

The Effect of 400 mg of Caffeine on Untrained Subjects Performance of Simulated Ocular Microsurgery

Jack Henderson*, Andreas Katsimpris, Frederick Burgess and Andrew J Tatham

Department of Ophthalmology, Princess Alexandra Eye Pavilion, University of Edinburgh, Edinburgh, UK

*Corresponding author: Jack Henderson, Department of Ophthalmology, Princess Alexandra Eye Pavilion, University of Edinburgh, Edinburgh, UK, Tel: +441315361628; Fax: +441315363897; E-mail: jackhenderson1996@hotmail.co.uk

Received date: November 20, 2016; Accepted date: December 22, 2017; Published date: December 29, 2017

Copyright: ©2017 Henderson J, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Objective: To investigate the effects of 400 mg of caffeine ingestion on previously untrained students' performance on simulated microsurgical tasks.

Methods: 10 previously untrained students were included and randomised into two groups: a control or caffeine group. Each group received a 15-min orientation session on a microsurgical simulator (VRMagic eyes surgical simulator, Mannheim, Germany). Each group then performed three repetitions of each task: a navigation task, a forceps task and a bimanual task. The control group repeated the testing sequence after a 30-min break. The caffeine group orally ingested 400 mg of caffeine and 30 min later repeated the same sequence. An ECG was performed on the caffeine group before and after caffeine ingestion to assess for arrhythmia. Overall score (%) was the primary outcome. Secondary outcomes included odometer (mm), time taken (s) and injured cornea and lens area (mm²).

Results: 10 subjects fulfilled all inclusion criteria. Mean age was 22.42 ± 0.92 years old. 4 subjects were male, 6 were female. 9 were right handed and 1 was left handed. The learning curve effect was significant and varying across subjects. There was no significant difference between baseline testing parameters of the two groups. There was no significant difference between the overall performance of the caffeinated and control groups. The control group did however complete the navigation and forceps tasks faster than the caffeine group. A reduction in the heart rate of the caffeine group was observed after caffeine dose.

Conclusion: Our results show no significant change of simulated microsurgical ability after 400 mg of caffeine ingestion.

Keywords: Caffeine; Simulated microsurgery; ECG; Microsurgical tasks; VR magic eyes

Introduction

Ophthalmological surgical training has historically been a challenge. The recent advancements in simulation technology have opened new solutions in this field; eye surgery simulators use computerised graphic displays and accurate sensors to mimic eye surgery that allow ophthalmologists of all experience levels to enhance their surgical skills before using them in the operating room. The Royal College of Ophthalmologists currently detail surgical simulation an "essential" component in the training curriculum [1] and details 16 centres across the UK with this technology.

The concept of a learning curve was first described in aircraft manufacturing to describe how performance improved with time and experience, with productivity increasing as a result [2]. The learning curve is especially significant in surgical training as it is important to know how many procedures a surgeon must perform to become safe and competent. Simulators allow surgeons to overcome the learning curve of completing new tasks in a controlled environment without jeopardising patient safety [3]. Furthermore, simulators identically replicate tasks and produce quantitative measures of the simulated surgical process, for example, time to complete a task or area of

surrounding tissue damage; meaning their use in a research setting can be useful.

External factors such as distractions, drugs and fatigue have the potential to influence surgical ability and ultimately patient safety. The use of caffeine as a stimulant is common in surgeons; one study of 95 [1] surgeons found that 66.8% reported drinking caffeinated coffee, with the most common reasons for doing so being: 'to reduce fatigue', 'night-shift working' or 'working long hours' [4]. Antagonising the A1 and A2 adenosine receptors, caffeine acts by promoting the effects of the sympathetic nervous system [5] and reaches a peak plasma concentration after 30-60 min of ingestion [6,7]. Caffeine ingestion impacts individuals differently; however tremor and restlessness are established side effects, making its common use in a microsurgical setting debatable. Despite some surgeons actively avoiding caffeine before operating, previous small studies which analysed its effect on simulated eye surgery have shown no conclusive correlation [8-10].

In this study, we aim to investigate the association between 400 mg of caffeine intake and the simulated microsurgical performance of subjects who have no previous experience on simulated microsurgical tasks. The 400 mg caffeine dosage used in this study is the maximum recommended daily caffeine ingestion in the UK, and contains the caffeine equivalent of 2-4 large cups of caffeinated coffee [11].

Methods

This was a prospective randomised study of 10 fourth year students recruited from the University of Edinburgh, Edinburgh, Scotland. The study methods, which adhered to the tenets of the Declaration of Helsinki, were prospectively approved by University of Edinburgh

Ethics Committee. Written informed consent was obtained prospectively from all participants. Surgical simulation was performed using the VRMagic eyesi Surgical Simulator (VRMagic, Mannheim, Germany), the most commonly available ocular microsurgery simulator in the United Kingdom.

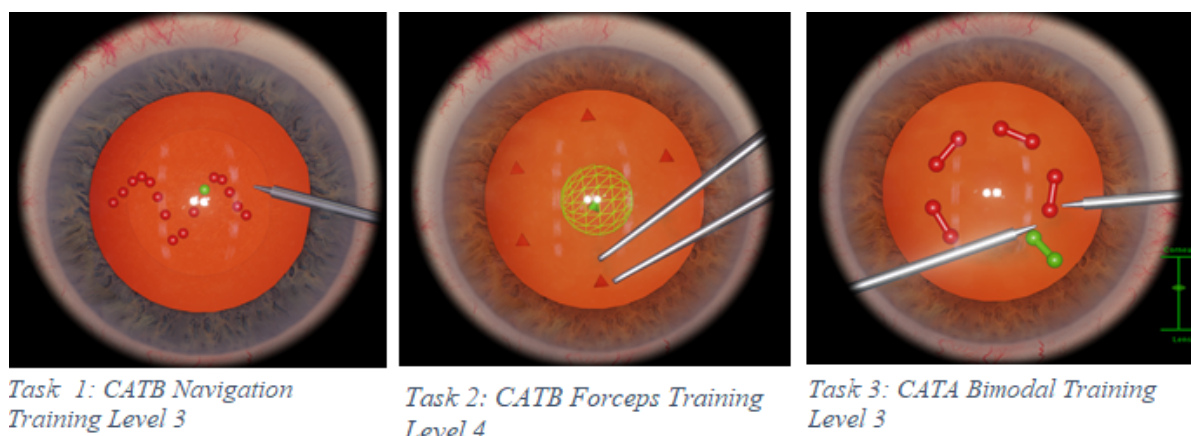


Figure 1: Screenshots showing each of the simulated tasks.

All subjects had no previous experience of microsurgery, and all had good corrected visual acuity in both eyes with normal stereoscopic vision. Exclusion criteria included any history of tremor disease, cardiovascular or neurological disease, or limitation of upper limb function. All subjects abstained from caffeine and alcohol the day before testing. Testing commenced with a short standardised 15-min period of supervised demonstration of the surgical simulator, allowing subjects to become familiar with its operations. Three tasks were selected for the assessment: 1) A navigation task (CATB Navigation Training Level 3) which required subjects to utilise an instrument to turn 16 intraocular red spheres to green spheres. 2) A forceps task (CATB Forceps Training Level 4) which involved subjects using forceps to grab and drag 6 intraocular triangular objects into a central sphere area. 3) A bimodal task (CATA Bimodal Training Level 3) which required subjects to bimanually use two instruments to turn 5 bipolar red objects to green. Screenshots from the tasks are shown in Figure 1.

Following the initial demonstration, all subjects were required to complete the 3 simulated surgical tasks, with each task repeated 3 times (first set) in the order of: 3 x navigation task, 3 x forceps task, 3 x bimodal task for each set. This was followed by a rest period of 30 min to reduce the impact of fatigue before the second repetition with each task completed a further 3 times (second set). Subjects were randomised to a control group or to a group that completed the second set of tests 30 min after consuming 400 mg of caffeine (caffeine group). Caffeine was ingested orally in the form of 8 50 mg tablets. For safety reasons, subjects in the caffeine group received a 12 lead ECG before and 1 h after caffeine consumption to screen for arrhythmia; ECG parameters were analysed. The average half-life of caffeine is 4 h [12], therefore caffeine group subjects were observed for this length of time after consumption to screen for adverse side effects. A summary of the assessment process is shown in Figure 2.

Surgical ability was assessed using several simulator-generated outcomes. The primary outcome was overall score percentage, with

100% indicating a perfect score. Secondary outcomes included the time taken to complete each task; odometer (distance in mm travelled by the instrument(s) within the anterior chamber); and tissue injury to the cornea or lens caused by contact of instruments with internal eye structures (measured as mm² of injury).

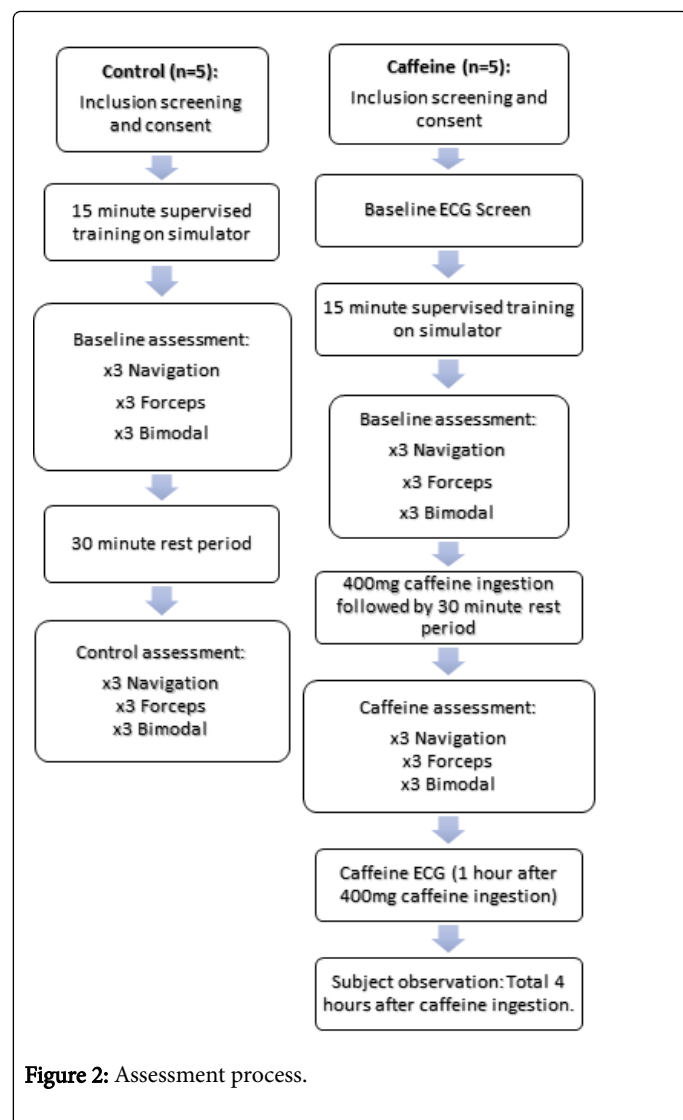
Statistical analysis

Learning curves have a slope representing the rate of learning that is likely to eventually plateau, however the shape of learning curves may be very different between individuals making statistical comparisons difficult. Learning curves for each subject were therefore displayed graphically for each task (Navigation, Forceps and Bimodal) and each outcome variable (overall score, time, odometer and tissue injury) in figures 3-5. Performance in the first 3 baseline repetitions was averaged and compared to performance in the second 3 repetitions for each task. The primary outcome was to compare overall score performance between control subjects and those taking caffeine based on the average of three tasks performed after minimising learning effect (Figures 6 and 7).

ECG changes were analysed using paired t-tests (95% CI) comparing ECG produced parameters between individuals at baseline and 1 h after 400 mg caffeine ingestion.

Results

11 previously untrained students who fulfilled inclusion criteria and consented were enrolled in the study. One subject in the caffeine group was excluded at ECG testing due to the finding of an arrhythmia. Of the remaining 10 subjects, the mean age was 22.42 ± 0.92 years old. 4 subjects were male, 6 were female. 9 were right handed and one was left handed.



There was no significant difference in baseline performance across all parameters between the control and caffeine groups (Table 1). After caffeine ingestion, there was also no significant difference in overall test performance between the control and caffeine groups for each task (Table 2). The control group did however complete the navigation and forceps tasks faster than the caffeine group (Table 2). The caffeine group had a non-significant higher performance in the bimodal task than control across overall score, odometer and injured cornea area parameters (Table 2). However, overall the caffeine group had a non-significant reduced performance compared to control on forceps task for odometer, injured lens area and overall score (Table 2).

There was no significant difference between control and caffeine improvement in performance between the first and second testing sets (Table 3). No adverse side effects were recorded in the caffeine group. Analysis of the ECG findings was performed on the 5 subjects in the caffeine group. The control group were not tested for comparison.

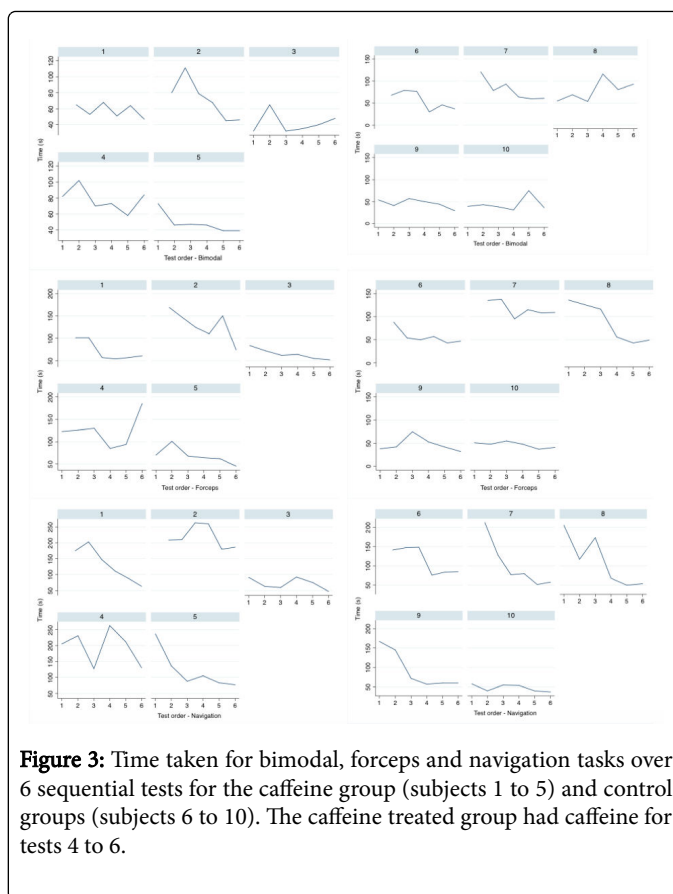


Figure 3: Time taken for bimodal, forceps and navigation tasks over 6 sequential tests for the caffeine group (subjects 1 to 5) and control groups (subjects 6 to 10). The caffeine treated group had caffeine for tests 4 to 6.

At baseline, the average heart rate was 77 ± 8.6 beats per minute (BPM). One hour after 400 mg caffeine ingestion, this reduced to 67.6 ± 11.5 BPM. This reduction in heart rate was significant ($p < 0.01$). Other ECG changes were not significant.

Discussion

Caffeine is believed to be the most widely consumed psychoactive drug in the world [12]. Naturally present at varying concentrations as a xanthine derivative in coffee and tea, caffeine has multisystem effects including: cardiovascular, respiratory, endocrine, gastrointestinal and central nervous system [13]. Caffeine's nervous system effects are known to include an increase in arousal, vigilance and reduced reaction times [13]; considered by some as performance enhancing qualities in a surgical environment. However, caffeine's effects are known to be dose dependent, with previous studies suggesting at concentrations that vary between individuals, side effects such as tremor, restlessness and anxiety become present [14,15]: qualities unwanted in the operating room. This study found no significant translation of these potential effects of caffeine on microsurgical performance. However, it is possible that some of the unwanted side effects of caffeine contributed to the caffeine group completing two of the three tasks slower on average than control.

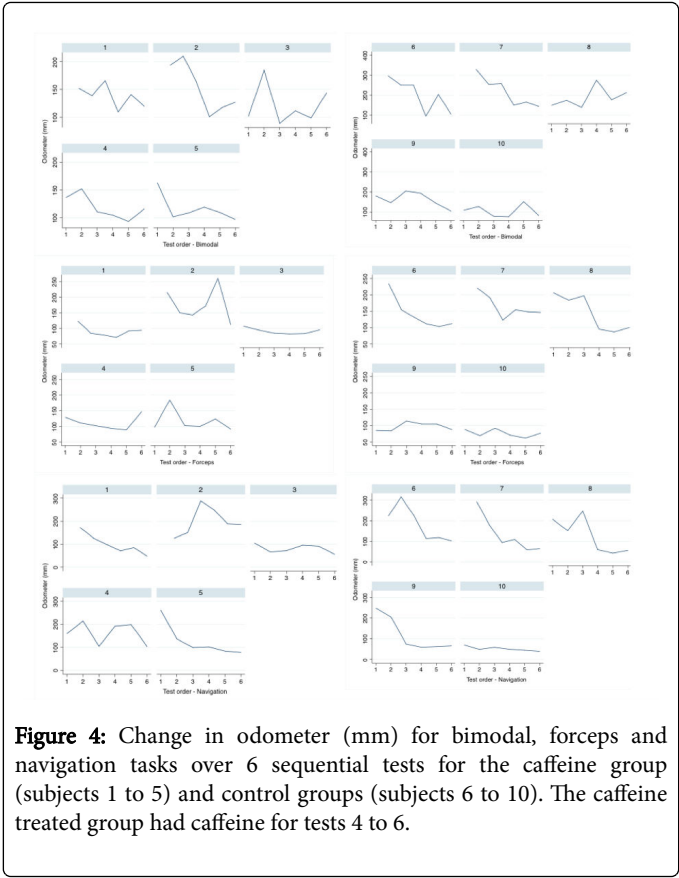


Figure 4: Change in odometer (mm) for bimodal, forceps and navigation tasks over 6 sequential tests for the caffeine group (subjects 1 to 5) and control groups (subjects 6 to 10). The caffeine treated group had caffeine for tests 4 to 6.

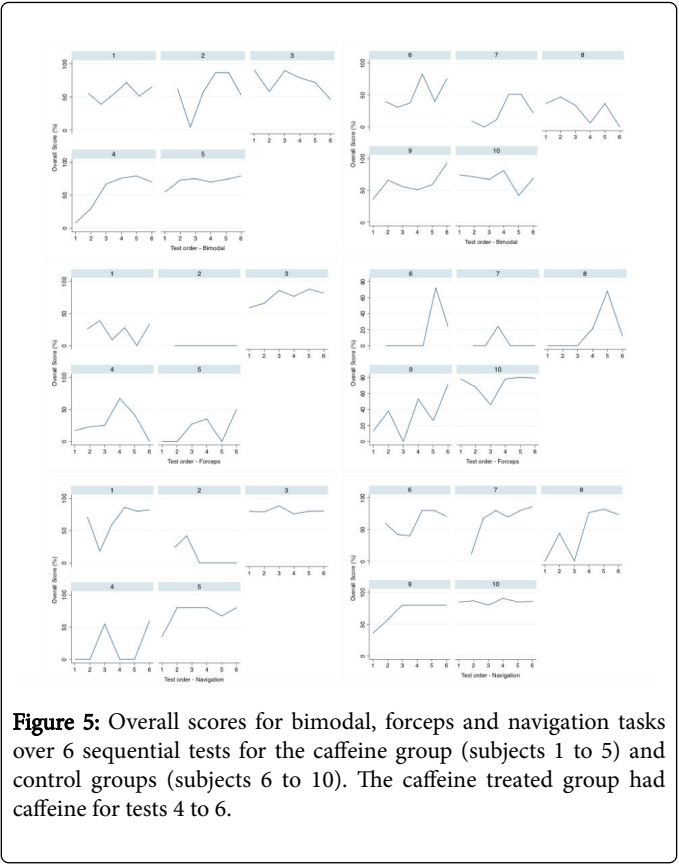


Figure 5: Overall scores for bimodal, forceps and navigation tasks over 6 sequential tests for the caffeine group (subjects 1 to 5) and control groups (subjects 6 to 10). The caffeine treated group had caffeine for tests 4 to 6.

	Control group (n=5)	Caffeine group (prior to caffeine) (n=5)	P-value (Wilcoxon rank sum)
Task 1-Navigation			
Time (s)	167 (141 to 205)	205 (175 to 209)	0.40
Odometer (mm)	224 (208 to 249)	160 (126 to 172)	0.35
Injured cornea (mm ²)	0 (0 to 1.7)	0 (0 to 0.5)	0.64
Injured lens (mm ²)	0	0	NA
Overall score (%)	36 (11 to 60)	35 (24 to 71)	1.00
Task 2-Forceps			
Time (s)	88 (51 to 135)	101 (84 to 123)	0.60
Odometer (mm)	206 (88 to 220)	123 (107 to 129)	0.75
Injured cornea (mm ²)	10.9 (1.5 to 12.4)	2.3 (1.8 to 13.5)	0.83
Injured lens (mm ²)	4.5 (3.1 to 6.9)	8.4 (3.4 to 8.9)	0.25
Overall score (%)	0 (0 to 13)	17 (0 to 26)	0.58
Task 3-Bimodal			
Time (s)	55 (54 to 68)	73 (65 to 80)	0.60
Odometer (mm)	180 (149 to 297)	152 (137 to 163))	0.35

Injured cornea (mm ²)	0.3 (0 to 1.4)	0	0.41
Injured lens (mm ²)	0	0	NA
Overall score (%)	37 (36 to 40)	55 (55 to 62)	0.35

Table 1: Baseline performance using microsurgical simulator for control and caffeine groups based on the first test performed. Results show median (interquartile range).

	Control group (n=5)	Caffeine group (after caffeine) (n=5)	P-value (Wilcoxon rank sum)
Task 1-Navigation			
Time (s)	59 (57 to 63)	88 (87 to 202)	0.02
Odometer (mm)	62 (53 to 78)	87 (81 to 165)	0.08
Injured cornea (mm ²)	0 (0 to 0.1)	0 (0 to 0.1)	0.91
Injured lens (mm ²)	0	0	NA
Overall score (%)	79 (78 to 80)	76 (20 to 79)	0.21
Task 2-Forceps			
Time (s)	49 (42 to 49)	57 (57 to 111)	0.045
Odometer (mm)	99 (94 to 109)	105 (87 to 110)	0.75
Injured cornea (mm ²)	3.6 (1.5 to 3.9)	3.4 (1.7 to 5.3)	0.60
Injured lens (mm ²)	1.6 (1.4 to 2.6)	2.8 (1.8 to 4.4)	0.25
Overall score (%)	34 (32 to 50)	28 (21 to 36)	0.68
Task 3-Bimodal			
Time (s)	47 (41 to 62)	53 (41 to 54)	0.83
Odometer (mm)	147 (135 to 153)	115 (109 to 118)	0.12
Injured cornea (mm ²)	0.19 (0 to 2.2)	0	0.09
Injured lens (mm ²)	0	0	NA
Overall score (%)	64 (41 to 66)	74 (66 to 75)	0.12

Table 2: Comparison of average of final three tests for control and caffeine group, i.e. the three tests after the caffeine dose for the caffeine group.

	Control group (n=5)	Caffeine group (after caffeine) (n=5)	P-value (Wilcoxon rank sum)
Task 1-Navigation			
Time (s)	108 (59 to 148)	20 (3 to 88)	0.25
Odometer (mm)	155 (112 to 187)	41 (-5 to 104)	0.08
Injured cornea (mm ²)	0 (0 to 1.5)	0 (-0.1 to 0.5)	0.28
Injured lens (mm ²)	0	0	NA
Overall score (%)	-44 (-68 to -17)	-12 (-20 to 1.3)	0.12

Task 2-Forceps			
Time (s)	24 (9 to 39)	27 (13 to 44)	0.75
Odometer (mm)	71 (18 to 112)	20 (19 to 34)	0.46
Injured cornea (mm ²)	6 (0 to 9)	-0.2 (-3 to 0.1)	0.17
Injured lens (mm ²)	3 (-0.3 to 4.3)	1 (0.6 to 5)	0.60
Overall score (%)	-32 (-34 to -1)	-19 (-23 to 0)	0.21
Task 3-Bimodal			
Time (s)	13 (-8 to 30)	11 (10 to 27)	0.92
Odometer (mm)	33 (5 to 162)	32 (28 to 54)	0.75
Injured cornea (mm ²)	0 (-0.2 to 0.2)	0	0.83
Injured lens (mm ²)	0	0	NA
Overall score (%)	-26 (-32 to 10)	-14 (-19 to -8)	0.75

Table 3: Difference in performance for control and caffeine groups (average of second set minus baseline assessment).

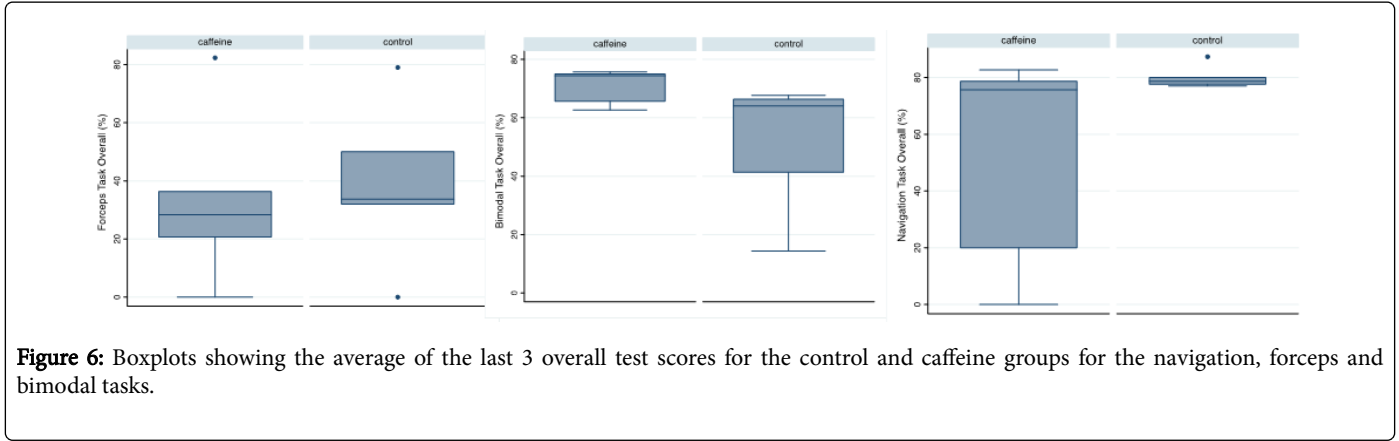


Figure 6: Boxplots showing the average of the last 3 overall test scores for the control and caffeine groups for the navigation, forceps and bimodal tasks.

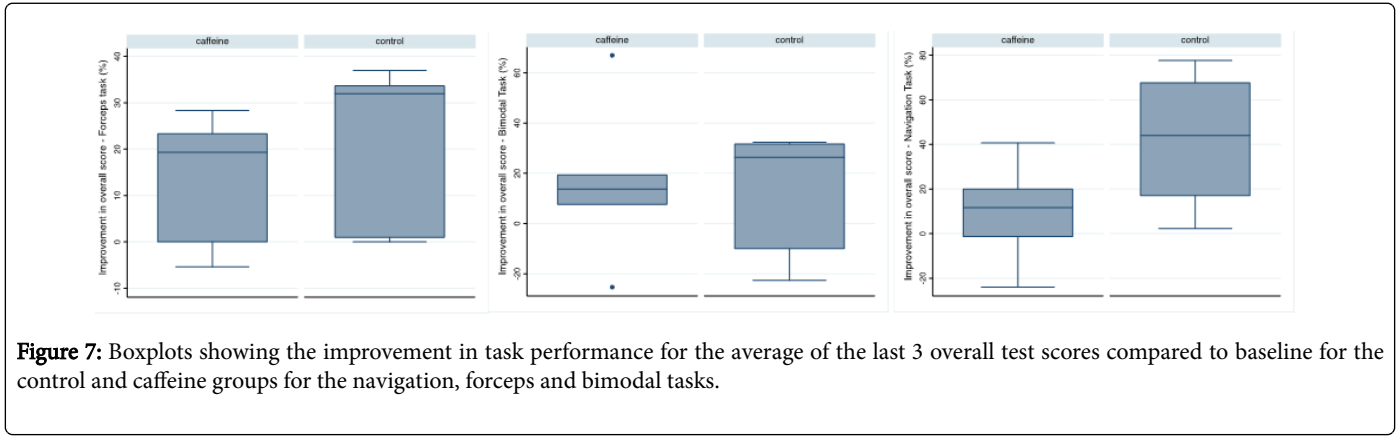


Figure 7: Boxplots showing the improvement in task performance for the average of the last 3 overall test scores compared to baseline for the control and caffeine groups for the navigation, forceps and bimodal tasks.

The small sample size (n=5) of this study's ECG findings supports other investigations which show a transient reduction in heart rate and increase in blood pressure at high caffeine doses (>150 mg/person) [16-18]. Interestingly, other studies do not elicit this cardiovascular response at lower doses of caffeine [6,10]. At an individual's caffeine threshold, it is hypothesised that enough adenosine receptors are

antagonised that blood pressure increases through a combination of stimulation of the myocardium, vascular tone, sympathetic nervous system and activation of the renin-angiotensin system [18]. According to the Frank-Stirling mechanism, this increase in blood pressure consequently causes a reduction in heart rate, as potentially demonstrated in this study. Although it is unlikely that these

cardiovascular pharmacological effects of caffeine are clinically significant for microsurgeons, they may be involved in the more important central nervous system effects of this drug.

Caffeine may improve concentration and reduce reaction times; however, it may also have an impact on dexterity and fine motor precision. This study has not statistically shown that a large 400 mg dose of caffeine is detrimental for performance enhancing in a microsurgical setting in untrained subjects. However, the action of caffeine is dosage dependent and its effects impact individuals differently, thus its usage in surgeons performing microsurgery should continue to be carefully considered at an individual level.

Limitations

Emphasis should be placed on the primary outcome of overall score as this study was limited by inclusion of a relatively small number of subjects, therefore there is the possibility of falsely rejecting or accepting the null hypothesis by chance. Furthermore, the stability of learning curves does not equate to competency as subject's surgical ability appeared to plateau at different stages. Caffeine inherently is an active drug that affects individuals differently, however this study did not account for tolerance nor compensate for subject's normal caffeine consumption. In addition, subject performance after caffeine ingestion could have been impacted by the placebo effect.

Disclosure

A.J.T speaking honorarium and travel support from Allergan and Heidelberg Engineering. Travel support from Santen and Thea. The remaining authors declare no conflict of interest.

References

1. Simulation Group of Education Committee (2014) Surgical Skills Simulation: for the curriculum. Royal College of Ophthalmologists.
2. Wright TP (1936) Factors affecting the cost of airplanes. *J Aeronautical Sci* 3: 122-128.
3. Khan N, Abboudi H, Khan MS, Dasgupta P, Ahmed K, et al. (2014) Measuring the surgical 'learning curve': methods, variables and competency. *BJU Int* 113: 504-508.
4. Franke GA, Bagusat C, McFarlane C, Tassone-Steiger T, Kneist W, Lieb K et al. (2015) The use of caffeinated substances by surgeons for cognitive enhancement. *Ann Surg* 261: 1091-1095.
5. Ludwig IA, Mena P, Calani L, Cid C, Del Rio D, et al. (2014) Variations in caffeine and chlorogenic acid contents of coffees: what are we drinking? *Food Funct* 5: 1718-1726.
6. Cano-Marquina A, Tarín JJ, Cano A (2013) The impact of coffee on health. *Maturitas* 75: 7-21.
7. Shirlow MJ, Mathers CD (1985) A study of caffeine consumption and symptoms: indigestion, palpitations, tremor, headache and insomnia. *Int J Epidemiol* 14: 239-248.
8. Ahmad H, Ahmad R, Pointdujour M, Liu E, Smith F, et al. (2010) The Effect of Caffeine and Beta Blockade on Surgical Performance Using the EYESi VRMagic Anti-Tremor, Forceps and Capsulorhexis Surgical Simulator Modules in Experienced vs. Novice Surgeons. *Invest Ophthalmol Vis Sci* 51: 5439.
9. Koenigsman H, Troupe J (2012) The Objective Measure Of The Effects Of Caffeine And Caffeine Withdrawal On Microsurgical Skills Using The Eyesi Simulator Module For Anterior Segment Surgery. *Invest Ophthalmol Vis Sci* 53: 6728.
10. Arriola-Lopez A E, Morales-Canton V, Garcia-Aguirre G, Salcedo-Villanueva G, Dalma-Weiszhausz (2016) Effect of caffeine intake on retinal microsurgical performance. *J Clin Exp Ophthalmol* 7: 581.
11. ProPlus® Caffeine Information Leaflet (2001), United Kingdom.
12. Cappelletti S, Daria P, Sani G, Aromatario M (2015) Caffeine: Cognitive and Physical Performance Enhancer or Psychoactive Drug. *Curr Neuroparmacol* 13: 71-88.
13. Benowitz NL (1990) Clinical Pharmacology of Caffeine. *Annu Rev Med* 41: 277-88.
14. Kaplan GB, Greenblatt DJ, Ehrenberg BL, Goddard JE, Cotreau MM, et al. (1997) Dose-Dependent Pharmacokinetics and Psychomotor Effects of Caffeine in Humans. *J Clin Pharmacol* 37: 693-703.
15. James JE (1991) Cardiovascular system: Caffeine and Health, Academic Press, London, 96-138.
16. Green P J, Kirby R, Suls J (1996) The effects of caffeine on blood pressure and heart rate: a review. *Ann Behav Med* 18: 201-216.
17. Myers MG (1988) Effects of caffeine on blood pressure. *Arch Intern Med* 148: 1189-1193.
18. Robertson D, Frölich JC, Carr RK, Watson JT, Hollifield JW, et al. (1978) Effects of Caffeine on Plasma Renin Activity, Catecholamines and Blood Pressure. *N Engl J Med* 298: 181-186.