Gene Polymorphism Linked to Depression in CHD

BY BRUCE JANCIN
Denver Bureau

VIENNA — Patients with coronary heart disease who carry the short allele of the serotonin transporter gene have significantly higher rates of major depression and perceived stress than do those who are homozygous for the long allele, Dr. Christian Otte said at the annual congress of the European College of Neuropsychopharmacology.

Moreover, patients with coronary heart disease (CHD) who carry the s (or short) allele of a functional polymorphism in the promoter region of the serotonin transporter gene also have higher 24-hour norepinephrine excretion than do those who have two long alleles (the l/l genotype), according to data from the prospective Heart and Soul Study.

"Since both depression and higher norepinephrine values have been associated with worse cardiac outcome, this might be a mechanism by which carriers of the short allele of the serotonin transporter gene might be at greater risk to suffer from cardiac events," explained Dr. Otte, a psychiatrist at University Hospital Hamburg-Eppendorf (Germany).

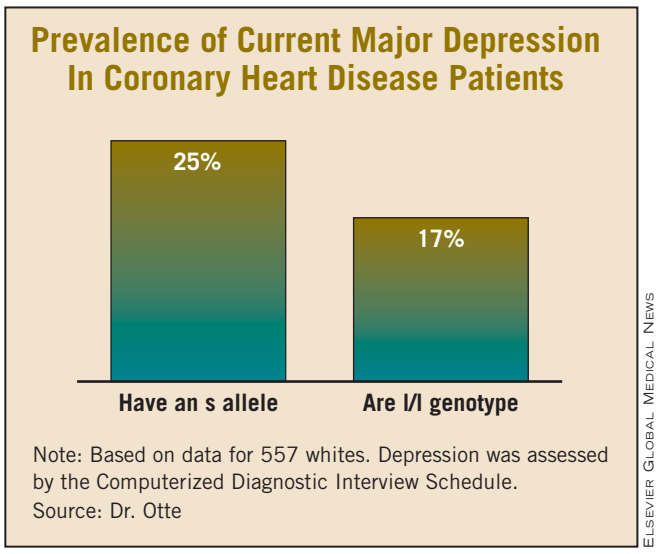
The Heart and Soul Study is an ongoing prospective cohort study based at the University of California, San Francisco, and involving 1,024 patients with CHD. The aim of the study is to shed new light on the association between depression and cardiovascular events. For purposes of the genetic study of serotonin transporter gene polymorphism, Dr. Otte restricted the analysis to the 557 whites, the largest racial group in the study. Of this group, 17% were homozygous for the s/s genotype, 52% were s/l, and 31% were l/l.

The prevalence of current major depression as assessed by the Computerized Diagnostic Interview Schedule was 25% among participants carrying an s allele, a significantly higher rate than the 17% in l/l subjects. After statistical adjustment for age and gender, CHD patients with an s allele for the serotonin transporter gene had a 60% increased rate of major depression. They also were 60% more likely to score in the moderate to high range for perceived stress, as reflected in a score greater than 5 on the Perceived Stress Scale.

Moreover, s allele carriers had a mean 24-hour norepinephrine excretion of 55.6 mg/day, compared with 50.2 mg/day in l/l patients, and they were 70% more likely to fall within the top quartile for 24-hour norepinephrine.

Dr. Otte said his research was inspired by a "classic" study of conducted by investigators at King's College London, who demonstrated that carriers of one or two copies of the s allele who experienced stressful life events were much more likely to develop depression than were l/l individuals with a comparable degree of life stress (Science 2003;301:386-9).

The Heart and Soul Study investigators reasoned that a chronic debilitating medical illness such as CHD might operate as an ongoing major stressor that would permit them to learn whether the s allele is related to depression, an extremely common CHD comorbidity.



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Increased Mortality Seen in Those With Changes in Sleep Duration

BY TIMOTHY F. KIRN
Sacramento Bureau

Both too much sleep and not enough sleep appear to be associated with increased mortality, according to a new longitudinal study.

Sleeping less than 6 hours per night or more than 9 hours per night was associated with almost twice the mortality risk of sleeping 6-8 hours per night, according to an analysis of sleep data from a prospective cohort study of more than 10,000 British civil servants.

The findings were recently presented at a meeting of the British Sleep Society, and the research article has been accepted for publication in the journal Sleep.

The investigators found that a decrease in the amount of time slept was associated with increased mortality from cardiovascular causes. An increase in sleep time was associated with an excess of mortality from all other causes, according to Jane Ferrie, Ph.D., of University College London, and her colleagues.

Previous studies have reported a U-shaped relationship between time spent sleeping and mortality, the investigators said. What has not been looked at by a sleep study before is the effect a change in sleep patterns might have.

The researchers examined sleep data collected from British civil service employees aged 35-55 years who were enrolled beginning in 1985 in a long-term study known as Whitehall II. Baseline sleep duration data were available for 9,781 subjects who were interviewed in 1985-1988, while follow-up data were available for 7,729 who were interviewed again in 1992-1993. Mortality data were available through September 2004.

After adjustment for factors such as age, sex, smoking status, body mass index, cholesterol, and physical activity, those Whitehall II participants who reported sleeping 5 hours or less a night at the first interview had a hazard ratio of death from all causes of 1.24, relative to those who slept 7 hours per night. Those who slept 9 hours or more had a fully adjusted hazard ratio of 1.54.

The fully adjusted hazard ratios of all-cause mortality were slightly higher for those who reported sleep for 5 hours or less and 9 hours or more at the second interview, 1.78 and 1.95, respectively. The risk of death due to cardiovascular causes was relatively greater for those who slept less after the baseline period than for those who slept more.

Participants whose sleep decreased from 6-8 hours a night at the first interview to less than 6 hours at the second interview had a fully adjusted hazard ratio of mortality from cardiovascular cause of 2.04, compared with 1.22 for those who slept more. Those whose sleep increased from 7-8 hours at the first interview to more than 8 hours at the second interview had a fully adjusted hazard ratio of mortality from noncardiovascular causes of 2.06, compared with 1.44 for those who slept less.

Investigators found a positive association between marital status and sleep duration. Married women were more likely to sleep longer, while married men were more likely to average 7-8 hours of sleep per night.

The connection between sleep duration and body mass index wasn't as clear cut. At the Whitehall II study's baseline, higher BMI was associated both with short and long sleep duration in women, but only with short sleep duration in men. By 1992-1993, BMI and sleep duration showed no association in women, but both short and long sleep durations were associated with higher BMI in men.

"Patients reporting a decrease in sleep should be regarded as higher risk populations for cardiovascular and all-cause mortality," according to the investigators. Advising patients who may sleep too long to curtail their sleep should "at least be considered," the investigators wrote. ■

CBT Shows Promise for Irritable Bowel Syndrome

BY BRUCE JANCIN
Denver Bureau

VIENNA — Irritable bowel syndrome can be conceptualized as an anxiety disorder—and, as such, responsive to cognitive-behavioral therapy, according to Dr. Sergej Andreewitch.

"Core symptomatology of IBS is clearly physiological, but the cause of suffering and severe loss of function affecting many patients is better accounted for by the catastrophizing appraisal of symptoms and the related avoidance behavior," Dr. Andreewitch said at the annual congress of the European College of Neuropsychopharmacology.

A program of cognitive-behavioral therapy (CBT) targeting the negative evaluation of GI symptoms and resultant dysfunctional avoidance behaviors associated with IBS brought substantial improvement to participants in his pilot study. Next, Dr. Andreewitch, who is affiliated with the Karolinska Institute, Stockholm, plans to develop the treatment program into an Internet-based intervention.

He reported on 13 consecutive women with a mean age of 32 years and an 11.5-year history of IBS who had been referred for CBT from Stockholm-area GI clinics. The treatment program involved a 2-hour session weekly for 10 weeks, with four or five patients per group. The therapeutic strategy was modeled on well-established CBT programs for a variety of anxiety disorders.

As is typical in IBS, psychiatric comorbidity was common. Nine of the 13 patients met diagnostic criteria for a specific phobia, panic disorder, generalized anxiety disorder, or dysthymia.

The psychotherapeutic intervention showed substantial efficacy. Scores on the daily patient-rated GI Symptoms Checklist of abdominal pain, tenderness, bloating, diarrhea, and constipation dropped from a baseline mean of 31.4 to 17.2 at conclusion of the CBT program and remained there at reassessment 4 weeks later.

Similarly, mean scores on the Sheehan Disability Scale plummeted from 13.2 to 3.8, while Montgomery-Asberg Depression Rating Scale scores dropped from a baseline of 12.7 to 6.8.

These outcomes compare quite favorably with conventional treatments, which typically are only moderately effective. These treatments include stool-modifying agents, analgesics, antidepressants, and dietary restriction, Dr. Andreewitch continued.

The etiology of IBS is poorly understood. It is second only to the common cold as a cause of work absences, he noted. ■

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