Early Trauma Tied to Adult Mental, Physical Health

BY NANCY WALSH
New York Bureau

NEW YORK — Traumatic stress in youth is the single most important contributor to later psychiatric morbidity and mortality, and the American Psychiatric Association should make violence and its sequelae a major organizational priority, according to a new report.

The report of the APA Task Force on the Biopsychosocial Consequences of Childhood Violence, which is being submitted by the association's joint reference committee for approval, also concluded that the prevention of trauma and violence is potentially the single most effective strategy for the prevention of mental illness.

Much of the epidemiologic data on exposure to violence during childhood has emerged from the Adverse Childhood Experiences (ACE) study, which is a collaboration of the Centers for Disease Control and Prevention and the Kaiser-Permanente Medical Care Program in San Diego. This ongoing study, which is investigating the impact of adverse childhood experiences on adult health, includes approximately 175,000 members of the Kaiser health plan, coprincipal investigator Vincent J. Felitti said at the American Psychiatric Association's Institute on Psychiatric Services. The subjects in the study are predominantly white and well educated.

The ACE study has identified several specific categories of adverse childhood experiences that are associated with numerous health risk factors later in life and has found these experiences to be far more common than was previously appreciated. (See box.)

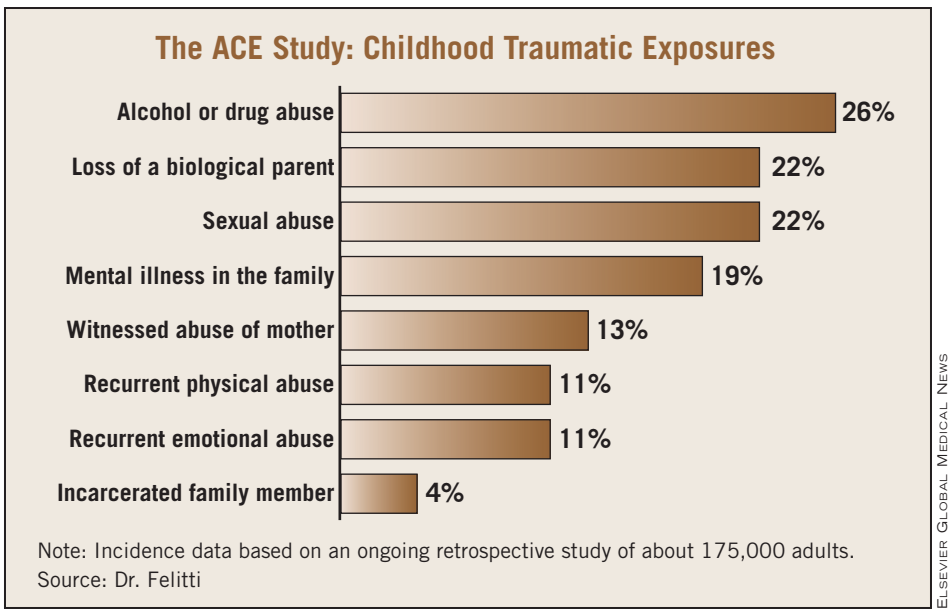
Nonetheless, more than half of the subjects reported having experienced at least one of these early life adverse events (ACE score 1) and one-quarter reported having two or more, according to Dr. Felitti, who is an internist with Kaiser-Permanente and clinical professor of medicine, University of California, San Diego.

Serious physical and emotional abuse was reported by one in nine people, and sexual abuse was reported by 28% of women and 16% of men. "This is hard to believe unless you routinely ask people—in which case it becomes blatantly obvious," he said.

Then the ACE researchers looked at the impact of these events on health risk factors in adulthood. Smoking and self-acknowledged alcohol abuse strongly correlated with childhood exposure to violence, as did intravenous drug use. For men who had an ACE score of 6 or higher, there was a 46-fold increase in likelihood of intravenous drug use. An ACE score of 6 or higher also was associated with a 30- to 51-fold increase in the likelihood of attempted suicide in later life, he said.

In addition, the report highlights the fact that traumatic stress is not only linked to psychological disorders such as depression and posttraumatic stress disorder (PTSD), but is also a major etiologic factor in medical morbidity and mortality. For example, regular smoking before the age of 14 years not only correlated with early life exposure to violence, but also with later development of chronic obstructive pulmonary disease.

"This was an important conceptual shift, the conversion of life experience into biomedical disease," Dr. Felitti said. And this conversion extended to ischemic heart disease, cancer, fractures, and liver disease.



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Nonetheless, although exposure to violence heightens the risk for the development of PTSD, other stress-related disorders, and medical morbidity, it is not necessarily predictive of psychopathology. Another task force member, Dr. Carl C. Bell, who is chief executive officer of Community Mental Health Council Inc. in Chicago, emphasized this point. "Risk factors are not predictive factors because of protective factors," he said.

Only one-third of individuals exposed to violence develop PTSD. The rest are characterized by a variety of protective factors, such as intellectual ability, a feeling of connectedness, and having an internal locus of control and blame, according to Dr. Bell, who is also clinical professor of psychiatry and public health, University of Illinois in Chicago.

These protective factors together cultivate resilience and stress resistance in the individual, and psychiatrists have an important role in helping individuals cultivate resiliency by means of a community psychiatry model, the task force report states.

The task force recommended that the APA make a long-term commitment to addressing issues of trauma, establishing a committee with a 5-year mandate to raise consciousness within psychiatry, and to address fiscal issues, training, research, prevention, and public education.

"The only way this is going to happen politically is to form many partnerships, both within the APA and other professional organizations, the police, Head Start, and early childhood care teachers, so that they begin to understand more about these kids," said William W. Harris, Ph.D., another task force member and president of KidsPac, a political action committee dedicated to obtaining federal government assistance for disadvantaged children. ■

Antidepressant Targets Circadian Cycle, Has Fewer Side Effects

BY JANE SALODOF MACNEIL
Southwest Bureau

PARIS — Two clinical trials have found agomelatine, an investigational drug targeting dysfunction in circadian rhythm, to be as effective as venlafaxine in treating major depressive disorder, but with fewer side effects.

In particular, sexual dysfunction occurred at significantly lower rates in patients who remitted on agomelatine, compared with those who remitted on venlafaxine (Effexor), Dr. Sidney H. Kennedy said at the annual congress of the European College of Neuropsychopharmacology.

He also presented a pooled analysis from three placebo-controlled trials that showed agomelatine's sexual side-effect profile to be similar to placebo and better than that of selective serotonin reuptake inhibitors (SSRIs).

Servier, a French pharmaceutical firm, sponsored the studies. It is seeking approval of agomelatine for major depressive disorder in Europe and has licensed the new agent to Novartis for development in the United States.

If approved, agomelatine could become the first melatonergic antidepressant. It is an agonist of the melatonin 1 and melatonin 2 receptors and also has antagonist properties against the serotonergic 5-HT_{2C} receptors. Other analyses have shown that it improves sleep quality.

"Its mechanisms appear to be normalizing a disruptive circadian rhythm," said Dr. Kennedy, psychiatrist-in-chief at the University Health Network in Toronto and a professor of psychiatry at the University of Toronto.

Both agomelatine-venlafaxine trials were randomized, double-blind, and parallel-group studies conducted in multiple countries. Patients ranged in age from 18 to 60 years and met criteria for major depressive disorder in the studies, reported by Dr. Kennedy with Dr. Christian Guilleminault of Stanford (Calif.) University.

In particular, sexual dysfunction occurred at significantly lower rates in patients who remitted on agomelatine.

DR. KENNEDY

The first study randomized 165 patients to agomelatine and 167 to venlafaxine IR. Patients started on 25 mg/day of agomelatine or 75 mg/day of venlafaxine. If they did not improve over 2 weeks, the doses could be increased to 50 mg/day of agomelatine or 150 mg/day of venlafaxine.

After 6 weeks, 76.4% of the agomelatine group and 70.6% of the venlafaxine cohort had responded to treatment. In both groups, total Hamilton Rating Scale for Depression scores fell from about 26 points to about 9 points. Responders were allowed to stay on their study drug for 6 months, at which point the investigators found a statistically significant benefit for agomelatine in Clinical Global Impression-Improvement scores.

The second study randomized 137 patients to agomelatine and 140 to venlafaxine IR. Doses were fixed at 50 mg/day of agomelatine and 75 mg daily of venlafaxine IR, which increased after 2 weeks to 150 mg/day. Dr. Kennedy and Dr. Guilleminault reported the remission rates were similar at 12 weeks: 73% on agomelatine and 67% on venlafaxine. Total scores on the Montgomery-Asberg Depression Rating Scale fell from 27.9 points to about 10 points in both groups.

Combined data from both trials showed fewer patients on agomelatine withdrew because of adverse events, compared with those on venlafaxine: 4.3% vs. 13.2%, respectively, at 6 weeks and 2.2% vs. 8.6%, respectively, at 12 weeks. The most frequent adverse events at 6 weeks in 303 patients on agomelatine included psychiatric disorders (1.7%), nervous system disorders (1%), and gastrointestinal disorders (0.7%).

The sexual function data, reported by Dr. Kennedy with Beata S. Eisfeld of the University of Toronto, showed 80% of people who remitted on agomelatine had no dysfunction in drive-desire/arousal or orgasm, compared with 58.8% and 53%, respectively, on venlafaxine. In the pooled placebo-controlled data, 3.2% of 1,120 patients on agomelatine, 2.6% of 998 patients on placebo, and 10.8% of 567 patients on an SSRI had "at least one emergent sexual dysfunction event." ■

Pages 34a—34b