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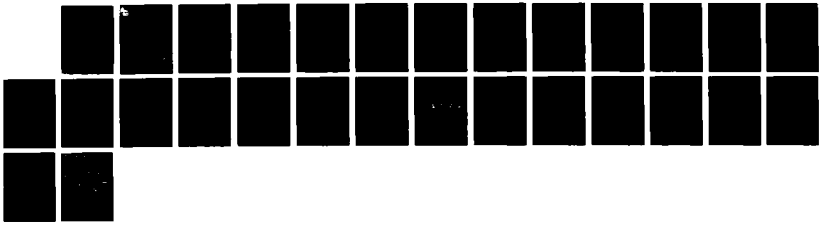

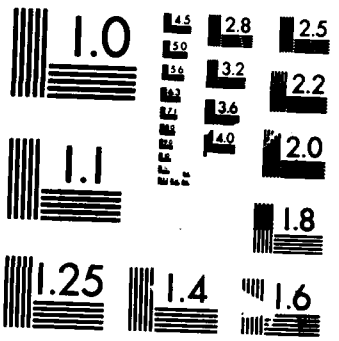

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ATROPINE EFFECTS ON THE OPERATION OF THE TOW MISSILE LAUNCHER

DAVID M. PENETAR, PhD, MAJ MS
DAVID A. STAMPER, MA
and
JEROME W. MOLCHANY, BS

DIVISION OF OCULAR HAZARDS

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Atropine effects on the operation of the TOW missile launcher

12 PERSONAL AUTHOR(S)

David M. Penetar, David A. Stamper, Jerome W. Molchany

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ABSTRACT

The effects of one and two autoinjector equivalents of atropine sulfate (2 and 4 mg/70 kg im) were tested in eight volunteers, ages 22 to 39 yr. Drug effects on the volunteers were assessed on the basis of their ability to operate the Army's current infantry antitank weapon--the TOW missile launcher. Soldiers were required to optically track and manually maintain the cross hairs of the sight on a moving target vehicle 2 km away for 15 s under both daylight and simulated dusk/dawn conditions. Results indicate no significant impairment of tracking capability after a 2 mg/70 kg injection; however, significant decrements were observed 150 min after a 4 mg/70 kg injection under both light conditions.

PREFACE

We express our appreciation to physicians CPT Peter Maningas, MAJ Donald Marks, MAJ William Bickell, and COL John J. Kearney. We thank Dr. Virginia Gildengorin for her advice and assistance with the statistical analysis of the data. Most of all, we express our appreciation to the volunteers who willingly bore the atropine effects.

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INTRODUCTION

Threats to the soldier on current and future battlefields include chemical warfare nerve agents. These agents can kill quickly by irreversibly binding essential neural enzymes called acetylcholinesterases. Without these enzymes, cholinergic synapses--in particular the peripheral neuromuscular junctions controlling respiration--undergo continual cholinergic stimulation and thus almost immediately cease functioning properly. Two complementary methods exist for reversing the effects of excess cholinergic stimulation: 1) prevention of the binding of excess acetylcholine through competitive receptor blockade and 2) reactivation of the inhibited enzyme by freeing it from its organophosphate bonds. Competitive receptor blockade is accomplished by anticholinergics such as atropine, while enzyme reactivation is accomplished by various oxime nucleophilic agents such as 2-PAM Cl (pyridine-2-aldoxime methyl chloride or pralidoxime) (1,2).

Because of the widespread cholinergic innervations throughout the human nervous system, any perturbation of the cholinergic receptors and enzyme functions can be expected to have profound physiological and behavioral consequences. The physiological and visual effects of anticholinergics and cholinesterase reactivators have been studied for many years (3, 4). A few studies have dealt with the effects of atropine on military-type tasks. Six milligrams of atropine did not produce significant decrements in the soldiers' ability to dig trenches (5). Two and 4 mg did not affect accuracy in a rifle fire exercise (5,6). Four milligrams did, however, affect the performance of radio operators. Atropine's effects on complex military tasks have not been studied, and rarely has there been an attempt to quantify the dose-effect relationship measures of behavior or performance.

The TOW (tube-launched, optically-tracked, wire-guided) missile launcher is one of the US Army's primary weapons to meet and defeat enemy armored targets. Mounted on either ground, vehicle, or helicopter, this system works by having a soldier detect and identify a Threat armored target, then fire and guide a missile to the

target. Soldiers are required to maintain the cross hairs of a 13-power optical system on the target for up to 20 s. This visual-motor coordination task often requires a soldier to follow or "track" the vehicle while it is moving. In the ground-mounted TOW, the cross hairs of the sight are kept on the target manually by the soldier operating two circular grips located on either side of the sight. The soldier can adjust vertical placement by turning the grips and horizontal placement by turning the entire sight/weapons system located on a viscous-damped traversing unit. An unaltered visual system, steady hand, and clear head are required to hit and destroy the target.

The Division of Ocular Hazards, Letterman Army Institute of Research, has a modified ground TOW I missile launcher (see Apparatus, below) that allows for the collection of pursuit-tracking data as operators optically track moving targets at tactical ranges (1-3 km). The modified TOW allows researchers to study the visual-motor behaviors required for acquiring, tracking, and engaging armored targets in a field setting.

In recent years, we have studied the effects of atropine and 2-PAM Cl alone and in combination on a visual motor task in the laboratory (4, 7), using the BLASER tracker, which is presumed to simulate those skills required to accurately operate Army systems such as the Ground Laser Locater Designator (GLLD) and TOW. Neither atropine in doses up to 2 mg/70 kg im nor 2-PAM Cl in doses up to 1200 mg/70 kg im was found to affect tracking performance significantly (4, 8). Four mg/70 kg atropine did degrade performance significantly in both the bright and dim light conditions, and its peak effect was 150 min after injection (4, 7). Once these data were known, a specific field study on a real Army system was the necessary and next logical step. The field study would validate our laboratory findings and provide reliable data to field commanders about the effects nerve agent antidotes would have on troop performance. Data on the performance of a real Army system would be more easily understood and incorporated into our tactical knowledge. Given the above, we set out to assess the dose-response effects of atropine on the operators of the TOW missile launcher.

METHODS

Participants: Eight adult male soldiers, ages 22 to 39, gave their free and informed voluntary consent prior to the study. They were screened and found to be in excellent physical and mental health, to have normal slit lamp and fundus examinations, and to be free of ocular disease. Special emphasis was made to determine whether the volunteers had good cardiovascular fitness and were nonsusceptible to atropine-related glaucoma or other anticholinergic contraindications.

Apparatus: Data on pursuit tracking performance were collected utilizing a ground-mounted TOW launcher. The system consists of a TOW launcher that has been augmented by the addition of an Apple II Plus microprocessor which permits recording of the error signals generated by the TOW's Missile Guidance Unit (MGU). The MGU operates in conjunction with the TOW sight to provide both azimuth (X) and elevation (Y) error signals. The operation of the system may be summarized as follows: The TOW sight contains a 13-power telescope with adjustable cross hairs, and an infrared tracker. The tracker generates an analog error signal proportional to the deviation of an infrared source from the center of the sight cross hairs. The M-70 infrared source is located on a target combat vehicle (M1009 CUCV--the military version of a diesel-powered 4WD Chevy Blaser). The TOW is boresighted daily using the M-70 source mounted on a stationary target to provide an accurate 0,0 point of reference for the generation of the analog error signals. The X and Y error signals are then processed by the TOW's MGU, digitized within the Apple by a 12-bit hybrid analog-to-digital converter and recorded on disk. The resulting time series is processed off-line via specially written software yielding percent time-on-target, standard deviation (SD), root mean square (RMS), and maximum absolute tracking error (MAT) scores for each trial. The system is powered by a 1-KW gasoline-driven motor/generator whose voltage is stabilized and filtered to remove unwanted ignition noise by means of an uninterruptible power supply.

Field Site: All training and testing was conducted at Hamilton Army Air Field, Novato, CA (about 20 miles north of the Presidio of San Francisco). The TOW was set up on a small rise about 10 feet above the overall ground level. Two kilometers away, on a curved runway access road, the target vehicle was driven at 20 mph in a left-to-right direction for approximately 20 s. TOW operators and

observers had a clear line of sight to the target vehicle unobscured by vegetation and somewhat above the heat scintillation radiating from the ground.

Training of Subjects: Each volunteer received two days of training on the TOW. The first day consisted of 22 one-minute tracking trials under two ambient lighting conditions (daylight and dawn/dusk)[1]. Dawn/dusk conditions were simulated by inserting a 2.7 OD neutral density filter in the optical pathway and placing a lightproof cloth hood over the volunteer seated behind the TOW and allowing him to dark-adapt partially for 5 min. The second training day consisted of 32 twenty-second trials (16 light and 16 dim). This training schedule, used in previous TOW field studies, has been found to produce accurate and stable tracking performance (9).

Drug Testing: After training, all volunteers were scheduled for a baseline/no drug day. Following this, three experimental days were scheduled: saline placebo, 2 mg/70 kg, and 4 mg/70 kg. The injections followed a counterbalanced design and were scheduled no closer than 72 hr to allow for complete clearance of the drug and to minimize behavioral tolerance effects. Injections were intramuscular (in the arm). Volunteers performed 20 tracking trials (10 light, 10 dim) on each experimental day. Tracking commenced 150 min (2-1/2 hr) after injection. Volunteers had access to a temperature-controlled motor home where they rested while not actually tracking. Medical supervision and support consisted of the responsible physician trained in emergency medicine, an enlisted soldier (91A Combat Medic from Letterman Army Medical Center) and ambulance with driver. The responsible physician administered all injections and he or the medic took vital signs at the following time periods: 1 hr preinjection, 15 and 30 min after injection, and then every half hour thereafter while at the field site. A SPARK (Systematic Pulmono/cardiac Anaphylaxis Resuscitation Kit) kit (complete with drugs and equipment to handle cardiopulmonary arrest and anaphylactic shock), oxygen, and defibrillator were on hand and available in the unlikely event that adverse anticholinergic effects (cardiac, heat, or otherwise) required treatment. A specific atropine antidote, physostigmine (ANTILIRIUM^{R}, O'Neal, Jones & Feldman Pharmaceuticals, St. Louis) was available in addition to the SPARK Kit drugs. Coordination was made with the nearest hospital (Novato Community) for volunteers to be transported to in the event of a medical emergency. Volunteers were cleared by the attending physician and ophthalmologist either on site or upon

[1]Measured daylight luminance levels averaged approximately 4000 nits while dusk/dawn luminance levels were calculated to be approximately 25 nits.

return to LAIR before being transported to their residence. At that time, heart rate had to be at baseline levels ±15% with temperature, mental status, and intraocular pressure normal. They were cautioned not to drive or ride a bicycle/motorcycle, use workshop tools, or exercise for the remainder of the day. While in the study, volunteers carried a card which listed the phone numbers of personnel to contact and how to obtain medical care in the event of a delayed drug reaction or emergency. On days following experimental days, volunteers reported to the Visual Function Laboratory, LAIR, for readings of vital signs (heart rate, blood pressure, temperature) and check of visual functions (pupil size, accommodation, intraocular pressure).

Experimental Design and Statistical Analysis: Volunteers were tested with atropine sulfate in a repeated measures design. Each volunteer received both doses of the drug as well as a saline control injection. Dosing order was balanced across volunteers. The raw horizontal and vertical tracking error scores for only the first 10 s of the trial were used to calculate the variability in tracking error (standard deviation (SD), root mean square (RMS)), and maximum absolute tracking (MAT) error for each trial. Analysis of variance (ANOVA) (10) was performed to evaluate drug effects on tracking performance under low light and bright light conditions separately. Standard deviations were log transformed prior to the ANOVA analysis. The ANOVA is a 2 X 4 factorial design generated by the two light levels and four injection conditions. Significant Fs were further evaluated by the least square difference test (11). The significance level is set at $p=0.05$ for all comparisons.

RESULTS & DISCUSSION

Vertical Axis Analysis: Mean standard deviation (SD), root mean square (RMS), and maximum absolute tracking errors (MAT) data for the Y-axis component of the tracking task are presented in Table 1. All three measures of the tracking error analysis revealed increases following the 4 mg/70 kg injection, especially for the dim light condition, but these increases were not statistically significant (Table 2). This result is not surprising given the horizontal-only nature of the task. When a vertical element was added to the laboratory tracking task by means of three gentle up-and-down hills,

a significant atropine effect was found (4). Very often tracking vehicles as they travel up and down hills adds to the complexity of the task not simply because of the addition of the vertical component, but also because there will be changes in speed (i.e. slowing down on the uphill and speeding up on the downhill). These local variations make the tracking much more difficult than a constant-speed, one-direction task. Tracking accuracy is known to decrease as the speed of the target increases (12). Tracking tasks where targets move in two dimensions and at modulating speeds presumably will be more difficult than the presently tested task. Drug effects may be potentiated under this more difficult task. From a tactical point of view, these questions are important since even when moving on relatively open and level terrain, small hills, ditches and the like will produce vertical components to the tracking task. Additionally, cross-country travels can be at rates of speed in excess of 20 mph, possibly up to 50 mph. Drug effects on tracking targets moving at higher velocities remain to be explored.

Horizontal Axis Analysis: Percent time on target represents the time the sight cross hairs were maintained within a 1-mrad horizontal "window" (2.2 m square) on the moving target vehicle. Percent time on target under bright light conditions decreased from 99% during baseline conditions to 89% after the 4 mg/70 kg dose (Fig 1). These effects were nonsignificant ($F=3.54$, $df=3,21$, $p=0.08$). Dim light conditions produced substantially less accurate performance under baseline conditions when compared to bright light conditions (87% vs 99%). A significant drug effect was observed at the 4 mg/70 kg dose where percent time on target decreased to 63% ($F=5.51$, $df=3,21$, $p=0.03$). This means that on the average, operators only were able to maintain the cross hairs within the 2.2 m square center of mass for less than 7 out of the 10 analyzed seconds of tracking.

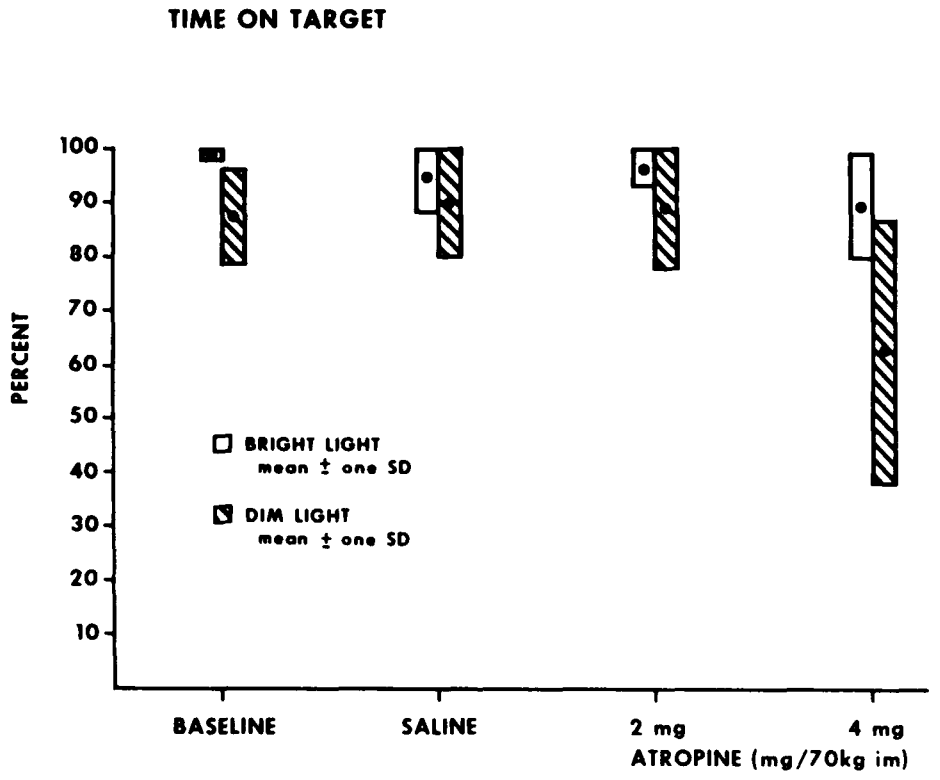

FIGURE 1. Mean (N=8) percent time on target for 4 injections and 2 light conditions (open bars: daylight; striped bars: dusk/dawn). Target is defined as a 1-mrad window (2.2m square), the center of mass for the vehicle. The vehicle was a CUCV tactical vehicle, the military version of a diesel-powered 4 WD Chevy Blaser.

Mean SD horizontal tracking error scores increased significantly from 0.138 mrad under bright baseline conditions to 0.255 mrad after the 4 mg/70 kg injection (Fig 2). Under dim light conditions, mean SD errors increased significantly (Table 2) from a 0.25-mrad baseline to 0.47 mrad under the 4 mg/70 kg dose. Large variability around the mean at the highest dose can be observed by the shaded bars under this condition.

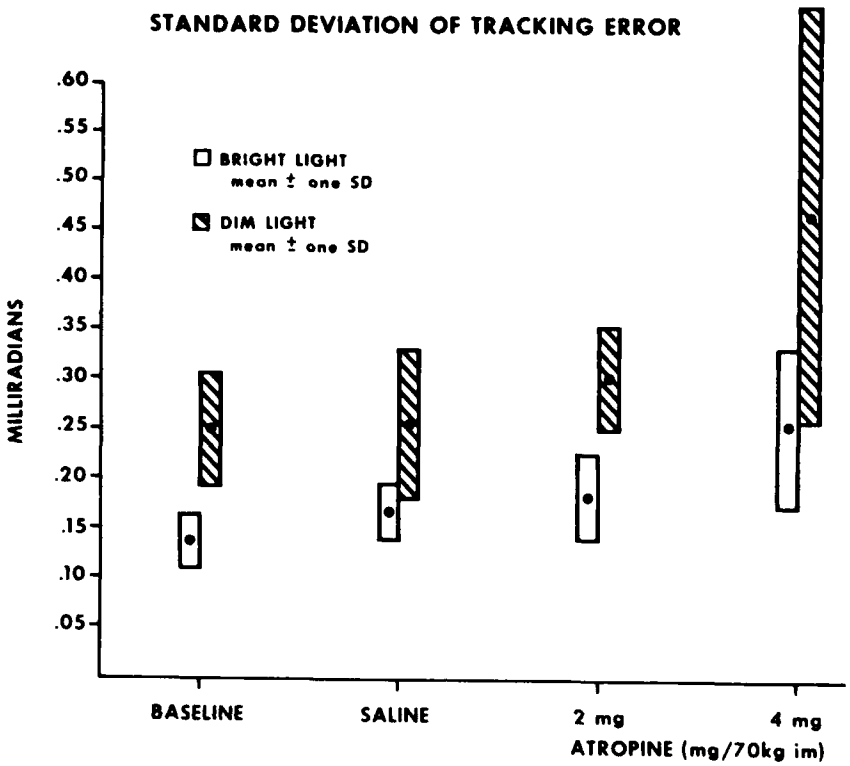

FIGURE 2. Mean (N=8) standard deviation of the horizontal tracking error under daylight (open bars) and dusk/dawn (striped bars) conditions. Significant effects are observed following the 4 mg/70kg injection under both light conditions.

Mean horizontal RMS tracking error is presented in Table 3. Graphically, the drug effect picture is similar to that for the SD error scores and is not presented. Increases under bright light conditions were over 2-fold, from an averaged baseline of 0.17 mrad to 0.292 mrad after 4 mg/70 kg, but missed statistical significance (Table 2). Under dim light conditions, atropine produced significant increases to 0.562 mrad from a baseline of 0.302 mrad.

MAT scores were significantly increased (Table 2) by the higher doses of atropine in both bright light (from 0.446 to 0.746 mrad) and dim light (from 0.736 to 1.197 mrad) (Fig 3). Variability around the MAT means was larger than the variability around either the SD or RMS means.

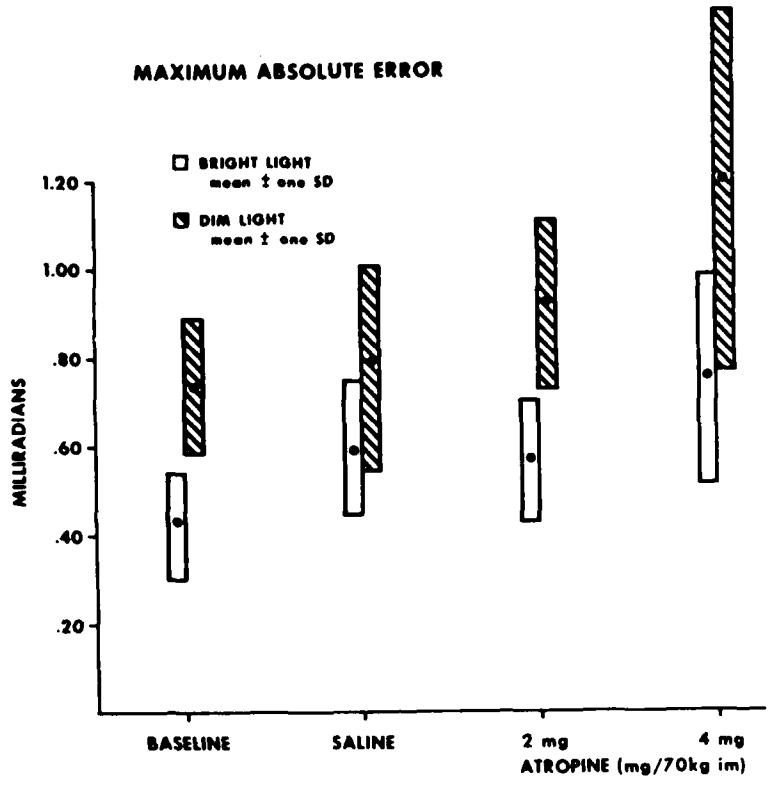

FIGURE 3. Mean (N=8) maximum absolute tracking errors under daylight (open bars) and dusk/dawn (striped bars) conditions. Significant increases in errors are observed for the 4 mg/70 kg dose in both light conditions.

The MAT scores of each volunteer at 0.5-s intervals throughout the trial were averaged and plotted separately for each injection condition (Fig 4). Under bright baseline conditions, tracking errors remained fairly constant, averaging 0.139 mrad. Except for an unexplained upswing in the saline line during the final 2 s of the plots, there was virtually no difference between baseline, saline, and 2 mg/70 kg atropine values. Overall, a significant difference was observed for the 4 mg/70 kg dose. Average MAT for this condition was 0.259 mrad. Performance could be seen as more variable under the dim conditions, fluctuating about 1/10 mrad on the average. As under bright light conditions, tracking performance under dim light for baseline, saline, and 2 mg/70 kg atropine was equivalent. A clear and significant atropine effect was observed for the 4 mg dose. MAT averaged 0.449 and fluctuated between 0.34 and 0.54 mrad.

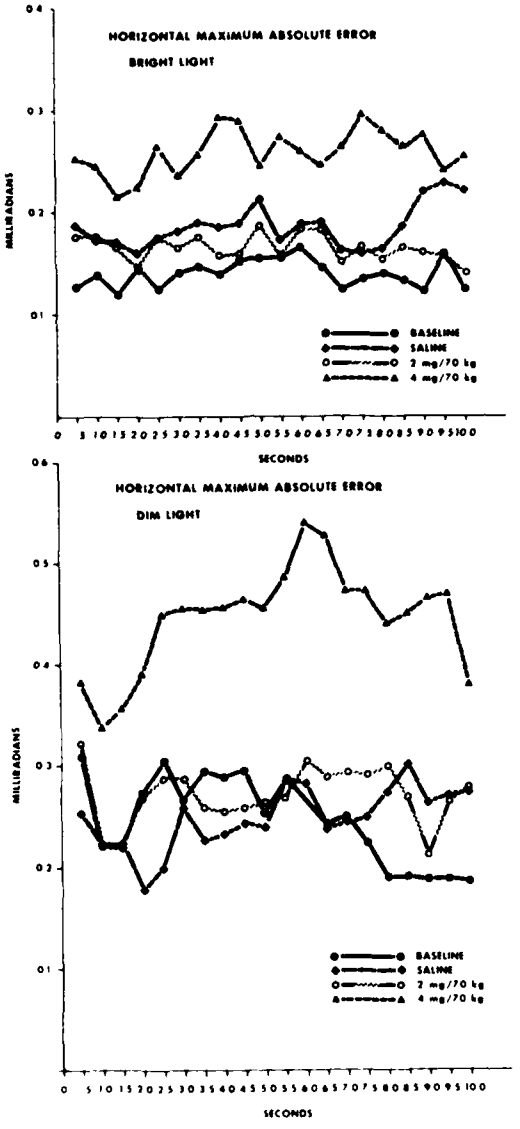

FIGURE 4. Tracking steadiness for 4 injection and 2 light conditions (open bars: daylight; striped bars: dusk/dawn). Mean (N=8) maximum errors are plotted by 0.5 s intervals for the first 10 s of the target's traverse. Maximum absolute errors report the largest off-center excursions made by the cross hairs at each sample point. Significant effects are observed for the 4 mg/70 kg injection under both light conditions.

At the distance tested (2 km), the 4.6 m long CUCV subtended a horizontal angle of 2.07 mrad. Average MAT scores for the different light and drug conditions do not reveal that atropine produces off-target tracking. Overall, under bright light, operators were fluctuating somewhere within a 0.3 m center of mass area during baseline and 0.58 m after the 4 mg/70 kg dose. Under dim light conditions, fluctuations were within a 0.55 m center of mass area during baseline and 1.0 m after the 4 mg/70 kg dose. However, inspection of the individual performance records following the 4 mg/70 kg injection revealed numerous instances in which operators were lagging behind the vehicle for several seconds. These lags were often followed by a swing past the center to beyond the front of the target (lead error). Although the averaged performance reports on-target tracking, individual records reveal this was not the case in many instances. To support this observation, we analyzed the horizontal MAT scores further for the number of seconds soldiers were completely off the truck (i.e. when the cross hairs were $\pm$2.07 mrad). Under bright light, average time off truck was less than 0.01 s for baseline, saline, and 2 mg/70 kg conditions (Fig 5). This was increased to 0.255 s following the 4 mg/70 kg injection. In the dim light, soldiers averaged 0.2, 0.1, and 0.3 s off the truck for the baseline, saline, and 2 mg/70 kg conditions, respectively. This was dramatically increased to an average of 1.7 s following a 4 mg/70 kg injection. This averaged amount of time off truck tends to underestimate the effect, however.

In the tactical sense, what is important is an analysis of the number of times the drug in question will cause soldiers to be off the target vehicle and for how long they will stay off. Fig 6 represents such an analysis. It can be seen for the bright light condition that only the 4 mg/70 kg dose causes any soldier to be off the truck for more than 0.1 s. The dim light condition alone caused one soldier to be off the target for greater than 0.5 s while the 4 mg/70 kg dose in the dim light caused six of the eight soldiers to be off the truck for this duration or longer. In this dim light condition, five soldiers exhibited off-truck tracking in excess of 1 sec. The scores of these five soldiers ranged from an average of 1.5 s to 4.3 s. These soldiers were completely off the truck from 15% to almost 50% of the tracking trial. These data have important tactical significance. If the missile reaches the target during an instance of substantial lead/lag error when the cross hairs are off the target, the missile would miss the target. We

generalize from this observation and conclude that performance following the 4 mg/70 kg dose will substantially decrease the probability of both hits and kills.

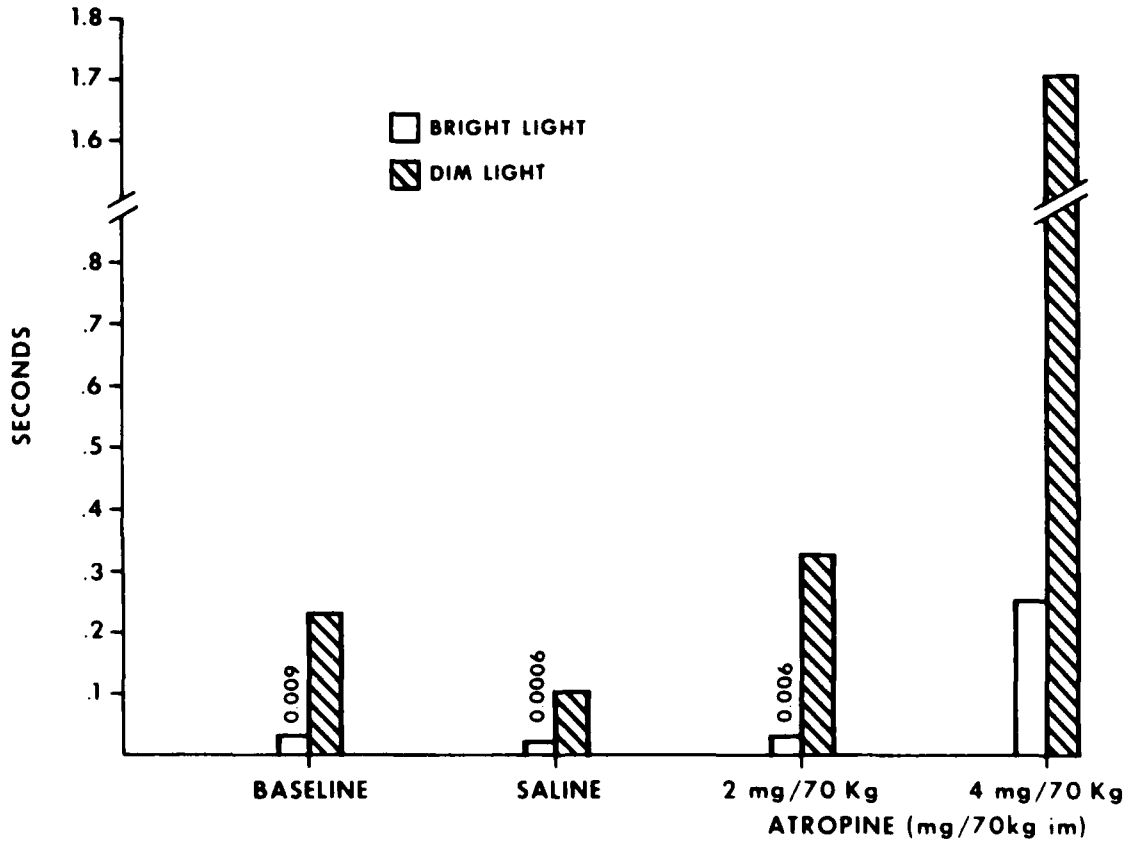

FIGURE 5. Mean (N=8) tracking seconds off vehicle target for 4 injection and 2 light conditions (open bars: daylight; striped bars: dusk/dawn). Off-vehicle tracking occurred when operators led or lagged the vehicle by more than 2.07 mrad. Numbers above the open bars are the averages for those conditions.

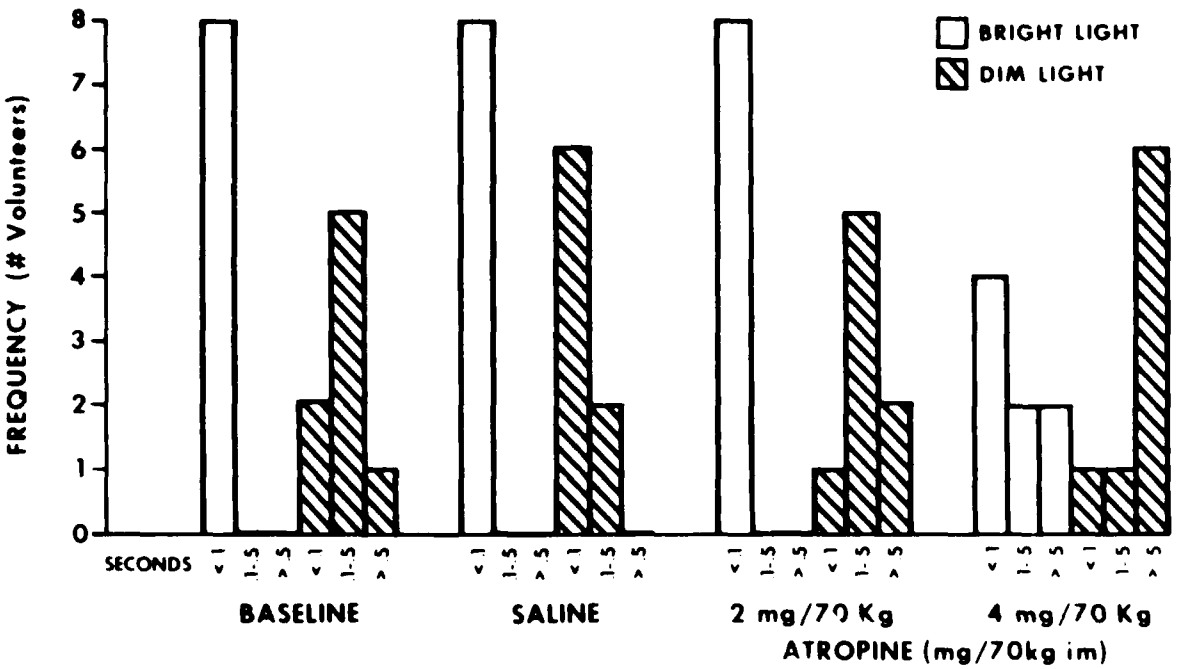

FIGURE 6. The number of operators who tracked beyond 2.07 mrad (i.e. led or lagged the cross hairs off the vehicle) for less than 0.1 s, for 0.1 s thru 0.5 s, and for greater than 0.5 s during the 4 injection conditions and 2 light conditions (open bars: daylight; striped bars: dusk/dawn).

In our analysis, we have shown substantially more drug effect under dim light conditions than under bright light. The reasons for such differences are not readily apparent. Atropine is known to produce loss of accommodation and cycloplegia resulting in reduced near vision acuity (especially for low-contrast tasks) but without significant effects on distance acuity tasks (2,4). These classic atropine effects do not account for the greater tracking deficits observed in dim light since the target and cross hairs are at optical infinity. Since most of the soldiers report instances of cross hairs disappearing during dim light trials, the reduced contrast of the target/background in combination with a possible atropine

effect on contrast sensitivity possibly may be the cause. Atropine effects on contrast sensitivity are unclear at the present time (13), and more research needs to be done in this area.

SUMMARY

All three measures of tracking errors reveal basically the same picture of drug effects. Under bright light conditions, 2 mg/70 kg atropine produced no statistically significant increases while the 4 mg/70 kg produced consistent and statistically reliable increases in the error measures producing tracking deficits. Drug effects under dim-light conditions are greater, but again, 2 mg/70 kg produces nonsignificant increases in the error measures while 4 mg/70 kg produces significant increases. Inspection of the individual summary statistics indicates that some volunteers are severely affected by the drug while others show only slight increases. This is most readily apparent in the analysis of tracking time off the target vehicle.

CONCLUSIONS

In an unstressed environment, soldiers can successfully engage armored targets with the TOW system following a 2 mg/70 kg injection of atropine. Performance after a 4 mg/70 kg dose indicates significant decreases in tracking ability and reduced probability to hit and destroy targets, especially under periods of reduced light and visibility.

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Table 1: Mean Standard Deviation (SD), Root Mean Square (RMS), and Maximum Absolute Tracking Error (MAT) for the Vertical (Y) axis.*

	Injection Conditions			
	Baseline	Saline	2 mg/70 kg	4 mg/70 kg
SD				
Bright	0.112±0.014	0.104±0.015	0.113±0.014	0.133±0.026
Dim	0.151±0.032	0.131±0.033	0.160±0.048	0.204±0.078
RMS				
Bright	0.166±0.055	0.143±0.027	0.194±0.056	0.217±0.109
Dim	0.225±0.089	0.185±0.058	0.223±0.086	0.336±0.194
MAT				
Bright	0.492±0.163	0.383±0.058	0.465±0.081	0.515±0.172
Dim	0.552±0.133	0.486±0.120	0.543±0.152	0.781±0.337

*All values are expressed in milliradians ±1 standard deviation

Table 2: Analysis of Variance Results on Vertical & Horizontal Scores for Three Measures of Tracking Performance

		Mean Square	DF	Greenhouse Geisser Probability
Vertical Axis				
Bright Light SD	Dose	0.01486	3	
	Error	0.00517	21	0.0802
Dim Light SD	Dose	0.04302	3	
	Error	0.01841	21	0.1267
Bright Light RMS	Dose	0.00831	3	
	Error	0.00568	21	0.2671
Dim Light RMS	Dose	0.03367	3	
	Error	0.01541	21	0.1697
Bright Light MAT	Dose	0.02677	3	
	Error	0.01852	21	0.2664
Dim Light MAT	Dose	0.13545	3	
	Error	0.04613	21	0.1132
Horizontal Axis				
Bright Light SD	Dose	0.08716	3	
	Error	0.00890	21	0.0015
Dim Light SD	Dose	0.10395	3	
	Error	0.01627	21	0.0123
Bright Light RMS	Dose	0.02120	3	
	Error	0.00606	21	0.0698
Dim Light RMS	Dose	0.12077	3	
	Error	0.02437	21	0.0408
Bright Light MAT	Dose	0.12159	3	
	Error	0.02767	21	0.0371
Dim Light MAT	Dose	0.34049	3	
	Error	0.07747	21	0.0409

Table 3: Average Root Mean Square (in milliradians) of Horizontal Tracking Error (±1 SD)

Baseline	Saline	2 mg/70 kg	4 mg/70 kg
Bright Light			
0.170±0.042	0.241±0.087	0.211±0.048	0.292±0.104
Dim Light			
0.302±0.058	0.310±0.119	0.344±0.057	0.562±0.259

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OFFICE OF NAVAL RESEARCH
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