

THE EFFECTS OF ANTIDEPRESSANTS ON OBSTRUCTED AND UNOBSTRUCTED GAIT IN THE HEALTHY ELDERLY

LF Draganich¹, PhD, J Zacny², PhD, J Klawns², MD, and T Karrison³, PhD

1. Section of Orthopaedic Surgery and Rehabilitation Medicine, Department of Surgery

2. Department of Anesthesiology and Critical Care, 3. Department of Health Studies

The University of Chicago, Chicago, Illinois 60637

INTRODUCTION

Falls are the leading cause of death from injury in people 65 years or more of age. Most falls by elderly persons occur during activities such as walking or changing position, and tripping or tripping over an obstacle is among the most reported causes of falls. Antidepressants have been found to be associated with falling. We hypothesized that single doses of amitriptyline, a tertiary-amine tricyclic antidepressant, desipramine, a secondary-amine tricyclic antidepressant, and paroxetine, a selective serotonin reuptake inhibitor, would affect temporal-distance variables and the kinematics of the trailing limb when stepping over obstacles.

METHODS

Twelve healthy subjects, 10 male and 2 female, were tested. Their mean (SD) age was 66.9 yr (3.0 yr), their mean height was 170.0 cm (14.0 cm) and their mean weight was 761 N (12.4 N). Inclusion in the study required that each subject be 65 to 75 years of age, report being able to walk several blocks without rest, and be able to successfully step over an 8-inch high obstacle. A medical history was obtained and a physical (including neurologic) examination was conducted to exclude the presence of poor uncorrected vision or chronic conditions, including a history of heart disease, hip fracture, active cancer, or stroke, as these have been reported to be associated with loss of mobility. Subjects also passed a psychiatric symptomatology test, a psychiatric screening interview, an alcoholism screening test, and a resting 12-

lead EKG. Subjects reported that they did not use central nervous system-active drugs within 30 days of their participation.

The University of Chicago Institutional Review Board approved the protocol and informed consent was obtained.

Subjects arrived for testing by livery service at approximately 0615 h. At 0630 h subjects were given a baseline resting EKG. At 0715 h subjects were given a standardized breakfast adjusted for body weight. Drugs were administered with 100 cc to 200 cc of water at 0800 h. Doses of paroxetine 20 mg, amitriptyline 50 mg, desipramine 50 mg, or placebo were tested in a four-period, double blind, crossover design. Treatment orders were randomly assigned from those residing in three, 4 × 4 Latin squares. The washout periods between treatments were at least 6 days. Drug and placebo capsules were identical in size, weight, and appearance. The randomization schedule was generated by the project statistician at the beginning of the study and given to the pharmacist. The pharmacist placed the appropriate capsule in a white envelope with the subject number and trial number noted on it and gave it to the nurse who administered the drug to the subject on the morning of the gait tests. The treatment team was blind to treatment assignment. Gait testing began at 1200 h, four hours after the drug had been ingested and when drug plasma levels were predicted to be at or close to peak levels.

The motion analysis laboratory included a 9.5 meter walkway. The kinematic parameters were measured using the Watsmart (Northern

Digital, Inc., Waterloo, Ontario, Canada) optical electronic three-dimensional digitizing and analysis system which detected the positions of infrared light-emitting diodes. Rigid segments of infra-red light emitting diodes were attached using elastic straps to the foot, shank, thigh, and pelvis of the left lower extremities of the subjects. Three sets of experiments were performed. Subjects first performed several practice trials. In experiment 1, the subject was asked to walk on the walkway, without encountering obstacles, in a self-selected manner. In experiment 2, the subject was asked to walk on the walkway, step over an obstacle (a white plastic dowel, 6 mm in diameter, placed across an aluminum frame) positioned 102, 153, or 204 mm high in a self-selected manner and continue walking to the end of the walkway. Trials for the three heights were in a random order.

The variables investigated for unobstructed gait consisted of velocity, stride length (normalized to lower limb length), cadence, maximum hip, knee, and ankle flexion and extension. Those for obstructed gait consisted of those temporal distance variables listed above, toe-obstacle clearance for the trailing limb (limb crossing obstacle last), angular velocity of hip, knee, and ankle flexion, and hip, knee, and ankle flexion when the toe of the trailing limb was directly over the obstacle.

All variables were separately analyzed by repeated measures analysis of variance (ANOVA). P levels ≤ 0.05 were regarded as statistically significant. The Greenhouse-Geiser adjustment to the degrees of freedom was used in assessing significance levels based on the overall F-test. If the overall F-test was significant, pairwise comparisons among treatment means were performed using paired t tests for the variables of gait, and Tukey tests for the variables of

psychomotor function and

RESULTS

None of the subjects fell during any of the experiments. None of the subjects tripped during unobstructed gait. Compared with placebo, amitriptyline reduced maximum knee flexion during the swing phase of gait by 4.2%. This was marginally significant ($p = 0.051$). None of the drugs were found to have other statistically significant effects on unobstructed gait. None of the subjects tripped when stepping over obstacles in a self-selected manner. Compared with placebo, amitriptyline significantly affected four dependent variables, reducing velocity by 8.0%, cadence by 4.9%, angular velocity of hip flexion by 10.0%, and angular velocity of knee flexion by 8.0% when stepping over obstacles ($p \leq 0.028$).

DISCUSSION

To our knowledge, this is the first placebo-controlled study of the effects of antidepressants on the gait of the healthy elderly. The data confirm our hypothesis on amitriptyline, demonstrating causal effects on the temporal-distance measures and on the kinematics of the trailing limb when stepping over obstacles. These abnormalities may result in falling. However, neither desipramine nor paroxetine had deleterious effects on gait, suggesting that these latter drugs may be safer to use with regard to gait.

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