EXPLORING HYPERTENSION AND COGNITION IN EARLY-MIDDLE-AGED ADULTS VIA SACCADIC EYE MOVEMENTS

by

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(Under the direction of Jennifer E. McDowell)

Hypertension is a risk factor for cerebrovascular disease and is associated with cognitive decline. The extent to which this affects neurocognition in non-elderly adults remains unclear. Saccade tasks are a reliable measure of neurocognition. This study evaluated pro and antisaccade performance in early-middle-aged adults with low, medium, and high mean arterial blood pressure (MAP) by comparing models of speed accuracy and saccadic main sequences. A canonical correlation analysis compared associations between saccade performance/lifestyle factors and blood pressure. Results found no significant group differences in any of the models. Direct comparisons revealed slower reaction times for participants in the high MAP group compared to the low group and no differences in accuracy across groups. This suggests that the high blood pressure group took longer to reach the same level of performance as the healthy individuals. CCA results showed that BMI and saccade performance were most associated with MAP. Collectively, these results may highlight an association between neurocognition and blood pressure in adults.

INDEX WORDS: Hypertension, Blood Pressure, Cognition, Saccades, Eye-Movements

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Introduction

The brain cannot function properly if the body is in dysfunction. Neurological changes associated with general health do not happen overnight but accumulate throughout a lifetime. A major factor under-considered compared to other health-related risks to neuro-cognitive dysfunction (e.g., aging) is hypertension. Hypertension is a state of persistently elevated blood pressure and has a prevalence rate of 50% among American adults, and 25% of afflicted adults are managing symptoms with pharmaceuticals (Centers for Disease Control and Prevention [CDC] 2024; Chobufo et al., 2020). Recent findings indicated that early onset of hypertension is increasing in the United States (CDC, 2024). With a substantial increase in the prevalence of hypertension, there is a massive gap in research on how hypertension in young, middle-aged adults influences later-in-life cognition. Cognition and associated neurological processes can be reliably measured by saccadic eye movement tasks, which probe for reflexive and higher-level volitional processes (McDowell et al., 2008; Peirce et al., 2019). Analyzing saccadic task performance across adults with low, medium, and high blood pressure levels may shed light on potentially impacted cognitive processes to inform early and efficient intervention.

Hypertension and the brain.

Blood pressure is defined as the pressure against the arterial wall as blood pushes from the heart out into the rest of the body (CDC, 2024). Blood pressure is captured by measuring the amount of pressure when the heart beats (systolic pressure) and the amount of pressure between beats (diastolic pressure), measured by units of millimeters of mercury or mmHg (Mayo Clinic, 2024). Hypertension is clinically described as a systolic pressure above 130mmHg or diastolic pressure above 80mmHg (CDC, 2024). Another metric used to index blood pressure is mean arterial pressure (MAP). MAP is the average pressure against the arteries during a cardiac cycle and is associated with cerebrovascular and cardiovascular health (Kandil et al., 2023). It can be derived from systolic and diastolic blood pressure or measured independently. Having a MAP reading of above 99.01 is considered high, and a MAP below 93.33 is considered optimal (Kandil et al., 2023).

Organs in the human body require a steady flow of oxygen and nutrients via the bloodstream to work efficiently and maintain proper health. The brain makes up 2% of one's body weight and utilizes 25% of the body's overall blood supply (NIA, 2024). Chronic exposure to hypertension is associated with narrowing, scarring, and threat to the structural integrity of capillaries in the brain (Cheon, 2022; NIA, 2024). Alterations to capillaries can cause cascading damaging effects such as vascular stiffening, regulation impairments, microbleeds, and hemorrhages (Cheon, 2022). Ultimately, this decreases the volume of vital nutrients entering the brain, possibly resulting in cell death and tissue loss over time (Cheon, 2022; NIA, 2024). Elevated blood pressure throughout childhood can predict biological markers of cardiovascular risk later in life (American Heart Association, CDC, 2024; Hao, 2017). Although hypertension has been researched throughout the lifespan, including in childhood (Hao et al., 2017; Su et al., 2015) and elderly adulthood (George et al., 2023; Gottesman et al., 2014), the progressive impact it has on the brain and cognitive functioning needs to be further examined.

Neuro-cognitive effects of hypertension.

Hypertension is linked to cognitive decline and dementia, partially due to quantifiable neuroanatomical changes (Cheon, 2022). This includes differences in brain matter volume and disrupted white matter microstructure, which is assessed by magnetic resonance imaging (MRI) diffusion tensor imaging (DTI) and measures the diffusion of water across white matter tracts across the brain (Lockhart & DeClarli, 2014). One recent study compared multiple structural MRI variables among early adults in different progressive states of hypertension (normotension, transition to hypertension, and hypertension) across several visits at least one year apart (George et al., 2023). Results found that decreased cerebellar volumes and decreased volumes of the frontal and parietal cortices were associated with the transitioning-to-hypertension group compared to the normotensive group. In addition to these regions, the hypertension group showed an overall reduction of hippocampal volumes, an enlargement of the lateral and third ventricles, and decreased overall white matter microstructure compared to the normotensive group (George et al., 2023).

White matter hyperintensities are bright spots in the white matter on MRI brain images and are associated with lesions or abnormalities in axon myelination (Sharma et al., 2024). These imaging markers are commonly found in elderly adults and are strongly associated with multiple cardiovascular risks, such as small vessel disease of the brain and hypertension (Dufouil et al., 2001; Hajjar et al., 2011; Sharma et al., 2024). Hypertensive patients with impairments in gait, mood, and cognition are shown to have white matter hyperintensities that possibly mediate the relationship between hypertension and symptomology (Haijer et al., 2011). Furthermore, treating high blood pressure significantly reduces the risk of white matter hyperintensities (Dufouil et al., 2001), which underlines the importance of early intervention measures to prevent further damage to the brain. Although these findings highlight the progressive loss of brain matter and related cognitive deficits in hypertensive pre-middle-aged adults, further research exploring specific aspects of neuro-cognition and how these may be directly impacted by hypertension is crucial in developing more informative intervention measures.

Ocular motor paradigms.

Ocular motor (eye movements), measured during saccade tasks, are a reliable measure of behavioral and neurocognitive functioning. Saccades are quick eye movements extensively researched and functionally mapped in the human brain (McDowell et al., 2008). Saccadic eye movements are broadly classified into two groups: those that are exogenously (reflex-like) driven, such as prosaccades, or endogenously (voluntarily) driven, such as antisaccades (McDowell et al., 2008). Prosaccades are typically used to observe baseline eye movements and behaviors, where subjects are instructed to look at a stimulus as it appears. Prosaccades can be used as a simple yet reliable baseline measure due to their known neurological circuitry (Hutton, 2008; McDowell et al., 2008). Differing in basic performance can provide researchers with key insight when interpreting the performance on more complex tasks.

Anti-saccades are commonly used to measure multiple other aspects of cognitive control, including working memory, attention, and decision-making (Hutton, 2008; McDowell, 2008; Opwonya, 2022a; Pierce et al., 2019). Antisaccade tasks add to the cognitive load of the task, as one must inhibit looking at the stimulus and instead direct their gaze to the opposite location. Additionally, subjects must pay attention to making the correct decision and maintaining the goal of the task. The extra complexity of the antisaccade task leads to more variable results in performance, including increased error rates and prolonged correct reaction times compared to the prosaccade task (Pierce et al., 2019). The performance on pro and antisaccade tasks can be compared across different neurological and psychiatric conditions that impact cognition, such as schizophrenia, anxiety, depression, attention deficit, obsessive-compulsive, and bipolar disorders (Bittencourt et al., 2013). Furthermore, saccade tasks have been historically used in researching cognition-associated health conditions and age-related disorders such as Alzheimer's disease and dementia (Opwonya et al., 2022a; Opwonya et al., 2022b), which have both been linked to the early onset of a hypertensive state (Gottesman et al., 2015; Lockhart & DeCarli, 2014).

Main sequence effects.

Saccadic metrics can be used to compare behavioral performance, including associations between measurements. One relationship of importance in saccadic eye movement data is the main sequence effects. The saccadic main sequence is the stereotyped relationship between saccade velocity, amplitude, and duration. Peak velocity is measured as degrees per second, indicating the maximum speed of a saccade, and tends to be faster in prosaccade conditions (Hutton, 2008). Amplitude is the position of the saccade in degrees, and duration is how long the saccadic movement took in milliseconds. In healthy individuals, the relationship between peak velocity and amplitude appears linear at lower amplitudes and begins to level off as amplitude increases (Guadron et al., 2023).

It has been suggested that the saccadic main sequence is designed for the evolutionary purpose of conserving time and energy while also maintaining the task goal (Harris & Wolpert, 2006; Wang & Hsiang, 2011). As amplitude increases, this prioritization may shift more to conserving energy rather than optimizing time, which may be explained by the leveling off of peak velocity when higher amplitudes are reached (Wang & Hsiang, 2011). The relationship between these metrics can be used to evaluate neurological processes (Gibaldi & Sabatini, 2021; Pierce et al., 2019). Specifically, defects in this purposeful relationship in pro and antisaccade tasks may highlight the underlying neurological deficits. Multimetric analyses of main sequence effects may be a useful tool to parse out neuro-cognitive differences (Ramat et al., 2007) and may serve as an additional, more sensitive measure than evaluating saccade metrics alone.

Timing differences in saccade tasks.

In saccadic eve-movement tasks, the on/offset timing of the peripheral stimuli and central fixation can be changed to manipulate task performance. For example, in “gap” conditions, the target fixation is extinguished before stimulus onset, while in “overlap” conditions, the target fixation remains on the screen slightly after peripheral stimulus presentation (Pierce et al., 2019; McDowell et al., 2008). Another example of timing manipulation is referred to as the “synchronous” condition, where the central fixation disappears in sync with the onset of the peripheral stimulus. Manipulating the fixation timings results in significant differences in saccade performance, including reaction times and peak velocity. An example of this is the “gap effect,” a phenomenon with decreased reaction times and increased peak velocity in gap conditions when compared to synchronous conditions. Comparatively, increased reaction times and decreased peak velocity are observed in overlap conditions when compared to synchronous conditions (Pierce et al., 2019; McDowell et al., 2008). In people exhibiting cognitive impairment in various psychiatric conditions, the gap effect seems slightly amplified when compared to healthy controls (McDowell & Clementz, 1997; Huang et al., 2023).

Saccadic speed-accuracy as a cognitive measurement.

Another association to review is between saccade reaction time and response correctness throughout the task. The relationship between speed and accuracy trade-off (SATO), which is associated with main sequence effects in healthy individuals (Guadron et al., 2022), has been extensively researched in cognitive psychology and historically used to quantify the decision-making process (Heitz, 2014). Multiple attempts have been made to model this phenomenon, which involves finding a "happy medium" between accuracy and reaction time, referred to as the optimum decision threshold (Heitz, 2024). If the reaction time is too fast, the brain might not completely process visual information, and the probability of making a mistake increases. If reaction time is too slow, it may indicate an issue in breaking attention from the stimulus. This relationship between speed and accuracy can also be applied to saccade tasks (Huang et al., 2021; Polli et al., 2006). Evaluating the tight relationship and trade-off rates between the speed and accuracy of saccades may provide additional details about the behavioral performance between the two groups. Specifically, comparing this relationship can provide insight into potential impairments in neurocognitive processes, such as visual processing, attentional inhibition, and goal maintenance (Heitz, 2024; Opwonya, 2022).

Neural underpinnings of saccades.

Saccade tasks help to elucidate underlying neurological mechanisms involved in saccade generation and saccadic task performance. As summarized by McDowell et al. (2008) and Hutton (2008), prosaccade generation involves cortical regions, including the primary visual, extrastriate, and parietal cortices, and the frontal and supplementary eye fields (FEF and SEF), and subcortical areas, including the striatum, thalamus, superior colliculus, and cerebellar vermis. As the cognitive load of a task increases, such as in antisaccade tasks, additional activation in the prefrontal and anterior cingulate cortices (PFC and ACC) is observed, along with cortical activation of prosaccade-generating circuitry to the prosaccade regions (McDowell et al., 2008).

These findings are supported by functional magnetic resonance imaging (fMRI) studies where participants completed pro- and anti-saccade tasks. Results indicated increased activation in the frontal, supplementary, and parietal eye fields, as well as the lenticular nuclei and occipital cortex, during both pro and anti-saccade trials. Additionally, the dorsal-lateral PFC (dlPFC), ACC, and supramarginal gyri show activation specific to the antisaccade task (Matsuda et al., 2003). These regions are known to be heavily involved in cognition and decision-making (Broche-Pérez et al., 2016). The activation observed between pro- and anti-saccade task performance is attributed to differences in task instruction rather than motor movement (DeSouza et al., 2003).

*Sociodemographic considerations***.**

Studying the long-term effects of hypertension can be complicated, given the heterogeneous nature of the disease. In hypertension, there are numerous, often converging covariates of high blood pressure that add to the complexity of studying its effects. Sociodemographic and associated economic differences can contribute to the population differences observed in hypertension, especially in Black Americans. Previous studies have shown that Black adults are disproportionally diagnosed with hypertension compared to white Americans (Dolezar et al., 2014; Hicken et al., 2014). Further results have shown that this disparity lacks a biological basis and has been consistently linked to discrimination-related stress and hypervigilance (Dolezar et al., 2014; Hicken et al., 2014). Meta-analyses have shown that differences in age, sex, and education level significantly moderate the association between discrimination and hypertension (Dolezar et al., 2014). The influences of sociodemographic differences, stress, and other mental and physical health factors will all be considered in the current study. These factors, along with saccade performance, will be evaluated to determine which ones potentially contribute the most to hypertension.

Current study directions.

Previous research has indicated that hypertension in early and middle life is associated with later cognitive deficits. Research on non-elderly populations in the early-middle adulthood range is key to better understanding hypertension progression, becoming familiar with the associated degradation of cognitive functioning, and using that information to develop effective early intervention measures. Saccadic eye movement tasks are infrequently used in researching cardiovascular health but may provide the necessary tools to better understand this association. Literature has shown that MAP may be a stronger predictor of cardiovascular risk and may even be a more consistent and reliable measure than using systolic and diastolic bp alone (Kandil et al., 2023). For this reason, this study will use groups of low, medium, and high MAP to identify hypertension.

This paper seeks to bridge the gap in current research by looking at saccadic task performance as a marker of cognitive and behavioral functioning in early middle-aged adults with and without severe hypertension. It is hypothesized that models of main sequence effects will differ the most between the high and low MAP groups. It is also hypothesized that the high MAP group will show the most differences in performance (increased errors and prolonged reaction times) on antisaccade tasks compared to the medium and low MAP groups and that such differences will be heightened in the antisaccade overlap task. In SATO analyses, it is hypothesized that the models will differ the most between the high and low MAP groups. Lastly, comparisons from a canonical correlation will be made to review the correlation strength of saccade variables and other lifestyle factors, such as body mass index (BMI), exercise, and stress, and how they are associated with blood pressure. It is hypothesized that poorer saccade performance will be moderately associated with higher blood pressure and that lifestyle factors (particularly high BMI and stress) will have the strongest associations.

Methods

Participants.

Participants were recruited by the Georgia Stress and Heart Study (Hao et al., 2017; Su et al., 2015) located in the Georgia Prevention Institute at Augusta University, GA, as detailed in Reeves et al. (2023). Subjects were initially screened during a phone interview, and anyone pregnant, nursing, or with a history of congestive heart failure was excluded from the study. **Table 1**. contains sociodemographic and health information for the sample, which consisted of 69 low MAP, 74 medium MAP, and 71 high MAP subjects. All participants virtually completed multiple questionnaires measuring various health and lifestyle factors, including perceived stress (Cohen et al., 1983), nicotine and alcohol use (occurrences per month), and frequency of physical exercise (measured by times per week). Information on self-reported race, sex, and age were also collected.

Health metrics. Blood pressure was measured via a Dinamap vital signs monitor (Soller, 2015), which recorded systolic/diastolic blood pressure and MAP accordingly. Height and weight measures were also taken during the visit, and BMI was calculated by dividing weight (kg) by height (m^2). The average BMI per group is listed in **Table 1.**, as well as group averages for all three blood pressure measures. It was decided that mean arterial pressure (MAP) would be used in grouping low, medium, and high blood pressure groups, given its accuracy in predicting risk over time (Kandil et al., 2023). Data for each subject's MAP was graphed and separated into groups based on the tertile method as shown in **Table 1**., and the criteria for each group are as follows: 60 mmHg < low < 84.99 mmHg, 85 mmHg < medium < 95.99 mmHg, and high > 96 mmHg. These groups align with previous literature, stating that the average MAP for a healthy individual is around 90mmHg (Kandil et al., 2023).

Saccade tasks.

Saccade paradigms were administered, as detailed by Huang et al. (2022). Eye movements were recorded using the Eyelink II head-mounted eye tracking system, which used a lens system to track movements of both the left and right pupils at a sampling rate of 500 Hz. Associated SR software (SR Research Ltd., Mississauga, Canada) monitored eye movements for data quality and task performance. Data were collected in a darkened room while the participants had their heads placed on a chin rest to control for motion and visual angle. Task paradigms were presented using the Presentation software (Version 16.1; NeuroBehavioral Systems, Inc. Berkeley, CA, www.neurobs.com). Tasks were given in order: prosaccade gap, prosaccade synchronous, prosaccade overlap, antisaccade gap, antisaccade overlap. Tasks were administered consecutively for each participant, as presented in **Figure 2.**

Prosaccade. For the prosaccade tasks, each participant was instructed to look at the center cross and then at the white dot when it appeared. The prosaccade task consisted of 96 trials separated into 3 blocks of 32 trials for each timing condition (gap, synchronous, and overlap). **Figure 2a.** shows an example of each prosaccade task condition. Tasks began with a dark screen and a red fixation cross presented size 1°. A white circle was presented on either side of the cross at 10° or 15° at random—the time the stimulus was presented varied between 1500ms and 2500ms. In the synchronous condition, the fixation cross disappeared in sync with the stimulus onset. For the gap and overlap condition, the stimulus was presented at ±200ms before/after removing the fixation cross. Rest periods were administered after each block of 32 trials. Each rest period lasted approximately 30 seconds, during which the word 'rest' was presented on a black screen. Participants were allowed to close their eyes to rest but were instructed not to move their heads from the chin rest.

Antisaccade. For the antisaccade tasks, participants were instructed to look at the center fixation and then at the opposite or mirrored direction of the stimulus when it appeared. Each antisaccade task consisted of 80 trials intermitted by 2 rest periods. **Figure 2b.** shows an example of each antisaccade task condition. Similar to the prosaccade task, a red fixation cross was presented at 1°, and the stimulus (for antisaccade, this was a white square) was presented left and right, 10° and 15° at random. For the antisaccade gap condition, the fixation was extinguished 200ms before stimulus presentation. For antisaccade overlap, the fixation cross was extinguished 200ms after stimulus presentation. Afterward, a red cross appeared on the mirrored side, indicating where participants should have looked. A practice run consisting of a few trials was run before the task to ensure participants understood the directions.

Statistical analyses.

Quantifying saccade performance. Eye movements were scored using a house-made script on Matlab (version 2014b; MathWorks Inc., Natick, MA). Metrics used in analyses were quantified on a trial-by-trial basis using the same script, manually inputting the start and endpoints. The metrics calculated from this include reaction time (measured by how long in milliseconds (ms) for the saccade to start) and amplitude (how far, in degrees, the eyes moved during the saccade). Saccade data were gathered, and analyses were run using SAS base software (version 9.4; SAS Institute Inc., Cary, NC, USA) and the statistical software IBM SPSS (version 29; IBM Corp. Armonk, NY). Saccades that occurred before 90ms were in anticipation of the incoming stimulus; these trials were automatically excluded from further analyses. Furthermore, conditions in which less than 25% of trials were scorable were excluded (6 tasks total), and only subjects who completed each condition were included in the analyses (N=213).

Main sequence effects. Main sequence effects were modeled and compared according to a modified protocol originally used by Guadron et al. (2022). Before analysis, the saccadic amplitude was binned to the nearest .2 degrees, and the maximum velocity was averaged for each bin. Functions depicting the relationships between velocity and amplitude were fitted and plotted for each group using the following equations adapted from Guadron et al. (2022).

$$\text{Average velocity} = 1 \div \frac{b}{A+(a)}$$

In this model, A indicates amplitude, and *a* is the velocity constant (°/ms), the seed of which was initially set at .01 °/ms, representing the minimum possible velocity. Similarly, the minimum time in milliseconds was represented by *b,* originally placed at .1ms for each model. Ten models were created for each of the five conditions, for both correct and error trials, making up each group. After each model was fitted, they were compared based on correctness and group membership.

Direct comparisons. Multiple analyses of variance (MANOVAs) were run to evaluate direct comparisons between saccadic variables. Comparisons were made between reaction times for trials performed correctly for the prosaccade gap, synchronous, and overlap conditions, as well as the antisaccade gap and overlap condition. A MANOVA was also run to compare all MAP groups in trials where an error was made for the antisaccade gap and overlap conditions. Percent correct for the antisaccade gap and overlap conditions were also compared in the low, medium, and high MAP groups. Additional ANOVAs were run to test for group differences in sex and race.

Speed-Accuracy Trade-off (SATO) Comparisons. Following initial comparisons, the relationship between percent correct and correct reaction times was fitted to logistic functions for low, medium, and high MAP groups, similar to Huang et al. (2021) and Polli et al. (2006). Correct reaction times for each trial were grouped into 10ms latency bins. For each bin, the number of correct trials was tallied, and portion correct ratios were computed by dividing the number of correct trials by the total number of trials. Logistic functions were then selected using the following format for the antisaccade gap and overlap conditions, as detailed in Haung et al., 2021:

$$\text{Proportion correct} = 100 - \frac{A}{I + e^{(B-t)*r}}$$

Where A represents the maximum correct rate (100%), which is the upper limit of the proportion correct. B represents the time of maximum trade-off or the time it takes in ms for participants to reach 50% correct, which is also the turning point of the model. Lastly, r indicates the maximum trade-off rate, which is 0.1, and represents the starting slope of the model. This formula is also constrained by the maximum possible error rate, which is 100% (Haung et al., 2021). These functions were then graphed using Matlab, and group differences for each function were analyzed by comparing the estimates and confidence intervals of each model.

Canonical correlation analysis. A canonical correlation analysis (CCA) explored saccadic performance metrics and other lifestyle factors compared to continuous blood pressure measurements (MAP, systolic, and diastolic blood pressure). Saccade variables included correct reaction time, peak velocity, gain (a measure of how close subject gaze is to stimulus position) for each metric collapsed over timing condition, and percent correct for antisaccade. Additional factors included various lifestyle metrics that are associated with high blood pressure, including BMI, alcohol and nicotine use, physical exercise, and perceived stress. Each set of variables was run in the CCA using SPSS, and their components were compared. Significant components were then graphed according to group membership.

Results

Main Sequence effects.

Saccadic main sequence effects were modeled for each condition and group membership and were compared using a 95% confidence interval approach. No significant group differences were found between the main sequence models for the prosaccade task in any timing condition, $p > .05$. The main sequence model for the prosaccade task (collapsed across conditions after finding no significant differences) is shown in **Figure 3a**. Additionally, no significant differences were found between antisaccade tasks in either condition, for correct or error trials, $p > .05$. Models of main sequences for correct antisaccade trials are shown in **Figure 3b**. and incorrect trials in **Figure 3c**.

Direct Comparisons.

Prosaccade. To evaluate direct comparisons in saccade performance in groups with low, medium, and high MAP values, MANOVAs compared the percent correct and reaction times for each condition for correct and error trials in each group. **Table 2.** shows reaction time results for all prosaccade conditions performed correctly. No Significant group differences were found in the reaction times of correct trials in the PS gap $F(2, 211) = .098$, $p=.907$, PS synchronous, $F(2, 211) = 6.13$, $p=.543$ and PS overlap $F(2, 211) = 6.87$, $p=.504$ conditions. Although insignificant, the average reaction times for all prosaccade conditions were prolonged in the high MAP group compared to the low and medium groups. These results are graphed in **Figure 4a**.

Antisaccade. Results for percent correct and antisaccade reaction times for trials performed correctly and incorrectly can be found in **Table 2**. Significant, longer reaction times were noted for the high MAP group in the correctly performed trials of the antisaccade overlap condition, $F(2, 211) = 3.86$, $p = .023$ compared to the low MAP group, but did not significantly differ from the medium MAP group. No significant group differences in the reaction times of correct trials were observed in the gap condition $F(2, 211) = 9.47$, $p = .390$. Additionally, no significant group differences were found in error reaction times for the AS gap condition $F(2, 211) = .581$, $p = .560$, or the antisaccade overlap condition, $F(2, 211) = 1.35$, $p = .261$. Additionally, there were no significant group differences in percent correct for the antisaccade gap $F(2, 211) = 2.01$, $p = .126$, or overlap conditions $F(2, 211) = .496$, $p = .610$ as shown in **Figure 5**. Group reaction times for correct and incorrect trials are shown in **Figure 4b.** Additional ANOVAs were run to test for group differences in sex and race, and no significant group differences or interactions were found for either of these variables or any of the saccade performance metrics.

Speed-Accuracy Trade-Offs.

Models were created depicting saccade speed and accuracy trade-offs for each group for the antisaccade gap and overlap conditions. The models were stable and ran within less than 9 iterations. Overall, both models explained at least 95% of the variance. Group differences were compared using a 95% confidence interval approach. Models were collapsed across timing conditions after finding no significant group differences between the models $p>.05$ for the antisaccade gap or overlap conditions. The final model is shown in **Figure 6**. Overall, the high MAP group took longer to reach 50% correct in both conditions than the low and medium MAP groups. The high MAP took roughly ~10ms longer [212.8ms] than the medium MAP group [205.9ms] and ~15ms longer than the low MAP group [197.1] to reach optimal performance.

Canonical Correlation Analysis.

A canonical correlation analysis was run to compare blood pressure measures (mean arterial pressure, systolic, and diastolic blood pressure) and lifestyle variables (BMI, perceived stress, alcohol use, nicotine use, and physical exercise) / saccade metrics (Pro and Antisaccade correct reaction time, initial gain, and peak velocity, and antisaccade percent correct). There were three correlation combinations, one of which was significant $r = .557$, $F(36, 429) = 2.34$, $p < .001$, with loadings for each set shown in **Table 3**. Component 1 positively loaded MAP, systolic, and diastolic blood pressure in that respective order (loading weight - MAP:.873; systolic: .865; diastolic: .489). BMI contributed the most to component 2 (loading weight - BMI: .926), with antisaccade peak velocity, reaction time, and prosaccade peak velocity following suit, all moderately contributing to component 2 (loading weight - antisaccade peak velocity: -.285; antisaccade reaction time: .242; prosaccade peak velocity: -.233). Weekly exercise, alcohol use, and prosaccade gain contributed mildly to the model. Nicotine use, antisaccade gain, perceived stress, prosaccade reaction time, and antisaccade percent correct were the weakest contributors. **Figure 7**. depicts a scatterplot of canonical correlations for all three MAP groups.

Discussion

Cardiovascular diseases and risks such as hypertension are a steadily rising epidemic in the United States, especially in young adults. With this, a dire need is emerging for early intervention measures and research, especially given the strong association between high blood pressure, cerebrovascular disease, and cognitive decline. The current study compared subject performance on eye-tracking tasks, a strong measure of multiple aspects of behavior and cognition tied to multiple, well-documented neurological processes. The current study directly compared these measures and created more sensitive and descriptive models of neuro-cognitive processes by evaluating speed accuracy and main sequence effects. Furthermore, this was evaluated in early-middle-aged adults to provide findings on non-elderly populations and to fuel early intervention measures.

Saccade performance.

Results found no significant differences in reaction times in the prosaccade gap, synchronous, or overlap conditions. These findings are expected and align with previous literature, finding no significant differences between healthy individuals and individuals with psychiatric conditions (Hutton, 2008; McDowell & Clementz, 1997). Past research has argued that the prosaccade reaction time may be a measurement of spatial attention (Hutton, 2008). In the current study, prosaccade reaction time and the lack of significant group differences suggest that the basis neuro-circuitry of saccades is intact in our population. These findings provide a basis for comparing other measurements in subsequent analyses.

Our results found that the high MAP group had significantly prolonged reaction times in correct antisaccade overlap trials compared to the medium and low MAP groups. While significant group differences were found in antisaccade correct reaction time, no significant group differences were found in percent correct. This suggests that the high MAP group takes longer to perform than those without high blood pressure. This could be due to the increased cognitive resources needed to create correct responses, and accessing these resources may take longer in the hypertensive brain. Past research has found that prolonged reaction times in saccade tasks are associated with overall cognition, including deficits in social functioning and negative symptoms in schizophrenia (Huang et al., 2023).

Past research in cognitively impaired adults showed that performance on the antisaccade overlap condition distinguishes schizophrenia the most out of all the other conditions (McDowell et al., 2008). Antisaccade responses vary around 100ms longer than prosaccades in healthy adults (Hutton et al., 2008), and even more so in the antisaccade overlap condition. Current findings suggest that cognitive processing, such as breaking attention from the central fixation, may take longer in the high MAP group compared to the low and medium groups. This difference becomes distinct as task complexity increases, as observed in the antisaccade overlap task, distinguishing the higher and lower MAP groups most of all. This is supported by past research, showing an increase in demand for cerebral blood flow as the complexity of a visual task increases (Spence et al., 2021).

Regardless of statistical significance, overall reaction time appears to differ; the reaction time is higher overall in the high MAP group in all task conditions compared to the low and medium MAP groups. The high MAP group also took the longest time to reach the maximum trade-off rate in the SATO models compared to the medium and low MAP groups. Additionally, the high MAP group exhibited lower peak velocity as a function of amplitude across conditions compared to the two other groups. It has been proposed that the fixed relationships between speed accuracy and the saccadic main sequence are evolutionarily designed to maximize accuracy while conserving energy and visual acuity (Harris & Wolpert, 2006; Wang & Hsiang, 2011). Such a goal is reflected in the shape of the main sequence model in that speed is prioritized at shorter amplitudes and energy conservation at larger amplitudes and can vary depending on the task context (Harris & Wolpert, 2006). Although the high MAP group showed prolonged reaction times in the SATO models and slower peak velocities in the main sequence models, the model shapes do not deviate between the three groups. This suggests that this mechanism is preserved in the high MAP group.

One could argue that differences in reaction time shown in this study could be related to ocular degeneration due to neurobiological changes associated with hypertension. Hypertension affects the ocular system in the form of retinopathy and arteriosclerosis in more severe cases (Modi & Arsiwalla, 2024). While ocular impairments become more incidental to high blood pressure, the significant differences in reaction times observed in the more cognitively complex antisaccade tasks dispute this theory. While changes in eye function and degeneration are important considerations, the results of this study are not fully explained. This suggests that these changes may be primarily driven by cognitive dysfunction rather than ocular impairments.

Comparing lifestyle and sociodemographic factors

To compare these results with those of other known contributors to hypertension, a canonical correlation was run comparing blood pressure measures and saccade metrics/lifestyle factors. Results found that higher BMI was the strongest contributor to high blood pressure. This is to be expected, as BMI is a known factor in high blood pressure (Landi et al., 2018). Saccade metrics capturing speed and reaction time were the next highest contributors to the model. Lifestyle factors, including alcohol use and smoking, were weakly associated with high blood pressure. Collectively, these results suggest that poorer saccade performance, mainly speed, is correlated with higher blood pressure, even more so than known lifestyle risks. While other studies have shown cognitive differences in hypertensive adults (Cheon, 2022), the results of the current study provide key information that puts cognitive decline into perspective with other factors in hypertension. Changes in cognition associated with hypertension are observable even in non-elderly adults and should be an additional consideration in health-risk analyses.

While these findings support the importance of understanding cognitive differences in hypertension, this study's sample may not be representative of the general population. Aside from having hypertension and high BMI, this population sample practices relatively healthy lifestyles (or may have underreported on certain measures): having, on average, one cigarette and drink per month and exercising roughly three days a week. In the current study, the high MAP group in the current sample reported slightly lower perceived stress levels on the perceived stress scale than the low and medium MAP groups. This finding differs greatly from prior research that shows people with hypertension tend to have higher levels of stress, which is known to contribute greatly to high blood pressure (Dolezsar et al., 2014).

Hypertension disproportionately affects Black Americans due to current and historical differences in access to reliable health care and the presence of additional life stressors, such as racial discrimination (Dolezsar et al., 2014). These differences are observed in the current study, as the number of Black individuals was higher in the high MAP group, making up nearly 72% of the high MAP group, compared to the other MAP groups where black individuals made up 46% of the low group and 64% of the medium group. Due to these differences, MANOVAs were run, considering race as an additional factor to the MAP group. No significant main effects for race or interaction between race and MAP were found. While the current study did not find any significant differences, these are factors that, due to the disproportionate effects of hypertension, will continue to be considered in future studies.

While considering these results, it is important to remember that the sample of this study is comprised of middle-aged adults. In non-elderly adults, not as much is known about the initial influences that high blood pressure has on the brain and cognition, especially regarding saccade task performance. Age can serve as a protective factor in many ailments and has also been shown to correlate with saccade task performance (Opwonya et al., 2022b). It is possible that the current sample is younger and has likely not had hypertension for as long, making their cognition more intact than older, hypertensive samples. One study evaluating psychomotor reaction time, measured by a button press in response to an auditory, visual, or tactile stimulus, in middle-aged hypertensive and non-hypertensive individuals found no significant group differences (Edwards et al., 2007). Hypertension and cognitive decline is a complex issue, which is why the current study used a variety of sensitive measurements to parse out potential differences. The findings of this study provide early evidence of changes in cognitive behavior. The current sample also captures a single time point throughout the life course; it would be interesting to compare the performance of these individuals after time has passed.

Other Considerations and Future Directions.

When reviewing these results, it is important to note that this is not an epidemiological sample, and our subject pool encompasses only a portion of northern Georgia. While our sample is particularly interesting because it is taken from the American South, where hypertension is more common and severe, it is important to consider that these results may not be generalizable.

Another thing to consider is that the threshold for diagnosing hypertension has changed to become more sensitive throughout the years; this should be kept in mind when comparing our results to past research. Lastly, while our sample holds valuable information on blood pressure throughout the life course, some information on subject demographics is lacking, such as race, ethnicity, and gender. Since this is an ongoing, longitudinal study, only subjects who self-reported as White or Black, male or female, were recruited for this study. Decades later, we know that a diverse sample that better reflects the population is necessary for generalizability. These are considerations that will be better encompassed in future studies.

Conclusion.

Hypertension affects nearly half of American adults. Prolonged hypertension threatens the integrity of the brain and can lead to multiple neurological issues that ultimately affect cognition. Few research studies to date examine this issue in non-elderly adults, leaving much unknown to fuel early intervention causes. This study used saccade tasks, a sensitive and reliable measure that captures multiple aspects of behavior and cognition with known neurological circuitry, to examine this issue from multiple angles. Findings suggest: 1. Individuals with high blood pressure take longer to perform as accurately on cognitively complex tasks as individuals without high blood pressure. This is shown by significant group differences found in the antisaccade condition but not the prosaccade condition, suggesting impaired cognitive control in the high MAP group. 2. Saccade performance metrics are correlated with high blood pressure on a similar level as lifestyle metrics, including alcohol use and stress. Collectively, this study highlights the beginnings of neuro-cognitive differences associated with hypertension in early-middle-aged adults, which can be used to inform early intervention measures.

References

American Heart Association. *Facts About High Blood Pressure*. (n.d.). Www.Heart.Org. Retrieved July 23, 2024, from https://www.heart.org/en/health-topics/high-blood-pressure/the-facts-about-high-blood-pressure

Bittencourt, J., Velasques, B., Teixeira, S., Basile, L. F., Salles, J. I., Nardi, A. E., Budde, H., Cagy, M., Piedade, R., & Ribeiro, P. (2013). Saccadic eye movement applications for psychiatric disorders. Neuropsychiatric Disease and Treatment, 9, 1393–1409. https://doi.org/10.2147/NDT.S45931

Broche-Pérez, Y., Herrera Jiménez, L. F., & Omar-Martínez, E. (2016). Neural substrates of decision-making. Bases neurales de la toma de decisiones. *Neurologia (Barcelona, Spain)*, *31*(5), 319–325. https://doi.org/10.1016/j.nrl.2015.03.001

CDC. (2023, July 6). *Facts About Hypertension | cdc.gov*. Centers for Disease Control and Prevention. https://www.cdc.gov/bloodpressure/facts.htm

Cheon, E.-J. (2022). Hypertension and cognitive dysfunction: A narrative review. *Journal of Yeungnam Medical Science*, *40*(3), 225–232. https://doi.org/10.12701/jyms.2022.00605

Chobufo, M. D., Gayam, V., Soluny, J., Rahman, E. U., Enoru, S., Foryoung, J. B., Agbor, V. N., Dufresne, A., & Nfor, T. (2020). Prevalence and control rates of hypertension in the USA: 2017-2018. *International Journal of Cardiology. Hypertension*, *6*, 100044. https://doi.org/10.1016/j.ijchy.2020.100044

Cohen, S., Kamarck, T., & Mermelstein, R. (1983). *Perceived Stress Scale* [Database record]. APA PsycTests. https://doi.org/10.1037/t02889-000

DeSouza, J. F., Menon, R. S., & Everling, S. (2003). Preparatory set associated with pro-saccades and anti-saccades in humans investigated with event-related FMRI. *Journal of neurophysiology*, *89*(2), 1016–1023. https://doi.org/10.1152/jn.00562.2002

Dolezsar, C. M., McGrath, J. J., Herzig, A. J. M., & Miller, S. B. (2014). Perceived Racial Discrimination and Hypertension: A Comprehensive Systematic Review. *Health Psychology : Official Journal of the Division of Health Psychology, American Psychological Association*, *33*(1), 20–34. https://doi.org/10.1037/a0033718

Dufouil, C., de Kersaint–Gilly, A., Besançon, V., Levy, C., Auffray, E., Brunnereau, L., Alpérovitch, A., & Tzourio, C. (2001). Longitudinal study of blood pressure and white matter hyperintensities. *Neurology*, *56*(7), 921–926.https://doi.org/10.1212/WNL.56.7.921

Edwards, L., Ring, C., McIntyre, D., Carroll, D., & Martin, U. (2007). Psychomotor speed in hypertension: Effects of reaction time components, stimulus modality, and phase of the cardiac cycle. *Psychophysiology*, *44*(3), 459–468. https://doi.org/10.1111/j.1469-8986.2007.00521.x

Eggers, S. D. Z., Horn, A. K. E., Roeber, S., Härtig, W., Nair, G., Reich, D. S., & Leigh, R. J. (2015). Saccadic palsy following cardiac surgery: A review and new hypothesis. *Annals of the New York Academy of Sciences*, *1343*(1), 113–119. https://doi.org/10.1111/nyas.12666

George, K. M., Maillard, P., Gilsanz, P., Fletcher, E., Peterson, R. L., Fong, J., Mayeda, E. R., Mungas, D. M., Barnes, L. L., Glymour, M. M., DeCarli, C., & Whitmer, R. A. (2023).

Association of Early Adulthood Hypertension and Blood Pressure Change With Late-Life Neuroimaging Biomarkers. *JAMA network open*, *6*(4), e236431. https://doi.org/10.1001/jamanetworkopen.2023.6431

Gibaldi, A., & Sabatini, S. P. (2021). The saccade main sequence revised: A fast and repeatable tool for oculomotor analysis. *Behavior Research Methods*, *53*(1), 167–187. https://doi.org/10.3758/s13428-020-01388-2

Guadron, L., Titchener, S. A., Abbott, C. J., Ayton, L. N., van Opstal, J., Petoe, M. A., & Goossens, J. (2023). The Saccade Main Sequence in Patients With Retinitis Pigmentosa and Advanced Age-Related Macular Degeneration. *Investigative Ophthalmology & Visual Science*, *64*(3), 1. https://doi.org/10.1167/iovs.64.3.1

Guadron, L., van Opstal, A. J., & Goossens, J. (2022). Speed-accuracy tradeoffs influence the main sequence of saccadic eye movements. *Scientific Reports*, *12*, 5262. https://doi.org/10.1038/s41598-022-09029-8

Hajjar, I., Quach, L., Yang, F., Chaves, P. H., Newman, A. B., Mukamal, K., Longstreth, W., Jr, Inzitari, M., & Lipsitz, L. A. (2011). Hypertension, white matter hyperintensities, and concurrent impairments in mobility, cognition, and mood: the Cardiovascular Health Study. *Circulation*, *123*(8), 858–865. https://doi.org/10.1161/CIRCULATIONAHA.110.978114

Hao, G., Wang, X., Treiber, F. A., Harshfield, G., Kapuku, G., & Su, S. (2017). Blood Pressure Trajectories From Childhood to Young Adulthood Associated With Cardiovascular Risk: Results From the 23-Year Longitudinal Georgia Stress and Heart Study. *Hypertension (Dallas, Tex. : 1979)*, *69*(3), 435–442. https://doi.org/10.1161/HYPERTENSIONAHA.116.08312

Harris, C. M., & Wolpert, D. M. (2006). The main sequence of saccades optimizes speed-accuracy trade-off. *Biological Cybernetics*, *95*(1), 21. https://doi.org/10.1007/s00422-006-0064-x

Heitz, R. P. (2014). The speed-accuracy tradeoff: History, physiology, methodology, and behavior. *Frontiers in Neuroscience*, *8*, 150. https://doi.org/10.3389/fnins.2014.00150

Hicken, M. T., Lee, H., Morenoff, J., House, J. S., & Williams, D. R. (2014). Racial/Ethnic Disparities in Hypertension Prevalence: Reconsidering the Role of Chronic Stress. *American Journal of Public Health*, *104*(1), 117–123. https://doi.org/10.2105/AJPH.2013.301395

Hutton, S. B. (2008). Cognitive control of saccadic eye movements. *Brain and Cognition*, *68*(3), 327–340. https://doi.org/10.1016/j.bandc.2008.08.021

Kandil, H., Soliman, A., Alghamdi, N. S., Jennings, J. R., & El-Baz, A. (2023). Using Mean Arterial Pressure in Hypertension Diagnosis versus Using Systolic or Diastolic Blood Pressure Measurements. *Biomedicines*, *11*(3). https://doi.org/10.3390/biomedicines11030849

Landi, F., Calvani, R., Picca, A., Tosato, M., Martone, A. M., Ortolani, E., Sisto, A., D'Angelo, E., Serafini, E., Desideri, G., Fuga, M. T., & Marzetti, E. (2018). Body Mass Index is Strongly Associated with Hypertension: Results from the Longevity Check-Up 7+ Study. *Nutrients*, *10*(12), 1976. https://doi.org/10.3390/nu10121976

Lockhart, S. N., & DeCarli, C. (2014). Structural imaging measures of brain aging. *Neuropsychology Review*, *24*(3), 271–289. https://doi.org/10.1007/s11065-014-9268-3

Matsuda, T., Matsuura, M., Ohkubo, T., Ohkubo, H., Matsushima, E., Inoue, K., Taira, M., & Kojima, T. (2004). Functional MRI mapping of brain activation during visually guided saccades and antisaccades: cortical and subcortical networks. *Psychiatry Research*, *131*(2), 147–155. https://doi.org/10.1016/j.pscychresns.2003.12.007

Mayo Clinic. *High blood pressure (hypertension): Controlling this common health problem- High blood pressure (hypertension) - Symptoms & causes*. (n.d.). Mayo Clinic. Retrieved July 23, 2024, from https://www.mayoclinic.org/diseases-conditions/high-blood-pressure/symptoms-causes/syc-20373410

McDowell, J. E., Dyckman, K. A., Austin, B. P., & Clementz, B. A. (2008). Neurophysiology and neuroanatomy of reflexive and volitional saccades: evidence from studies of humans. *Brain and cognition*, *68*(3), 255–270. https://doi.org/10.1016/j.bandc.2008.08.016

McDowell, J. E., & Clementz, B. A. (1997). The effect of fixation condition manipulations on antisaccade performance in schizophrenia: Studies of diagnostic specificity. *Experimental Brain Research*, *115*(2), 333–344. https://doi.org/10.1007/PL00005702

National Institute on Aging. *Cognitive Health and Older Adults*. (2024, June 11). National Institute on Aging. https://www.nia.nih.gov/health/brain-health/cognitive-health-and-older-adults

Modi, P., & Arsiwalla, T. (2024). Hypertensive Retinopathy. In *StatPearls*. StatPearls Publishing.http://www.ncbi.nlm.nih.gov/books/NBK525980/

Opwonya, J., Doan, D. N. T., Kim, S. G., Kim, J. I., Ku, B., Kim, S., Park, S., & Kim, J. U. (2022a). Saccadic Eye Movement in Mild Cognitive Impairment and Alzheimer's Disease: A Systematic Review and Meta-Analysis. *Neuropsychology Review*, *32*(2), 193–227. https://doi.org/10.1007/s11065-021-09495-3

Opwonya, J., Wang, C., Jang, K.-M., Lee, K., Kim, J. I., & Kim, J. U. (2022b). Inhibitory Control of Saccadic Eye Movements and Cognitive Impairment in Mild Cognitive Impairment. *Frontiers in Aging Neuroscience*, *14*, 871432. https://doi.org/10.3389/fnagi.2022.871432

Pierce, J. E., Clementz, B. A., & McDowell, J. E. (2019). Saccades: Fundamentals and Neural Mechanisms. In C. Klein & U. Ettinger (Eds.), *Eye Movement Research: An Introduction to its Scientific Foundations and Applications* (pp. 11–71). Springer International Publishing. https://doi.org/10.1007/978-3-030-20085-5_2

Polli, F. E., Barton, J. J., Vangel, M., Goff, D. C., Iguchi, L., & Manoach, D. S. (2006). Schizophrenia patients show intact immediate error-related performance adjustments on an antisaccade task. *Schizophrenia research*, *82*(2-3), 191–201. https://doi.org/10.1016/j.schres.2005.10.003

Ramat, S., Leigh, R. J., Zee, D. S., & Optican, L. M. (2007). What clinical disorders tell us about the neural control of saccadic eye movements. *Brain*, *130*(1), 10–35. https://doi.org/10.1093/brain/awl309

Sharma, R., Sekhon, S., Lui, F., & Cascella, M. (2024). White Matter Lesions. In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK562167/

Soller, B., McCombie, D., & Kanter, B. (2015). *GE DINAMAPTM CARESCAPETM V100*.

Su, S., Wang, X., Pollock, J. S., Treiber, F. A., Xu, X., Snieder, H., McCall, W. V., Stefanek, M., & Harshfield, G. A. (2015). Adverse childhood experiences and blood pressure trajectories from childhood to young adulthood: the Georgia stress and Heart study. *Circulation*, *131*(19), 1674–1681. https://doi.org/10.1161/CIRCULATIONAHA.114.013104

The MathWorks Inc. (2022). MATLAB version: 9.13.0 (R2022b), Natick, Massachusetts: The MathWorks Inc. https://www.mathworks.com

Veldink, J. H., Scheltens, P., Jonker, C., & Launer, L. J. (1998). Progression of cerebral white matter hyperintensities on MRI is related to diastolic blood pressure. *Neurology*, *51*(1), 319–320. https://doi.org/10.1212/WNL.51.1.319

Wang, X., & Hsiang, S. M. (2011). Modeling trade-off between time-optimal and minimum energy in saccade main sequence. *Biological Cybernetics*, *104*(1), 65–73. https://doi.org/10.1007/s00422-011-0420-3

Tables

Variable	Mean Arterial Pressure Group: Low	Medium	High
Overall N = 213	69	74	71
Mean (SD)			
MAP	78.8 (4.9)	91.0 (2.9)	104.2 (5.8)
Systolic BP	108.5 (9.6)	116.5 (7.5)	138.5 (10.4)
Diastolic BP	66.6 (5.8)	74.0 (4.5)	84.0 (6.4)
Age	38.2 (4.8)	38.2 (4.5)	41.2 (3.1)
BMI	26.6 (4.7)	32.7 (7.5)	35.1 (7.4)
Perceived Stress	13.2 (6.6)	14.0 (6.4)	12.3 (6.6)
Exercise (per week)	3.8 (1.4)	3.2 (1.4)	3.2 (1.5)
Nicotine use (per month)	1.0 (2.0)	1.1 (2.1)	.9 (2.1)
Alcohol use (per month)	1.6 (1.3)	1.7 (1.8)	1.3 (1.5)
% of total N (N)			
Sex			
Male	15.0% (32)	14.5% (31)	15.5% (33)
Female	17.0% (37)	20.0% (44)	18.0% (38)
Race			
Black	17.0% (37)	12.0% (27)	7.0% (15)
White	15.0% (32)	22.0% (48)	27.0% (58)

Table 1. Demographic Information. Table 1. Depicts the demographic information of the final sample according to group membership, including the overall sample size, age, sex, and race. Lifestyle metrics, such as exercise per week (in days) and monthly nicotine and alcohol use (in days per month), are also included. Age is the mean and standard deviation (SD) in years. Sex and race are shown as the number (N) of each group and the percent of the sample each category makes up.

	Group mean (SD)			Statistics	
Variable	**Low MAP**	**Medium MAP**	**High MAP**	***f***	***p***
PS Gap RT	153.8 (25.5)	154.95(25.2)	155.6 (24.7)	.10	.907
PS Synchronous RT	172.6 (26.3)	174.5 (25.6)	177.4 (26.9)	.61	.543
PS Overlap RT	186.1 (38.1)	192.0 (39.3)	177.4 (26.9)	.69	.504
AS Gap Correct RT	312.8 (82.8)	324.9 (71.3)	329.7 (70.2)	.95	.390
AS Overlap Correct RT	349.7 (72.6)	370.4 (84.4)	386.6 (78.0)	3.89	**.023***
AS Gap Error RT	200.2 (39.0)	193.3 (32.2)	197.3 (42.9)	.58	.560
AS Overlap Error RT	221.6 (53.0)	222.3 (41.2)	233.8 (54.3)	1.35	.261
AS Gap % correct	72.3 (23.0)	64.3 (25.2)	67.1 (23.7)	2.10	.126
AS Overlap % correct	70.9 (22.9)	67.9 (20.9)	67.7 (19.9)	.50	.610

Table 2. MANOVA Results. Table 2 depicts group means for the low, medium, and high MAP groups, standard deviations for variables of interest, and *f* and *p* values resulting from multiple ANOVAs. Significant group differences were found in antisaccade reaction times for correct trials for the antisaccade overlap condition. **MAP=Mean Arterial Pressure, RT=Reaction Time SD=Standard Deviation, PS=prosaccade, AS = Antisaccade, * = *p*<.05.**

Component 1	Component 2
Mean Arterial Pressure .873	BMI .926
Systolic Blood Pressure .865	Antisaccade Reaction Time .242
Diastolic Blood Pressure .489	Monthly nicotine use -.029
	Antisaccade gain -.044
	Perceived stress -.047
	Prosaccade reaction time -.059
	Antisaccade percent correct -.093
	Prosaccade gain -.118
	Monthly alcohol use -.180
	Weekly exercise -.196
	Prosaccade Peak Velocity -.233
	Antisaccade Peak Velocity -.285

Table 3. Canonical correlation components. Table 3 shows a heatmap of correlations for sets 1 and 2 components. Set 1 shows loadings for blood pressure measurements (mean arterial pressure (MAP), systolic, and diastolic blood pressure), and set 2 shows loadings for saccade performance (pro and antisaccade reaction time, gain, and peak velocity, and antisaccade percent correct) and lifestyle factors (body mass index (BMI), monthly alcohol and nicotine use, and weekly exercise). Red indicates a positive association, and blue indicates a negative one. Higher absolute values indicate a stronger correlation. In set 1, all measures are strongly correlated, with MAP and systolic blood pressure being the strongest. In set 2, BMI and antisaccade reaction time have strong and moderate positive contributions, and pro and antisaccade peak velocity have moderate negative contributions.

Figures

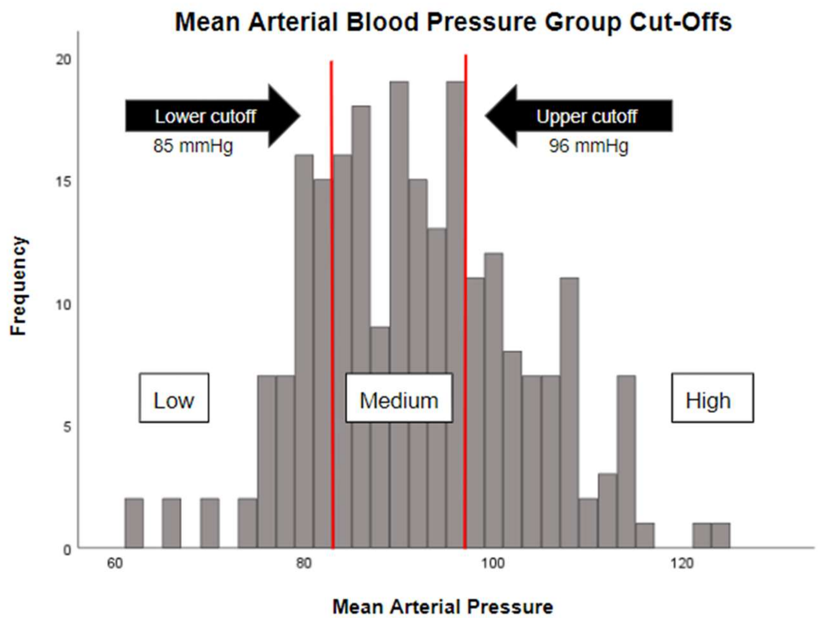


Figure 1. Mean Arterial Blood Pressure Group Cut-Offs. Figure 1. shows the frequency distribution of mean arterial blood pressure in this sample. Mean arterial pressure (MAP) is shown on the x-axis, and frequency is on the y-axis. Cut-offs are marked by a vertical, red line at 85 mmHg and 96 mmHg, with arrows indicating the lower and higher ends. Cut-offs were determined by calculating each tertile. The low MAP group is marked below 85 mmHg, the medium group between 85 mmHg and 96 mmHg, and the high group above 96 mmHg.

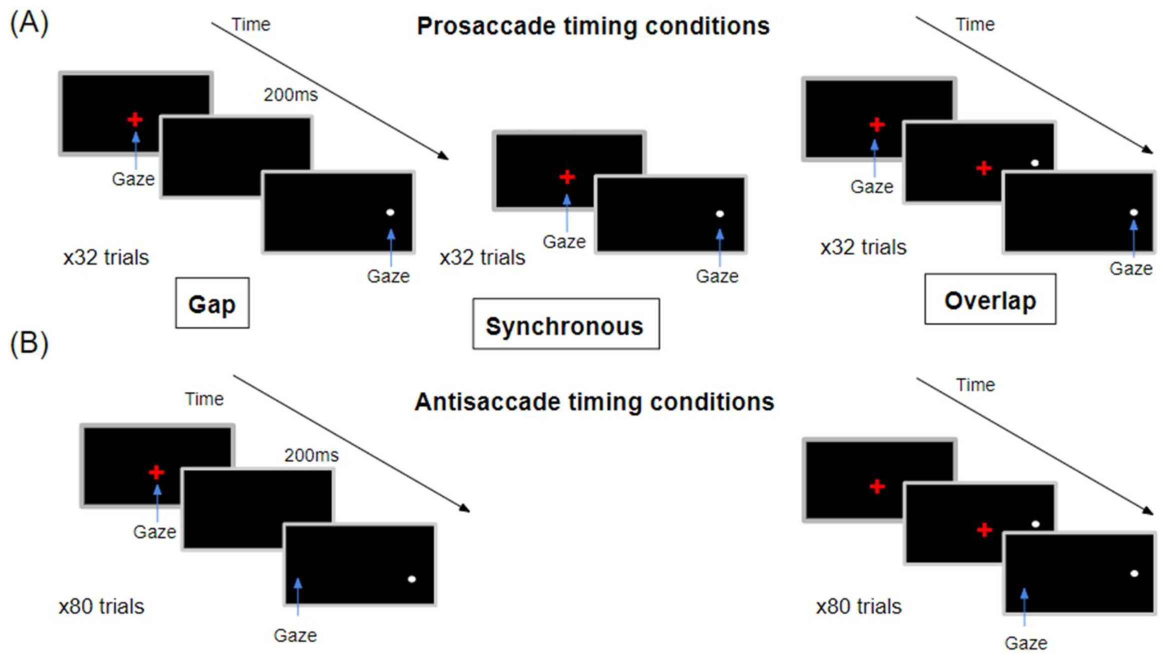


Figure 2. Saccade Task Example. Figures 2a and 2b show examples of each prosaccade and antisaccade condition. Figure 2a describes what the experiment screen looks like for prosaccade gap, synchronous, and overlap conditions, respectively. Figure 2b describes the antisaccade gap and overlap conditions. Each task begins with a red fixation cross in the center, where subjects are instructed to keep their gaze. For the gap condition, the central fixation is removed 200 milliseconds before stimulus presentation. For the synchronous condition, fixation removal and stimulus onset happen simultaneously. For the overlap condition, the central fixation remains on the screen for 200 milliseconds after the stimulus appearance. A blue arrow indicates the correct gaze position throughout each task and did not appear in the tasks. For the prosaccade, the gaze should be on the stimulus, whereas, in the antisaccade condition, the gaze should be in the mirrored direction of the stimulus. There are 32 trials for each prosaccade condition and 80 trials for each antisaccade condition.

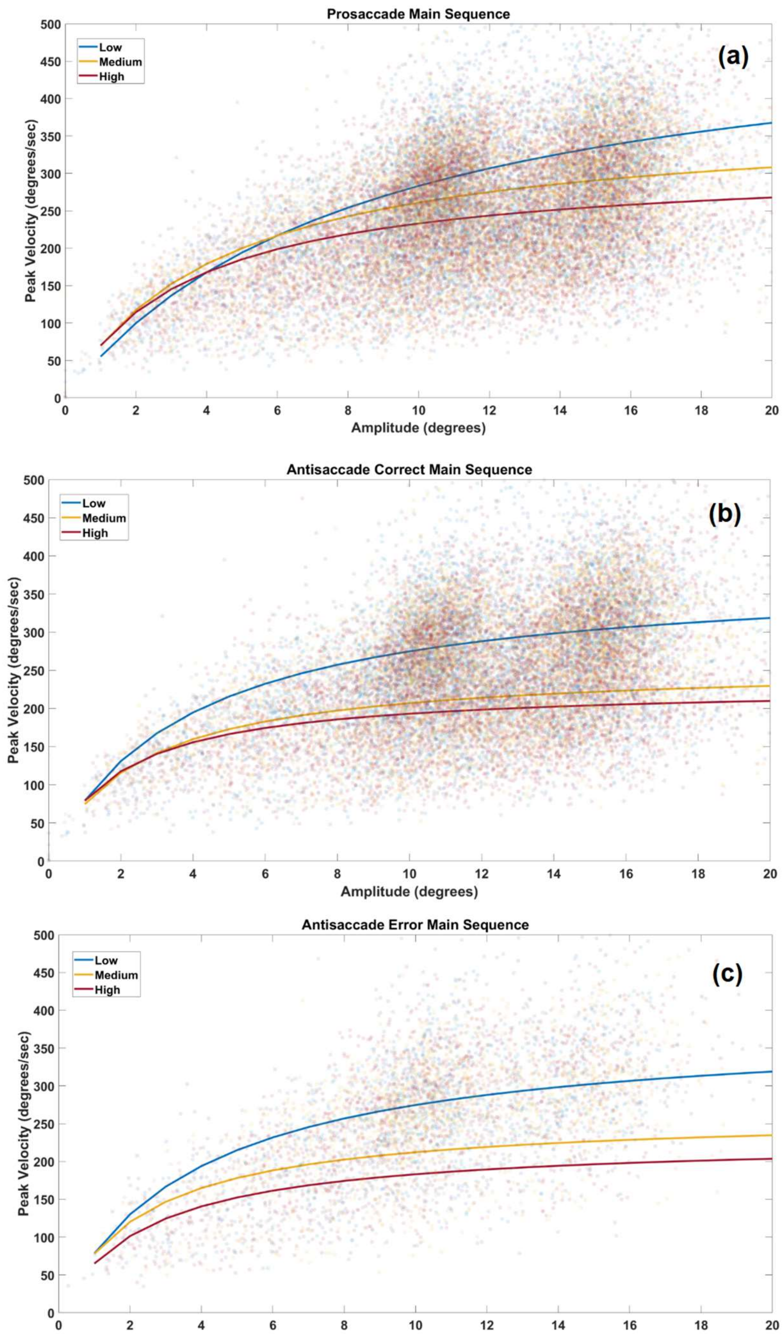
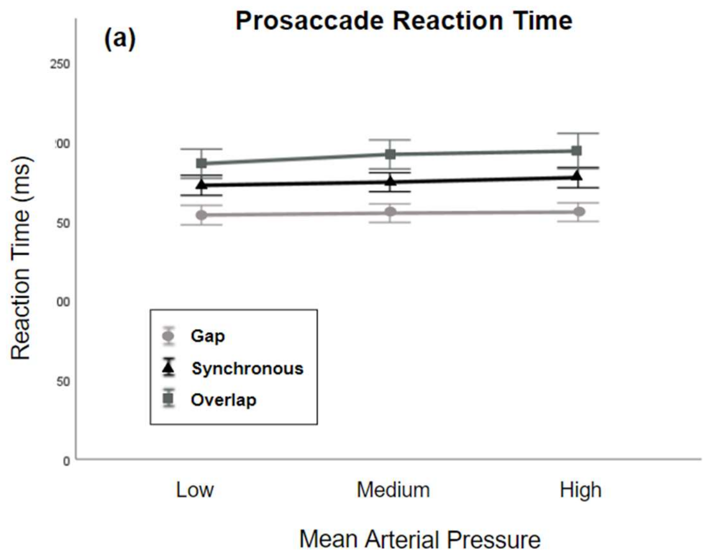
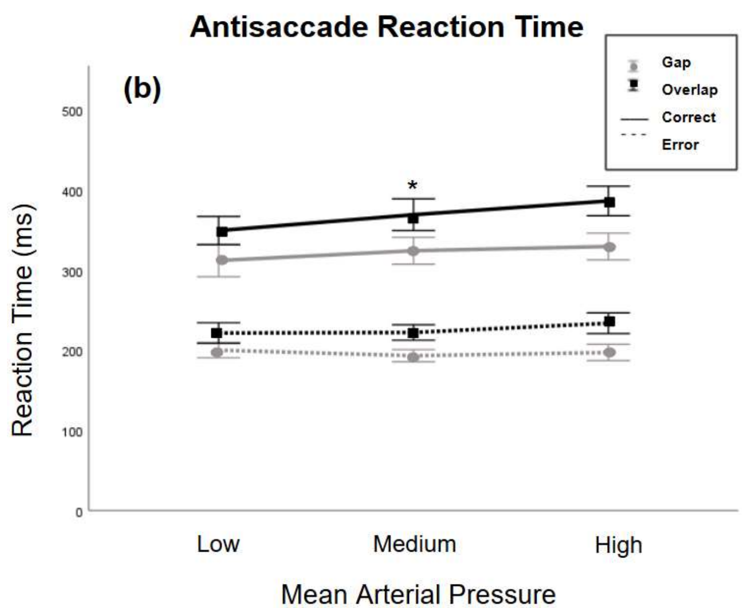


Figure 3a, b, and c. Models of main sequence effects. Figure 3 depicts models of the saccadic main sequence for each task condition per group. Figure 3a shows this for the prosaccade condition (correct trials only), Figure 3b shows models for antisaccade trials that were performed correctly, and Figure 3c models antisaccade trials that an error was made. For all three models, a blue line marks performance for the low MAP group, a yellow line marks the medium MAP group and a red line for the high MAP group. Scatter points indicate the responses of individual trials. No significant group differences were found for any of the models.





Figures 4a and 4b. Reaction time results. Figures 4a and 4b depict average reaction times for the low, medium, and high mean arterial pressure (MAP) groups. Figure 4a compares average group reaction times in the prosaccade task for gap, synchronous, and overlap conditions. For each group, the average prosaccade gap reaction time is marked by a circle, the synchronous by a triangle, and the overlap with a square. Figure 4b compares average group reaction times in the antisaccade task for gap and overlap conditions in trials performed correctly and incorrectly (error). For each group, antisaccade reaction time is marked with a circle for the gap condition and a square for the overlap condition. Results for correct trials are shown as a continuous line, and error trials are shown as a dashed line for each respective timing condition. Results found significant group differences between correct and incorrect antisaccade overlap trials. *** = *p*<.05.**

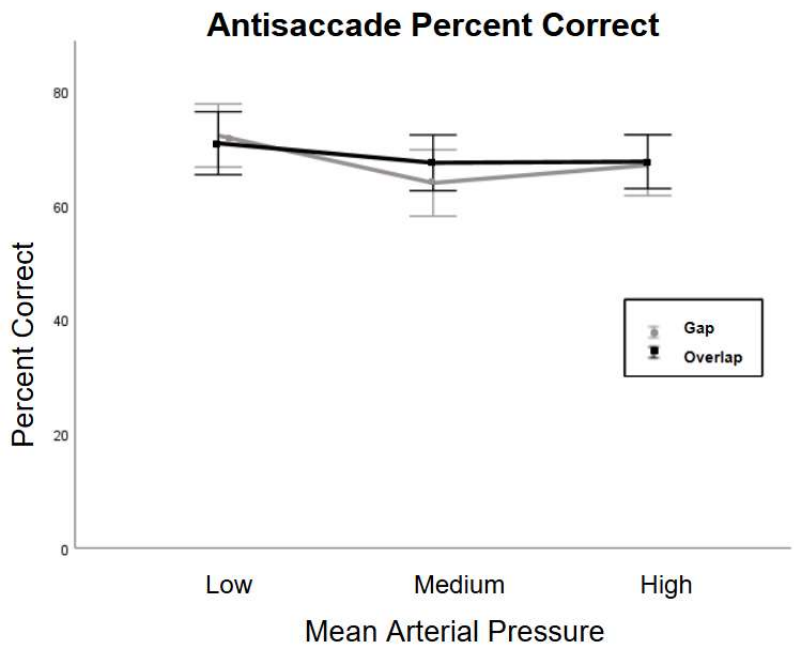


Figure 5. Antisaccade percent correct. Figure 5. shows the average percent correct values for the low, medium, and high MAP groups for the antisaccade gap and overlap conditions. The gap condition is indicated by a gray line and circles, and the overlap condition is indicated by a black line and squares. There were no significant group differences in either the antisaccade gap or overlap conditions.

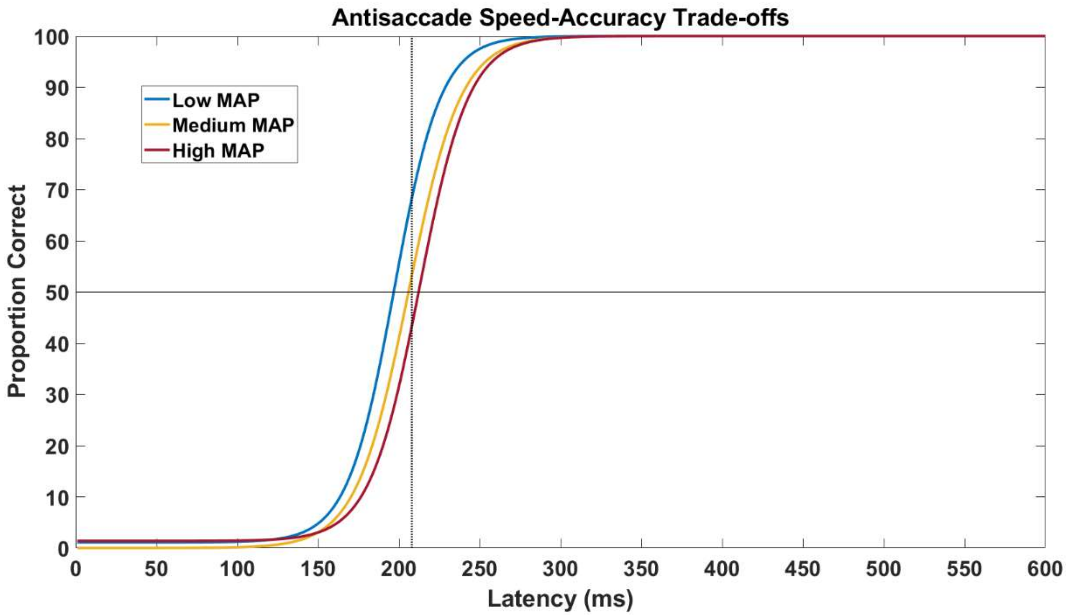


Figure 6. Speed-accuracy models for antisaccade tasks. Saccadic speed accuracy was modeled for the antisaccade task (collapsed across timing conditions). The x-axis shows saccade latency, binned by 10 milliseconds, and the y-axis shows the proportion of correct responses, which was calculated for each latency bin. The horizontal line marks 50% correct, and the vertical line marks the time (ms) where 50% correct is reached. The crosshairs of these two lines indicate the point of maximum speed-trade-off for the medium MAP group. A blue line indicates performance for the low MAP group, the medium MAP group is in yellow, and the high MAP group is in red.

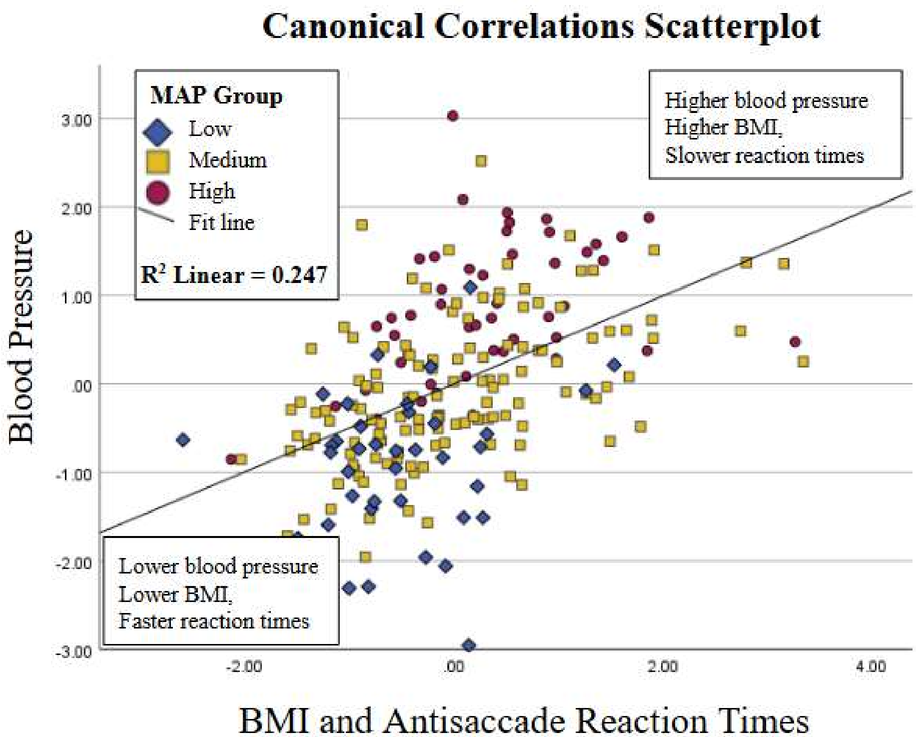


Figure 7. Scatterplot of Canonical Correlations. Figure 7 shows a scatterplot of the canonical loadings per group and the fit line. Component 1 (y-axis) compromises blood pressure measurements: MAP, systolic, and diastolic blood pressure. Component 2 (x-axis) mostly comprises BMI, saccade speed, and reaction time. Low MAP is indicated by a blue diamond, medium by a red circle, and high by a yellow square. The black line indicates the estimated fit line, with an R-squared value of .247.