

## Effect of Caffeine Intake on Retinal Microsurgical Performance

Andrea Elizabeth Arriola-Lopez<sup>1\*</sup>, Virgilio Morales-Canton<sup>1</sup>, Gerardo Garcia-Aguirre<sup>1,2</sup>, Guillermo Salcedo-Villanueva<sup>1</sup>, Jose Dalma-Weiszhausz<sup>1</sup> and Raul Velez-Montoya<sup>1,2</sup>

<sup>1</sup>Asociación Para Evitar la Ceguera en Mexico I.A.P. "Hospital Dr. Luis Sanchez Bulnes", Retina Department, Mexico City, Mexico

<sup>2</sup>Macula Retina Consultores, Mexico City, Mexico

\*Corresponding author: Andrea Elizabeth Arriola-Lopez, Vicente Garcia Torres No. 46, Barrio San Lucas, Delegación Coyoacan, CP 04100, Mexico, Tel: +52.55.1084.1400. (ext 1172); Fax: +52.55.1084.1404; E-mail: [aearriola7@gmail.com](mailto:aearriola7@gmail.com)

Received date: May 20, 2016; Accepted date: July 27, 2016; Published date: July 29, 2016

Copyright: © 2016 Arriola-Lopez AE, 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 assess the effects of prior caffeine intake on tremor control and internal limiting membrane peeling proficiency of experienced retinal surgeons using a microsurgical simulator.

**Methods:** Experienced vitreoretinal surgeons were included. On two separate days, each subject underwent a test on a level 4 anti-tremor test and internal limiting membrane peeling test on a microsurgical simulator (Eye-Si/ Series 199, VRMagic, Software 2.9, Mannheim, Germany) first with no caffeine intake and after 40 minutes of taking an oral dose of caffeine (200 mg and 400 mg). Each subject underwent blood pressure and heart rate measurements before and 40 min after caffeine intake. The same technician measured both surgical performances.

**Results:** Mean age was  $46.4 \pm 10.1$  years. All subjects were male. The mean anti-tremor results were: baseline scores  $61.2 \pm 19.15$ , 200 mg  $61.6 \pm 12.63$  and 400 mg  $75.4 \pm 15.09$ . The mean internal limiting membrane peeling results were: baseline score  $55.9 \pm 5.46$ , 200 mg  $54.8 \pm 10.05$  and 400 mg  $62.6 \pm 9.63$ . Blood pressure and heart rate remained stable. After consumption of higher doses of caffeine some adverse effects were reported such as headache and a transient episode of anxiety.

**Conclusion:** Caffeine consumption prior to surgery is discouraged by microsurgeons due to potential adverse effects. Our results showed no significant change on the surgical ability after 200 and 400 mg of oral caffeine. There was a non-significant improvement on the overall score after 400 mg.

**Keywords:** Caffeine; Microsurgery; Retina; Simulator; Tremor; Dexterity; Performance

### Background

Caffeine is one of the most widely consumed behaviorally active substances in the world. It mainly acts upon the central nervous system, with widely known physiological and psychological effects (increased alertness, enhanced vigilance, reduced fatigue) [1-6]. All its effects are through the antagonism of the A1 and A2 subtypes of the adenosine receptor, potentiating the effects of sympathetic nervous system stimulation [6].

However, there are negative aspects of caffeine intake: a high dose can result in a state of excitement and anxiety including adverse reactions like tachycardia, headache, palpitations, insomnia, restlessness, nervousness, and tremor. Dose response and tolerance to regular consumption vary between individuals; so, for some people, even a single cup may cause sleeplessness with a racing mind, while for others, drinking ten times this amount can still be pleasant and not interfere with sleep [6]. Caffeine has a half-life of approximately 4-6 h, with a plasma peak time concentration following its ingestion between 30-60 minutes (average 40) [7].

Microsurgeons may choose to avoid caffeine to prevent potentially deleterious caffeine-induced tremor and a possible detrimental effect

on surgical performance, despite the fact that an adverse effect on surgical skills has never been shown [8].

Simple simulators, or "box trainers" emerged and facilitated the development of surgical skills, and the surgeons who practiced with box trainers or simulators arrived to the operating room with greater skill, with shorter learning curves. In the area of ophthalmology, the Eye-Si (Eye-Si/Series 199, VRMagic, Software 2.9, Mannheim, Germany) has been scientifically validated for most ophthalmologic microsurgical tasks; novices perform worse than experts who already have the skill that is to be taught on the simulator [9-11]. A direct correlation has been found between surgical experience and the performance of the navigation task. Surgical experience was associated with fewer retinal contacts per average time and shorter membrane peeling time, indicating that training results in better surgical skills and that the vitreoretinal surgical simulator has the potential to evaluate specific surgical skills that are training-related. The Eye-Si simulator also has the capability of training surgeons in new techniques and has the potential to model and simulate surgical scenarios to assist surgeons defining strategies before human intervention [12].

In this study, we aimed to investigate the association between caffeine intake and microsurgical performance by having experienced retinal surgeons perform standardized tasks in a microsurgical simulator under different doses of caffeine (0 mg, 200 mg and 400 mg).

## Design

Cross sectional and interventional study.

Carried out in Asociación para Evitar la Ceguera en México, Hospital "Luis Sánchez Bulnes", University hospital.

## Participants or samples

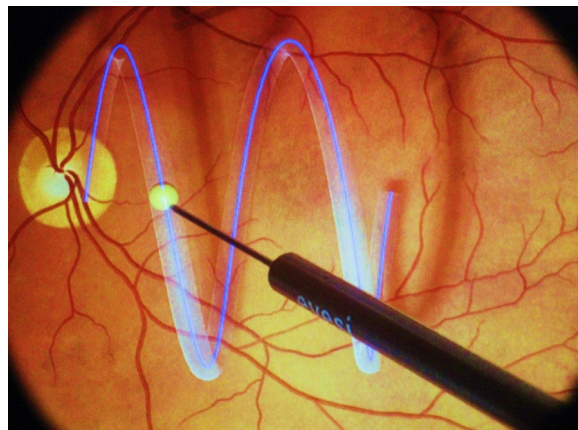
Vitreoretinal surgeons with at least 5 years of experience, female/male, without previous consumption of any form of caffeine (at least 6 hours) and any associated motor pathology (e.g. Parkinson, Corea, Arthritis), exercise or prior performance of intraocular surgery.

## Methods

The study was conducted on a single center. The study was approved by the local institutional review board and was conducted according to the tenets of the declaration of Helsinki and good clinical practice guidelines. All sensitive data were handling according to the Health Insurance Portability and Accountability act of 1996 and its Mexican counterpart: the Federal law for Protection of Personal Data in Possession of Individuals (NOM-024-SSA3-2010). All participants signed an informed consent form prior to enrollment. Vitreoretinal surgeons with at least five years of experience after completion of fellowship were included in this study. A validated retinal microsurgical simulator (Eye-Si Series 199, VRMagic, Software 2.9, Mannheim, Germany) was used. The simulator platform provides a virtual operating microscope, a model eye and handheld probes (cut-suction probe, light probe, forceps, diamond-dusted scraper) that are inserted into the model eye. The simulator generates a virtual stereoscopic image through the oculars, and provides several different modules with different levels of difficulty (in the vitreosurgical module: one to four from easiest to most difficult). The simulator calculates a performance score between 0 and 100 for each interaction and gives metrics providing feedback on microscope handling, tissue treatment, target achievement, efficiency and instrument handling. All subjects underwent a level 1 test-run simulation that was not graded, in order to become familiarized with the instruments and images provided by the simulator. The simulations performed by each subject were:

**Anti-Tremor Test Level 4:** A spiral trajectory is displayed inside the vitreous. A sphere marks the starting point of the trajectory. The

sphere turns green when the instrument tip is within the sphere. Then the surgeon guides the sphere along the trajectory to the end point. The sphere will follow the instrument tip as long as the tip of the instrument is inside the sphere. The goal is to train manual dexterity, learn how to perform accurate movements and reduce tremor (Figure 1).



**Figure 1:** Antitremor test level 4. The Sphere travels through the spiral only when the tip is touching the center. Once it started moving, the surgeon must keep the tip on the center at all times while "pushing" it, following the spiral pathway. If the tip loses the center, the sphere will change color to red and the sphere will not move further, until the tip touches the center again. The software takes away points, if the tip loses the center, if the exercise last too long and if the instrument is pulled out of the simulated eye.

**ILM-Peeling Test Level 4:** The internal limiting membrane (ILM) has to be removed. The ILM shows as a lightly ICG-stained surface membrane. The goal is to create a flap, with a strong adherent ILM that fragments easily. ILM should be peeled with end-gripping forceps on a circular fashion. Training goal is to control the movements of instruments inside the eye (Figure 2).



**Figure 2:** Internal limiting membrane-peeling test level 4. Left, creating the flap. Right, peeling the membrane with the forceps. The surgeon will be qualified according to the amount of ILM left after the exercise, the amount and extension of the retina damage/bleeding and the time needed for completion of the exercise.

On a random day, having abstained from caffeine for at least 6 hours, all subjects underwent blood pressure and heart rate

measurements and performed both simulations. After finishing the simulations, surgeons ingested 200 mg of caffeine, and after 40

minutes, blood pressure and heart rate were measured and both surgical feets were performed.

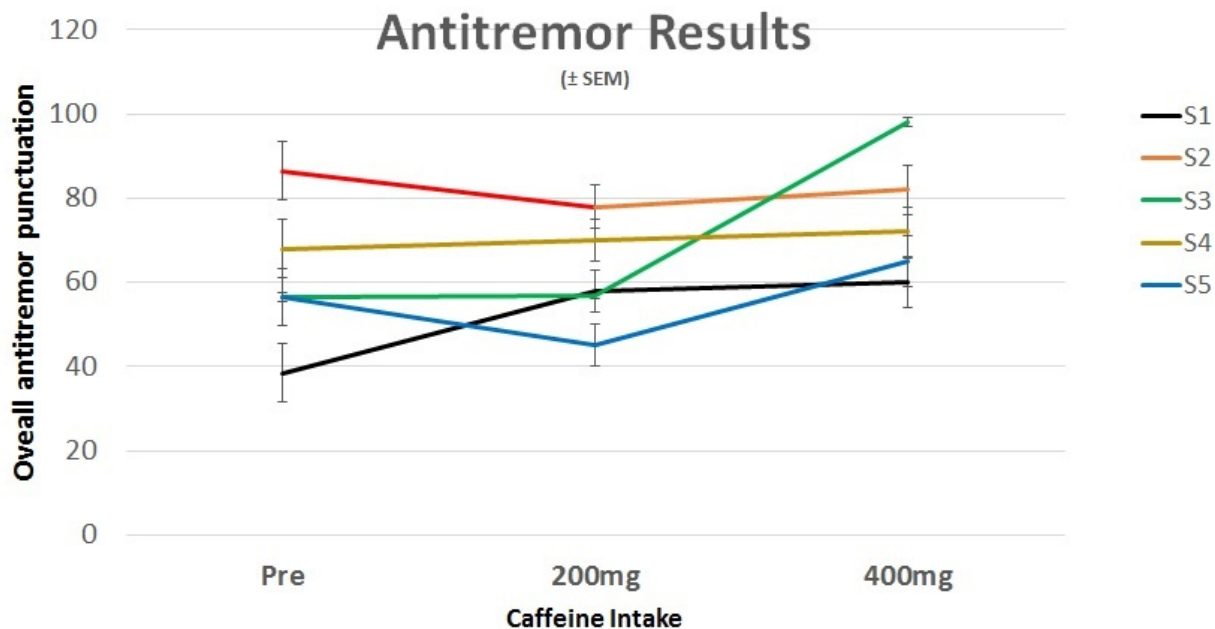


Figure 3: Anti-Tremor Test Overall Scores. Discrete improvement on 400 mg caffeine intake.

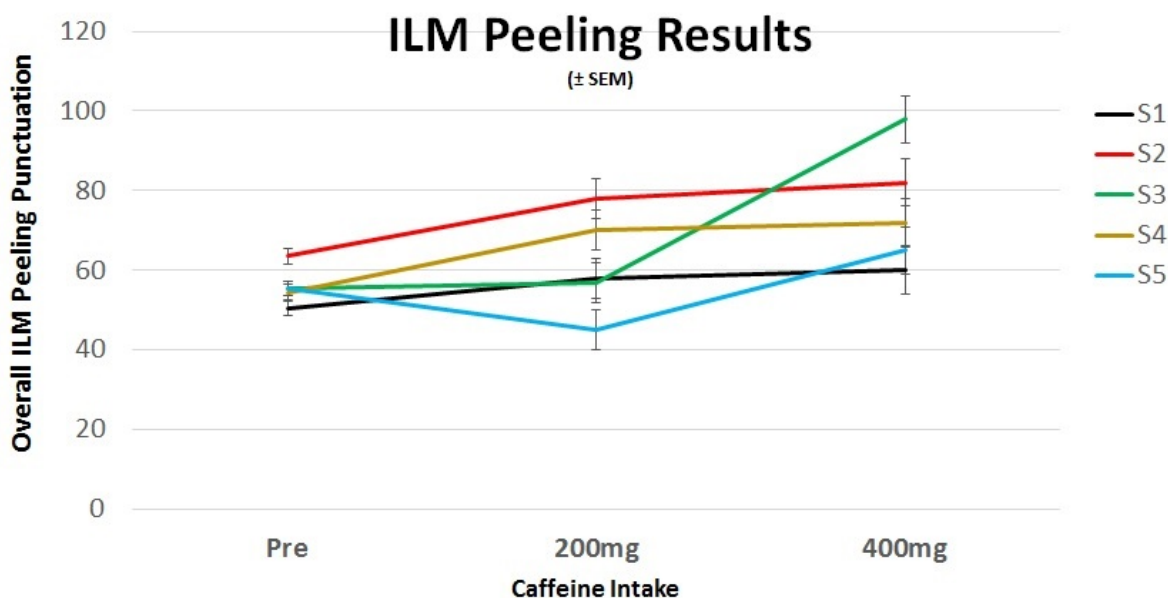


Figure 4: ILM Peeling Test Overall Scores. Slight improvement of performance on 400 mg caffeine intake.

On another random day two month later, all measurements and processes were performed again, but caffeine intake increased to 400 mg. The same technician measured all surgical performances (baseline, 200 mg and 400 mg). The final score was calculated by the simulator's software, provided by the manufacturer and according to their instructions. The score for each test was used for statistical analysis. Statistical analysis was done using an excel spreadsheet (Excel 2007; Microsoft Corp., Redmond, WA). Changes in final scores of each test were assessed using Kruskal-Wallis test with an alpha value of 0.05 or less for statistical significance.

### Main outcome measures

Final Scores of each 4 level test (anti-tremor test and ILM-peeling test).

### Results

Five experienced retinal surgeons, who fulfill the inclusion/exclusion criteria, were consented and enrolled on the study; all participant were healthy with no history of previous diseases like high blood pressure, diabetes mellitus, thyroid diseases or tremor diseases. The mean age was  $46.4 \pm 10.1$  years, all male subjects. After three different measurements on each subject, Anti-Tremor results were: baseline score mean  $61.2 \pm 19.15$ , 200 mg group mean  $61.6 \pm 12.63$  and 400 mg group mean  $75.4 \pm 15.09$ . ILM-Peeling results were: baseline scores  $55.9 \pm 5.46$ , 200 mg  $54.8 \pm 10.05$  and 400 mg  $62.6 \pm 9.63$ . Systolic blood pressure (SBP) was  $116.1 \pm 11.59$  at baseline,  $118.4 \pm 4.77$  after 200 mg and  $117.6 \pm 18.33$  after 400 mg. There was no statistically significant difference between groups (Kruskal-Wallis p-value 0.298 Anti-Tremor Test versus p-value 0.3772 ILM-Peeling Test). (Figures 3-4) Diastolic blood pressure (DBP) was  $74.4 \pm 10.97$  at baseline,  $69.6 \pm 8.26$  after 200 mg and  $74 \pm 8.39$  after 400 mg. Heart rate was  $64.1 \pm 9$  beats per minute (BPM) on baseline,  $65.8 \pm 8.25$  BPM after 200 mg and  $63.6 \pm 6.42$  BPM after 400 mg. Blood pressure remained stable, maintained in ranges between 90/60 and 140/90 mmHg and heart rate between 51 to 80 BPM. The Kruskal-Wallis test showed no differences ( $p=0.882$ ). After consumption of 400 mg of caffeine some adverse effects were reported as headache (2 subjects) and transient episode of anxiety (1 subject).

### Discussion

Caffeine is a xanthine derivative present in tea (black/green), coffee (mostly depends of variety of brewed coffee and tea) and, to a lesser extent, chocolate [2,13]. Caffeine consumption enhances alertness and concentration, which could be useful for a microsurgions embarking on a lengthy procedure. Most studies appear to indicate that the tremor-inducing effect of caffeine is dose-dependent. In ophthalmic surgeons, 100 mg caffeine consumption failed to increase operative hand tremor measured using a noncontact position tracking system, whereas 200 mg caffeine increased hand tremor amplified by a hand-held laser pointer, without evidence of changes on surgical skills. In low-caffeine users, moderate doses (2.5 mg/kg body weight) elicited hand tremor and high doses (5 mg/kg) worsened dexterity [8]. Under the effect of relatively high doses of caffeine (200 mg and 400 mg) our experienced retina surgeons, who consume caffeine on a daily basis (180-240 mg equivalent to 1 to 3 cups of regular coffee), did not experience change on their microsurgical skills. On the contrary, there was a slight tendency to improve, which was statistically non-significant.

Coffee consumption has been associated with acute increases in blood pressure (BP) in caffeine-naive people but exerts negligible effects on the long-term levels of BP in habitual coffee drinkers. The acute effects of coffee are transient, and, with regular intake, tolerance develops to its hemodynamic and humoral effects [14,15]. A recent meta-analysis of 10 randomized controlled trials and 5 cohort studies assessed BP and the incidence of arterial hypertension in coffee consumers did not find significant changes in mean systolic or diastolic BP in coffee drinkers compared with the control group. Evidence analyzed from this large study showed no clinically important effects of long-term coffee consumption on BP or risk of arterial hypertension [7,15-17]. Considering the effects of caffeine, controlled interventional studies show that in normal adults, even high-dose caffeine does not affect prevailing cardiac rhythm and rate. Moreover, it does not cause clinically significant ventricular or supraventricular arrhythmias [14,18,19]. As shown in this study, there were no blood pressure or heart rate abnormalities in any of the subjects, and all fluctuations were between normal ranges.

In addition to the small sample and therefore a possible type 2 error; our study has several limitation that we would like to address: First, we considered the coffee tolerance intake of the study subjects, who have a daily intake of 1 to 3 cups of coffee (180-240 mg of caffeine) that probably create a "resistance" or tolerance to its effect on performing microsurgical procedures. Second, the number of study subjects restricts the collection of statistically significant data.

Caffeine consumption enhances alertness and concentration, although adverse effects such as tremor or anxiety discourage its consumption by some microsurgions (in training or seasoned experienced). Most studies appear to indicate that its effects are dose dependent. Its regular use typically causes mild physical dependence as evidenced by the development of tolerance, withdrawal symptoms and cravings with abstinence. In this study, microsurgical performance had a slight tendency to improve with caffeine intake in a dose-dependent fashion, but results were statistically non-significant. The small number of subjects limited meaningful results; a study with larger numbers of subjects probably would yield significant data.

### Financial Support & Conflict of Interests

The current manuscript has never been published or submitted for publication. The authors do not have any economic, proprietary or financial interest to disclose in the publication of this paper. There were no funds allocated to the realization of this study. The authors state that they have full control of all primary data and they agree to allow the Journal of Clinical & Experimental Ophthalmology to review their data upon request.

### References

1. Dömötör Z, Szemerszky R, Köteles F (2015) Subjective and objective effects of coffee consumption - caffeine or expectations? *Acta Physiol Hung* 102: 77-85.
2. Kim YS, Kwak SM, Myung SK (2015) Caffeine intake from coffee or tea and cognitive disorders: a meta-analysis of observational studies. *Neuroepidemiology* 44: 51-63.
3. Nurminen ML, Niittynen L, Korpela R, Vapaatalo H (1999) Coffee, caffeine and blood pressure: a critical review. *Eur J Clin Nutr* 53: 831-839.
4. Smith A (2002) Effects of caffeine on human behavior. *Food Chem Toxicol* 40: 1243-1255.



5. Smith A, Sutherland D, Christopher G (2005) Effects of repeated doses of caffeine on mood and performance of alert and fatigued volunteers. *J Psychopharmacol* 19: 620-626.
6. 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.
7. Cano-Marquina A, Tarín JJ, Cano A (2013) The impact of coffee on health. *Maturitas* 75: 7-21.
8. Urso-Baiarda F, Shurey S, Grobbelaar AO (2007) Effect of caffeine on microsurgical technical performance. *Microsurgery* 27: 84-87.
9. McCannel CA (2015) Simulation Surgical Teaching in Ophthalmology. *Ophthalmology* 122: 2371-2372.
10. McCannel CA, Reed DC, Goldman DR (2013) Ophthalmic surgery simulator training improves resident performance of capsulorhexis in the operating room. *Ophthalmology* 120: 2456-2461.
11. Selvander M, Åsman P (2012) Virtual reality cataract surgery training: learning curves and concurrent validity. *Acta Ophthalmol* 90: 412-417.
12. Rossi JV, Verma D, Fujii GY, Lakhnpal RR, Wu SL, et al. (2004) Virtual vitreoretinal surgical simulator as a training tool. *Retina* 24: 231-236.
13. Mitchell D, Hockenberry J, Teplansky R, Hartman TJ (2015) Assessing dietary exposure to caffeine from beverages in the U.S. population using brand-specific versus category-specific caffeine values. *Food and Chemical Toxicology* 80: 247-252.
14. O'Keefe J, Bhatti SK, Patil HR, DiNicolantonio JJ, Lucan SC, Lavie CJ (2013) Effects of Habitual Coffee Consumption on Cardiometabolic Disease, Cardiovascular Health, and All-Cause Mortality. *J Am Coll Cardiol* 62:1043-51.
15. Steffen M, Kuhle C, Hensrud D, Erwin PJ, Murad MH (2012) The effect of coffee consumption on blood pressure and the development of hypertension: a systematic review and meta-analysis. *J Hypertens* 30: 2245-2254.
16. Myers MG (1988) Effects of caffeine on blood pressure. *Arch Intern Med* 148: 1189-1193.
17. Corti R, Binggeli C, Sudano I, Spieker L, Hänseler E, et al. (2002) Coffee acutely increases sympathetic nerve activity and blood pressure independently of caffeine content: role of habitual versus nonhabitual drinking. *Circulation* 106: 2935-2940.
18. Newcombe PE, Renton KW, Rautaharju PM, Spencer CA, Montague TJ (1988) High-dose caffeine and cardiac rate and rhythm in normal subjects. *Chest* 94: 90-94.
19. Farag NH, Vincent AS, McKey BS, Whitsett TL, Lovallo WR (2005) Hemodynamic mechanisms underlying the incomplete tolerance to caffeine's pressor effects. *Am J Cardiol* 95: 1389-1392.