

# Early Adversity Linked to Risk of Adult Obesity

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Some stressful childhood emotional experiences are associated with an increased likelihood of adult obesity and, therefore, a greater risk for type 2 diabetes, according to findings of a British population-based study of more than 9,000 participants.

Claudia Thomas, Ph.D., and her associates studied 9,310 participants of a 1958

British birth cohort followed longitudinally up to age 45 years. They were asked about emotional and physical neglect, household dysfunction, and abuse at different evaluations during the longitudinal study. The investigators looked for associations with midlife body mass index (BMI), central obesity, and glucose control (Pediatrics 2008;121:e1240-9 [doi:10.1542/peds.2007-2403]).

"We found that several different experiences, ranging from severe adversities,

such as physical abuse, to other experiences, such as less severe forms of emotional neglect, increased the risk for obesity and, in doing so, increased the risk for poor glucose control," wrote Dr. Thomas and her associates from the Centre for Paediatric Epidemiology and Biostatistics, Institute of Child Health, University College London.

The investigators found some significant correlations, some nonsignificant trends, and even an inverse relationship (between parental depression and later adverse health outcomes measured).

Of the adversities measured during childhood, low parental aspirations and little paternal or maternal interest in education were significantly associated with increased BMI, central obesity, and a glycosylated hemoglobin (HbA<sub>1c</sub>) of 6% or greater at 45 years. Children who reported that they hardly ever took outings with their father had significantly higher midlife BMI and central obesity rates, but a nonsignificant increased risk of an HbA<sub>1c</sub> of 6% or greater.

In contrast, children who reported that their mother hardly ever read to them or they did not "get on with either parent" were not at an increased risk. Likewise, those who appeared scruffy or dirty (at 7 and 11 years, according to teachers), experienced domestic tension and/or parental alcoholism or were placed in lo-

cal or voluntary care before age 16 years were not more likely to have a higher adiposity or worse glucose control.

Dr. Thomas and her associates also adjusted for possible confounders. When they did, only a few correlations remained significant. All children who reported their mother had little interest in their education had significantly increased BMI and likelihood of HbA<sub>1c</sub> of 6% or greater. Girls in this group also had a significantly increased likelihood of later central obesity. Socioeconomic position at birth, type of accommodation (owned vs. rented), number of persons per room in household, and whether any child received free school meals at age 11 or 16 years were the possible confounders.

Dr. Thomas and her associates also retrospectively asked participants at age 45 about childhood adversity. They found a strict upbringing significantly related to increased BMI, central obesity, and an HbA<sub>1c</sub> of 6% or greater. Reported physical abuse also was significantly associated with increases in adiposity.

Previous studies have linked abusive and neglectful experiences early in life with increased risks of obesity, cardiovascular disease, diabetes, and liver disease. Associations between lower childhood socioeconomic status and increased risk of insulin resistance and type 2 diabetes also are proposed in several studies. ■

## LEXAPRO® (escitalopram oxalate) TABLETS/ORAL SOLUTION

(5% and 4%); Fatigue (5% and 2%). **Psychiatric Disorders:** Insomnia (9% and 4%); Somnolence (6% and 2%); Appetite Decreased (3% and 1%); Libido Decreased (3% and 1%). **Respiratory System Disorders:** Rhinitis (5% and 4%); Sinusitis (3% and 2%). **Urogenital:** Ejaculation Disorder\* (9% and <1%); Impotence\* (2% and <1%); Anorgasmia\* (2% and <1%). \*Events reported by at least 2% of patients treated with Lexapro are reported, except for the following events which had an incidence on placebo > Lexapro: headache, upper respiratory tract infection, back pain, pharyngitis, inflicted injury, anxiety. \*Primarily ejaculatory delay. \*Denominator used was for males only (N=225 Lexapro; N=188 placebo). **Generalized Anxiety Disorder Table 3** enumerates the incidence, rounded to the nearest percent of treatment-emergent adverse events that occurred among 429 GAD patients who received Lexapro 10 to 20 mg/day in placebo-controlled trials. Events included are those occurring in 2% or more of patients treated with Lexapro and for which the incidence in patients treated with Lexapro was greater than the incidence in placebo-treated patients. The most commonly observed adverse events in Lexapro patients (incidence of approximately 5% or greater and approximately twice the incidence in placebo patients) were nausea, ejaculation disorder (primarily ejaculatory delay), insomnia, fatigue, decreased libido, and anorgasmia (see TABLE 3). **TABLE 3: Treatment-Emergent Adverse Events: Incidence in Placebo-Controlled Clinical Trials for Generalized Anxiety Disorder\* (Percentage of Patients Reporting Event) Body System/Adverse Event Lexapro (N=429) and Placebo (N=427): Autonomic Nervous System Disorders:** Dry Mouth (9% and 5%); Sweating Increased (4% and 1%). **Central & Peripheral Nervous System Disorders:** Headache (24% and 17%); Paresthesia (2% and 1%). **Gastrointestinal Disorders:** Nausea (18% and 8%); Diarrhea (8% and 6%); Constipation (5% and 4%); Indigestion (3% and 2%); Vomiting (3% and 1%); Abdominal Pain (2% and 1%); Flatulence (2% and 1%); Toothache (2% and 0%). **General:** Fatigue (8% and 2%); Influenza-like symptoms (5% and 4%). **Musculoskeletal:** Neck/Shoulder Pain (3% and 1%). **Psychiatric Disorders:** Somnolence (13% and 7%); Insomnia (12% and 6%); Libido Decreased (7% and 2%); Dreaming Abnormal (3% and 2%); Appetite Decreased (3% and 1%); Lethargy (3% and 1%); Yawning (2% and 1%). **Urogenital:** Ejaculation Disorder\* (14% and 2%); Anorgasmia\* (6% and <1%); Menstrual Disorder (2% and 1%). \*Events reported by at least 2% of patients treated with Lexapro are reported, except for the following events which had an incidence on placebo > Lexapro: inflicted injury, dizziness, back pain, upper respiratory tract infection, rhinitis, pharyngitis. \*Primarily ejaculatory delay. \*Denominator used was for males only (N=182 Lexapro; N=195 placebo). \*Denominator used was for females only (N=247 Lexapro; N=232 placebo). **Dose Dependency of Adverse Events** The potential dose dependency of common adverse events (defined as an incidence rate of ≥ 5% in either the 10 mg or 20 mg Lexapro groups) was examined on the basis of the combined incidence of adverse events in two fixed-dose trials. The overall incidence rates of adverse events in 10 mg Lexapro-treated patients (66%) was similar to that of the placebo-treated patients (61%), while the incidence rate in 20 mg/day Lexapro-treated patients was greater (86%). **Table 4** shows common adverse events that occurred in the 20 mg/day Lexapro group with an incidence that was approximately twice that of the 10 mg/day Lexapro group and approximately twice that of the placebo group. **TABLE 4: Incidence of Common Adverse Events\* in Patients with Major Depressive Disorder Receiving Lexapro (N=311), 10 mg/day Lexapro (N=310), 20 mg/day Lexapro (N=125); Insomnia (4%, 7%, 14%); Diarrhea (5%, 6%, 14%); Dry Mouth (3%, 4%, 9%); Somnolence (1%, 4%, 9%); Dizziness (2%, 4%, 7%); Sweating Increased (<1%, 3%, 8%); Constipation (1%, 3%, 6%); Fatigue (2%, 2%, 6%); Indigestion (1%, 2%, 6%).** \*Adverse events with an incidence rate of at least 5% in either the Lexapro groups and with an incidence rate in the 20 mg/day Lexapro group that was approximately twice that of the 10 mg/day Lexapro group and the placebo group. **Male and Female Sexual Dysfunction with SSRIs** Although changes in sexual desire, sexual performance, and sexual satisfaction often occur as manifestations of a psychiatric disorder, they may also be a consequence of pharmacologic treatment. In particular, some evidence suggests that SSRIs can cause such untoward sexual experiences. Reliable estimates of the incidence and severity of untoward experiences involving sexual desire, performance, and satisfaction are difficult to obtain, however, in part because patients and physicians may be reluctant to discuss them. Accordingly, estimates of the incidence of untoward sexual experience and performance cited in product labeling are likely to underestimate their actual incidence. **Table 5** shows the incidence rates of sexual side effects in patients with major depressive disorder and GAD in placebo-controlled trials. **TABLE 5: Incidence of Sexual Side Effects in Placebo-Controlled Clinical Trials [In Males Only: Adverse Event: Lexapro (N=407) and Placebo (N=383)];** Ejaculation Disorder (primarily ejaculatory delay) (12% and 1%); Libido Decreased (6% and 2%); Impotence (2% and <1%). [In Females Only: Lexapro (N=737) and Placebo (N=636)]; Libido Decreased (3% and 1%); Anorgasmia (3% and <1%) There are no adequately designed studies examining sexual dysfunction with escitalopram treatment. Priligis has been reported with all SSRIs. While it is difficult to know the precise risk of sexual dysfunction associated with the use of SSRIs, physicians should routinely inquire about such possible side effects. **Vital Sign Changes** Lexapro and placebo groups were compared with respect to (1) mean change from baseline in vital signs (pulse, systolic blood pressure, and diastolic blood pressure) and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses did not reveal any clinically important changes in vital signs associated with Lexapro treatment. In addition, a comparison of supine and standing vital sign measures in subjects receiving Lexapro indicated that Lexapro treatment is not associated with orthostatic changes. **Weight Changes** Patients treated with Lexapro in controlled trials did not differ from placebo-treated patients with regard to clinically important change in body weight. **Laboratory Changes** Lexapro and placebo groups were compared with respect to (1) mean change from baseline in various serum chemistry, hematology, and urinalysis variables, and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed no clinically important changes in laboratory test parameters associated with Lexapro treatment. **ECG Changes** Electrocardiograms from Lexapro (N=625), racemic citalopram (N=351), and placebo (N=527) groups were compared with respect to (1) mean change from baseline in various ECG parameters and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed (1) a decrease in heart rate of 2.2 bpm for Lexapro and 2.7 bpm for racemic citalopram, compared to an increase of 0.3 bpm for placebo and (2) an increase in QTc interval of 3.9 msec for Lexapro and 3.7 msec for racemic citalopram, compared to 0.5 msec for placebo. Neither Lexapro nor racemic citalopram were associated with the development of clinically significant ECG abnormalities. **Other Events Observed During the Premarketing Evaluation of Lexapro** Following is a list of WHO terms that reflect treatment-emergent adverse events, as defined in the introduction to the ADVERSE REACTIONS section, reported by the 1428 patients treated with Lexapro for periods of up to one year in double-blind or open-label clinical trials during its premarketing evaluation. All reported events are included except those already listed in Tables 2 & 3, those occurring in only one patient, event terms that are so general as to be uninformative, and those that are unlikely to be drug related. It is important to emphasize that, although the events reported occurred during treatment with Lexapro, they were not necessarily caused by it. Events are further categorized by body system and listed in order of decreasing frequency according to the following definitions: frequent adverse events are those occurring on one or more occasions in at least 1/100 patients; infrequent adverse events are those occurring in less than 1/100 patients but at least 1/1000 patients. **Cardiovascular - Frequent:** palpitation, hypertension. **Infrequent:** bradycardia, tachycardia, ECG abnormal, flushing, varicose vein. **Central and Peripheral Nervous System Disorders - Frequent:** light-headed feeling, migraine. **Infrequent:** tremor, vertigo, restless legs, shaking, twitching, dysequilibrium, tic, carpal tunnel syndrome, muscle contractions involuntary, sluggishness, coordination abnormal, faintness, hyperreflexia, muscular tone increased. **Gastrointestinal Disorders - Frequent:** heartburn, abdominal cramp, gastroenteritis. **Infrequent:** gastroesophageal reflux, bloating, abdominal discomfort, dyspepsia, increased stool frequency, belching, gastritis, hemorrhoids, gagging, polyposis gastric, swallowing difficult. **General - Frequent:** allergy, pain in limb, fever, hot flashes, chest pain. **Infrequent:** edema of extremities, chills, tightness of chest, leg pain, asthenia, syncope, malaise, anaphylaxis, fall. **Hemic and Lymphatic Disorders - Frequent:** bruise, anemia, nosebleed, hematoma, lymphadenopathy cervical. **Metabolic and Nutritional Disorders - Frequent:** increased weight. **Infrequent:** decreased weight, hyperglycemia, thirst, bilirubin increased, hepatic enzymes increased, gout, hypercholesterolemia. **Musculoskeletal System Disorders - Frequent:** arthralgia, myalgia. **Infrequent:** jaw stiffness, muscle cramp, muscle stiffness, arthritis, muscle weakness, back discomfort, arthropathy, jaw pain, joint stiffness. **Psychiatric Disorders - Frequent:** appetite increased, lethargy, irritability, concentration impaired. **Infrequent:** jitteriness, panic reaction, agitation, apathy, forgetfulness, depression aggravated, nervousness, restlessness aggravated, suicide attempt, amnesia, anxiety attack, bruising, carbohydrate craving, confusion, depersonalization, disorientation, emotional lability, feeling unreal, tremulousness nervous, crying abnormal, depression, excitability, auditory hallucination, suicidal tendency. **Reproductive Disorders/Female\* - Frequent:** menstrual disorder. **Infrequent:** menorrhagia, breast neoplasm, pelvic inflammation, premenstrual syndrome, spotting between menses. \*Based on female subjects only. **Respiratory System Disorders - Frequent:** bronchitis, sinus congestion, coughing, nasal congestion, sinus headache. **Infrequent:** asthma, breath shortness, laryngitis, pneumonia, tracheitis. **Skin and Appendages Disorders - Frequent:** rash. **Infrequent:** pruritus, acne, alopecia, eczema, dermatitis, dry skin, folliculitis, lipoma, furunculosis, dry lips, skin nodules. **Special Senses - Frequent:** vision blurred, tinnitus. **Infrequent:** taste alteration, earache, conjunctivitis, vision abnormal, dry eyes, eye irritation, visual disturbance, eye infection, pupils dilated, metallic taste. **Urinary System Disorders - Frequent:** urinary frequency, urinary tract infection. **Infrequent:** urinary urgency, kidney stone, dysuria, blood in urine. **Events Reported Subsequent to the Marketing of Escitalopram** - Although no causal relationship to escitalopram treatment has been found, the following adverse events have been reported to have occurred in patients and to be temporally associated with escitalopram treatment during post marketing spontaneous and clinical trial experience and were not observed during the premarketing evaluation of escitalopram: **Blood and Lymphatic System Disorders:** hemolytic anemia, leukopenia, thrombocytopenia. **Cardiac Disorders:** atrial fibrillation, cardiac failure, myocardial infarction, torsade de pointes, ventricular arrhythmia, ventricular tachycardia. **Endocrine Disorders:** diabetes mellitus, hyperprolactinemia, SIADH. **Eye Disorders:** diplopia, glaucoma. **Gastrointestinal Disorders:** gastrointestinal hemorrhage, pancreatitis, rectal hemorrhage. **General Disorders and Administration Site Conditions:** abnormal gait. **Hepatobiliary Disorders:** fulminant hepatitis, hepatic failure, hepatic necrosis, hepatitis. **Immune System Disorders:** allergic reaction. **Investigations:** electrocardiogram QT prolongation, INR increased, prothrombin decreased. **Metabolism and Nutrition Disorders:** hypoglycemia, hypokalemia. **Musculoskeletal and Connective Tissue Disorders:** rhabdomyolysis. **Nervous System Disorders:** akathisia, choreoathetosis, dysarthria, dyskinesia, dystonia, extrapyramidal disorders, grand mal seizures (or convulsions), hypoaesthesia, myoclonus, neuroleptic malignant syndrome, nystagmus, seizures, serotonin syndrome, tardive dyskinesia. **Pregnancy, Puerperium and Perinatal Conditions:** spontaneous abortion. **Psychiatric Disorders:** acute psychosis, aggression, anger, delirium, delusion, nightmare, paranoia, visual hallucinations. **Renal and Urinary Disorders:** acute renal failure. **Reproductive System and Breast Disorders:** priapism. **Respiratory, Thoracic and Mediastinal Disorders:** pulmonary embolism. **Skin and Subcutaneous Tissue Disorders:** angioedema, ecchymosis, erythema multiforme, photosensitivity reaction, Stevens Johnson Syndrome, toxic epidermal necrolysis, urticaria. **Vascular Disorders:** deep vein thrombosis, hypotension, orthostatic hypotension, phlebitis thrombosis. 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## Psychosocial Competence May Affect Diabetes Control

BY KERRI WACHTER  
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WASHINGTON — Total social competence and externalizing behavior may play a role in how well children and adolescents control their diabetes, according to the results of a study involving 78 patients.

"Lower total psychosocial competence is a strong predictor of poor metabolic control in diabetic youth," Dr. Ivana Balic, a general psychiatry resident, and Dr. Burselon W. Daviss, a child psychiatrist, both of the University of Texas Health Sciences Center at San Antonio, wrote in a poster. Externalizing psychopathology was a lesser predictor.

The researchers recruited 78 children and adolescents (mean age 12 years) from a clinic or a diabetes camp for this study, presented at the annual meeting of the American Psychiatric Association. Using the Child Behavior Checklist, they assessed total social competence and externalizing symptoms. Along with sociodemographics, the researchers assessed these factors as predictors of poor metabolic control 3 months later. Poor metabolic control was defined as an HbA<sub>1c</sub> level of 10 mg/dL or greater.

In all, 56% of the youth had poor metabolic control. On univariate analysis, age and living with a single parent were significant predictors of poor metabolic control, along with lower total social competence, family conflict, dietary noncompliance, and externalizing symptoms. Interestingly, internalizing symptoms did not significantly predict poor metabolic control.

All of the significant predictors from univariate analysis were incorporated into the backward stepwise logistic regression. The final predictive model included age, living with a single parent, lower total social competence, dietary noncompliance, and family conflict. This model correctly classified 74% of the youth with poor metabolic control.

Total competence, as tested by the Child Behavioral Checklist, describes children's capability in school activities, social activities, and other areas of competence. "Children who do a good job at the things that total competence is measuring also are more likely to do a better job at handling their diabetes," said Dr. Balic in an interview. Children who have trouble in these areas might have more trouble managing diabetes. ■

**Age and living with a single parent also were significant predictors of poor metabolic control.**

DR. DAVISS

