ABSTRACT

In order to verify the sensitivity of the Cogtest system to subtle cognitive changes, we administered a single 0.3mg subcutaneous dose of scopolamine to N=8 elderly study participants. Scopolamine has been routinely used to induce cognitive dysfunction in a bid to mimic the loss of acetylcholine transmission seen in patients with Alzheimer’s disease. All participants were compliant and had a high probability of compliance. No attrition occurred on a battery of three Cogtest assessments: a test of continuous performance, one of strategic target detection and a word-learning task. Participants were assessed 1-hour prior to drug administration and at 2.5, 5, 7.5 and 11 hours after dosing. Consistent with the known effects of scopolamine, a marked decline in performance was seen 1.45 hours after drug administration. Also consistent with known effects, cognitive decline was most marked on the word-learning task, with performance falling from a mean total score of 10.1 (SE 0.93) at baseline levels (9.9 (SE 1.2)). This effect was found to be statistically significant when analysed by ANOVA (F=3.75, P=0.01). Peak drug effects on a test of continuous performance showed a prolongation of latency for correct responses of 60msec, reducing to a 16msec prolongation 7.5 hours after dosing. Consistent with our hypothesis, the duration of the stimulus, so the average ITI is (1.5 + 2msec) + 16msec (the duration of the stimulus), so the average ITI is 2.0 seconds This is consistent with the known effects of scopolamine. The outcome measure selected for analysis in this study was latency for correct responses.

INTRODUCTION

Traditionally assessments have been made using ‘paper-and-pencil’ testing, but there is considerable data has suggested that computerized assessments improve the quality of psychometric data collected, though at the expense of the validity of collected data (Waeses & Harrison, 2000). Such tests are often designed and administered by opinion leaders in the field of cognitive testing. Although computerized systems have been developed as a means of aiding the use of trained human testing in clinical trials. One such system is the Cogtest system, which has already found utility in a number of clinical drug studies (Barker et al., 2006). It has been used for the development of the Cogtest system, including  measures of new learning, compro- mising the practicability of the system. Performance on our third task, STD, showed a marked decline in performance was seen 1.45 hours after drug administration. Also consistent with known effects, cognitive decline was most marked on the word-learning task, with performance falling from a mean total score of 10.1 (SE 0.93) at baseline levels (9.9 (SE 1.2)). This effect was found to be statistically significant when analysed by ANOVA (F=3.75, P=0.01) and is shown in Fig. 1. Participants were white females with an average age of 69.1 years. Precise ages and years of education for each study participant are shown in Table 1.

RESULTS

In this study we employed a word list learning task and a continuous performance task, both of which we expected to be negatively affected by the administration of scopolamine. The results of this study confirm our hypothesis that a strategic target detection task that has some similarities with the IQED and WSCA which measures concept use, that performance on this task would be negatively affected by the administration of scopolamine.

Consistent with the known effects of scopolamine, a decline in performance was seen on the word memory task, with performance falling from a mean total score of 10.1 (SE 0.93) at baseline levels (9.9 (SE 1.2)). Also consistent with our knowledge of scopol- amine’s effects, performance at 7.5 hours was restored to baseline levels (9.9 (SE 1.2)). This effect was found to be statistically significant when analysed by ANOVA (F=3.75, P=0.01) and is shown in Fig. 1.

All participants were white females with an average age of 69.1 years. Precise ages and years of education for each study participant are shown in Table 1.

Continuous Performance Task (CPT): This is an experiment of conditional target-non-target dis- crimination, assessing the ability to sustain effort in a cognitively demanding situation. In this task, the participant is instructed to respond to a white mouse press when an “X” is preceded by an A. The left mouse button is pressed for all stimuli including an A, X that was not preceded by an A, and any other letter. Stimuli are selected according to the structure and randomization algorithm set out in this document. Twenty percent of the test consists of targets (AX). Stimuli are presented for 200msec each. The inter-trial interval varies across trials and may be 1.5, 2.0 or 2.5 seconds (depending on the duration of the stimulus), so the average ITI is 2.0 seconds. This is consistent with the known effects of scopolamine. The outcome measure selected for analysis in this study was latency for correct responses.

Strategic Target Detection (STD): This test is sim- ilar to the paper-and-pencil ‘completion’ tests or the ‘cross-out’ subset of the WAIS-III, where study participants are required to cross out target stimuli embedded among distractors. In this com- puterised version, the study participant touches the target stimuli (shapes) directly on the touch- screen.

Word List Memory (WLM): This is an auditory- verbal memory test which addresses the well- known inability to decline in dementia, and particularly prob - lemes such as dementia and Parkinsonism. (SE 0.3) to 5.9 (SE 0.8). Performance at 7.5 hours after dosing was 7.5 (SE 0.8). This effect was found to be statistically significant when analysed by ANOVA (F=1.262, p=0.3123). Latency returned to values close to predrug levels 7.5 hours after adminis- tration (P=0.1235). Finally, whilst modest elevations of latency were seen on the STD task at the 1.45 and 7.5 hours, these effects were slight and were not found to be statistically signif- icant (P>0.1)

REFERENCE

McKeith I, Del Ser T, Spano P, Emre M, Wesnes K, Anand R, Cummings J, 2000. The inclusion of computerized laboratory based tests in the Cogtest system pro- vides developers with an excellent opportunity to monitor comprehensively and assess effectively the effects of their drug.

Finally, a number of commentators have suggest- ed that well-assembled batteries of cognitive tests provide a way to not just to measure change, but also to assess cognitive decline. Cognitive decline was assessed by using the Cogtest system, including  measures of new learning, compro- mising the practicability of the system. Performance on our third task, STD, showed a marked decline in performance was seen 1.45 hours after drug administration. Also consistent with known effects, cognitive decline was most marked on the word-learning task, with performance falling from a mean total score of 10.1 (SE 0.93) at baseline levels (9.9 (SE 1.2)). This effect was found to be statistically significant when analysed by ANOVA (F=3.75, P=0.01) and is shown in Fig. 1.

Analysis of latency for correct responses on the CPT task showed a moderate increase in latency of 59msec from predrug assessment (588msec, SD=146) to peak drug activity (648msec, SD=148). This peak drug effect was not significant (F=1.426, p=0.3123). Latency returned to values close to predrug levels 7.5 hours after administra- tion (F=0.1235). Finally, whilst modest elevations of latency were seen on the STD task at the 1.45 and 7.5 hours, these effects were slight and were not found to be statistically signif- icant (P>0.1)