THE EFFECTS OF BRAND-SPECIFIC HEMP-DERIVED CANNABIDIOL ON PSYCHOMETRICS IN HEALTHY ADULT MALES AND FEMALES OVER 12 WEEKS

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ABSTRACT

INTRODUCTION: The *Cannabis sativa* plant contains several phyto-cannabinoids, among which Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD) are the most widely known. Although CBD is not a strong agonist of cannabinoid receptors and lacks psychotropic activity, it interacts with several other target sites, leading to its potential pharmacological properties. The sedative effects of CBD, as well as its agonistic effect on serotonin (5-HT3 receptors), lead to anxiolytic and sleep-inducing properties. There is scientific consensus that THC can be effective in treating chronic pain, little is known about the pain-relieving properties of products containing CBD, nor has this work been done in healthy populations. **PURPOSE**: This double-blind, randomized, placebo-controlled study aimed to assess the sex-specific psychometric effects of CBD consumption over 12 weeks in healthy adults. **METHODS**: 27 healthy males (age=24 ± 5y; BMI=26.1 ± 2.7 kg/m^2) and 27 females (24 ± 8y; BMI=23.7 ± 3.4 kg/m^2) completed this study. Participants arrived at the laboratory after >8 h of fasting, and >48 h without alcohol consumption and vigorous exercise. Following baseline measurements (height, weight, blood pressure, EKG, and blood work to ensure health status), participants were stratified by sex and randomized to CBD or placebo groups. Products were given in liquid form and contained medium-chain triglyceride oil. The CBD product contained 50 mg/mL CBD. Participants were instructed to consume 1mL of their product twice daily and were given enough product to last until their next laboratory visit. Psychometric data were collected at baseline and on days 30±3, 60±3, and 90±3. Perceived stress was assessed using the Cohen Perceived Stress Scale, sleep quality was assessed using the Pittsburgh Sleep Quality Index, and a 10-item Likert scale was used to measure perceived pain. Change from baseline was calculated for each measure, and ANOVA was used to determine differences between groups over time while adjusting for baseline values (α=0.05). Males and females were analyzed separately. **RESULTS**: There was a significant Group main effect in females for perceived stress (p=0.047), indicating perceived stress was lower those consuming the placebo product compared to CBD. No differences in perceived stress were found in males (p=0.954). There were no differences between the groups in terms of sleep quality (males: p=0.86; females: p=0.337) and perceived pain (males: p=0.109; females: p=0.449). **CONCLUSIONS**: These findings show slightly differential psychometric responses to chronic CBD consumption in males and females. Females consuming CBD had higher perceived stress compared to placebo, while there were no differences in males, suggesting sex-specific effects of CBD. No differences were identified in sleep or pain. This may indicate products containing only CBD are not sufficient for sleep or pain reduction in healthy individuals. There may be a difference in the effects of CBD upon healthy individuals as compared to those with comorbidities. **PRACTICAL APPLICATIONS**: Consumption of CBD may not improve stress in healthy adult females. Future investigations should assess the sex-specific differences in response to CBD products on various outcomes to further elucidate the effects of CBD dependent on sex. Furthermore, research should include more objective markers to measure stress levels, such as cortisol measurements in both healthy individuals and those with comorbidities.

INTRODUCTION

- CBD is rationalized to improve sleep, anxiety, and depression via sedative effects resulting from its influence on 5-HT3 receptors
- CBD appears to have positive effects on attenuating anxiety when used in acute, experimentally manipulated stressful situations
- While THC is understood to alleviate pain, the effects of CBD ingested in isolation are mixed
- Most research on CBD has been conducted with small sample sizes, acute doses, and in clinical populations

Purpose: To assess the sex-specific psychometric effects of CBD consumption in healthy adult males and females over 12 weeks

CONCLUSIONS AND PRACTICAL APPLICATIONS

- These exploratory findings indicate that males and females experienced different responses to 12 weeks of CBD ingestion
- Females experienced lower perceived stress in the placebo group as compared to the CBD group when adjusting for baseline values at visits 1 and 2, but not at visit 3
- We found no evidence that 100mg daily CBD ingestion over 12 weeks provided benefits to perceived stress, sleep quality, or body discomfort in healthy adults
- Future studies should further investigate possible sex-specific responses to CBD and higher doses in healthy populations

METHODS

Subjects: Healthy adults
- 27 males (age=24 ± 5y; BMI=26.1 ± 2.7 kg/m^2)
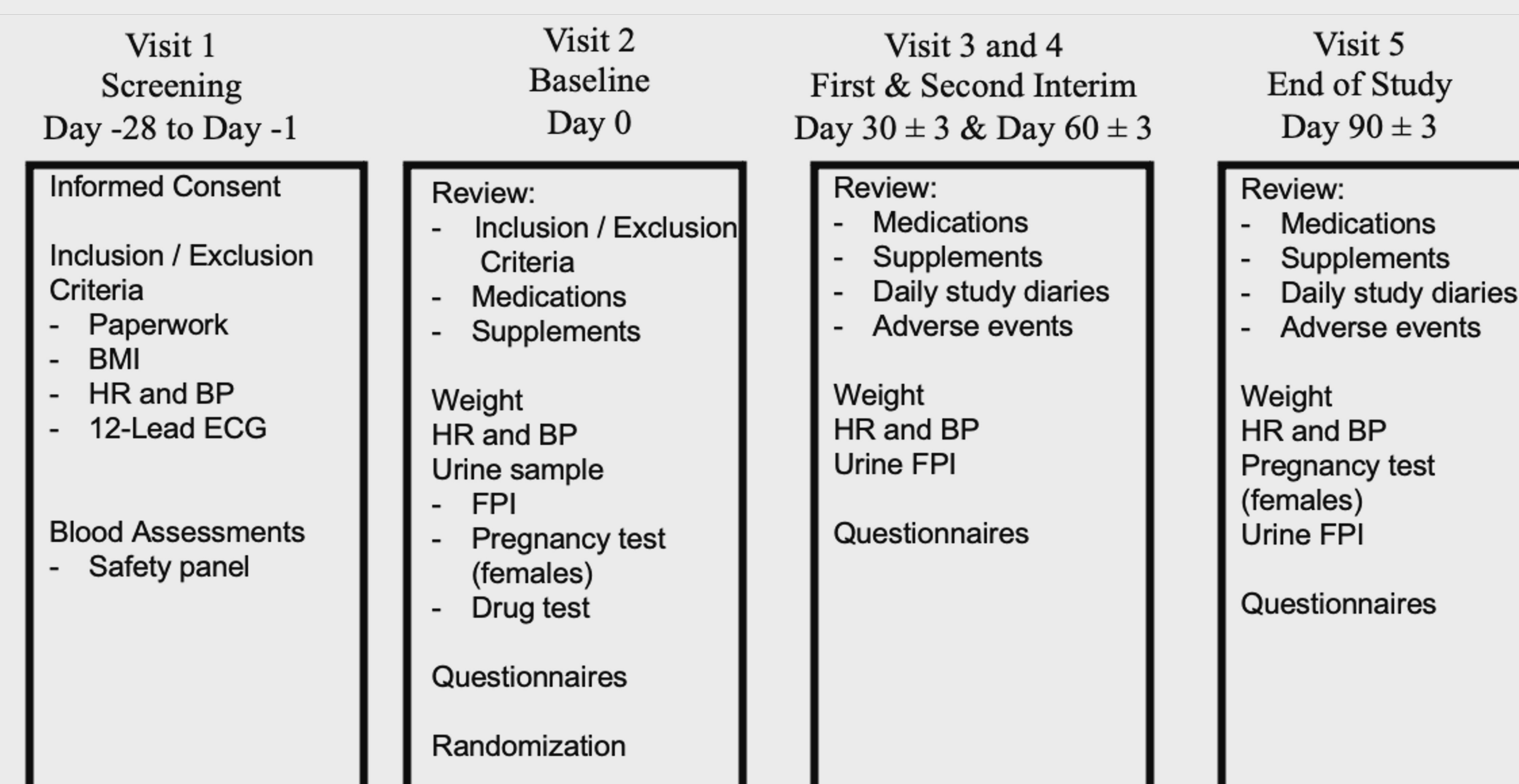- 27 females (age=24 ± 8y; BMI=23.7 ± 3.4 kg/m^2)

Procedures:
- Participants arrived at the lab after >8h of fasting and >48h without alcohol consumption and vigorous exercise

Study Products:
- The CBD and placebo products were suspended in medium-chain triglyceride oil
- The CBD product contained 50mg/mL of CBD
- Participants were instructed to consume 1mL twice daily

Questionnaires:
- Perceived Stress Scale
- Pittsburgh Sleep Quality Index
- Overall Body Discomfort, 10-item Likert scale

Visit 1 Screening Day -28 to Day -1	Visit 2 Baseline Day 0	Visit 3 and 4 First & Second Interim Day 30 ± 3 & Day 60 ± 3	Visit 5 End of Study Day 90 ± 3
Informed Consent	Review: - Inclusion / Exclusion Criteria - Medications - Supplements	Review: - Medications - Supplements - Daily study diaries - Adverse events	Review: - Medications - Supplements - Daily study diaries - Adverse events
Inclusion / Exclusion Criteria - Paperwork - BMI - HR and BP - 12-Lead ECG	Weight HR and BP Urine sample - FPI - Pregnancy test (females) - Drug test	Weight HR and BP Urine FPI	Weight HR and BP Pregnancy test (females) Urine FPI
Blood Assessments - Safety panel	Questionnaires	Questionnaires	Questionnaires
	Randomization		

Statistical Analysis:
- A linear mixed-effects model was used to determine differences between groups over time while adjusting for baseline values (α=0.05). Males and females were analyzed separately. Post hoc t-tests were performed on significant effects using a Bonferroni correction.
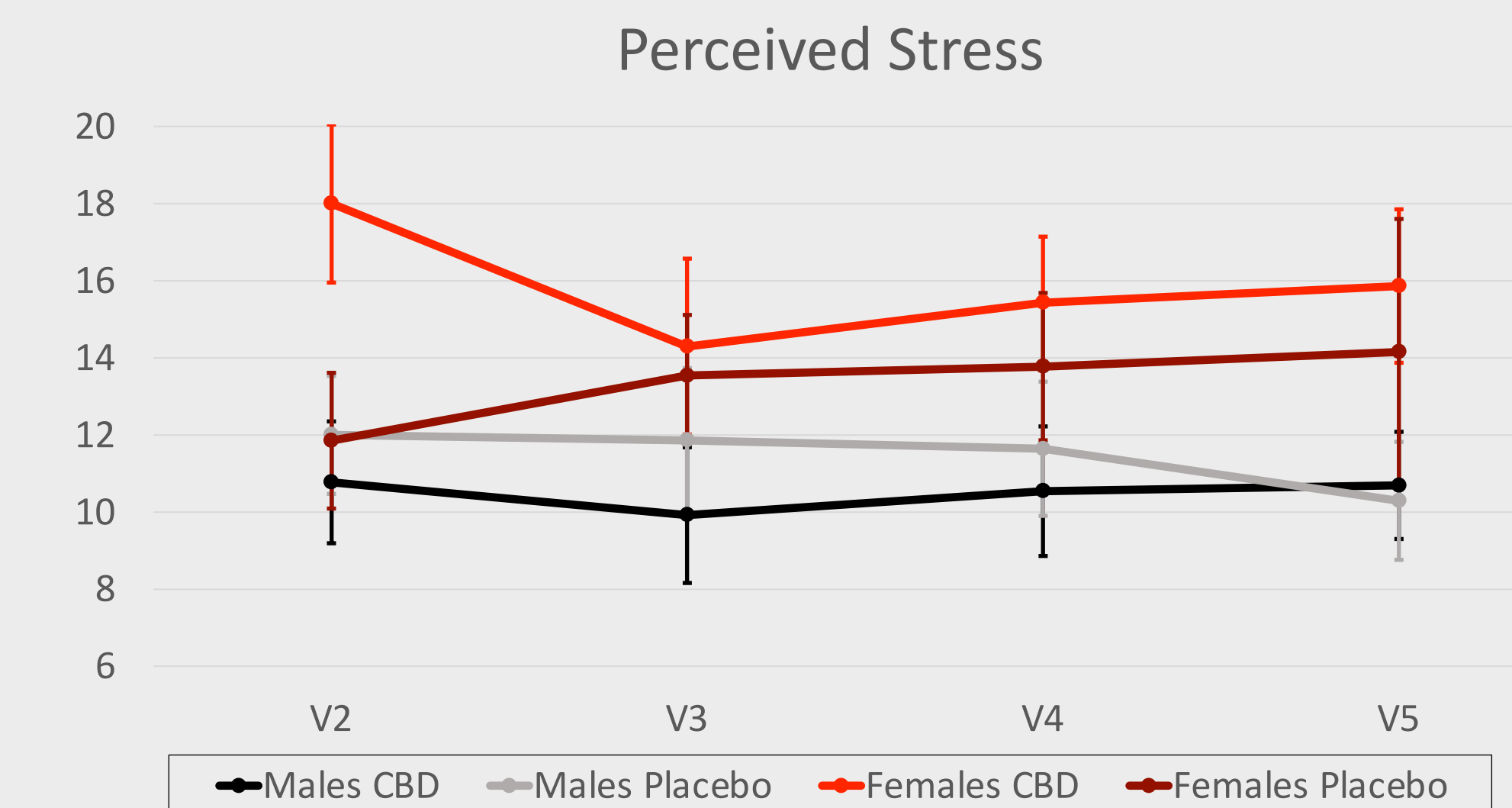
RESULTS

Figure 1. Changes over time with a significant main effect of group in females for perceived stress (p=0.047).
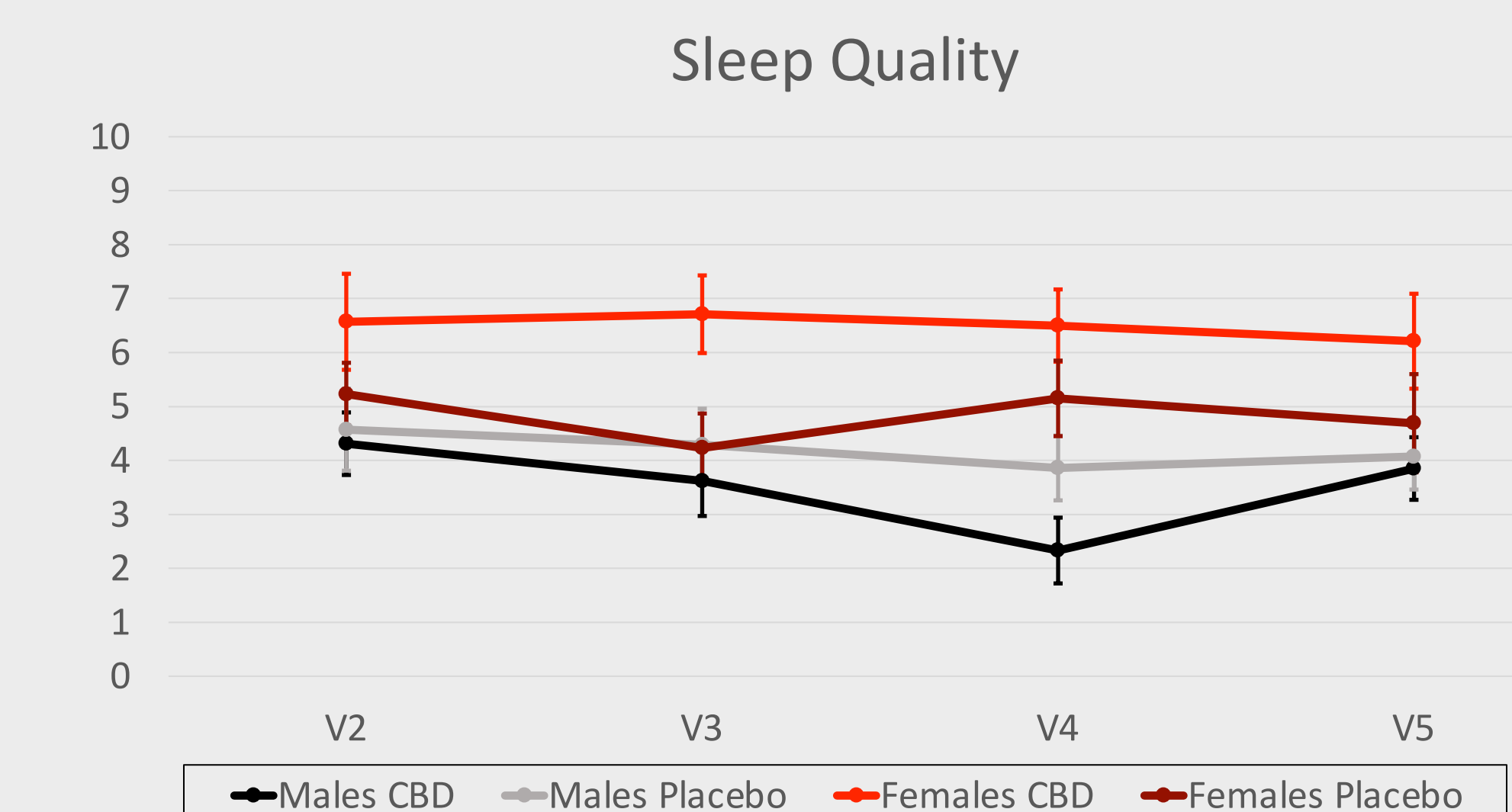

Figure 2. No changes in sleep quality were detected (males: p=0.860; females: p=0.337).
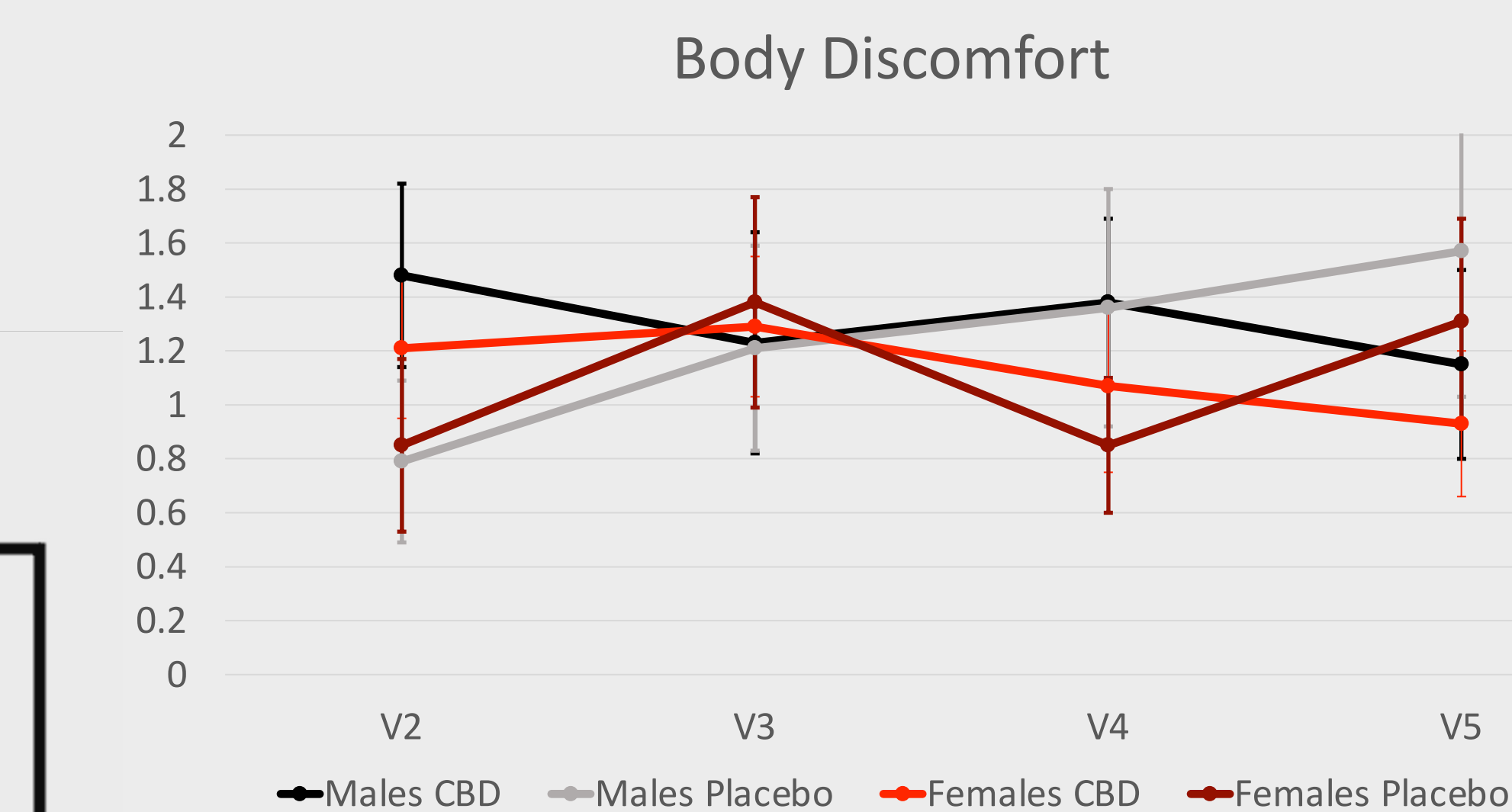

Figure 3. No changes in body discomfort were found (males: p=0.109; females: p=0.449).

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