Efficacy of Lisdexamfetamine Dimesylate for Promoting Occupational Success in Young Adults With ADHD

NCT03446885

Document Date: September 23, 2020

Participants were recruited through flyers at local venues (e.g., coffee shops, restaurants), social media advertisements, flyer mailing to psychiatrists, pediatricians, and other professionals, and direct mailings to participants who had previously expressed interest on being included on a mailing list. All participants had to have an estimated full-scale IQ above 70, a valid driving license or permit, no history of severe motion sickness, and no current psychoactive medication for another psychological disorder. Participants taking medication for ADHD had to agree to participate in the laboratory activities on a day that they did not take their current prescribed medication.

To determine eligibility for the study, participants completed (1) a self-report of ADHD symptoms using the Disruptive Behavior Disorders rating scale ADHD Items (Molina, Smith, & Pelham, 2001; Pelham et al., 1992); (2) the Impairment Rating Scale modified to include functional domains appropriate for a young adult (Fabiano et al., 2006; Sibley et al., 2012a) based on the last six months; (3) a semi-structured Disruptive Behavior Disorders interview to obtain contextual information on symptoms and impairment over the last six months (Hartung McCarthy, Milich, & Martin, 2005); and (4) the Wechsler Abbreviated Scale of Intelligence (Wechsler, 2011). A collateral rater (i.e., the participant's parent in 90% of cases or another adult who knew the participant's developmental history) also reported on the participant's ADHD symptom ratings for the past six months and retrospectively using the Disruptive Behavior Disorder Rating Scale ADHD items. Collaterals also completed an Impairment Rating Scale based on the last six months. Collateral raters were compensated with a $25 gift card for completing the forms. Participants were diagnosed with ADHD if they had (1) five or more inattentive and/or hyperactive impulsive behaviors endorsed as present in the last six months

across the self-report, collateral, and interview sources, (2) evidence of historical ADHD symptoms (e.g., the collateral rater endorsed a clinically significant amount of childhood symptoms), and (3) present psychosocial impairment significant enough to warrant treatment as rated by self and/or collateral (Sibley et al., 2012a; Sibley et al., 2012b).

Participants received a $25 gift card for completing a physical visit, and $75 for attending each laboratory visit. Thus, they had an opportunity to earn up to $175 in gift cards for completing the entire study. Of the 22 participants that met the study's eligibility criteria, 36% met criteria for the primarily inattentive presentation, 55% met criteria for combined presentation, 5% met criteria for hyperactive/impulsive presentation, and 5% met criteria for ADHD, unspecified (American Psychiatric Association, 2013). Table 1 lists demographic information on the participants.

The majority of participants were also currently employed (75%). Of the employed participants, two were in their first job, with the remainder having other, prior jobs in the last five years (*Range* = 1-5; *Median* = 4). For these currently employed participants, two were in salaried, full-time professional positions ($34,500 and $54,000 salaries), three worked full-time in hourly positions (i.e., 40 hours a week), and the remainder worked 23 or fewer hours per week. Removing the salaried positions, the average hourly pay rate for the currently employed participants was $11.47 (*SD* = $1.08). Considering the entire employment history of the participants, 95% (*N* = 19) had been employed at some time. For these participants, eight had worked in a food service or delivery position (e.g., dishwasher, barista, fast food, waiter/waitress, cook). Other occupations included lifeguarding, retail (e.g., cashier),

production (e.g., in a factory that made boxes), and clerical office work (e.g., reception, scanning papers).

Procedures

The study was approved by the Institutional Review Board and registered at clinicaltrials.gov (NCT03446885). Upon enrollment into the study, participants were scheduled for two, three-hour visits to the Laboratory Assessment of Behavior in Occupational Roles (LABOR; Fabiano et al., 2018). The study utilized a within-subjects crossover design with two conditions: (1) single dose of placebo (micronized methylcellulose powder) and (2) a single dose of 40 mg lisdexamfetamine dimesylate (Vyvanse® Shire Pharmaceuticals). Lisdexamfetamine is a Schedule II central nervous stimulant prodrug that is converted to the active component dextroamphetamine. It was approved by the FDA as a treatment for ADHD in 2007 (www.drugs.com/history/vyvanse.html).

At the start of each visit to LABOR, participants first confirmed that they did not take any medication for ADHD that day. Order of study condition was randomized and counter-balanced by the unblinded study pharmacist. Medication and placebo were placed in identical opaque blue capsules by the unblinded study pharmacist. Both the participant and the study staff were blinded to the medication condition and order of medication or placebo dose administration. Participants were then administered either placebo or 40 mg lisdexamfetamine dimeslyate prior to engaging in the simulated workplace environment. Several studies of both children and adults have shown that the mean plasma concentration of dextroamphetamine (i.e., the active component) reaches above the limit of quantitation within 30 minutes of the administration of lisdexamfetamine dimesylate, with many participants experiencing

therapeutic effects within the 1st hour of drug administration (Boellner, Stark, Krishnan, & Zhang, 2010; Elbe, Macbride, & Reddy, 2010; Krishnan, Pennick, & Stark, 2008). Thus, a medication wait period of 30-60 minutes was implemented to promote ecological validity (e.g., administration of medication immediately prior to beginning work shift) and to ensure that participants were experiencing therapeutic levels of the drug by the time they started the workplace paradigm.

After completing the medication wait period, during which they completed several psychosocial surveys, participants were introduced to the LABOR analogue workplace. The LABOR analogue workplace setting included the completion of an online job application, which consisted of a series of questions typical of job applications for fast food restaurants, and participation in a video-recorded job interview, in which the interviewer asked a set of 13 open-ended questions. Interviewers were trained to ask the question and wait for the participant's response prior to going to the next question. At the completion of the final question, the interviewer congratulated the participant on completing the interview and "offered the job" by providing the participant an apron to put on before starting work.

Participants subsequently completed an orientation session where the job tasks, delivery procedures, and driving simulator were introduced and practiced (See Figure 2). The LABOR assessment included 40-minutes of job tasks commonly associated with working in a pizza place (i.e., creating 100 napkin bundles enclosing a fork, knife, and spoon, preparing 100 to-go bags with napkin bundles and condiments, and folding 25 pizza boxes) and a 5-min menu search task, in which participants were given a pizzeria menu and asked to find and calculate prices for a series of guest checks. This was followed by approximately 30-minutes of delivery

preparation and simulated delivery on a high-fidelity driving simulator. Following the completion of the final delivery and a return to the pizza restaurant, the participant completed some final ratings and was debriefed (see Figure 2 and Fabiano et al., 2018 for more details regarding the LABOR analogue workplace.) The LABOR analogue workplace setting and procedures were identical for both visits.

Measures

Job Application and Interview

Application rating. Five independent coders reviewed each application and completed a rating form asking them to make an overall evaluation regarding whether the person was an acceptable job candidate for an interview using a scale of 1 ("definitely not") to 5 ("definitely"). The intra-class correlation for the ratings of overall acceptability of the job candidate was .91. The average score across raters was used as a dependent measure.

Interview rating. Five coders who were unaware of the study participant identities or medication/placebo status viewed the job interview videotape and completed a form. Raters provided a rating of their overall impression of the interview behavior ranging from a score of one (Poor) to four (Outstanding). The intra-class correlation for the ratings of overall impression of the interview behavior was .90. The average score of the five coders for each participant was utilized as a dependent measure.

In addition to these ratings of the interview performance, the rater also completed the five-item inattentive/overactive (I/O) factor of the Iowa Conners rating scale to assess the participants' level of ADHD symptoms during the interview (Atkins, Pelham, & Licht, 1989; Milich, Loney, & Landau, 1982; Pelham, Milich, Murphy, & Murphy, 1989). The five items were

rated on a scale of *Not at all* (0) to *Very much* (3) and the sum of these items represents the score. Inter-rater reliability for the job interview codes were acceptable, with intra-class correlations ranging from .75 to .89.

Job Performance

Item completion. Each participant was instructed on how to complete item preparation, similar to the expectations within the front end of a restaurant. All participants were instructed to complete the napkin rings first, then the take-out bags, and then the pizza boxes, in that order. Participants were instructed that they had to complete one entire task prior to proceeding to the next task. The dependent measures from this aspect of the study were the number of items completed correctly. The total number of items assigned was 223. Similar to studies of child productivity, participants were purposely given many more items to complete than could be reasonably done in 40 minutes to prevent a ceiling effect (e.g., Fabiano et al., 2007; Pelham, et al., 1993).

Delivery Performance. Participants completed two simulated deliveries on the high fidelity driving simulator. In order to complete these tasks, participants had to put together the order from the laboratory "kitchen", they had to package the order appropriately, and then drive to the address in the simulator, exit the vehicle, deliver the correct items, and make change correctly from the customer. The experimenter also completed a checklist of each item that was delivered, and indicated whether this was a correct item according to the order. Further, for each delivery, the experimenter noted whether the participant made correct change from the payment. The percentage of delivery tasks completed correctly was used as the dependent measure.

Delivery Rating. Following the deliveries, the experimenter made a rating of the overall neatness and organization of the presented items delivered.

Driving Rating. During the deliveries, the experimenter watched each participant on the driving simulator and completed a survey of the participant's driving. Number of roadway rule violations, imprudent decisions, and collisions were noted. Following the two delivery trips, the experimenter provided an overall rating of the driving performance (i.e., 1 = "Poor" to 10 = "Excellent").

Integrity of LABOR Environment and Experimental Manipulation

To ensure an identical workplace environment at both visits and across all participants, the laboratory set-up was operationalized in a written protocol. In addition to a manual that specified the placement of all workplace materials, the environment used in the driving simulation was programmed to be consistent at both visits and across all the participants. A script was used for the job application instructions, job interview questions, and all interactions used to orient and prompt the participants during the experiment.

Independent observations of the laboratory sessions indicated that the laboratory was correctly set-up for the LABOR evaluation 93% of the time (e.g., on three instances the delivery/job task items were incorrectly placed). On 98% of occasions, all components of the visit were completed. That is, one participant in the placebo condition did not complete the workplace task or the delivery task due to illness not related to the experiment. Furthermore, a second participant elected to not complete the second visit. The data from these two participants were not included in the final analysis.

Following the completion of the laboratory tasks, participants were asked to rate their experiences within the environment. There were no significant differences between groups on ratings of workplace realism (1 = *Not at all realistic* to 10 *Very realistic*); mean scores were 6.95 (*SD* = 1.70) and 7.10 (*SD* = 1.45) for placebo and medication conditions, respectively. When asked about driving simulator realism, the mean scores were 7.10 (*SD* = 1.62) and 6.65 (*SD* = 1.84) for placebo and medication conditions, respectively. Participants were also asked to rate their effort during the experience (1 = *No effort at all* to 10 *All my effort*), and the mean scores were 7.40 (*SD* = 2.06) and 8.15 (*SD* = 1.60) for placebo and medication conditions, respectively. Finally, participants were asked "To what degree was your behavior the same as it would be in a real workplace setting?" and ratings ranged from one (*Not at all the same*) to 10 (*Exactly the same*), and mean scores were 7.40 (*SD* = 1.93) and 7.75 (*SD* = 1.55) for placebo and medication conditions, respectively. These self-ratings from the participants indicate that, in general, the environment reasonably approximated a workplace environment, and participants' own effort and behavior approximated an authentic workplace.

Statistical Analysis

Data were analyzed using a repeated measures, multivariate analysis of variance (MANOVA). Analyses were conducted for the pre-employment application and interview variables (application rating, interview rating, and I/O score during the interview), for the productivity variable (items completed), and for the delivery variable (delivery performance, delivery rating, and driving rating), separately. Medication status (medication, placebo) was entered as a within-subjects variable, and for all analyses order (placebo first vs. medication first) was entered as a covariate. Following the overall multivariate analysis, univariate tests

were conducted. Estimates of effect size were calculated by calculating *partial eta*^{2}. The primary outcomes listed in clinicaltrials.gov (NCT03446885) were application ratings, ratings of job interview performance, observed workplace productivity, and I/O rating.