# Fine Motor Differences and Prenatal Serotonin Reuptake Inhibitors Exposure

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**Objective** To examine fine motor differences between preschoolers with prenatal exposure to serotonin reuptake inhibitor (SRI) and children of mothers with major depressive disorder.

**Study design** A subset of children (N = 40) from a larger study on the effects of prenatal SRI and untreated major depressive disorder participated in a kinematic task of visual motor and fine motor functions at ages 4-5 years: exposure to SRI (n = 15), untreated major depressive disorder exposure (n = 10), and the control group (n = 15). The task was to reach and secure a peg, then drop it in a small hole near the start position in the light condition with full visibility or in the glow condition in which a phosphorescent peg glows in the dark. Movement-tracking software measured the positioning of the moving hand and fingers.

**Results** In the glow condition, the group exposed to SRIs had a greater proportion of maximum aperture than the group with major depressive disorder, and the group exposed to SRIs was slower than the group with major depressive disorder to drop the peg into the hole. In the glow condition, the trajectory of the group exposed to SRI was less straight than the group with major depressive disorder, and the group with major depressive disorder had a straighter trajectory than the control group.

**Conclusion** This study provides evidence that preschool aged children with prenatal SRI exposure have poorer fine motor and visual-motor control compared with those with prenatal untreated major depressive disorder. *(J Pediatr 2016;175:144-9)*.

Newborns exposed to serotonin reuptake inhibitors (SRIs) demonstrate significantly poorer motor quality compared with infants who are not exposed.[1-6] At 18 months of age, children exposed to SRIs showed worse performances in motor quality on the Bayley Behavioral Rating Scale[7] and delayed motor milestones up to age 40 months.[8] Few studies, however, have examined motor development and motor control skills in children beyond 4 years of age exposed to SRIs. Moreover, the measurement tools used may not be precise enough to detect more nuanced effects of SRIs that could suggest delay in neural processes involved in motor control that may be of clinical importance.

A highly precise methodology to evaluate variation in fine motor movements is kinematics analysis, in which the trajectory of the reaching hand and the finger aperture are monitored by an optoelectronic motor analysis system. Acquisition and execution of fine motor skills requires the coordinated participation of multiple structures in the motor cortex, basal ganglia, cerebellum, and spinal cord.[9] Fine motor development involves modifications of the cortical representations of the body caused by sensory input, including sensorimotor input affecting somatotopin maps, efference copy development, and visual-motor coordination.[10] Somatotopin maps refer to adjacent neurons in neural tissue that respond selectively to stimuli presented to adjacent locations on the body.

Efference copy is a series of copies of efferent signals from the motor cortex into the sensory cortex and the periphery. Together with internal models, efference copies can enable the brain to predict the effects of an action system.

Although kinematic analysis has been applied to normative preschool age children,[11,12] this study takes advantage of kinematic analysis to evaluate the impact of prenatal exposure to SRI on motor function at later preschool ages (4-5 years). Our hypotheses are that prenatal exposure to SRI will result in less-efficient reaching (eg, increased movement units [MUs], shorter proportion of time to the end of the first MU, slower peak velocity; longer phase duration; and less straightness). Further, we hypothesize that the glow condition when the peg is seen but not the moving hand will be less efficient because of efference copy.

## Methods

The subsample consisted of 40 children with a mean age of 4.75 years (range, 4.33-5.25 years) who participated in a larger study[13] on the effects of prenatal

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| GEE | Generalized estimating equation |
| MU | Movement unit |
| SRI | Serotonin reuptake inhibitor |

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exposure to SRI on fetal, infant, and child outcomes: 15 exposed to SRI, 10 exposed to untreated mothers with major depressive disorder, and 15 control patients. The study was approved by the Institutional Review Board at Women and Infants Hospital of Rhode Island, and written informed consent was obtained from the parents.

Women ages 18-40 years were recruited in the community and through mental health professionals and were enrolled between 22 and 34 weeks of pregnancy. Women were included in the group with SRI exposure if they were on an SRI for a minimum of 4 weeks during the pregnancy. Inclusion in the group with major depressive disorder exposure required a minimum of 4 consecutive weeks of symptomatic major depressive disorder, as defined by the Structural Clinical Interview for *The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, Psychiatric Diagnoses.[14] The nonexposure control group included women with no psychiatric diagnoses during pregnancy and at least 1 year previously, no use of psychotropic or other medications during the pregnancy, and mild or no depressive symptoms. The majority of the women taking SRIs were using sertraline (64%); the remainder used citalopram (24%) or escitalopram (4%). Exclusion criteria for the mothers were the use of anticonvulsants or antipsychotics,[15,16] alcohol consumption (>1 drink/wk), cigarette and/or illegal drug use during pregnancy, and diagnoses of psychotic or bipolar disorders, thyroid conditions, hypertension, and diabetes. Anxiety disorders were allowed in the SRI and major depressive disorder groups as well as medications such as zolpidem, diphenhydramine, and other types of antidepressants/anxiolytics. Premature births (<36 weeks of gestation) or infants with known genetic, medical, or physical anomalies were excluded.

Children were instructed to reach and grasp a series of identical cylindrical pegs (5 cm in height × 2.5 cm in diameter) roughly an arm's length away on a table, return with the peg toward the start position, and drop the peg in a small opening (**Figure**; available at www.jpeds.com). The task was performed in 2 experimental conditions. In the light condition, both hand and peg were visible. In the glow condition, the lights were turned off and only the peg, coated with phosphorescent paint, was visible. The small opening for the drop also was coated with phosphorescent paint and was visible in both conditions.

The children grasped and dropped a total of 15 pegs in each lighting condition. The pegs were separated into sets with 5 pegs each. The light and glow conditions alternated every 5 pegs. If trials were unsuccessful or likely to be unscorable, an additional set of 5 pegs of the same condition were conducted.

Two cameras with infrared illuminator rings recorded the procedure from different angles. The children wore a glove on their dominant hand that had reflective markers on the distal aspect of the thumb and index finger and on the proximal region between these 2 fingers that we called the "web." Reflective markers also were placed on the pegs. The reflective markers appear as bright spots on the camera footage, allowing for later digitizing and tracking of movements of each marker with the Vicon Motus software (Vicon Motus, Boston, Massachusetts) at 100 frames per second. This provided coordinates for each marker in each frame.

The task had 2 phases of primary interest: reach and drop. The reach phase began with the web marker's first movement towards the peg and ended when the child grasped the peg. The drop phase began when the mid-pinch (defined as the center between the index and thumb markers) was exactly at 4 cm from where the child dropped the peg. The reach involved control of the hand and entire upper extremity and was evaluated by use of the coordinates of the centrally located web marker. The drop involved fine motor control of the fingers, and the variables in this phase used the coordinates of the distally located mid-pinch.

The dependent measures derived from the kinematic record of each trial are shown in **Table I** (available at www.jpeds.com).[12,17-19] Definitions are included. The reach measures were chosen to allow comparison with other kinematic studies and to provide a detailed assessment of the development of reaching. The drop measures are unique to this study and provide additional challenge for a young child not only to release the peg into a small opening but also to recalibrate speed during the approach to the target area. Final analyses tested kinematic parameters by study groups.

## Statistical Analyses

Demographic characteristics were assessed with ANOVA for continuous measures or $\chi^2$ for categorical measures. Before statistical analysis, the frame-by-frame coordinates were incorporated into trials then into outcome variables within study groups. Generalized estimating equations (GEEs) were used to compare the 3 groups (SRI, major depressive disorder, and control) in each of the light and glow conditions independently. This extension of the general linear model allows more flexibility in the distributions of the dependent variable and accounts for the correlated nature of the observations within each subject. The general form of the GEE model used for these analyses incorporated a categorical variable for depression group (SRI, major depressive disorder, and control) as well as the specification for the repeated nature of the data based on the subject. Light and glow conditions were examined in separate GEE models. Furthermore, 3 covariates that were related to one or more reaching conditions were included in the models: mothers' level of depression at the study visit, child's mean age (months) at the study visit, and gestational age (**Table II**). In addition, children varied in the number of sets (5 trials each) that were completed in the session. The greater the number of sets, the greater the likelihood of practice effects. Thus, number of sets was included as a covariate as well. Pairwise comparisons of the parameter estimates for any significant group main effects were examined with the Fisher least significant difference. Peak velocity models were adjusted for arm length.