

# White-Matter Deficit Seen in Stuttering Children

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ATLANTA — Children who stutter have been found to have deficiencies in white-matter organization in a tract that interconnects the frontal speech/motor planning region and the posterior speech comprehension region, suggesting that inefficient connectivity among speech-relevant regions of the left hemisphere may be a possible neuroanatomical basis for stuttering, Soo-Eun Chang, Ph.D., reported in a poster at the annual meeting of the Society for Neuroscience.

Adults who stutter show the same tract abnormalities as do children, but also show asymmetry in gray-matter volume, suggesting that the gray-matter findings in adults reflect neuroplastic changes secondary to a lifetime of stuttering.

This shows “that the adult studies are compromised because there are two things going on: the original deficit, and then the

neuroplasticity that is laid on top of that. This gives us a clear picture of” the actual deficit, Christy L. Ludlow, Ph.D., section chief of the National Institute of Neurological Disorders and Stroke and a coauthor of the study, said in an interview.

In their study, 22 monolingual, right-handed boys aged 9-12 years underwent high-resolution, diffusion-weighted imaging MRI studies. The group was categorized into three subgroups: normal fluent controls (seven), children who showed persistent stuttering (eight), and children who previously stuttered but had recovered and had been fluent for at least 2 years prior to scanning (seven).

When compared with normal controls, children who stutter had reduced white-matter integrity only in the left arcuate fasciculus (a tract that underlies the oral-facial motor regions).

Studies by other investigators have shown that stuttering adults manifest increased gray-matter volume in the right

hemisphere, whereas fluent adults show greater left hemisphere volume. No such gray-matter asymmetry could be found in children. “In fact, they show less volume in both sides of the brain in speech areas,” which suggests that the initial deficit is different from what people see in adults, Dr. Ludlow said.

Interestingly, the left rolandic operculum abnormality was not related to ongoing stuttering, because no difference was found in this region between children

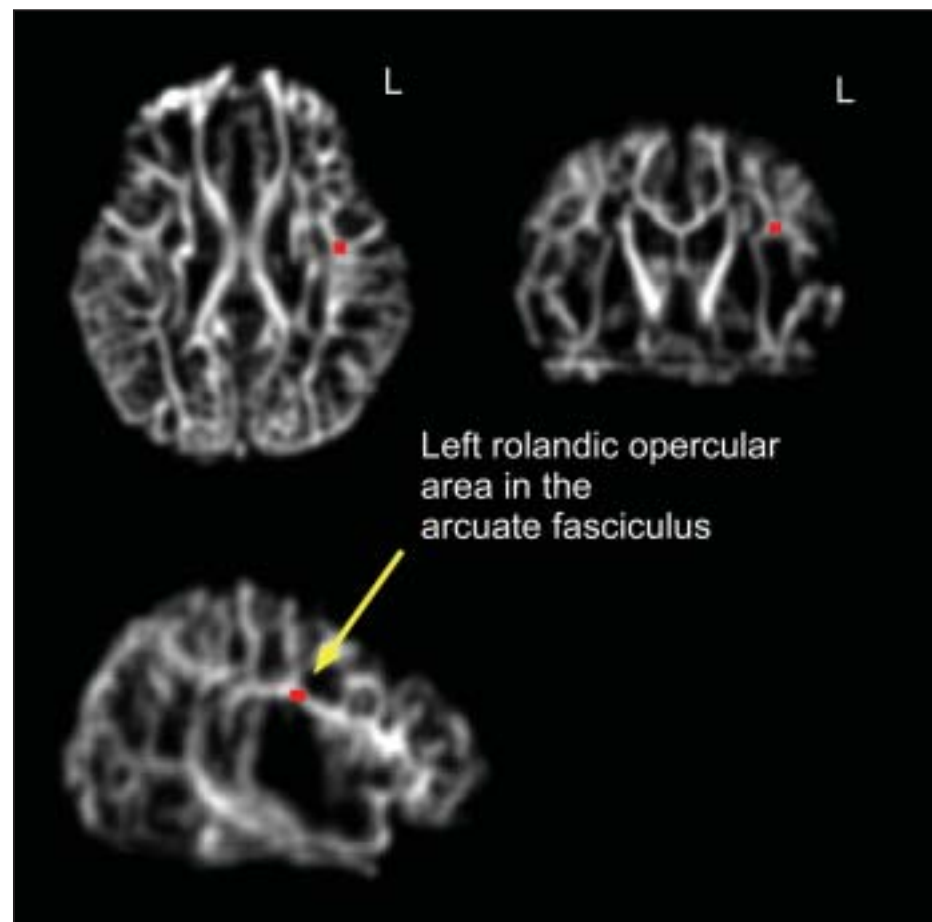
who recovered and children who continued to stutter. This may indicate that the abnormality indicates a risk for stuttering, not whether there is a chance of recovery, the investigators noted.

“This is a novel finding because there haven’t been any studies to date looking at the brains of children who stutter. . . . Our research suggests that some of the brain-imaging differences found in stuttering adults may be the result of a lifetime of coping with stuttering,” Dr. Chang said. ■



Children ‘show less volume in both sides of the brain in speech areas.’

DR. LUDLOW



Left rolandic opercular area in the arcuate fasciculus

MRI demonstrates significantly less white-matter integrity in the rolandic operculum in children with stuttering (both persistent and recovered).

disorder **Central & peripheral nervous system:** Dizziness, Parkinsonism, Akathisia, Dystonia **Psychiatric:** Somnolence, Anxiety, Confusion **Respiratory system:** Rhinitis, Pharyngitis, Coughing **Body as a whole - general:** Asthenia **Urinary system:** Urinary incontinence **Heart rate and rhythm:** Tachycardia **Metabolic and nutritional:** Weight increase **Skin and appendages:** Rash. **Dose Dependency of Adverse Events:** Data from two fixed-dose trials provided evidence of dose-relatedness for extrapyramidal symptoms associated with risperidone treatment. These symptoms include: sleepiness, increased duration of sleep, accommodation disturbances, orthostatic dizziness, palpitations, weight gain, erectile dysfunction, ejaculatory dysfunction, orgasmic dysfunction, asthenia/lasitudin/increased fatigability, and increased pigmentation. **Vital Sign Changes:** RISPERDAL® is associated with orthostatic hypotension and tachycardia (see PRECAUTIONS). **Weight Changes:** A statistically significantly greater incidence of weight gain for RISPERDAL® (18%) compared to placebo (9%). **Laboratory Changes:** A between-group comparison for 6- to 8-week placebo-controlled trials revealed no statistically significant RISPERDAL®/placebo differences in the proportions of patients experiencing potentially important changes in routine serum chemistry, hematology, or urinalysis parameters. Similarly, there were no RISPERDAL®/placebo differences in the incidence of discontinuations for changes in serum chemistry, hematology, or urinalysis. However, RISPERDAL® administration was associated with increases in serum prolactin (see PRECAUTIONS). **ECG Changes:** Between-group comparisons for pooled placebo-controlled trials revealed no statistically significant differences between risperidone and placebo in mean changes from baseline in ECG parameters, including QT, QTc, and PR intervals, and heart rate. When all RISPERDAL® doses were pooled from randomized controlled trials in several indications, there was a mean increase in heart rate of 1 beat per minute compared to no change for placebo patients. In short-term schizophrenia trials, higher doses of risperidone (8-16 mg/day) were associated with a higher mean increase in heart rate compared to placebo (4-6 beats per minute). **Adverse Events and Other Safety Measures in Pediatric Patients With Autistic Disorder:** In the two 8-week, placebo-controlled trials in pediatric patients treated for irritability associated with autistic disorder (n=156), two patients (one treated with RISPERDAL® and one treated with placebo) discontinued treatment due to an adverse event. **Incidence of Treatment-Emergent Adverse Events in Two 8-Week, Placebo-Controlled Trials in Pediatric Patients With Autistic Disorder.** **Body System Preferred Term: Psychiatric:** Somnolence, Appetite increased, Confusion **Gastrointestinal:** Saliva increased, Constipation, Dry mouth **Body as a whole - general:** Fatigue **Central & peripheral nervous system:** Tremor, Dystonia, Dizziness, Automatism, Dyskinesia, Parkinsonism **Respiratory:** Upper respiratory tract infection **Metabolic and nutritional:** Weight increase **Heart rate and rhythm:** Tachycardia **Other Events Observed During the Premarketing Evaluation of RISPERDAL®:** During its premarketing assessment, multiple doses of RISPERDAL® were administered to 2607 adult patients with schizophrenia and 1923 pediatric patients in Phase 2 and 3 studies and the following reactions were reported: (Note: frequent adverse events are those occurring in at least 1/100 patients; infrequent adverse events are those occurring in 1/100 to 1/1000 patients. It is important to emphasize that, although the events reported occurred during treatment with RISPERDAL®, they were not necessarily caused by it). Serious adverse reactions experienced by the pediatric population were similar to those seen in the adult population (see WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS). **Psychiatric Disorders:** Frequent: increased dream activity\*, diminished sexual desire\*, nervousness. Infrequent: impaired concentration, depression, apathy, catatonic reaction, euphoria, increased libido, amnesia. Rare: emotional lability, nightmares, delirium, withdrawal syndrome, yawning. **Central and Peripheral Nervous System Disorders:** Frequent: increased sleep duration\*. Infrequent: dysarthria, vertigo, stupor, paraesthesia, confusion. Rare: aphasia, cholinergic syndrome, hypoesthesia, tongue paralysis, leg cramps, torticollis, hypotonia, coma, migraine, hyperreflexia, choreoathetosis. **Gastrointestinal Disorders:** Frequent: anorexia, reduced salivation\*. Infrequent: flatulence, diarrhea, increased appetite, stomatitis, melena, dysphagia, hemorrhoids, gastritis. Rare: fecal incontinence, eructation, gastroesophageal reflux, gastroenteritis, esophagitis, tongue discoloration, cholelithiasis, tongue edema, diverticulitis, gingivitis, discolored feces, GI hemorrhage, hematemesis. **Body as a Whole/General Disorders:** Frequent: fatigue. Infrequent: edema, rigors, malaise, influenza-like symptoms. Rare: pallor, enlarged abdomen, allergic reaction, ascites, sarcoidosis, flushing. **Respiratory System Disorders:** Infrequent: hyperventilation, bronchospasm, pneumonia, stridor. Rare: asthma, increased sputum, aspiration. **Skin and Appendage Disorders:** Frequent: increased pigmentation\*, photosensitivity\*. Infrequent: increased sweating, acne, decreased sweating, alopecia, hyperkeratosis, pruritus, skin exfoliation. Rare: bullous eruption, skin ulceration, aggravated psoriasis, furunculosis, verruca, dermatitis lichenoid, hypertrichosis, genital pruritus, urticaria. **Cardiovascular Disorders:** Infrequent: palpitation, hypertension, hypotension, AV block, myocardial infarction. Rare: ventricular tachycardia, angina pectoris, premature atrial contractions, T wave inversions, ventricular extrasystoles, ST depression, myocarditis. **Vision Disorders:** Infrequent: abnormal accommodation, xerophthalmia. Rare: diplopia, eye pain, blepharitis, photopsia, photophobia, abnormal lacrimation. **Metabolic and Nutritional Disorders:** Infrequent: hyponatremia, weight increase, creatine phosphokinase increase, thirst, weight decrease, diabetes mellitus. Rare: decreased serum iron, cachexia, dehydration, hypokalemia, hypoproteinemia, hyperphosphatemia, hypertriglyceridemia, hyperuricemia, hypoglycemia. **Urinary System Disorders:** Frequent: polyuria/polydipsia\*. Infrequent: urinary incontinence, hematuria, dysuria. Rare: urinary retention, cystitis, renal insufficiency. **Musculo-Skeletal System Disorders:** Infrequent: myalgia. Rare: arthrosis, synostosis, bursitis, arthritis, skeletal pain. **Reproductive Disorders, Female:** Frequent: menorrhagia\*, orgasmic dysfunction\*, dry vagina\*. Infrequent: nonpuerperal lactation, amenorrhea, female breast pain, leukorrhea, mastitis, dysmenorrhea, female perineal pain, intermenstrual bleeding, vaginal hemorrhage. **Liver and Biliary System Disorders:** Infrequent: increased SGOT, increased SGPT. Rare: hepatic failure, cholestatic hepatitis, cholecystitis, cholelithiasis, hepatitis, hepatocellular damage. Platelet, Bleeding, and Clotting Disorders: Infrequent: epistaxis, purpura. Rare: hemorrhage, superficial phlebitis, thrombophlebitis, thrombocytopenia. **Hearing and Vestibular Disorders:** Rare: tinnitus, hyperacusis, decreased hearing. **Red Blood Cell Disorders:** Infrequent: anemia, hypochromic anemia. Rare: normocytic anemia. **Reproductive Disorders, Male:** Frequent: erectile dysfunction\*. Infrequent: ejaculation failure. **White Cell and Resistance Disorders:** Infrequent: granulocytopenia. Rare: leukocytosis, lymphadenopathy, leucopenia, Pelger-Huet anomaly. **Endocrine Disorders:** Rare: gynecomastia, male breast pain, antidiuretic hormone disorder. **Special Senses:** Rare: bitter taste. \*Incidence based on elicited reports. **Postintroduction Reports:** Adverse events reported since market introduction which were temporally (but not necessarily causally) related to RISPERDAL® therapy include the following: anaphylactic reaction, angioedema, apnea, atrial fibrillation, cerebrovascular disorder, including cerebrovascular accident, diabetes mellitus aggravated, including diabetic ketoacidosis, hyperglycemia, intestinal obstruction, jaundice, mania, pancreatitis, Parkinson's disease aggravated, pituitary adenomas, pulmonary embolism, precocious puberty, and QT prolongation. There have been rare reports of sudden death and/or cardiopulmonary arrest in patients receiving RISPERDAL®. A causal relationship with RISPERDAL® has not been established. It is important to note that sudden and unexpected death may occur in psychotic patients whether they remain untreated or whether they are treated with other antipsychotic drugs.

## DRUG ABUSE AND DEPENDENCE

**Controlled Substance Class:** RISPERDAL® (risperidone) is not a controlled substance.

For more information on symptoms and treatment of overdose, see full Prescribing Information.

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## Depression History a Possible Marker For Auras Following Epilepsy Surgery

SAN DIEGO — A presurgical history of depression appears to predict the persistence of auras after an anterotemporal lobectomy in which patients became free of disabling seizures, Dr. Andres M. Kanner reported during a poster session at the annual meetings of the American Epilepsy Society and the Canadian League Against Epilepsy.

While the cause of the association remains unclear, one hypothesis is that the aura “may be an expression of epileptogenic activity in the insula, because sometimes the insula can be a culprit in the generation of the aura in patients with temporal lobe epilepsy,” said Dr. Kanner, associate director of epilepsy and clinical neurophysiology at Rush University Medical Center, Chicago. “It opens up a lot of questions that I don’t have answers for.”

He and his associates studied 58 men and 39 women (mean age of 31 years) who underwent an anterotemporal lobectomy at the Rush Epilepsy Center. Of the 97 patients, 60 had mesial temporal sclerosis, 18

had lesional temporal lobe epilepsy, and 19 had idiopathic temporal lobe epilepsy.

All patients had undergone presurgical psychiatric evaluation and had a mean postsurgical follow-up time of 7 years.

Dr. Kanner reported that of the 97 patients, 37 (38%) were free of any disabling seizures and auras since having their surgery, while 43 patients (44%) were free of disabling seizures but had auras. Nearly half of the patients (47) had a lifetime history of depression.

Logistic regression analysis revealed the absence of a lifetime history of depression as the only variable that predicted a seizure-free outcome without auras.

“There is a bidirectional relationship between depression and epilepsy that has been pretty well recognized,” Dr. Kanner said. “If you have a history of epilepsy you are more likely to be at risk for depression, and if you have a history of depression you have a four- to seven-times greater risk of developing epilepsy.”

—Doug Brunk