

# **Project title**

"Effects of Anxiolytics on Fine Tuning (Neuromuscular) Activity Performance"

# **Reference number: 08D01EE**

# **RESEARCH TEAM**

- 1. Emin Ergen, Professor, MD Sports medicine specialist Ankara University
- 2. Caner Açıkada, Professor, Ph.D. Sport scientist Hacettepe University
- 3. Rüştü Onur, Professor, MD Ph.D. Pharmacologist Hacettepe University
- 4. Rüştü Güner, Professor, MD Sports medicine specialist Ankara University
- 5. Nursabah Başçı, Professor, Ph.D. Chemical engineer Hacettepe University
- 6. Tahir Hazır, Associate Professor, Ph.D.-Sport scientist (Exercise physiology)– Hacettepe University
- 7. Ziya Koruç, Associate Professor, Ph.D.-Sport scientist (Clinical psychology)- Hacettepe University
- 8. Murat Çilli, Associate Professor, Ph.D.- Sport scientist Hacettepe University

# 9. Ergün Acar, Research Assistant, Sport sciences – Hacettepe University

- 10. Yıldırım Sara, Associate Professor, MD Pharmacologist Hacettepe University
- 11. Hülya Savaş, Ph.D. Chemist Hacettepe University
- 12. Aydın Balcı, MD, Resident in sports medicine Ankara University
- 13. Mesut Çelebi, MD Sports medicine specialist Ankara University
- 14. Serdar Arıtan, Associate Professor, Ph.D.- Sport scientist (biomechanics) Hacettepe University
- 15. Öznur Oztaş Atalan, M.Sc. chemist Hacettepe University

# **ARCHERS (SUBJECTS)**

1.	Damla GUNAY	(F)
2.	Neslihan CAKIROGLU	(F)
3.	Selen OZKAYA	(F)
4.	Zeynep ISIL SU UNAL	(F)
5.	BEGUL LOKLUOGLU	(F)
6.	Selma KAYA	(F)
7.	Zekiye KESKIN SATIR	(F)
8.	Aybüke AKTUNA	(F)
9.	Goktug Ergin	
10.	Fatih BOZLAR	
11.	Yusuf CORBA	
12.	Sermet CINAR	
13.	Yagiz YILMAZ	
14.	Hasan ORBAY	
15.	Enes UGURLU	
16.	Burak BEYDILLI	
17.	Osman ESKICI	
18.	ibrahim Etem GULACAR	
19.	Talha GORUCU	
20.	Kerem KIRSEVER	
21.	Bugra ERBAY	
22.	Seyit Zor	
23.	Zehra Ece YİĞİTER	(F)
24.	Begunhan UNSAL	(F)
"F den	otes female"	. /

# **ACKNOWLEDGEMENTS**

Françoise Dagouret Turkish Archery Federation Abdullah Topaloğlu Sirer Aydın Alper Aytaçoğlu Gülşen Balcı Turkish Doping Control Center Engin Kıran

# **ABBREVIATIONS**

HEART RATE (HR) RESTING HEART RATE (RHR) SHOOTING HEART RATE (SHR) MECHANICAL CLICKER REACTION TIME (MCRT) CENTER OF PRESSURE (CoP) COMPETITIVE STATE ANXIETY INVENTORY (CSAI-2)

# 1. Executive summary (project aims, results obtained during the granting year, conclusions and future plans).

The aim of the study was to investigate the effects of benzodiazepine on shooting performance and its components in archers. In order to evaluate the possible effects of benzodiazepine, some performance related parameters like body sway, mechanical clicker reaction time, aiming behaviour, anxiety and heart rate values were measured.

Subjects were 24 (10 females and 14 males) archers competing at international events and trained at least 4 years. Each archer was requested to perform under the influence of benzodiazepine, (diazepam 5 mg, oral). Their athletic performance was also evaluated after receiving placebo. Each archer competed as control, placebo and benzodiazepine under double blind crossover study. The competition was especially designed to simulate competition environment by having archers shooting in doubles each time, on a specifically designed platforms. One platform was mounted on two force plates, where all the data related to shooting and body swaying was collected. The second platform was a dummy platform, to provide the second subject with similar feelings as the subject on the first platform. With this set of data collection, the archers were asked to compete 6 times each in changing rounds, where they had 24 shots in each competition. Repeated measure of ANOVA was used to compare the differences between control, placebo and benzodiazepine shots.

Results show that there was no difference in shooting scores, resting heart rate, shooting heart rate, aiming behaviour (aiming displacement in) x and y axis on the target), the amount of changes in the center of pressure both in terms of displacement and velocity (front and rear foot), clicker reaction time between control, placebo and 5 mg diazepam administration shots.

It can be concluded that the use of 5 mg diazepam has no effect on shooting performance and related parameters on archers.

# 2. Background and aims

The use of prohibited substances is an unethical and health threatening practice in sport. This is clearly against fair-play and can be hazardous for health of athletes. Although the use of doping substances are rare in sports requiring fine tuning motor movements, there are rumours that some archers tend to use such medicines that diminish anxiety and reduce body sway during shooting which may positively affect the shooting performance. FITA (International Archery Federation) Medical and Sport Sciences Committee (MSSC) decided to carry out a project in order to find out whether there is such an effect of anxiolytic substances on performance.

In case benzodiazepines improve athletic performance in archery, these substances should be proposed as doping agents and they have to be taken into the monitoring list and then into the prohibited substances list. Such a result may also indicate abuse possibility of these substances in similar sports disciplines (shooting etc.). FITA concerns a Fair-Play in archery thoroughly.

# 3. Methods used

# **SUBJECTS**

Subjects were 24 elite Turkish archers (14 males and 10 females) having been trained for at least 4 years, 3-4 days a week and competing at the National Team. None of the subjects were taking any medication same or similar to benzodiazepines. They were also not consuming antacids, carbamazepine, isoniazid, and rifampicin that may affect absorption of benzodiazepine or its metabolism. Subjects were asked not to consume alcohol during the research period.

Property	Value <sup>*</sup>
Age (year)	$19.8 \pm 5.3$
Height (cm)	$172.0 \pm 9.18$
Body weight (kg)	72.7 ± 15.68

# Table 1: Demographic properties of the subjects (n=24):

\*: Values were given as mean + standard deviation

# SUBSTANCE

Diazepam 5 mg capsules were obtained from DEVA Holding AŞ, Istanbul-Turkey. Placebo capsules were also provided by the same company. The study protocol was approved by the local Ethics Committee at Hacettepe University Medical School.

The urine samples were taken before the diazepam and placebo ingestion in order to emptying the bladder and just and 2 hours after the match.

# MEASUREMENT OF AIMING BEHAVIOR AND IDENTIFYING PERFORMANCE DISTURBING PARAMETERS

#### **Body Sway**

Changes in the centre of pressure (COP) during shooting in archery was investigated by the use of two force plates placed under the feet during shooting stance and a 16 byte analogue-digital card. Table 1 shows the parameters which were evaluated during the body sways in shooting.

CoP Parameter		Definition					
	Range	Difference between maximum and minimum COP values					
Displacement	Standard deviation	Deviation of COP location					
	Length	Total length, or distance, traced by the COP path					
	Area	Percentage time spent within a given area					
	Average	Average of COP velocity					
Velocity/speed	Maximum	Maximum COP velocity values					
	Standard deviation	Deviation of COP velocity					

# Table 2 Summary of CoP parameters used in Olympic archery

# Aim point fluctuation (APF)

Originally, fluctuations during aiming on the target was planned to be traced by a special device (RIKA, Home Trainer, Finland). However, due to analoguous data output, another device was developed at Hacettepe University Technocity to measure aiming displacement in x and y axis on target. An infrared beamer system was used to evaluate aiming behaviour. A software was written to detect infrared beam on a video screen and transferred outputs to analoguous data. The accuracy of the system was verified whether the infrared beam and camera were working reliably for the purpose.

The aiming behavior was assessed using infrared beamer and a software developed to calculate relative travelling along x- and y-axis. The relative distance, which was calculated using integral method, according to the initial point in aiming (normalized), from the x and y axis were taken into account for 2 seconds before and half-a-second after the clicker drops and the parameters were recorded during aiming (Table 3).

APF Parameter		Definition			
Displacement	Range	Difference between maximum and minimum APF values			
	Standard deviation	Deviation of APF location			
Displacement	Length	Total length, or distance, traced by the APF path			
	Area	Percentage time spent within a given area			
	Average	Average of APF velocity			
Velocity/speed	Maximum	Maximum APF velocity values			
	Standard deviation	Deviation of APF velocity			
Points	APF position during shooting	APF points during shooting			
	Shooting points	Scored points			

Table 3. Summary of APF parameters used in Olympic archery



Picture 1. Experimental setting for the project

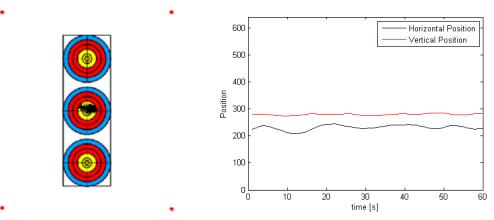


Figure 1.Aim point fluctuation around the target and its appearance on x(vertical) and y(horizontal) axis (in pixels).

# Mechanical Clicker Reaction Time (MCRT)

A device, installed with a microphone to detect the dropping sound of the metal piece of clicker and an infrared sensor to detect arrow's movement, was developed at Hacettepe University Technocity in order to measure the mechanical clicker reaction time (Picture 2).



Picture 2. Detector of clicker drop sound and infrared beamer box attached on a bow.

During shooting, the archer draws the string up to a position that the clicker drops from the arrow head and then the arrow is released. The sound of that drop is transferred to electrical signal by the microphone, amplified to 5V and considered as the initiation of mechanical clicker reaction time ( $t_{clk}$ ). Infrared sensor has a triggering potential of 2 kHz and amplification to 10V when the arrow travels after release. The infrared signal from the arrow head release is considered as the end of mechanical clicker reaction time ( $t_{inf}$ ). MCRT signals were recorded using a 16 bytes analogous-digital converter (NI-6210) to a computer with a 1/1000 second intervals (Figure 1 and 2).

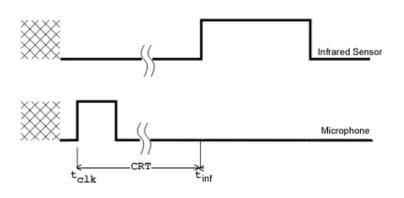


Figure 2. Data acquisition details during shooting.

#### Heart rate

Heart rate (HR) was recorded before (at resting state) and during shooting using telemetric heart rate monitor with one second interval (Polar RS800, Polar Electro Oy, Kempele, Finland). Resting state HR (RHR) values were obtained from the means of last five minutes of a ten minutes sitting position. Recording of shooting HR (SHR) values were initiated after stepping on the force plate and continued until the competition was over. The mean of SHR values during 8 series of three shots (24 shots in total) were considered for calculations. Archers pressed the marker button themselves to start recording the HR.

#### Shooting

Shootings took place according to regular indoor competition standards. Official judging, 18 m distance shooting, and normal indoor competition rules were considered. Match durations for benzodiazepine, placebo and control are given below.



Picture 3. Strapping the heart rate monitor.

# Table 4. Average shooting times during matches in different conditions (diazepam, placebo, control and mean values)

Avarage match duration for diazepam (min)	$20.9 \pm 3.18$
Avarage match duration for placebo (min)	$19.5 \pm 3.10$
Avarage match duration for control (min)	$21.8 \pm 3.46$
Avarage match duration in mean (min)	$20.7 \pm 3.33$

Archers were asked to compete in doubles as in official competition. It was announced that the highest scorer, both in males and females, were going to have a reward in order to create a competition environment motivation (Picture 4). In this specifically designed competition each archer had to compete 6 times during the course of the study, where they had to compete 3 times on data recording real, and 3 times on dummy platforms. In each round archerers shot 3 arrows in 8 series. Dummy platform was built to give similar feelings as in the real platform. The real and dummy platforms looked very similar in size, appearance and all the cabling, infrared beamer and other devices that were used, except there was no any data collection from the dummy platform. All the data was collected from the real platform. Below schedule indicating the course of competetion and 6 round shootings for each archer under control, placebo, and diazepam conditions in randomised double blind cross over study.

HEART RATE	x	Х			Х		
WARMING UP			х				
ANXIETY SCORE	x			х			х
SHOOTING - SCORING					Х		
AIMING BEHAVIOUR					Х		
BODY SWAY DATA RECORDING					Х		
CLICKER REACTION TIME					Х		
URINE SAMPLE	x					X	Х
ТІМЕ	70'	60'	20 - 30 MIN	5'	SHOOTING	5'	2 HRS

# MATCH PROGRAM

MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY	SUNDAY	ARCHERS
13 September	14September	15 September	16 September	17 September	18 September	19 September	1. Damla GUNAY
Introductions	1.MATCH	1.MATCH	1.MATCH	1.MATCH	1.MATCH	1.MATCH	2. Neslihan CAKIROGLU
10.00-11.00	1B 5DP DamlaBEGUL	5P 6DP	5C 7DP	5B 2DP	1 7DP	1C 3DP	3. Selen OZKAYA
Madical		BEGUL- Selma	BEGUL- Zekiye	BEGUL- Neslihan	Damla- Zekiye	Damla - Selen	4. Zeynep ISIL SU UNAL
Medical Examinations	2.MATCH	2.MATCH 2C 1DP	2.MATCH 2P 6	2.MATCH 3C 6DP	2.MATCH	2.MATCH 2B 5DP	4. Zeynep 1511 50 ONAL
14.00-15.00	6B 2 SelmaNeslihan	Neslihan - Damla	2P 6 Neslihan- Selma	Scien- Selma	6C 4DP Selma- Zeynep	2B 5DP Neslihan- BEGUL	5. BEGUL LOKLUOGLU
	3.МАТСН	3.MATCH	3.MATCH	3.MATCH	3.MATCH	3.MATCH	6. Selma KAYA
	3P 4DP	7B 3	4C 1	4B 7	3B 5	6P 8DP	7. Zekiye KESKIN SATIR
	SelenZeynep	Zekiye -Selen	Zeynep - Damla	Zeynep- Zekiye	Selen- BEGUL	Selma- Aybüke	,,.
	4.MATCH	4.MATCH	4.MATCH	4.MATCH	4.MATCH	4.MATCH	8. Aybüke Aktuna
	7C 8 Zekiye- Aybüke	4P 8DP Zeynep- Aybüke	8P 3DP Aybüke -Selen	<b>8C 1DP</b> Aybüke -Damla	8B 2DP Aybüke -Neslihan	7P 4 Zekiye -Zeynep	9. Goktug Ergin
			•	-	•		
20 September	21 September	22 September	23 September	24 September	25 September	26 September	10. Fatih BOZLAR
1.MATCH	1.MATCH	1.MATCH	1.MATCH	1.MATCH	1.MATCH		11. Yusuf CORBA
9B 13DP	13P 14DP	13C   15DP	13B 10DP	9P 15DP	9C 11DP	-	12. Sermet INAR
			,				
2.MATCH	2.MATCH	2.MATCH	2.MATCH	2.MATCH	2.MATCH		13. Yagiz YILMAZ
14B 10	10C 9DP	10P 14	11C 14DP	14C 12DP	10B 13DP		14. Hasan ORBAY
3.MATCH	3.MATCH	3.MATCH	3.MATCH	3.MATCH	3.MATCH		15. Enes UGURLU
11P 12DP	15B 11	12C 9	12B 15	11B 13	14P 16DP		16. Burak BEYDILLI
							iv. Durak DE i DIELI
4.MATCH	4.MATCH	4.MATCH	4.MATCH	4.MATCH	4.MATCH		17. Osman ESKICI
15C 16	12P 16DP	16P 11DP	16C 9DP	16B 10DP	15P 12		

27 September	28 September	29 September	30 September	1 October	2 October		18 ibrahim Etem GULACAR
1.MATCH	1.MATCH	1.MATCH	1.MATCH	1.MATCH	1.MATCH	•	19 Talha GORUCU
17B 21DP	21P 22DP	ZIC I9DP	21B 18DP	17P 18DP	17C 19DP		20 Kerem KIRSEVER
2.MATCH 22B 18	2.MATCH 18C 17DP	2.MATCH 18P 22	2.MATCH 19C 22DP	2.MATCH 22C 20DP	2.MATCH 18B 21DP		21 Bugra ERBAY
							22 M. Sahin KARACAM
3.MATCH 19P 20DP	3.MATCH 23B 24	3.MATCH 20C 17	3.MATCH 20B 17	3.MATCH 19B 21	3.MATCH		23 Zehra Ece YİĞİTER
							24 Begunhan UNSAL
4.MATCH 23C 24	4.MATCH 20P 19DP	4.MATCH 24P 23DP	4.MATCH 24C 23DP	4.MATCH 24B 23DP	4.MATCH 23P 24		

LEGENDS





Picture 4. Winners receiving awards.

# Shooting platforms

As two archers shot together (face to face match), in order to resemble competition situation (one experimental and one dummy), a shooting platform having one real (for testing) and one dummy (looking like identical to testing one) system were constructed (Picture 5).



Picture 5. Testing (right) and dummy (left) platforms.

# **PSYCHOLOGICAL (Psychomotor) TESTS**

Competitive State Anxiety Inventory (CSAI) was used to analyze anxiety of the subjects prior to competition. (Martens, R., Burton, D., Rivkin, F. & Simon, J. (1980). Reliability and validity of the Competitive State Anxiety Inventory (CSAI). In C. H. Nadeau, W. C. Halliwell, K. M. Newell & G. C. Roberts (Eds.), *Psychology of motor behavior and sport - 1979* (pp. 91-99). Champaign, IL: Human Kinetics and Competitive Anxiety in Sport, Rainer Martens, Robin S. Vealey, Damon Burton, 1990 ISBN: 0873229355 ISBN13: 9780873229357) A multi channel recording device (Procomp+) was planned to be used to measure EMG, EEG and inspiration parameters during shooting. However, during pilot studies it was found out that, the archers did not feel comfortable and no devices with wires were attached or placed on the subjects and only telemetric heart rate monitor was used.

Below are the results of psychological analysis of interventions;

Pre and post test procedure was used to evaluate the possible effect of wearing heart rate monitor by CSAI-2. No significant difference was found between pre and post anxiety levels(Table 6).

a) Diazepam									
		Ν	Mean	SD	Sd	Т	р		
Cognitive Anxiety	Pre	23	15.91	3.50	22	.000	1.0		
	Post	23	15.91	3.69					
Somatic Anxiety	Pre	23	13.52	2.57	22	.794	.436		
	Post	23	13.17	2.37					
Self - confidence	Pre	23	29.57	4.388	22	-1.249	.225		
	Post	23	30.39	4.649					

# Table 6. Pre and Post T-test results

b) Placebo									
		Ν	Mean	SD	Sd	Т	р		
Cognitive Anxiety	Pre	23	16.13	3.32	22	120	.906		
	Post	23	16.17	3.68					
Somatic Anxiety	Pre	23	13.22	1.95	22	.134	.894		
	Post	23	13.17	2.29					
Self - confidence	Pre	23	30.61	4.26	22	292	.773		
	Post	23	30.78	4.45					

# c) Control

			() C01	111 01			
		Ν	Mean	SD	Sd	Т	р
Cognitive Anxiety	Pre	23	15.96	3.39	22	.749	.462
	Post	23	16.30	3.56			
Somatic Anxiety	Pre	23	13.26	1.86	22	1.098	.284
	Post	23	12.96	2.08			
Self - confidence	Pre	23	30.61	4.53	22	222	.826
	Post	23	30.74	4.59			

	Wilk's λ	F	р	η²
Groups (with and without heart rate monitor)	.957	2.005	.116	.043

# Table 7. 2x3 MANOVA test results

MANOVA (2x3) and (3x2x3) were used for analysis to find differences between conditions. Statistical analysis did not show any difference between two conditions (pre and post), state (diazepam, placebo and control) and psychological measurements (cognitive and somatic anxiety and self-confidence) (Table 7 and 8). Upon obtaining insignificant results, single analysis of variance (ANOVA) was then used to analyse the parameters and again, no difference was found for each parameter (Table 9).

	Wilk's λ	F	р	$\eta^2$
Pre and post capsule results	.991	.384	.765	.009
Groups(Diazepam-placebo-control)	.984	.358	.905	.008
Pre and post capsule X Grup	.996	.084	.998	.002

#### Table 8 3x2x3 .MANOVAtest results

# Table 9. ANOVA test results

a) Cognitive Anxiety					
		Mean	SD	F	р
Cognitive Anxiety	Placebo	16.152	3.46	.060	.936
	Diazepam	15.913	3.56		
	Control	16.130	3.46		

#### b) Somatic Anxiety ANOVA

b) Somale Imaley Into II					
		Mean	SD	F	р
Somatic Anxiety		13.1957		.142	.868
	Diazepam	13.3478	2.45		
	Control	13.1087	1.96		

# c) Self-Confidence ANOVA

		Mean	SD	F	р
Self - confidence	Placebo	30.696	4.31	.389	.678
	Diazepam	29.978	4.49		
	Control	30.674	4.51		

Turkish version of CSAI-2 was adopted and modified by Koruc (1998).

Psychometric characteristics of CSAI-2 Turkish Version are;

Original scale was translated with double back translation procedure and translation validities of subscales were .92 for cognitive anxiety, .92 for somatic anxiety and .95 for self confidence subscales.

Validity and Reliability: Cronbach Alpha Internal coefficients were between .74 and .89 for subscales. Testretest procedure was used for examining consistency of test in one month, two weeks and two days before competition period. Test retest correlations in one month were .96 for cognitive anxiety, .92 for somatic anxiety and .94 for self confidence subscales. In a two weeks period test retest reliabilities were .56, .67 and .54 respectively. In a two days period test retest reliabilities were .23, .22 and .32 respectively. Construct validity was tested by exploratory factor analysis. Items were gathering under three main factors and explained 78% of total variance.

# DETERMINATION OF BENZODIAZEPINE METABOLITE LEVELS IN URINE

Measurement of diazepam metabolite (desmethyldiazepam) levels in urine samples was carried out by using a GC/MS device and method was optimized and validated in this project. Urine sample was added 25 µl ISTD (codeine-d3, 25 µg/ml), 1 ml sodium acetate buffer (1.1 M, pH: 5.2) and vortexed on a vortex-mixer for 5 seconds. After addition of 50 µl β- glucuronidase/aryl sulphatase, the mixture wasl gently vortexed for 5 seconds, and then was hydrolyzed at a 55°C water bath in 2 hours. The mixture was cooled to the room temperature, and then 1 ml of ammonium chloride buffer (pH: 9.0) was added. After mixing on a vortex-mixer 1 g NaCI was added. After centrifugation at 2500 rpm for 5 minutes, upper phase was transferred to a clean tube, and then chloroform: isopropanol (80:20, v/v) mixture containing %2 NH<sub>3</sub> was added. The mixture was mixed on a vortex-mixer for 1 minute, centrifuged and lower phase was transferred to a clean tube. Then 20 µl of MBTFA was added and mixed on a vortex-mixer for 5 seconds, and then it was evaporated to the dryness under nitrogen flow. After 1 hour in desiccators under vacuum atmosphere, the sample was added to 100 µl MSTFA, and mixed for 10 seconds on a vortex-mixer, and then was derivatized on a heating block. Samples was cooled to the room temperature, then 20µl MBTFA was added and mixed for 10 seconds on a vortex-mixer. After derivatization in the heating block for 10 minutes, samples was cooled to the room temperature and injected to the GC/MS system. The method was validated for the requirements of EUROCHEM method validation Guideline and FDA Guideline for Bioanalytical Method Validation (The Fitness for Purpose of Analytical Methods A Laboratory Guide to Method Validation and Related Topics December 1998 and Guidance for Industry Bioanalytical Method Validation U.S. Department of Health and Human Services Food and Drug Administration May 2001).

The samples before drug administration and after shooting were analyzed and there was no benzodiazepine metabolite in urine samples before drug intake. Urine samples obtained from subjects who received 5 mg diazepam displayed desmethyldiazepam 5 min and 2 h after the completion of the competition (Table 10).

At least a 48 hour period was given in between competitive shooting after diazepam administration in order to wash out the substance that would affect the performance.

Subject		Desmethyldiazepam Levels in Urine (µg/ml)		
No.	Subject Name	After shooting		
		5 min	2hrs	
1	Selma Kaya	0,04	0,10	
2	Damla Günay	0,02	0,16	
3	Zekiye Kekin Satır	-	0,28	
4	Begül Lokluoğlu	-	0,25	
5	Zeynep Işıl Su İnal	0,03	0,21	
6	Selen Özkaya	0,01	0,12	
7	Aybüke Aktuna	0,37	0,18	
8	Göktüğ Ergin	0,03	0,25	
9	Fatih Bozlar	-	0,08	
10	Hasan Orbay	-	0,06	
11	Sermet İnar	-	0,09	
12	Yağız Yılmaz	0,03	0,21	
13	Buğra Erbay	0,02	0,19	
14	Yusuf Çorba	0,08	0,30	
15	Tigin Beydilli	0,06	0,16	
16	Osman Eskici	0,09	0,67	
17	Seyit Zor Karaçam	0,04	0,48	
18	Zehra Ece Yiğiter	0,01	0,12	
19	Enes Uğurlu	-	0,46	
20	Kerem Kırsever	0,12	0,61	
21	Begünhan Unsal	0,05	0,22	
22	Neslihan Çakıroğlu	0,02	0,30	
23	Talha Görücü	-	0,26	
24	İbrahim Etem Gülaçar	0,04	0,43	
	Mean	0,06	0,26	
	Standard deviation	0,02	0,12	

Table 10: Diazepam metabolite (Desmethyldiazepam) levels in urine after shooting

# 4. Results (including graphs/tables with legends, number of samples/replicates, statistical methods, error bars).

#### **Statistics**

Descriptive analysis of all parameters (shooting scores, RHR, SHR, MCRT, psychological test scores, aiming behaviour and mechanical values measured on force plate, effects of benzodiazepine) were tested using T-Test, Repeated Measure of ANOVA and MANOVA. SPSS program was used for statistical analysis and 0.05 level of confidence was taken into consideration.

#### Results

#### **Shooting scores**

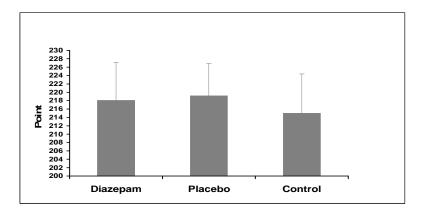


Figure 3. Archers' shooting scores (n = 24).

Shooting scores did not show any significant difference between the measurements F = 2.09; p > 0.05)(Figure 3). Thus, 5 mg diazepam administration did not affect shooting performance and other related performance components in archers.

#### **Resting heart rate values**

Resting heart rate values after taking benzodiazepine were similar in all measurements indicating that benzodiazepine has no effect (F = 0.082; p > 0.05) on heart rate (Table 11).

n = 22	HR (bpm)
Diazepam	$84.0 \pm 5.65$
Placebo	$83.6 \pm 11.11$
Control	$84.5 \pm 8.23$

#### Table 11. Resting heart rate

#### Heart rate during shooting

Despite the fact that benzodiazepine values presented slightly higher values for heart rate during shooting, there were no significant differences between three conditions F=2.59; p>0.05). Benzodiazepine did not cause any changes in heart rate during shooting (Table 12).

n = 22	HR (bpm)
Benzo	$113.1 \pm 12.2$
Placebo	$109.0 \pm 12.8$
~ .	
Control	$108.1 \pm 9.6$

#### Table 12. Heart rate during shooting

# Mechanical Clicker Reaction Time (MCRT)

Clicker reaction time values were not significantly different in all these three conditions (F = 0.23; p > 0.05)(Table 13).

n = 15	MCRT (s)
Diazepam	$0.1729 \pm 0.015$
Placebo	$0.1708 \pm 0.016$
Control	$0.1730 \pm 0.019$

# Table 13. Mechanical Clicker Reaction Time

# Aim point fluctuation

There were no difference between x and y axis displacement values prior to shooting during the aiming (for X axis F = 0.97; p > 0.05, for Y axis F = 1.32; p > 0.05) (Table 14).

Table 14. Aim point fluctuation around the target along X and Y
axis during aiming before shooting. (Mean ± SD).

n = 18	X axis	y axis
Diazepam	583,5 ± 278,0	535,6 ± 178,4
Placebo	605,2 ± 307,2	537,2 ± 174,5
Control	503,3 ± 152,5	478,2 ± 155,4

# Amount of changes in center of pressure

There were no difference in displacement values of front and rear feet between x and y axis (for front foot; x axis F = 3.07; p > 0.05, y axis F = 0.48; p > 0.05, for rear foot; x axis F = 0.85; p > 0.05, y axis F = 0.58; p > 0.05) (Table 15).

There were no difference in the velocity of center of pressure in x and y axis of the front and rear feet (for front foot; x axis F = 2.99; p > 0.05, y axis F = 2.12; p > 0.05, for rear foot; x axis F = 0.18; p > 0.05, y axis F = 0.33; p > 0.05) (Table 16).

		x axis (cm)	y axis (cm)
Front Foot	Diazepam	5.04 ± 2.38	1.68 ± 0.90
n = 17	Placebo	5.96 ± 2.63	$1.78 \pm 0.83$
	Control	$4.85 \pm 1.77$	$1.62 \pm 0.81$
Hind Foot n = 18	Diazepam	$4.35 \pm 1.84$	$1.25 \pm 0.47$
	Placebo	4.67 ± 1.94	$1.28 \pm 0.63$
	Control	$4.50 \pm 1.87$	$1.38 \pm 0.69$

# Table 15. Amount of changes in center of pressure in terms of distance along x and y axis on front and hind feet (Mean $\pm$ SD).

# Table 16. Amount of changes in center of pressure in terms of velocity along X and Y axis on front and hind feet (Mean $\pm$ SD).

		x axis (m.s <sup>-1</sup> )	y axis (m.s <sup>-1</sup> )
Front Foot n = 17	Diazepam	8.98 ± 4.21	2.76 ± 1.57
	Placebo	$10.96 \pm 4.89$	3.46 ± 2.19
	Control	8.89 ± 3.05	2.58 ± 1.31
Hind Foot n =18	Diazepam	$10.74 \pm 3.26$	3.82 ± 1.91
	Placebo	11.19 ± 2.84	3.61 ± 1.62
	Control	10.96 ± 3.26	3.51 ± 1.91

# 5. Discussion and conclusions.

It was hypothesised that benzodiazepines improve shooting performance in archery. However, after the completion of the study the hypothesis has been rejected. The hyphothesis were put forward to find an effect of benzodiazepine on shooting performance of archers, and hypothesising that there would be a positive effect on shooting performance components. However, the hypothesis were rejected.

The same applies to other performance related parameters like heart rate values, body sway, aiming behaviour, anxiety and clicker reaction time.

In fact, the latter findings can be considered supporting evidence for shooting performance indifferences.

Archery is a very specific sport discipline that relies on very individual differences. Previous studies have shown unique characteristics in aiming behaviour. Thus, anxiety may have effected differently and very individually to each subject and a general effect may have not been able to be shown.

# 6. Future plans.

- 1. The results will be shared with experts from other institutions working in the same field of interest and discussed the possible cooperation for future projects. Below issues may be questioned;
  - a. Study design
  - b. Dose
  - c. Subjects
- 2. The results will also be shared with International Shooting Federation for their opinion and suggestion.
- 3. The same setting may be used for testing the effect of other substances like beta blockers. This is another hot topic in archery and a project can be taken into account should there be an interest from International Federations, specifically from FITA.
- 4. Another substance, e.g. alprazolam which can be abused, may be taken into account for further research.

# 7. Expenditures incurred during the granting year

Project budget details are given in Item 12.

# 8. Publications/presentations related to the project, if applicable.

No publications were produced yet.

The results have not been presented by any means yet.

# 9. General conclusions.

The operation of the project was smooth and no major problems occurred.

Infrared beamer was a prototype and can be further developed for similar future studies.

Subjects' motivation for participating to this study was remarkable. Without their willingness, the results would have been questionable.

The amount of financial support from WADA was well projected.

The only unexpected problem was extending the schedule of the project due to an untimely illness of a key experimenter.

Any critics, opinions or suggestions would welcome from WADA.

# 10. Applicability for doping control and advantages over existing methods, if appropriate.

Project group is not in a position to propose to include benzodiazepine in the monitoring list since the results does not reveal any possible effect of the substance on athletic performance in the archery.

Literature will be closely followed by the project group in case any similar study showing different result than this one.

# 11. One page summary with Results and Conclusions to include in WADA's website.

It is well-known that athletes may experience some form of stress prior to or during a competition which may reduce or at least affect their athletic performance. Therefore, inhibition or reduction of stress may prove beneficial in athletes which can be easily achieved by utilizing an anxiolytic drug and benzodiazepines are the typical examples of these drugs. The purpose of the present study was to investigate whether the intake of a benzodiazepine would exert positive effects on physical performance capacity, such as an increase in shooting performance in elite archers. The research group has compared the effects of oral diazepam (5 mg) vs placebo. A randomized double-blind trial was used to assess shooting scores, heart rate values, body sway, aiming behaviour, anxiety and clicker reaction time in 24 athletes. The results did not show any difference between the groups, neither in physical performance characteristic nor in other parameters. It is concluded that as regards to the performance capacity, benzodiazepine use does not improve athletic performance in archery. However, the benzodiazepine was applied as a single relatively low dose (5 mg). Benzodiazepines exert calming effects with simultaneous reduction of anxiety at relatively low doses. These effects may be accompanied by some depressant effects on psychomotor and cognitive functions which were not observed in our study. Benzodiazepines, contrary to these depressant effects may also cause disinhibition of previously suppressed behaviour which may be related to their behavioural disinhibitory effects, including euphoria, impaired judgment, and loss of self-control which were also not observed in our study. Single-dose administration and selection of a moderate-low dose of a benzodiazepine derivative may explain why these disinhibitory effects are not observed in our study. It is well known that benzodiazepines also exert dose-dependent anterograde amnesic effects. Since benzodiazepines cause sedation and inhibition of motor activity in higher doses, they are expected to negatively affect motor performance in athletic competitions requiring fine tuning skills.

Date		CHF (Swiss Franc)
16.05.2008	Interface for computer	2.100,03
25.07.2008	Desmethyldiazepam + analytical colon	2.856,43
22.01.2010	Infrared laser beam	2.437,08
18.03.2010	Sensor Benzo Project 792.96€	1.179,21
16.09.2010	Accomodation of subjects Benzo Proj 9,500\$	10.031,05
21.09.2010	Cartridges+ext hard disc Benzo (347.51€)	476,16
21.10.2010	Petrol+meals + catering for experimenters Benzo Proj $(1,278.42\varepsilon)$	1.684,70
		20.764,66
Expenses	Summary	
	Amount	
Date	CHF	USD
2008	4956,46	4657,014
2009	0	0
1 January 22 November 2010	15808,2	14823,89
Total	20764,66	19480,90
Balance		+ 519,09

## 12. Overall financial summary covering years of grant