# ***The Effect of Caffeine on Velocity of Smooth Pursuit Eye Movements***

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## Abstract

The optokinetic reflex helps to position a moving target on the fovea via the combination of smooth pursuit and saccadic eye movements. Caffeine has been found to cause increased muscle movement and thus this has developed a growing interest to identify the effects of caffeine on eye movement, specifically on the function of the optokinetic reflex. Here, we aim to investigate eye movement, in particular smooth pursuit, by tracking eye movements relative to the position of a moving target on a screen. Eye positions were recorded by 100 images, captured as the eye tracked the target whilst the subject's head remained stationary. In a blind trial, the subject drank 200ml of caffeinated and decaffeinated coffee, 24-hours apart. Baseline data was obtained using water and was compared against caffeinated or decaffeinated conditions. The results showed a significant difference between these 3 conditions (one-way ANOVA, $p<0.05$, $n=8$). Eye velocities in the caffeinated condition compared to decaffeinated was 160% faster with mean velocities of 199 ± 46 for the caffeinated response and 127 ± 34 for decaffeinated. The study demonstrated that smooth pursuit velocity increased with caffeine intake, although the understanding remains unclear and further investigation is required.

## Introduction

The eyes are able to follow moving objects by focusing the image on the fovea whilst keeping the head still, achieved by a mechanism known as gaze shifting. The speed of eye tracking movements depends on the respective speed of the object[1]. Rapidly moving objects cause the eye to move in a rapid and jerky motion, known as saccades. The optokinetic reflex involves the synergistic movement of smooth pursuit (slow eye movements tracking the moving object) and saccades (rapid repositioning of the eye back into the visual field). Together this produces optokinetic nystagmus; jerky involuntary eye movements occurring as a result of the optokinetic reflex[2]. Studying the optokinetic reflex is important because it controls the ability for an image to be stabilised on the retina, preventing retinal slip. It involves a negative feedback system which compensates for the movement of objects by producing an equal and opposite retinal velocity signal. This is stimulated by brainstem nuclei signals, which results in an eye movement equal to the direction of the retinal slip to keep the image focussed on the fovea during smooth pursuit[3] (Figure 1).

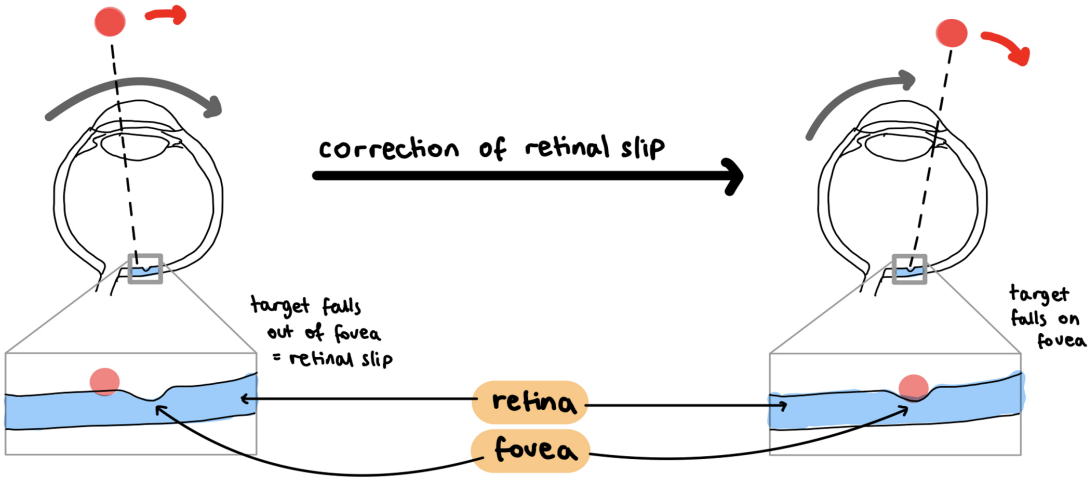


***Figure 1:*** *Diagram to show how retinal slip is corrected by the optokinetic reflex, resulting in image focus on the fovea.*

Saccades often occur during this process in order to correctly match and reduce the visual error between the visual axis and its image. The main brain nuclei responsible for the coordination of these processes is the pretectal nuclei (Figure 2A) sending information on the horizontal retinal error of the eye via direction-sensitive retinal slip neurons[4]. These signals are sent to the inferior olive then to the cerebellum, where the brain processes information on retinal slip and provides efferent information to the eye.

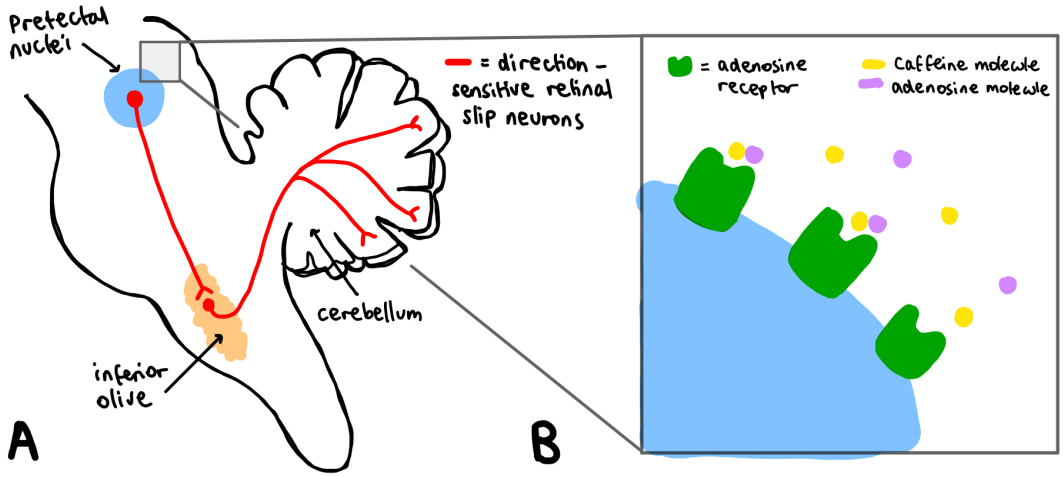


***Figure 2: A)*** *Diagram of the brainstem showing the pathway responsible for correcting retinal slip.* ***B)*** *Zoomed-in image to show the antagonistic characteristics of caffeine on adenosine receptors.*

Caffeine has been shown to cause an increase in velocity of rapid eye movements[5]. The interest of caffeine in the optokinetic reflex is relevant as its effects can be investigated to identify improvements or deterioration of the optokinetic reflex. Caffeine as a stimulant antagonises adenosine receptors (Figure 2B), which indirectly increases dopamine levels.

Adenosine receptors present on presynaptic terminals of dopaminergic neurons in the pretectal nucleus are found as a common target for caffeine[6]. Therefore, this investigation involves comparing the effects with and without caffeine on the optokinetic reflex, in particular measuring changes to the smooth pursuit of eye movement under the influence of caffeine. Traces of left and right eye movement in response to a slow tracking object were analysed to conclude whether smooth pursuit and saccadic movements increase after caffeine intake.

The aims of this investigation were to identify whether eye movement in the caffeinated response is the same as in the decaffeinated response, and to see if the intake of caffeine alters smooth pursuit tracking movements.

## Methods

In order to identify the effects of caffeine on the optokinetic reflex, we conducted a blind trial using two conditions; drinking caffeinated and decaffeinated coffee. The experiment consisted of 8 subjects, weighing between 50-85kgs. All participants were given the same type of coffee with the same amount of caffeine (94mg) in the caffeinated condition. Each cup of coffee in each variable had a total volume of 200ml. Participants underwent a blind trial, not knowing which type of coffee they were taking to remove bias.

An eye tracker phone application was used, where the subject followed the horizontal movement of a red dot across the screen. As the moving target was kept in the visual field at all times, only smooth pursuit was measured. The application took into account the positions of eve movement via images taken of the subject's pupil. To increase the reliability of the experiment we programmed the application to take 100 images of the eye whilst the subject followed the movement of the red dot without moving their head. The phone was placed 30cm and 90 degrees away from the subject (figure 3). This increased the accuracy of the experiment as the camera was able to effectively localise the subject's eyes to precisely locate the coordinates of their movement. Furthermore, controlling the distance and position of the phone relative to the eyes allowed for accurate comparison of the data.

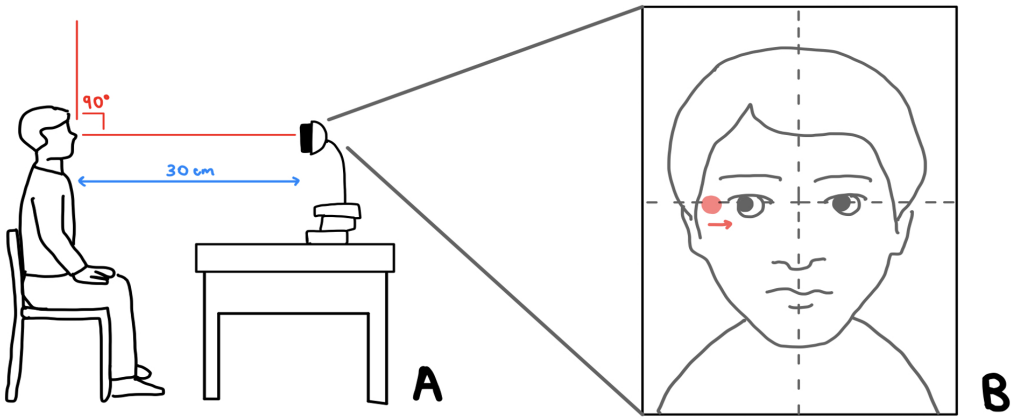


***Figure 3: A)*** *Experimental setup for recording of smooth pursuit eye movement.* ***B)*** *Setup on phone application, showing eye placement on guidelines to achieve accurate coordinate recordings.*

A preliminary eye test was conducted 3 times at the same time to deduce whether there were large variations between each recording. As no large variations were shown, we decided one recording of eye movement for each trial was sufficient. This also removed the effects of adaptation as risks of eye muscle memory can be eliminated due to the number of repeats being kept to a minimum. Subjects drank the same volume of water (200ml) 30 minutes before undertaking the experiment in the morning at the same time at 10am. This was to ensure that the results were not affected by fatigue. Furthermore, no caffeine was ingested at least 12 hours before the experiment to eliminate any residual effects of caffeine. The subject performed the eye test and data for their baseline eye movement was recorded. The positions of the left and right eye were calculated using coordinates relative to their eye position on the screen (measured in arbitrary units related to coordinates within the image) and these were plotted against time on a line graph to show the tracking movements of the eye. From this, average velocity (measured in arbitrary units per second (AU/s)) of the left and right eye were taken from the gradients of the minimum and maximum points of each eye movement in one direction (figure 4).

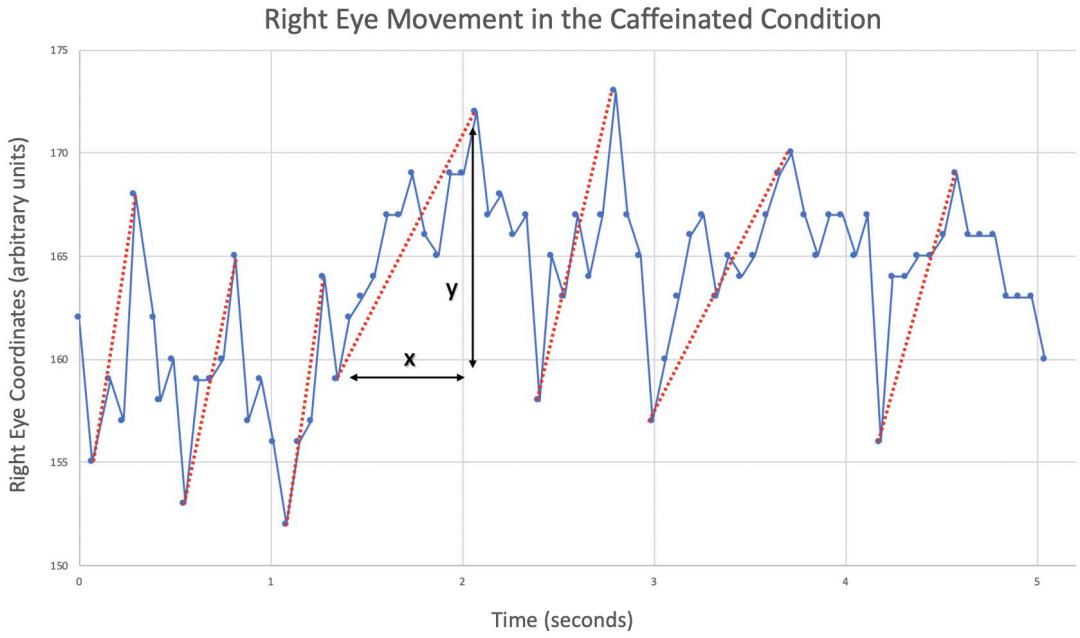


***Figure 4**: **Diagram to show how eye velocity was calculated**. Red dotted lines represent minimum-maximum point of each deflection. X and Y values were obtained from these points and used to find the gradient of the line (y/x) to record the eye velocity.*

Following the baseline test, subjects completed the blind trial drinking either caffeinated or decaffeinated coffee prepared at the same volume by the experimenter. The purpose of the decaffeinated condition was to eliminate placebo effects. The subjects were restricted from drinking caffeine 12 hours before the eye test was taken. Subjects drank 200ml of unknown coffee 30 minutes before the test to allow the effects to kick in. After which, the eye test was conducted at the same time as the baseline test, at 10am. This protocol was repeated 24 hours later with the second unknown cup of 200ml coffee. Data from both eyes were analysed in excel and presented as coordinates. The average velocities of the left and right eye were calculated using the same procedure described above (figure 4).

A paired t-test measuring 95% significance was carried out on the collected data to determine a statistically significant relationship between the caffeinated and decaffeinated trial. The average velocities were obtained from the graph, and mean velocity for both left and right eye movement was calculated. The standard deviations for both conditions were also calculated to identify the spread of data. Due to the variability in size of the recording device from each subject, the data was normalised with the baseline measurements to achieve results that can be compared with one another.

## Results

Figure 5a and 5b show typical responses of eye movement in response to caffeinated and decaffeinated conditions respectively. The downward deflections correspond to leftward eye movements and vice versa. Comparing both traces, it shows that eye movement in the caffeinated condition is jerkier in appearance. Eye movement is more sporadic when the eyes are following the red dot in a repeated left to right cycle, as denoted by its steeper gradient. In contrast, the eye movements in the decaffeinated condition are smoother in appearance and reflect tracking movements closer to smooth pursuit. This is not visible in the trace from the caffeinated condition. Rather, the trace shows a sudden saccadic eye movement as the eye moves from left to right. Unlike the eye movement in the decaffeinated condition where eye movement is kept to a similar range (161AU/s ± 11) and is uniformed in shape, the range of eye movement in the caffeinated condition (86AU/s ± 2) is more varied in between each deflection and the point at which the eye shifts direction is harder to identify.

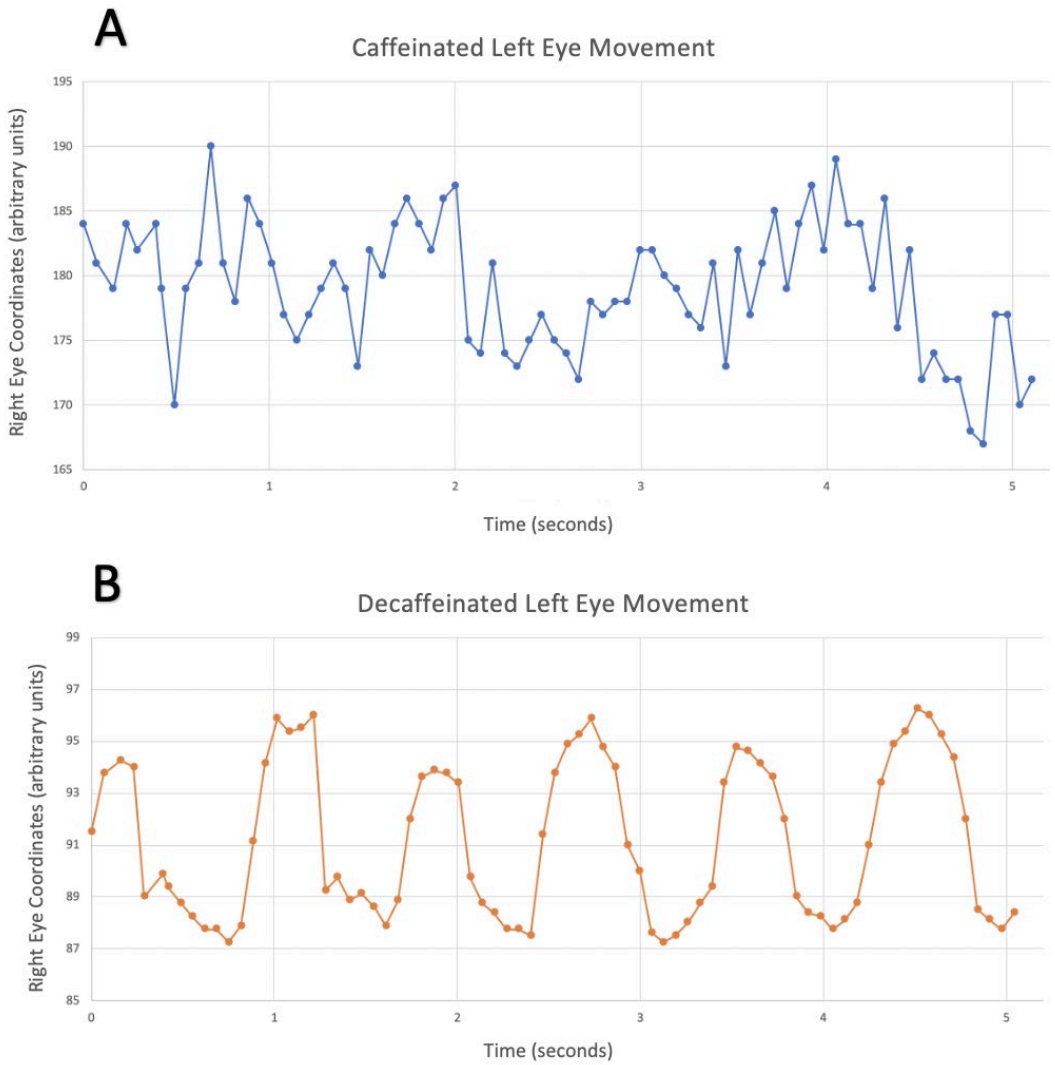


***Figure 5**: **Eye movement traces of smooth pursuit recordings**. **A)** caffeinated condition. **B)** decaffeinated condition.*

***Table 1:*** *Summary of Statistical Analysis of Data.*

| **Mean eye velocities of left and right eye in caffeinated and decaffeinated responses (mean ± SD)** | | |
|---|---|---|
| | **Caffeinated** | **Decaffeinated** |
| **Left Eye** | 152.11 AU/s ± 12.29 | 80.51 AU/s ± 2.34 |
| **Right Eye** | 170.0 AU/s ± 9.98 | 91.45 AU/s ± 2.15 |
| **Eye Velocity against Baseline (water)** | | |
| | **Caffeinated** | **Decaffeinated** |
| **Mean ± SD** | 199AU/s ± 46.3 | 127AU/s ± 33.5 |
| **Difference between baseline** | 2 times faster | 1.27 times faster |
| **Eye Velocity against Decaffeinated Condition** | | |
| | **Caffeinated** | |
| **Mean ± SD** | 159.7AU/s ± 33.9 | |
| **Overall Outcome** | 160% faster than decaffeinated condition (paired t-test, $p<0.05$, n=8) | |

On average (Figure 6), the velocity of eye movement in the caffeinated condition was twice as fast as the velocity of eye movement in the decaffeinated condition ($p<0.05$, n=100, paired t-test). These findings were found to be statistically significant with p values of $1.04 \times 10^{-151}$ and $1.27 \times 10^{-149}$ in both the left and right eyes respectively. The mean velocity of the eye movement during the caffeinated condition was 189% greater in the left eye and 186% greater in the right eye than that of its respective decaffeinated conditions.

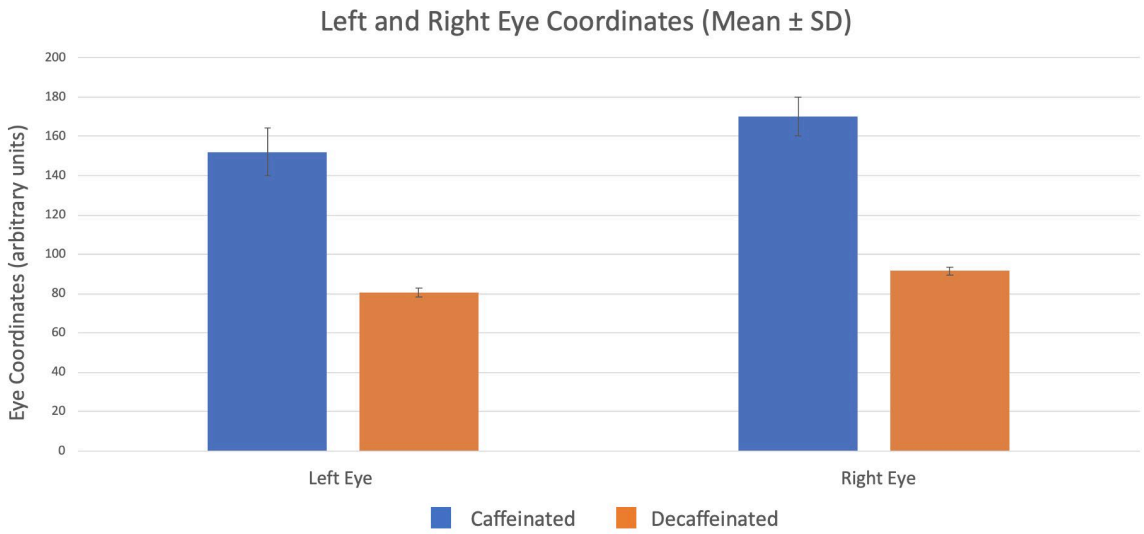


***Figure 6:*** *Bar chart showing mean eye velocities in the left and right eye of caffeinated and decaffeinated responses representative of one subject. Date represents mean ± SD. Left eye: unpaired t-test; p=0.46; n=100. Right eye: unpaired t-test; p=0.45; n=100.*

Furthermore, the velocity of eye movement in both the left and right eye (Figure 6), showed little differences with mean velocities of 152.11AU/s ± 12.29 (caffeinated) and 80.51AU/s ± 2.34 (decaffeinated) in the left eye as compared to 170.01AU/s ± 9.98 (caffeinated) and 91.45AU/s ± 2.15 (decaffeinated) in the right eye. A t-test was conducted between the data from the left and right eye in both conditions. The p-value was calculated to be 0.46 and 0.45 for eye movement in the left and right eye respectively ($p<0.05$, $n=100$, unpaired t-test). Therefore, the difference between left and right eye movements are not statistically significant, suggesting that eye movement is similar in both eyes. Thus, differences in both eyes can be omitted.

Figure 7 represents the increase in normalised eye velocity in the caffeinated and decaffeinated condition, from 8 subjects, relative to the baseline control results from water. Water was taken as a baseline measurement for normalisation to remove differences (such as caffeine metabolism) between subjects. On average, the eye velocity after caffeine intake (mean ± SD, 199AU/s ± 46.3) was 2 times faster than the eye velocity recorded at baseline conditions. On the other hand, eye velocity in the decaffeinated condition (mean ± SD, 127AU/s ± 33.5) was 1.27 times faster than at baseline.

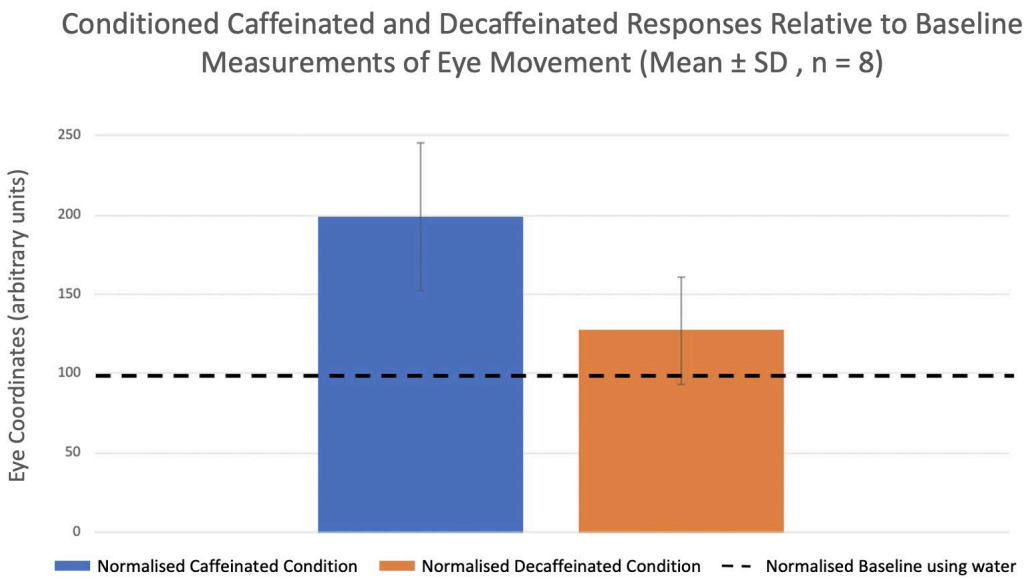


***Figure 7:*** *Bar chart showing normalised caffeinated and decaffeinated response relative to the baseline response. Data represents mean ± SD (error bars); one way ANOVA performed; p=4.52 x* $10^{-5}$*; n=8.*

As the findings between the decaffeinated and water condition were found to be statistically significant, a graph showing the eye velocities from the caffeinated condition (mean ± SD, 159.7AU/s ± 33.9) were normalised to the results obtained in the decaffeinated condition (Figure 8) to eliminate error due to placebo. Therefore, this allows for a clearer distinction of whether eye movements are indeed affected by effects of caffeine. On average, eye velocity after caffeine was 160% faster than the decaffeinated response and this was statistically significant (paired t-test, $p<0.05$, n=8).

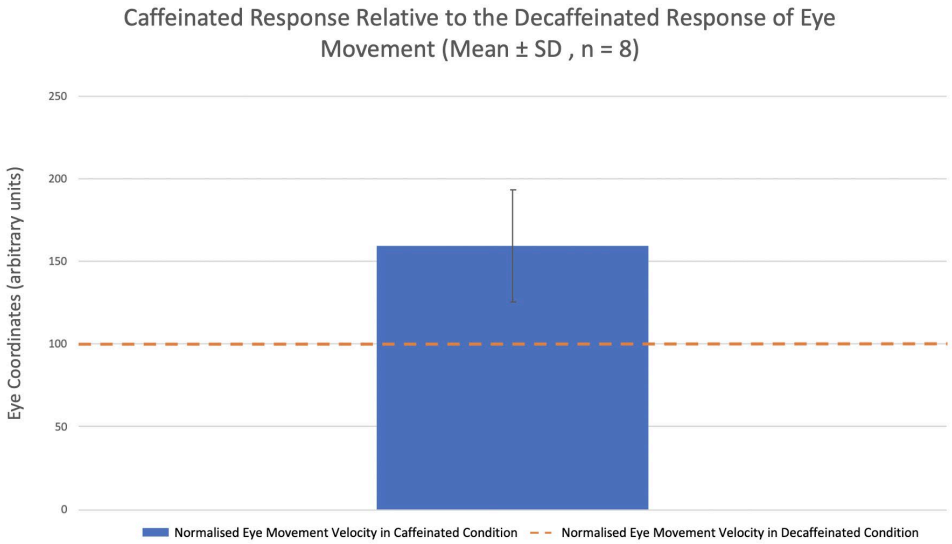


***Figure 8****: Bar chart showing normalised caffeinated response relative to decaffeinated response. Data represents mean ± SD (error bars); paired t-test performed; p=0.0016; n=8.*

## Discussion

Increase in average eye velocity by 160% was recorded in the caffeinated condition compared to the decaffeinated condition. These results reflect recent investigations[5] and can be explained by the fact that caffeine produces a stimulant effect on the central nervous system by antagonising adenosine receptors, thus resulting in disinhibition of dopamine. Caffeine intake also results in increased noradrenaline synthesis, further stimulating the release of dopamine, producing an excitatory efferent response which enhances eye movements. Another possible explanation is that noradrenaline release is linked to saccadic movements[7]. This study shows that inhibiting noradrenaline release caused eye tracking movements to slow down, resulting in smooth pursuit. However, other studies challenge these findings and argue that when caffeine was administered alone, eye movement velocities did not increase above baseline. This contradicts the results of our investigation and suggests that other factors could be producing the vast increase in eye movement velocity after caffeine administration. As the external factors were kept controlled in our experiment, a physiological factor could be providing an inhibitory input to disrupt the control of saccadic eye velocity achieved by noradrenaline. Studies have shown that a caffeine tolerance affects caffeine response[8]. Thus, the majority of subjects being non-regular caffeine drinkers could justify the intensified effects of caffeine. Research has also shown that caffeine increases intracellular calcium, which increases contractility rates in muscle cells, thus influencing extraocular muscles in the eye[9]. From this, it can be concluded that caffeine does indeed play a role in increasing eye movement velocity. Furthermore, the significant increase in the decaffeinated condition (by 127%) from baseline, can be explained as a result of glucose induced hyperactivity which increased overall eye movement velocity. Therefore, in future experiments, glucose level in both coffee drinks must also be taken into account.

Though smooth pursuit tracking movements were measured during the investigation, eye movement in the caffeinated condition produced sporadic saccadic-like movements explained by its larger SD values (SD = 46.2) as compared to the decaffeinated condition (SD = 33.5). These findings are consistent with the current understanding that caffeine stimulates saccadic eye movement as mentioned above[5]. Caffeine also has indirect effects on eye movement such as increasing reaction times[10]. By reducing the effects of fatigue, caffeine promotes alertness; achieved via blocking adenosine receptors in the brain. This aligns with recent findings suggesting that caffeine also improves processing speed[11], thus causes the eyes to move more frequently, which provides an explanation to the saccadic movements in our experiment. However, this study does not fully explain the presence of saccades appearing as the eyes

track the red dot in a smooth pursuit. Rashbass[12] pointed out that saccadic movements appear during smooth pursuit due to the increased position and velocity error in smooth tracking movements. As target velocity increases, smooth pursuit is unable to match the velocity of the target. Therefore, saccadic movement occurs to reposition the image on the fovea. This explanation is evident in patients with Alzheimer's, where smooth pursuit dysfunction resulted in a larger amplitude of saccadic interruption[13]. However, this explanation suggests that saccadic movement arises due to increased target velocity. As the target velocity in our experiment remained constant, this study fails to distinguish the presence of increased eye movement velocity and resulting saccades in our investigation. Moreover, Litman et al[14] concluded that caffeine had no effect on smooth pursuit velocity and found reduced saccadic movements after caffeine ingestion. The small sample size and lack of consistency in devices could have resulted in variability of our results, hence explaining the large SD values obtained in the caffeinated condition and appearance of saccadic-like movements. Further research into smooth pursuit and caffeine need to be carried out to identify their relationship in more detail. This can be achieved via blocking the saccadic movement pathway to identify effects only on smooth pursuit[15].

In conclusion, caffeine does affect the ability for vision to follow a moving target. Investigations on smooth pursuit eye movement resulted in a larger increase in eye velocity and induced saccadic movement after caffeine intake. However, the explanations of these findings are varied, thus further investigations are needed to determine the underlying mechanism for how caffeine affects smooth pursuit alone.

## References


1 Daube, J. R. a. R., D.I. (Oxford University Press, New York, NY., 2009).

2 Davies, D. (ebiolabs, Neurophysiology PHPH 20009, University of Bristol, 2020.).

3 de Brouwer, S., Missal, M. & Lefèvre, P. Role of retinal slip in the prediction of target motion during smooth and saccadic pursuit. *J Neurophysiol* **86**, 550-558, doi:10.1152/jn.2001.86.2.550 (2001).

4 Distler, C. & Hoffmann, K.-P. Visual Pathway for the Optokinetic Reflex in Infant Macaque Monkeys. *Journal of Neuroscience* **31**, 17659-17668, doi:10.1523/jneurosci.4302-11.2011 (2011).

5 Connell, C. J. W., Thompson, B., Turuwhenua, J., Srzich, A. & Gant, N. Fatigue-related impairments in oculomotor control are prevented by norepinephrine-dopamine reuptake inhibition. *Scientific Reports* **7**, 42726, doi:10.1038/srep42726 (2017).

6 Chatzifotis, S. *et al.* Effects of dietary caffeine on growth, body composition, somatic indexes, and cerebral distribution of acetyl-cholinesterase and nitric oxide synthase in gilthead sea bream (Sparus aurata), reared in winter temperature. *Aquaculture Nutrition* **14**, 405-415, doi:10.1111/j.1365-2095.2007.00541.x (2008).

7 Ball, D. M., Glue, P., Wilson, S. & Nutt, D. J. Pharmacology of saccadic eye movements in man. *Psychopharmacology* **105**, 361-367, doi:10.1007/bf02244431 (1991).

8 Yang, A., Palmer, A. A. & De Wit, H. Genetics of caffeine consumption and responses to caffeine. *Psychopharmacology* **211**, 245-257, doi:10.1007/s00213-010-1900-1 (2010).

9 Nehlig, A., Daval, J.-L. & Debry, G. Caffeine and the central nervous system: mechanisms of action, biochemical, metabolic and psychostimulant effects. *Brain Research Reviews* **17**, 139-170, doi:10.1016/0165-0173(92)90012-b (1992).

10 Santos, V. *et al.* Caffeine Reduces Reaction Time and Improves Performance in Simulated-Contest of Taekwondo. *Nutrients* **6**, 637-649, doi:10.3390/nu6020637 (2014).

11 Gillingham, R. L., Keefe, A. A. & Tikuisis, P. Acute caffeine intake before and after fatiguing exercise improves target shooting engagement time. *Aviat Space Environ Med* **75**, 865-871 (2004).

12 Rashbass, C. The relationship between saccadic and smooth tracking eye movements. *The Journal of Physiology* **159**, 326-338, doi:10.1113/jphysiol.1961.sp006811 (1961).

13 Fletcher, W. A. & Sharpe, J. A. Smooth pursuit dysfunction in Alzheimer's disease. *Neurology* **38**, 272-277, doi:10.1212/wnl.38.2.272 (1988).

14 Litman, R. E. *et al.* Smooth pursuit eye movements in schizophrenia: effects of neuroleptic treatment and caffeine. *Psychopharmacol Bull* **25**, 473-478 (1989).

15 Leigh, R. J. & Kennard, C. Using saccades as a research tool in the clinical neurosciences. *Brain* **127**, 460-477, doi:10.1093/brain/awh035 (2004).