Motivated behavior in adults with and without ADHD

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2.0 Methods

2.1 Participants. Participants were recruited from the Durham, North Carolina (n = 14 ADHD, 9 non-ADHD) and Little Rock, Arkansas (n = 14 ADHD, 9 non-ADHD) communities via social media, flyers, and word-of-mouth. Participants completed a phone interview and in-person screening session to determine eligibility. Eligible participants were between the ages of 18-45 years. To be eligible, ADHD participants had to have T-scores ≥ 65 for inattentive and/or hyperactive-impulsive symptoms on the Conners' Adult ADHD Rating Scale (CAARS) (Conners et al., 1998), and were evaluated to meet criteria for a primary diagnosis of ADHD based on the Conners' Adult ADHD Diagnostic Interview for DSM-IV (CAADID) (Epstein et al., 2001). Non-ADHD participants had to have T-scores < 55 for inattentive, hyperactive-impulsive, and total symptoms.

Participants were excluded if they reported serious health problems (e.g., uncontrolled cardiovascular disease) or neurological problems (e.g., seizure disorder or traumatic brain injury), met criteria for a psychiatric disorder other than ADHD (except for symptoms of depression or anxiety co-morbid with ADHD) based on the MINI International Neuropsychiatric Interview (Sheehan et al., 2009), reported drug or alcohol dependence in the past 12 months (other than tobacco), reported daily use of medication for ADHD in the past 6 months, had hypertension (i.e., blood pressure > 140/90 mmHg), or had contraindications for MPH (e.g., motor tics). Participants were also excluded if they tested positive for drugs (iCup, Alere Toxicology Services Portsmouth, VA), alcohol (Alco-Sensor III, Intoximeters Inc St. Louis, MO), or pregnancy (QuickVue+, Quidel Corporation San Diego, CA).

Seventy-nine individuals were consented and screened to participate in the study, and 28 participants were ineligible because they did not meet ADHD/non-ADHD criteria (n = 11), had hypertension (n = 6), had a positive drug screen (n = 4) had another Axis I diagnosis (n = 3), withdrew before the study day (n = 4). Of the 51 participants that met eligibility criteria and began the study, 46 participants completed all aspects of the study and were included in the

data analysis. Participants provided written informed consent and this protocol was approved by Duke University's and University of Arkansas for Medical Sciences' Institutional Review Boards.

2.2 Effort Expenditure for Rewards Task (EEfRT) (Treadway et al., 2009): In each trial of the EEfRT, participants choose between two task options to earn money. Both task options consist of repeated manual button presses within a short amount of time, and completed button presses are represented onscreen by the height of a vertical bar. The low effort option requires 30 button presses with the dominant index finger within 7 sec. The high effort option requires 100 button presses with the nondominant little finger within 21 sec. Participants were monitored during the task to ensure they used the correct finger.

In low-effort trials, participants could receive $1.00 if they completed the task on time. In high-effort trials, participants could receive a variable amount between $1.24 and $4.30 (i.e., reward magnitude). Across trials, the likelihood of receiving money upon successful completion of the task was either 12%, 50%, or 88% (i.e., reward probability). The probability level applied to both the low and high effort tasks. At the start of each trial, participants were shown the reward magnitude for both task options and the probability level. They had 5 sec to make a choice or else they would be randomly assigned to a task. Then, they completed the button press task and received feedback informing them if the task was completed successfully or not, and whether they received money for that trial. Participants were told a single trial that resulted in money reward would be selected at random at the end of the EEfRT, and the participant would be given this amount as bonus pay. See Figure 1.

Low-effort trials lasted approximately 15 sec, and high-effort trials lasted approximately 30 sec. Participants were told they had 20 min to play as many trials as possible. They were informed of the trade-off between choosing too many high-effort tasks and missing out on playing large-magnitude, large-probability trials later in the game to discourage the exclusive selection of either the low-effort or high-effort task. This also helped ensure that decisions were based on the expected value of the reward, and not based on a strategy to always select high-effort or

low-effort trials. Trials were presented in the same randomized order to all participants. The primary dependent variable was the percent high-effort selections by reward probability and magnitude (divided into 4 bins with an equal number of trials for analysis). Other performance metrics consisted of total number of trials completed and the ratio of high-effort trials completed/selected.

2.3 Attention Network Test (ANT) (Fan et al., 2002). The ANT combines a cued reaction-time test and flanker test to measure the efficiency and accuracy of three cognitive networks: alerting, orienting, and conflict (Posner and Petersen, 1990). On each trial, a row of five horizontal black lines, with arrowheads pointing left or right, is shown onscreen above or below a center fixation cross. The target is the center arrow. The target is flanked by arrows pointing in the same direction (congruent condition), or in the opposite direction (incongruent condition) or by lines (neutral condition). Participants indicate the direction of the target arrow using the arrow keys. The arrows are preceded by four types of cues (no cue, center cue, double, spatial cue), which either indicate the arrows will appear soon and/or predict the location of the arrows above or below the fixation cross. The primary dependent variables were the alerting, orienting, and executive function scores. The alerting score is the difference in reaction time between the temporally informative cue condition and the temporally uninformative cue condition. The orienting score is the difference in reaction time between the spatially informative cue condition and the spatially uninformative cue condition. The conflict score is the difference in reaction time between the congruent flanker condition and the incongruent flanker condition. Other performance metrics consisted of overall percent accuracy and average reaction time.

2.4 Procedure. After consenting and eligibility evaluation, the participants were scheduled for two study visits. These study visits were scheduled within two weeks of each other, but were at least 48 hours apart. For each participant, both study visits occurred either in the afternoon or the morning. Participants were instructed to skip the meal prior to the study visit (i.e., either breakfast or lunch). Participants were administered either immediate-release methylphenidate

(MPH: 40 mg) or a matching placebo (PLA) under double-blind conditions. Drugs were ordered and compounded through a pharmacy, and the placebo consisted of lactose. The prescription and medical oversight was provided by a study physician. After administration, participants were given two cereal bars, a fruit cup, and 8 oz of water and rested for 1 hour to allow for drug absorption. The study visit lasted for a total of 3 hours, and the EEfRT and ANT were completed approximately 2.5 hours after drug administration. The Positive and Negative Affect Scale (PANAS) (Watson et al., 1988) was administered prior to drug administration and at the end of the study visit. At the end of the visit, participants also rated to what extent they felt a drug effect on a scale from 1 (not at all) to 10 (extremely). Compensation for participation was provided at the end of the study and participants were told they could earn up to $5 in bonus pay for each task, depending on their task performance.

2.5 Data Analysis. Participant demographics were analyzed using independent-samples t-tests and Chi-Square tests. Age was included as a covariate in subsequent analyses due to differences between groups. The drug effects questionnaire, PANAS positive and negative scales, performance metrics in the EEfRT and ANT, and ANT dependent variables were analyzed using separate 2 (Group) x 2 (Drug) repeated-measures ANCOVAs. Percent high-effort selections in the EEfRT were analyzed using a 2 (Group) x 2 (Drug) x 4 (Reward Magnitude) x 3 (Reward Probability) repeated-measures ANCOVA. Follow-up comparisons were univariate ANCOVAs. Since participants could complete a variable number of trials during the 20 min of the EEfRT, only data from the first 50 trials were used for consistency (Treadway et al., 2012a). Associations between CAARS scores and the EEfRT and ANT dependent variables were performed using partial correlations (controlling for age). Data were analyzed using SPSS v24 (Chicago: SPSS Inc).

An initial exploration of the EEfRT and ANT performance metrics revealed no differences by site (UAMS vs Duke); thus, site was not included as a covariate in the analyses.