

Dysregulated Eating May Be Linked to Cortisol

BY KERRI WACHTER
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BALTIMORE — Children with greater food intake in the absence of hunger might have abnormal cortisol levels after stressful situations—a finding that could have implications for the development of obesity—data presented at the annual meeting of the American Psychosomatic Society show.

Lori A. Francis, Ph.D., of Pennsylvania

State University, Hershey, and her colleagues looked for associations between cortisol levels in response to stress and evidence of dysregulated eating in 43 children aged 5-9 years.

They found that children with dysregulated eating (eating in the absence of hunger) had increased cortisol levels immediately after the stress test and increasing cortisol levels during a recovery period.

"We think there's some sort of blunted stress response there," Dr. Francis said.

For the study, the children had baseline saliva measurements 15 minutes and 35 minutes after arrival. An hour after arrival, they were submitted to a stress test. A saliva sample was collected after the stress test, and two more samples were collected during the recovery period. Two hours after arrival, the children were given a meal, and 30 minutes later the eating in the absence of hunger protocol was started.

The researchers used a stress test that mainly consists of public speaking and

arithmetic tasks. The children were told that they must give a 4-minute speech that would be judged against the speeches of all of the other children.

The speech task was followed by either an arithmetic challenge (children aged 8-9 years) or a block design challenge (aged 5-7 years) for 4 minutes.

During the recovery period, the children completed questionnaires and participated in a craft project. After the recovery period, the children were given a standard meal and told to eat as much as they wanted.

The children were then given a small taste of each of 10 palatable snack foods. The children were then allowed free access to the snack foods and to a box of toys. Foods were weighed pre- and post access and caloric intake was calculated.

Two patterns of cortisol response were identified. Low reactors had cortisol levels that started out high but continued to decline. The high reactors started the stress period with lower cortisol levels that peaked right after the stress test and returned to baseline during the recovery period.

Dr. Francis said that in future studies, she and her colleagues hope to find that stress reactivity is an important marker in terms of the mechanism for developing overweight or obesity. ■

Genes May Make Some Vulnerable To Weight Gain

BALTIMORE — Genes appear to play a role not only in a child's vulnerability to weight gain but also in behaviors that can lead to weight gain, data presented at the annual meeting of the American Psychosomatic Society show.

Jane Wardle, Ph.D., director of the health behavior research center at University College London, and her colleagues analyzed data on 5,435 pairs of twins aged 8-11 years who are part of the Twins Early Development Study (TEDS). Parents rated each twin on satiety sensitivity and food cue responsiveness.

Using genetic model fitting, the researchers estimated that genes account for 63% of satiety sensitivity. Shared environment and nonshared environmental factors accounted for 21% and 16% of satiety sensitivity. The researchers also estimated that genes account for 75% of food cue responsiveness. Shared environment and nonshared environmental factors accounted for 10% and 15% of food cue responsiveness, respectively, she said.

The researchers also used genetic model fitting to estimate the influence of genes, shared environment, and nonshared environment on body mass index and waist circumference.

Genes account for roughly three-quarters of the variability in BMI and waist circumference in these children, shared environment accounts for about 10%, and nonshared environment accounts for roughly 15%.

—Kerri Wachter

Vyvanse™ (lisdexamfetamine dimesylate)

CII Rx Only

BRIEF SUMMARY: Consult the Full Prescribing Information for complete product information.

WARNING: POTENTIAL FOR ABUSE

AMPHETAMINES HAVE A HIGH POTENTIAL FOR ABUSE. ADMINISTRATION OF AMPHETAMINES FOR PROLONGED PERIODS OF TIME MAY LEAD TO DRUG DEPENDENCE. PARTICULAR ATTENTION SHOULD BE PAID TO THE POSSIBILITY OF SUBJECTS OBTAINING AMPHETAMINES FOR NON-THERAPEUTIC USE OR DISTRIBUTION TO OTHERS AND THE DRUGS SHOULD BE PRESCRIBED OR DISPENSED SPARINGLY. MISUSE OF AMPHETAMINES MAY CAUSE SUDDEN DEATH AND SERIOUS CARDIOVASCULAR ADVERSE EVENTS.

INDICATIONS AND USAGE

Vyvanse™ is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). The efficacy of Vyvanse in the treatment of ADHD was established on the basis of two controlled trials in children aged 6 to 12 and one controlled trial in adults who met DSM-IV-TR criteria for ADHD.

Special Diagnostic Considerations

Specific etiology of this syndrome is unknown, and there is no single diagnostic test. The diagnosis must be based upon a complete history and evaluation of the patient and not solely on the presence of the required number of DSM-IV characteristics.

Need for Comprehensive Treatment Program

Vyvanse is indicated as an integral part of a total treatment program for ADHD that may include other measures (psychological, educational, social) for patients with this syndrome.

Long-Term Use

The effectiveness of Vyvanse for long-term use, i.e., for more than 4 weeks, has not been systematically evaluated in controlled trials. Therefore, the physician who elects to use Vyvanse for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

CONTRAINDICATIONS

Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity or idiosyncratic reaction to sympathomimetic amines, glaucoma. Agitated states.

Patients with a history of drug abuse

During or within 14 days following the administration of monoamine oxidase inhibitors (hypertensive crises may result).

WARNINGS AND PRECAUTIONS

Serious Cardiovascular Events

Sudden Death and Pre-existing Structural Cardiac Abnormalities or Other Serious Heart Problems

Children and Adolescents

Sudden death has been reported in association with CNS stimulant treatment at usual doses in children and adolescents with structural cardiac abnormalities or other serious heart problems. Although some serious heart problems alone carry an increased risk of sudden death, stimulant products generally should not be used in children or adolescents with known serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, or other serious cardiac problems that may place them at increased vulnerability to the sympathomimetic effects of a stimulant drug.

Adults

Sudden death, stroke, and myocardial infarction have been reported in adults taking stimulant drugs at usual doses for ADHD. Although the role of stimulants in these adult cases is unknown, adults have a greater likelihood than children of having serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious cardiac problems. Adults with such abnormalities should also generally not be treated with stimulant drugs.

Hypertension and Other Cardiovascular Conditions

Stimulant medications cause a modest increase in average blood pressure (about 2-4 mm Hg) and average heart rate (about 3-6 bpm) and individuals may have larger increases. While the mean changes alone would not be expected to have short-term consequences, all patients should be monitored for larger changes in heart rate and blood pressure. Caution is indicated in treating patients whose underlying medical conditions might be compromised by increases in blood pressure or heart rate, e.g. those with pre-existing hypertension, heart failure, recent myocardial infarction, or ventricular arrhythmia.

Assessing Cardiovascular Status in Patients Being Treated with Stimulant Medications

Children, adolescents, or adults who are being considered for treatment with stimulant medications should have a careful history (including assessment for a family history of sudden death or ventricular arrhythmia) and physical exam to assess for the presence of cardiac disease, and should receive further cardiac evaluation if findings suggest such disease (e.g. electrocardiogram and echocardiogram). Patients who develop symptoms such as exertional chest pain, unexplained syncope, or other symptoms suggestive of cardiac disease during stimulant treatment should undergo a prompt cardiac evaluation.

Psychiatric Adverse Events

Pre-existing Psychosis

Administration of stimulants may exacerbate symptoms of behavior disturbance and thought disorder in patients with a pre-existing psychotic disorder.

Bipolar Illness

Particular care should be taken in using stimulants to treat ADHD in patients with comorbid bipolar disorder because of concern for possible induction of a mixed/manic episode in such patients. Prior to initiating treatment with a stimulant, patients with comorbid depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder. Such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder and depression.

Emergence of New Psychotic or Manic Symptoms

Treatment-emergent psychotic or manic symptoms, e.g. hallucinations, delusional thinking, or mania in children and adolescents without a prior history of psychotic illness or mania can be caused by stimulants at usual doses. If such symptoms occur consideration should be given to a possible causal role of the stimulant, and discontinuation of treatment may be appropriate. In a pooled analysis of multiple short-term, placebo-controlled studies, such symptoms occurred in about 0.1% (4 patients with events out of 3482 exposed to methylphenidate or amphetamine for several weeks at usual doses) or stimulant-treated patients compared to 0 in placebo-treated patients.

Aggression

Aggressive behavior or hostility is often observed in children and adolescents with ADHD, and has been reported in clinical trials and the post marketing experience of some medications indicated for the treatment of ADHD. Although there is no systematic evidence that stimulants cause aggressive behavior or hostility, patients beginning treatment of ADHD should be monitored for the appearance of, or worsening of, aggressive behavior or hostility.

Seizures

There is some clinical evidence that stimulants may lower the convulsive threshold in patients with prior history of seizures, in patients with prior EEG abnormalities in absence of seizures, and, very rarely, in patients without a history of seizures and no prior EEG evidence of seizures. In the presence of seizures, the drug should be discontinued.

Visual Disturbance

Difficulties with accommodation and blurring of vision have been reported with stimulant treatment.

Tics

Amphetamines have been reported to exacerbate motor and phonic tics and Tourette's syndrome. Therefore, clinical evaluation for tics and Tourette's syndrome should precede use of stimulant medications.

Long-Term Suppression of Growth

Careful follow-up of weight and height in children ages 7 to 10 years who were randomized to either methylphenidate or non-medication treatment groups over 14 months, as well as in naturalistic subgroups of newly methylphenidate-treated and non-medication treated children over 36 months (to the ages of 10 to 13 years), suggests that consistently medicated children (i.e. treatment for 7 days per week throughout the year) have a temporary slowing in growth rate (on average, a total of about 2 cm less growth in height and 2.7 kg less growth in weight over 3 years), without evidence of growth rebound during this period of development. In a controlled trial of amphetamine (d- to l-enantiomer ratio of 3:1) in adolescents, mean weight change from baseline within the initial 4 weeks of therapy was -1.1 lbs. and -2.8 lbs., respectively, for patients receiving 10 mg and 20 mg of amphetamine. Higher doses were associated with greater weight loss within the initial 4 weeks of treatment. In a controlled trial of Vyvanse in children ages 6 to 12 years, mean weight loss from baseline after 4 weeks of therapy was -0.9, -1.9, and -2.5 lb, respectively, for patients receiving 30 mg, 50 mg, and 70 mg of Vyvanse, compared to a 1 lb weight gain for patients receiving placebo. Higher doses were associated with greater weight loss with 4 weeks of treatment. Careful follow-up for weight in children ages 6 to 12 years who received Vyvanse over 12 months suggests that consistently medicated children (i.e. treatment for 7 days per week throughout the year) have a slowing in growth rate, measured by body weight as demonstrated by an age- and sex-normalized mean change from baseline in percentile, of -13.4 over 1 year (average percentile at baseline and 12 months, were 60.6 and 47.2, respectively). Therefore growth should be monitored during treatment with stimulants, and patients who are not growing or gaining weight as expected may need to have their treatment interrupted.

Prescribing and Dispensing

The least amount of amphetamine feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdose. Vyvanse should be used with caution in patients who use other sympathomimetic drugs.

ADVERSE REACTIONS

Clinical Studies Experience

The premarketing development program for Vyvanse included exposures in a total of 762 participants in clinical trials (348 pediatric patients, 358 adult patients and 56 healthy adult subjects). The information included in this section is based on data from the 4-week parallel-group controlled clinical studies in pediatric and adult patients with ADHD.

Adverse Reactions Associated with Discontinuation of Treatment in Clinical Trials

In the controlled pediatric (aged 6 to 12) trial, 10% (21/218) of Vyvanse-treated patients discontinued due to adverse reactions compared to 1% (1/72) who received placebo. The most frequent adverse events leading to discontinuation and considered to be drug-related (i.e. leading to discontinuation in at least 1% of Vyvanse-treated patients and at a rate at least twice that of placebo) were ECG voltage criteria for ventricular hypertrophy, tic, vomiting, psychomotor hyperactivity, insomnia, and rash (2/218 each; 1%). In the controlled adult trial, 6% (21/358) of Vyvanse-treated patients discontinued due to adverse events compared to 2% (1/62) who received placebo. The most frequent adverse events leading to discontinuation and considered to be drug-related (i.e. leading to discontinuation in at least 1% of Vyvanse-treated patients and at a rate at least twice that of placebo) were insomnia (8/358; 2%), tachycardia (3/358; 1%), irritability (2/358; 1%), hypertension (4/358; 1%), headache (2/358; 1%), anxiety (2/358; 1%), and dyspnea (3/358; 1%).

Pediatric

Table 1 Adverse Reactions Reported by 2% or More of Pediatric Patients Taking Vyvanse in a 4-Week Clinical Trial

Body System	Preferred Term	Vyvanse (n=218)	Placebo (n=72)
Gastrointestinal Disorders	Abdominal Pain Upper	12%	6%
	Vomiting	9%	4%
	Nausea	6%	3%
	Dry Mouth	5%	0%
General Disorder and Administration Site Conditions	Pyrexia	2%	1%
Investigations	Weight Decreased	9%	1%
Metabolism and Nutrition	Decreased Appetite	39%	4%
Nervous System Disorders	Dizziness	5%	0%
	Somnolence	2%	1%
Psychiatric Disorders	Insomnia	19%	3%
	Irritability	10%	0%
	Initial Insomnia	4%	0%
	Affect lability	3%	0%
	Tic	2%	0%
Skin and Subcutaneous Tissue Disorders	Rash	3%	0%

Note: This table includes those reactions for which the incidence in patients taking Vyvanse is at least twice the incidence in patients taking placebo.

Adult

Table 2 Adverse Reactions Reported by 2% or More of Adult Patients Taking Vyvanse in a 4-Week Clinical Trial

Body System	Preferred Term	Vyvanse (n=358)	Placebo (n=62)
Gastrointestinal Disorders	Dry Mouth	26%	3%
	Diarrhea	7%	0%
	Nausea	7%	0%
General Disorder and Administration Site Conditions	Feeling Jittery	4%	0%
Investigations	Blood Pressure Increased	3%	0%
	Heart Rate Increased	2%	0%
Metabolism and Nutrition Disorders	Anorexia	5%	0%
	Decreased Appetite	27%	3%
Nervous System Disorders	Tremor	2%	0%
Psychiatric Disorders	Insomnia	27%	8%
	Anxiety	6%	0%
	Agitation	3%	0%
	Restlessness	3%	0%
Respiratory Thoracic and Mediastinal Disorders	Dyspnea	2%	0%
Skin and Subcutaneous Tissue Disorders	Hyperhidrosis	3%	0%

Note: This table includes those events for which the incidence in patients taking Vyvanse is at least twice the incidence in patients taking placebo.

Vital Signs

Weight Loss — In the controlled adult trial, mean weight loss after 4 weeks of therapy was 2.8 lbs, 3.1 lbs, 4.3 lbs, for patients receiving final doses of 30 mg, 50 mg and 70 mg of Vyvanse, respectively, compared to a mean weight gain of 0.5 lbs for patients receiving placebo.

Adverse Reactions Associated with the Use of Amphetamine

Cardiovascular
Palpitations, tachycardia, elevation of blood pressure, sudden death, myocardial infarction. There have been isolated reports of cardiomyopathy associated with chronic amphetamine use.

Central Nervous System

Psychotic episodes at recommended doses, overstimulation, restlessness, dizziness, insomnia, euphoria, dyskinesia, dysphoria, depression, tremor, headache, exacerbation of motor and phonic tics and Tourette's syndrome, seizures, stroke.

Gastrointestinal

Dryness of the mouth, unpleasant taste, diarrhea, constipation, other gastrointestinal disturbances.

Allergic

Urticaria, rashes, and hypersensitivity reactions, including angioedema and anaphylaxis. Serious skin reactions, including Stevens Johnson Syndrome and Toxic Epidermal Necrolysis have been reported.

Endocrine

Impotence, changes in libido.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category C

Amphetamines should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Labor and Delivery

The effects of Vyvanse on labor and delivery in humans is unknown.

Nursing Mothers

Amphetamines are excreted in human milk. Mothers taking amphetamines should be advised to refrain from nursing.

Pediatric Use

Vyvanse has not been studied in children under 6 years of age or adolescents. Amphetamines are not recommended for use in children under 3 years of age.

Geriatric Use

Vyvanse has not been studied in the geriatric population.

DRUG ABUSE AND DEPENDENCE

Vyvanse is classified as a Schedule II controlled substance.

OVERDOSAGE

Toxic symptoms may occur idiosyncratically at low doses.

Treatment: Consult with a Certified Poison Control Center for up-to-date guidance and advice.

The prolonged release of Vyvanse in the body should be considered when treating patients with overdose.

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