorbidity, and risk factors. **Method:** Patients in the older group (age 60 and above) were further subdivided into early- and late-onset groups and compared. Phenomenology (number of panic symptoms, severity of anxiety, physiological symptoms, panic-associated cognitions, and overall severity of PD); comorbidity (depressive and anxiety disorders); and risk factors (family history of anxiety and life stressors) were assessed in 167 outpatients with PD. **Results:** Older patients reported fewer panic symptoms, less anxiety and arousal, less severe PD, lower levels of depression, and higher levels of functioning. Furthermore, within the older-patient group, late-onset patients were found to report less distress during panic attacks in relation to body sensations and panic-related cognitions and emotions. Multiple-regression analysis of the entire sample showed that chronological age and age at onset of PD distinctly predicted different domains of panic phenomenology. **Conclusion:** PD was consistently less severe in older patients across multiple domains, and a later age at onset was associated with less distress due to body sensations, cognitions, and emotions during panic attacks.

Two-Year Follow-up Status of Emergency Department Patients with Chest Pain: Was It Panic Disorder?
Fleet RP, Lavoie KL, Martel JP, Dupuis G, Marchand A, Beitman BD.
CJEM. 2003 Jul; 5(4):247–54.

Objectives: We previously reported that 25% (108/441) of consecutive patients presenting to the emergency department (ED) of the Montreal Heart Institute with a chief complaint of chest pain suffered from panic disorder (PD). The purpose of the present study was to re-examine these patients (with and without PD) 2 years after their initial ED visit to determine their psychiatric and psychosocial status. **Methods:** An interviewer, who was kept blind to patients' initial medical and psychiatric diagnoses, attempted to contact all patients who participated in the initial study by phone. Patients who completed the phone interview were sent a battery of psychological questionnaires by mail. **Results:** A total of 301 (70%) patients completed the phone interview, and 228 (52%) patients completed the self-report questionnaires. Participants and non-participants did not differ with respect to age, gender, initial self-report scores, or initial cardiac or psychiatric diagnoses. At follow-up, significantly ($p < 0.05$) more PD+ than non-PD (PD-) patients reported: 1) chest pains in the last month (57% vs. 31%); 2) one or more ED consultations in the past year for chest pain (40% vs. 14%); 3) one or more hospitalizations in the past year (31% vs. 11%); and 4) perceiving their general health as "poor" (22% vs. 9%). PD+ patients displayed a significant ($p < 0.05$) worsening of their panic symptoms, agoraphobic avoidance, depression,

and trait anxiety, and reported significantly ($p < 0.05$) greater suicidal ideation compared to PD− patients (32% vs. 9%). Of all PD+ patients, only 22% (18/82) reported receiving some form of mental health treatment for their symptoms. **Conclusions:** Unrecognized and untreated PD has a chronic and disabling course. Greater efforts should be made to screen for PD in patients complaining of chest pain in EDs.

Comparative Phenomenology of Ataques de Nervios, Panic Attacks, and Panic Disorder
Lewis-Fernández R, Guarnaccia PJ, Martínez IE, Salmán E, Schmidt A, Liebowitz M.
Cult Med Psychiatry. 2002 Jun; 26(2):199–223.

This article examines a clinical sample of 66 Dominican and Puerto Rican subjects who reported ataques de nervios and also psychiatric disorder, and disentangles the phenomenological experiences of ataque de nervios, panic attacks, and panic disorder. In-depth cultural interviews assessed the symptomatic phenomenology of ataque episodes from the local perspective as well as in terms of key panic features, such as recurrence, rapid peaking of symptoms, and lack of provocation. Independent diagnostic assessments of panic attacks and disorder were also used to establish the phenomenological overlap between ataque and panic. Our findings indicate that 36 percent of ataques de nervios fulfill criteria for panic attacks and between 17 percent and 33 percent for panic disorder, depending on the overlap method used. The main features distinguishing ataques that fulfill panic criteria from ataques that do not include whether the episodes were provoked by an upsetting event in the person's life and the rapidity of crescendo of the actual attack. A key finding is that ataques often share individual phenomenological features with panic episodes, but that these features usually do not "run together" during the ataque experience. This confirms previous findings that ataque is a more inclusive construct than panic disorder. The importance of these findings for the clinical diagnosis and treatment of persons with ataques is discussed.

NOTES