development. OBJECTIVES/GOALS: Spray-dried dispersion (SDD) tablet formulation is an approach to increase oral drug solubility and absorption. Methods to predict SDD performance in humans are poorly developed. We aim to develop an in vivo in vitro correlation (IVIVC) between in vitro dissolution and in vivo absorption of itraconazole SDD tablets. METHODS/STUDY POPULATION: This research project involves tablet manufacturing, in vitro dissolution experiments, and a clinical study. We manufactured fast-, medium-, and slow-release SDD tablets containing amorphous solid dispersion of itraconazole (100 mg) and different grades of the polymer hypromellose acetate succinate (HPMC-AS). Tablets differed in slug pressure, tablet compression force, and formulation composition. Dissolution studies were performed using the United States Pharmacopeia (USP) type II apparatus. The clinical study is an ongoing randomized, cross-over, open-label, fasted, single-dose trial in healthy participants (n=12). An IVIVC will be created by comparing the rank order of drug in vitro dissolution with in vivo absorption. RESULTS/ANTICIPATED RESULTS: Tablet manufacturing was successful, and the tablets displayed the same dissolution rate ranking order as anticipated. Fast-release tablets showed the highest percentage of drug dissolved by 10 min (74%) compared to medium-(62%) and slow-release (1.2%) tablets. Percentage drug dissolved differs by at least 10% at all time points among the different release-rate tablets. The clinical study is currently ongoing, and we expect that the pharmacokinetic (PK) profiles differ among the different tablets. We predict that the rank order of tablet absorption in humans will agree with the order of drug dissolved observed in the dissolution experiments. DISCUSSION/SIGNIFICANCE OF FINDINGS: Spray-dried dispersions are a formulation method to try to improve drug solubility and oral drug absorption. This research will elucidate manufacturing parameters that can impact tablet performance and expand on the ability of in vitro dissolution to predict human PK and streamline drug development of poorly soluble drug candidates.

Team Science

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Sensory mechanisms of atypical motor variability and regularity in autism spectrum disorder*

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ABSTRACT IMPACT: This project aims to better understand mechanisms of sensory and motor deficits in individuals with ASD with the goal of informing diagnosis and treatment development. OBJECTIVES/GOALS: Over-reliance on both visual and proprioceptive feedback have both been observed during motor behavior in persons with Autism Spectrum Disorders (ASD), suggesting that separate sensory feedback processes may be selectively altered during different behaviors. The objective of this study is to clarify sensory mechanisms of fine motor control in ASD. METHODS/STUDY POPULATION: Participants with ASD (N=43) and controls (N=23) matched on age (10-20 yrs) and non-verbal IQ completed tests of precision gripping. Participants were instructed to press on force sensors with their index finger and thumb so that a moving bar corresponding to their force output reached and stayed as stable as possible at the level of a stationary target bar. Visual feedback was manipulated by changing the visual gain of the force bar (low, medium and high). The force bar moved more per change in force

output at higher gains. Proprioceptive feedback was manipulated by applying 80 Hz tendon vibration at the wrist to induce an illusion of muscle contraction. This was compared to a condition with the tendon vibrator turned off. Force variability (standard deviation) and regularity (sample entropy) were examined. RESULTS/ANTICIPATED RESULTS: Controls showed increased force variability with the tendon vibration on compared to off ($t = -3.372$, $p < 0.001$); however, the ASD group showed no difference in force variability between the tendon vibration conditions ($t = -0.960$, $p = 0.338$). Individuals with ASD had stronger age-associated reductions in force variability relative to controls across tendon vibrator and gain conditions (Group x Age: $t = -4.05$, $p < .001$). The ASD group also had greater age-associated increases in force regularity relative to controls, especially at higher gain levels (Group x Gain Level x Age: $t = -3.22$, $p = 0.001$). Unlike the ASD group for whom regularity increased with age in both tendon vibration conditions, controls only showed these age-related gains when the tendon vibrator was off (Group x Vibration Frequency x Age: $t = 2.46$, $p = .014$). DISCUSSION/SIGNIFICANCE OF FINDINGS: Our findings indicate that while controls integrate proprioceptive and visual feedback online to accurately adjust fine motor behavior, persons with ASD rely mostly on visual feedback. Our results suggest delayed development of sensory integration and reduced reliance on multisensory feedback during online fine motor control in persons with ASD.

Translational Science, Policy, & Health Outcomes Science

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Daily relationship between social connectedness and health behaviors among dementia family caregivers

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ABSTRACT IMPACT: Knowledge of which aspects of social connectedness most strongly associate with caregiver health and health behaviors can inform intervention targets to improve caregiver health OBJECTIVES/GOALS: Stressed dementia caregivers are at risk of poor health. Social connectedness may reduce adverse health effects, yet it is unknown about which aspects relate most strongly to health. This is a barrier to intervention development. Our study identifies aspects of social connectedness most strongly associate with caregivers' daily health behaviors. METHODS/STUDY POPULATION: Data. Enrolled spousal caregivers completed 14 consecutive days of online surveys. Measures. We examined multiple health behaviors each day, which included: 1) number of occurrences of 3 potential binge-eating behaviors (range 0 to 30), 2) whether participants engaged in at least 30 minutes of physical activity, and 3) perceived sleep quality, rated 1 (very bad) to 5 (very good). We also examined a count of health symptoms caregivers experienced (e.g., backache; range: 0 to 7). Measures of social connectedness included: spousal emotional support, perceived spousal appreciation, emotional support from any source, and loneliness. Analysis. We applied bivariate multi-level mixed effects models to examine the association between each aspect of social connectedness and health behaviors day-to-day. RESULTS/ANTICIPATED RESULTS: Since November 2020, 5 of N=40 participants were enrolled, of whom 3 had completed all diary surveys. Participants were women ages 59 to 73, and included 4 non-Hispanic white and 1 Hispanic caregivers. Data included 51 days of surveys (93% adherence). No