Disturbances of postural sway components in cannabis users

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Highlights

- Cannabis use is associated with increased postural sway.

- A theoretically driven analysis indicated peripheral nervous system impairment.

- Findings indicate that long-term cannabis use adversely affects postural control.

Abstract

Introduction: A prominent effect of acute cannabis use is impaired motor coordination and driving performance. However, few studies have evaluated balance in chronic cannabis users, even though density of the CB1 receptor, which mediates the psychoactive effects of cannabis, is extremely high in brain regions critically involved in this fundamental behavior. The present study measured postural sway in regular cannabis users and used rambling and trembling analysis to quantify the integrity of central and peripheral nervous system contributions to the sway signal.

Methods: Postural sway was measured in 42 regular cannabis users (CB group) and 36 non-cannabis users (N-CB group) by asking participants to stand as still as possible on a force platform in the presence and absence of motor and sensory challenges. Center of pressure (COP) path length was measured, and the COP signal was decomposed into rambling and trembling components. Exploratory correlational analyses were conducted between sway variables, cannabis use history, and neurocognitive function.

Results: The CB group had significantly increased path length and increased trembling in the anterior-posterior (AP) direction. Exploratory correlational analyses suggested that AP rambling was significantly inversely associated with visuo-motor processing speed.

Discussion: Regular cannabis use is associated with increased postural sway, and this appears to be predominantly due to the trembling component, which is believed to reflect the peripheral nervous system's contribution to the sway signal.

1. Introduction

Cannabis is one of the most commonly used illicit drugs, with 22.2 million people in the United States reporting that they had used it in the past month during the 2015 National Survey on Drug Use and Health (SAMHSA, 2015). Acutely, administration of cannabis or delta-9-tetrahydrocannabinol (THC), the compound responsible for the psychoactive effects of cannabis, broadly impairs cognitive function. Chronic cannabis use has been associated with cognitive impairment in diverse domains including memory and attention, executive control, and decision-making (Lundqvist 2005; Sofuoglu et al., 2010; Thoma et al., 2011). Acute cannabis also impairs vehicle-driving performance (Hartman and Huestis 2013; Lenne et al., 2010), a major concern given the prevalence of use in the United States. However, the effects of chronic cannabis use on specific processes supporting motor and sensorimotor behaviors is not well characterized. In the present study, computational analysis of the neural systems involved in maintaining balance during upright posture was studied in cannabis users and control participants.

Cannabis interferes with normal endocannabinoid system function via THC's partial agonism at CB1 cannabinoid receptors. The heaviest CB1 receptor concentrations are in brain regions that largely reflect behavioral and cognitive effects of cannabis—i.e., the cerebral cortex,

basal ganglia, hippocampus, amygdala and cerebellum (Mackie 2005). Consistent with the distribution of CB1 receptors in the brain, chronic cannabis users differ in resting state functional connectivity patterns that encompass these same regions (Blanco-Hinojo et al., 2017; Wetherill et al., 2015). Neuroanatomical abnormalities in chronic cannabis users also largely map onto these same CB1-receptor rich regions; moreover, greater structural deviations appear to be associated with longer duration and earlier onset of use (Lorenzetti et al., 2016; Martin-Santos et al., 2010; Weinstein et al., 2016). However, one review concluded that structural brain alterations due to cannabis use are negligible (Martin-Santos et al., 2010).

Gross neuroanatomical changes following sustained cannabis use could occur as a consequence of changes in CB1 receptor density. Autoradiographic studies in mice have demonstrated that chronic THC exposure resulted in CB1 receptor down-regulation in all regions with high CB1 receptor density, with cerebellum and hippocampus showing particularly rapid and high magnitude desensitization to THC effects (Sim-Selley and Martin 2002). A recent positron emission tomography (PET) study in chronic cannabis users found evidence of reduced CB1 receptor density in cortical regions, although not in subcortical areas (Hirvonen et al., 2012).

Acute cannabis intoxication impairs motor coordination as well as complex motor behaviors, including driving. Investigations of motor functioning in chronic cannabis users suggest that these deficits are persistent (Bolla et al., 2002; Dervaux et al., 2013), although the relationship between motor effects, amount of cannabis used and age of onset of use is less clear.

Postural sway is a sensitive measure of largely unconscious sensorimotor processes involved in balance. In addition to being particularly densely populated with CB1 receptors, fronto-cerebellar circuits also critically mediate postural control (Ferraye et al., 2014; Ioffe et al., 2007; Jahn 2011; Jahn et al., 2008; Jahn et al., 2004). Neuroimaging studies indicate increased

cerebellar activity during quiet standing (Jahn et al., 2008; Ouchi et al., 1999). Decreased cerebellar volume (Birch et al., 2015) and reductions in regional cerebral blood flow (rCBF) in frontal cortex (Nakamura et al., 1997) are both associated with greater postural instability. Cerebellar damage is also associated with decreased postural control during quiet standing (Ilg et al., 2009; Mauritz et al., 1979). Moreover, transcranial direct current stimulation (tDCS) of cerebellum modulates postural sway (Ehsani et al., 2017; Foerster et al., 2017; Inukai et al., 2016). Cannabis users who were acutely intoxicated after smoking high THC cannabis cigarettes showed increased postural sway (Liguori et al., 2002; Liguori et al., 2003; Liguori et al., 1998). Similarly, acute exposure to pure THC increases postural sway in cannabis users (Klumpers et al., 2012; Zuurman et al., 2010). Hence, postural sway can be considered a sensitive test of the motor circuitry likely to be affected by cannabis use.

To our knowledge, the first study of postural sway in cannabis users was published recently by Pearson-Dennett, et al. (2017), who measured the major and minor hemi-axes and axis angle of the center-of-pressure (COP) ellipse and reported that these measures did not differentiate cannabis users from non-users. However, these sway variables are not commonly used to assess sway and appear to have been used in only one previous study by this same group (Thewlis et al., 2014). By contrast, COP path length is routinely used to assess postural sway, with numerous published studies employing this measure to quantify sway in just the last calendar year (Clark et al., 2017; Howard et al., 2017; Kalron 2017; Koyama and Yamauchi 2017; Lee and Brown 2017; Ludwig 2017; Pavao et al., 2017; Schmidt et al., 2017; Scholes et al., 2017).

The idea of 2-component COP was introduced in the 1990s and the rambling-trembling method (Zatsiorsky and Duarte 1999) in particular has garnered substantial empirical support. As

a result it has been widely accepted to successfully decompose these two components from the complex COP signal following numerous studies demonstrating that rambling and trembling change independently of each other in response to task manipulations (Danna-Dos-Santos et al., 2008; de Freitas et al., 2009; Mochizuki et al., 2006; Tahayor et al., 2012). The rambling-trembling model has also been used to successfully differentiate clinical groups with CNS disorders including developmental coordination disorder (Speedtsberg et al., 2017) and multiple sclerosis (Shin et al., 2011), suggesting it may be useful in clinical evaluation for some patient groups. The rambling component is defined by the migration of a series of centrally determined equilibrium points generated by the central nervous system (CNS) in order to maintain upright posture. The trembling component represents fluctuations about these equilibrium points. This component is believed to arise from "apparent muscle stiffness" and may primarily represent the peripheral nervous system's contribution to postural sway (Zatsiorsky and Duarte 1999).

We compared postural sway in non-cannabis users to regular cannabis users, employing traditional path length measures and rambling-trembling analyses. We also determined the association of sway variables with cannabis use variables, including age of onset of cannabis use and total estimated lifetime use, and with cognitive performance on standardized tests of processing speed, short-term memory, and intelligence quotient (IQ). Given the aforementioned findings suggesting motor systems are compromised by chronic cannabis use, we predicted that 1) cannabis users would have increased postural sway (sway path) compared to non-cannabis users; 2) that rambling would be significantly increased in cannabis users; and 3) that both of these sway measures would be positively correlated with lifetime cannabis use.

2. Methods

2.1 Participants

Participants were 42 cannabis users (CB group) and 36 non-cannabis users (N-CB group; see Table 1 for demographic information). Participants were recruited using advertisements in local newspapers and through posted flyers. The study procedures were approved by the Indiana University Institutional Review Board and the study was conducted in accordance with the Declaration of Helsinki (Edinburgh amendments). Written informed consent was obtained from all participants.

Inclusion criteria for all participants included being 18 years of age or older, completion of high school education, and no history of cardiovascular disease, hearing loss, neurological disease, learning disability, or head injury resulting in loss of consciousness. A specific inclusion criterion for the N-CB group was the stipulation that there be no history of illicit substance abuse or dependence, and no Diagnostic and Statistical Manual of Mental Disorders, fourth Edition (DSM-IV) Axis I diagnoses as determined using the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders-IV Axis I Disorders, non-patient version (SCID-NP)(First et al., 1995).

Specific inclusion criteria for the CB group included current cannabis use at least 1 time per week over a period including the past month, no other illicit substance use for the previous 3 months, and no DSM-IV diagnoses for Axis I disorders other than cannabis abuse or dependence. In addition to the SCID, a written drug use questionnaire and a six-month time line follow back assessment was used to estimate current and past use of CB. Three variables characterizing use of CB were chosen for statistical analyses: age of onset of first CB use, lifetime number of exposures to CB, and CB use in the past month. On average, the CB group had an average age of onset of cannabis use of 16.13 years (SD=2.23), with the last cannabis use 2.23 days (SD=4.51) before testing. The average monthly use was 30.5 joints (SD=24.7), and the mean lifetime

number of CB uses was 1423.4 (SD=2231). Participants underwent urine toxicology testing capable of detecting methamphetamine, opiates, phencyclidine, benzodiazepines, barbiturates, amphetamine, cocaine, and cannabis. Overall, 29 of 37 healthy controls and 20 of 42 cannabis users completed postural sway on the same day as toxicology testing. Because THC metabolites can be detected for days or weeks after use, urine analysis cannot differentiate between use in the previous 24 hours and more remote use. Participants were asked not to use cannabis on the day of assessment, and verbally confirmed that they were not acutely intoxicated prior to postural sway testing. On the basis of self-report and the SCID interview, none of the CB users had used other illicit psychoactive substances in the three months prior to the assessment. None of the CB users had positive urine screens for illicit psychoactive substances other than cannabis.

In terms of comorbidities, three CB subjects were experiencing an anxiety disorder, one was experiencing a major depressive episode, nine subjects had prior episodes of major depression, and one subject had past alcohol dependence. These findings are common comorbidities with CB use (Moore et al., 2007), and consistent with very high lifetime rates of psychiatric comorbidity, approaching 90%, in persons with cannabis dependence (Agosti et al., 2002).

2.2 Procedure

Participants were asked to stand as still as possible with their arms resting comfortably at their sides on an AMTI Accusway (Watertown, MA) force platform, sampling at 200hz, with eyes open and eyes closed, and with feet (base) together or shoulder-width apart, which resulted in 4 separate conditions. One-minute recordings of center of pressure (COP) were made for each condition for each participant.

Participants completed neurocognitive measures including the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler 1999) which provides a valid and reliable estimate of full-scale IQ using 2 subtests of the Wechsler neurocognitive battery: Vocabulary (which measures verbal intelligence) and Matrix Reasoning (a measure of non-verbal intelligence). Two additional Wechsler subtests were also administered: Digit-Symbol Coding and Digit Span, which measure processing speed and verbal working memory, respectively.

2.3 Data analysis

All data were analyzed using MATLAB version 2015b. Data were first subsampled using MATLAB's "decimate" function, which filters the data with an 8th order Chebyshev Type I low-pass filter with a cutoff frequency of 20 Hz, before resampling. A resampling value of 4 was used, resulting in a final sampling rate of 50 Hz. COP path length was computed using the following equation:

$$Path\ Length = \sum_{n-1}^{N} \sqrt{[x(n) - x(n-1)]^2 + [y(n) - y(n-1)]^2}$$

COP trajectories were decomposed into rambling and trembling components according to the approach described by Zatsiorsky and Duarte (1999; 2000). Briefly, an instant equilibrium point (IEP) occurs when the horizontal force component is zero meaning that the ground reaction force was vertical in that instant. Cubic spline was used to reconstruct an IEP trajectory from these points, which was the rambling trajectory. Trembling was estimated as the deviations of the COP trajectory from the IEPs. The root mean square (RMS) was then computed for both rambling and trembling trajectories in the medio-lateral (ML) and anterior-posterior (AP) directions.

2.4 Statistical analyses

Because sway variables were not normally distributed, they were log transformed prior to each analysis. Repeated measures Analysis of Variance (ANOVA) tests were used to analyze COP path length, rambling RMS, and trembling RMS data with Eye (Open, Closed) and Base (Open, Closed) as within-subjects conditions, and Group (CB and N-CB) as the between-subjects condition. Because weight is known to have effects on postural sway, we determined whether weight was significantly correlated with sway variables separately for each of the ANOVAs. In cases where there were one or more significant correlations with weight, it was included as a covariate in that ANOVA. If weight was significant as a covariate in the model, it was retained and results were reported accordingly. Because of evidence of sex differences associated with cannabis consumption (Calakos et al., 2017), repeated measures ANOVAs using both group and sex as between-subjects variables were conducted. These tests showed no significant sex effects for any dependent variables. For all statistical analyses, post-hoc comparisons using the Bonferroni correction were conducted when interactions were significant ($p<0.05$). Results of the major dependent variables are reported with their corresponding effect sizes in the form of partial eta^2 (ηp^2) where values of $\eta p^2<0.06$ were considered small, effect sizes of $0.06<\eta p^2<0.14$ were considered moderate, and effect sizes of $\eta p^2>0.14$ were considered large (Cohen 1973).

Pearson's correlations were computed to determine whether significant associations existed between total estimated lifetime cannabis use and both sway path and rambling in accordance with the stated hypotheses. In addition, exploratory Pearson's correlations were computed to determine whether significant associations existed between postural sway variables. Only the eyes-closed, closed-base condition was submitted to these analyses because it is the most challenging and should lead to the most between- subjects variability. Therefore, 5 sway variables (eyes-closed, closed-base for path length, AP rambling, AP trembling, ML rambling

and ML trembling) were correlated with WASI IQ, Digit Symbol scaled score, Digit Span scaled score, lifetime days of cannabis use, and age of onset of cannabis use.

3. Results

Exemplar plots of COP path length data from an N-CB and a CB participant in the eyes-closed, base-closed condition are shown in Figure 1, with corresponding plots of their rambling and trembling trajectories graphically depicted in Figure 2. These particular participants were chosen because their COP path length data were closest to the means within their groups.

3.1 Demographics and clinical variables

Groups did not differ on weight [$t(76)=-0.56$, $p=0.58$], age [$t(76)=1.20$, $p=0.24$], or sex [$X^2(1) = 0.005$, $p = 0.94$]. The N-CB group had significantly higher WASI IQ scores than the cannabis group, $t(76)=2.19$, $p=0.03$, although both groups are well above the population average. There were no group differences on Digit Symbol Coding or the Digit Span test.

Table 1. Demographic information for N-CB and CB groups.

3.2 Path length

The CB group had longer path length compared to controls, $F(1,76)=5.34$, $p<0.02$, $\eta p^2=0.07$. Overall, path length was also increased in the eyes-closed condition, $F(1,76)=273.83$, $p<0.001$, $\eta p^2=0.78$, and the base-closed condition, $F(1,76)=100.54$, $p<0.001$, $\eta p^2=0.57$. There was also an Eyes by Base interaction, $F(1,76)=29.34$, $p<0.001$, $\eta p^2=0.28$. Sway path data are represented graphically in Figure 3.

3.3 Rambling-Trembling analysis

3.3.1 Overview. The cannabis group showed increased trembling in both the anterior-posterior (AP) and medio-lateral (ML) directions but did not differ from the N-CB group for the rambling measures. Across groups, the eyes closed condition and the closed based position

produced increased rambling and trembling compared to the eyes open and open base conditions, respectively.

3.3.1.1 ML rambling RMS. No Group main effect or interactions were observed for ML rambling. A main effect of Eyes was observed, $F(1,76)=25.15$, $p<0.001$, $\eta p^2=0.25$, due to increased rambling in the eyes-closed condition. Similarly, increased rambling in the base closed condition produced a main effect of Base, $F(1,76)=317.29$, $p<0.001$, $\eta p^2=0.81$. Finally, there was an Eyes by Base interaction, $F(1,76)=9.10$, $p=0.003$, $\eta p^2=0.11$. Figure 4A depicts these results.

3.3.1.2 ML trembling RMS. The CB group had increased trembling in the ML direction compared to N-CB, $F(1,76)=6.11$, $p=0.02$, $\eta p^2=0.07$. There was a main effect of Eyes, in which trembling increased in the eyes closed conditions, $F(1,76)=141.68$, $p<0.001$, $\eta p^2=0.65$. Likewise, there was a main effect of base, $F(1,76)=184.42$, $p<0.001$, $\eta p^2=0.71$, where trembling increased in the base closed conditions. There was also an Eyes by Base interaction, $F(1,76)=31.79$, $p<0.001$, $\eta p^2=0.30$. No interactions were found between Group and ML trembling. These data are represented graphically in Figure 4B.

3.3.1.3 AP rambling RMS. Weight was correlated with AP RMS rambling and was significant as a between subjects covariate, $F(1,75)=4.59$, $p=0.04$, $\eta p^2=.06$, so it was included in the ANOVA. There was no main effect of group, nor were there any two-way interactions with group; however, there was a main effect of Eyes, $F(1,75)=21.47$, $p<0.001$, $\eta p^2=0.22$, with increased rambling in the eyes closed condition. There was also a significant 3-way Eyes by Base by Group interaction, $F(1,75)=5.70$, $p=0.02$, $\eta p^2=0.07$. Figure 4C shows data for AP rambling. Post-hoc tests showed that the CB group had significantly reduced trembling in the eyes-closed, closed base condition compared to the eyes-closed, open-base condition, $p=0.02$.

3.3.1.4 AP Trembling RMS. Weight was correlated with AP trembling and was significant as a between subjects covariate, $F(1,75)=8.14$, $p=0.006$, $\eta p^2=0.10$, so it was included in the ANOVA. In this model, the CB group had significantly increased trembling compared to N-CB, $F(1,75)=6.51$, $p=0.01$, $\eta p^2=0.08$. Trembling was increased in the eyes-closed conditions, resulting in a main effect of Eye, $F(1,75)=273.70$, $p<0.001$, $\eta p^2=0.79$. It was also increased in the base-closed conditions, $F(1,75)=11.57$, $p=0.001$, $\eta p^2=0.13$, for a main effect of Base. Finally, there was an Eyes by Base interaction, $F(1,75)=4.17$, $p=0.05$, $\eta p^2=0.05$. However, there were no interactions with Group. See Figure 4D for AP trembling data.

3.4 Correlations with demographic, and cannabis use

In the entire sample, the Digit Symbol Scaled Score was significantly inversely correlated with AP rambling, $r(76)=-0.302$, $p=0.008$, and to a lesser extent with ML trembling, $r(76)=-0.252$, $p=0.03$. In the CB group, there were no significant correlations between the sway measures and measures of current CB use, lifetime days of use or age of onset of CB use.

4. Discussion

The primary findings from the present study are that cannabis use is associated with increased path length and increased trembling in both the AP and ML directions. We had predicted that the CB group would primarily have increased rambling, but neither the ML nor AP directions showed significant differences between groups. Interpreted within the framework of the rambling-trembling model, this finding would indicate that CNS regulation of postural control was not impaired. However, one interpretation for this result that does implicate a CNS deficit is that the cerebellum is impaired by chronic cannabis use and this disrupts its ability to make use of incoming proprioceptive sensory information from muscle spindles in the spinocerebellar tract. In this case, the cerebellum would be unable to efficiently execute postural

adjustments and this would be reflected in excess trembling. This explanation is consistent with findings of neuroanatomical alterations in the cerebellum following chronic cannabis use (Lorenzetti et al., 2016).

An alternative explanation for the present finding of increased trembling in the CB group is that peripheral nervous system function is adversely affected by cannabis use in such a way as to impair postural control. The rambling-trembling model attributes trembling to peripheral spinal reflexes and the intrinsic properties of muscles themselves (Zatsiorsky and Duarte 1999), and, interpreted within this framework, the present results suggest that the efficacy of one or both of these are compromised in cannabis users. The expression of CB1 receptors by skeletal muscle tissue has now been demonstrated in mammals (Cavuoto et al., 2007; Crespillo et al., 2011; Hutchins-Wiese et al., 2012). Recent work has clarified the signaling pathways through which CB1 receptor signaling mediates excitation-contraction coupling in mammalian muscle fibers and determined that CB1 activation makes muscle fibers more prone to fatigue (Olah et al., 2016). Muscle fatigue can interfere with proprioceptive feedback (Forestier et al., 2002; Hiemstra et al., 2001) that is critical for normal postural control, and this appears to be the primary mechanism through which postural sway is increased following activities that incur muscle fatigue (Vuillerme et al., 2002a; Vuillerme et al., 2002b; Vuillerme and Nougier 2003). Interestingly, the effects of fatigue are most pronounced in the eyes-closed position, and fatigue can be counteracted by reinstating visual feedback (Vuillerme et al., 2001) at least under some conditions (Vuillerme et al., 2006). This latter result suggests that peripheral muscular effects induced by CB use may contribute to an increase in postural sway in regular users.

Because cannabis use has been suggested to accelerate the aging process (Reece et al., 2016), postural sway studies in aging populations may be particularly relevant to the present

findings. Interestingly, rambling-trembling analyses comparing aging and elderly participants during quiet standing found that the aged sample showed significantly increased trembling in the AP direction as well as increased COP RMS, but no significant differences in AP rambling, nor ML rambling or trembling (Sarabon and Rosker 2013). Therefore, although the present study found increased trembling in the AP and ML directions in cannabis users, the findings in Sarabon and Rosker in an aging sample are strikingly similar to the current results.

Although the correlational analyses in the present study were exploratory, significant negative associations were found between AP rambling RMS and scaled scores on Digit Symbol Coding, which measures visuo-motor processing speed and, to a lesser extent, memory (Joy et al., 2004). Several things suggest that this association may be independent of cannabis use, however. There were no group differences on either Digit Symbol Coding or AP Rambling. Moreover, while Digit Symbol Coding scores were impaired in cannabis users (Thames et al., 2014) they have also been reported to be unimpaired (Auer et al., 2016) and even improved (Becker et al., 2014). Nonetheless, it is interesting to note that a previous study reported that decreased DTI-based ponto-cerebellar tissue ratios significantly predicted both postural stability and digit symbol scores in HIV patients without alcohol use disorders or dementia (Sullivan et al., 2011).

4.1 Conclusions and limitations

The present study is the first to investigate association between long-term cannabis use and postural sway using rambling-trembling analysis. These findings are consistent with the hypothesis that cannabis use disrupts CNS processing of incoming peripheral nervous system information, which implicates the cerebellum. Alternatively, peripheral nervous system components of postural sway are themselves impaired.

Future studies could clarify several issues arising from the present work. First, it is important to note that the type of cannabis used by this the individuals included in the CB group was not tested, and the amount of THC present can vary significantly depending on the particular type of cannabis. Second, it is possible that withdrawal effects could contribute to sway deficits, especially in chronic heavy users. The hourly time course of withdrawal after cessation is not well characterized, but prior studies indicate that the average onset of withdrawal symptoms occur after two to three days (Budney et al., 2003; Copersino et al., 2006). Therefore, measures of withdrawal could be highly informative in future research. Third, it is possible that factors other than cannabis use contributed to differences between groups. For example, it is known that cannabis use is increased among individuals with psychotic experiences (Degenhardt et al., 2017), and it is also known that postural sway is increased in cases of severe psychotic illness such as schizophrenia (Kent et al., 2012; Marvel et al., 2004). While none of the participants in the present study met criteria for a psychotic illness, it is possible that higher rates of psychotic experiences existed in this group that increased sway independently of cannabis use. Fourth, although participants confirmed that they had abstained from cannabis use on the day of testing, there was no additional verification method that could reliably provide information to corroborate this. In addition, while every effort was made to measure postural sway and toxicology on the same day, this was not always possible. Therefore, we cannot confirm via toxicology that all participants were free from the effects of psychoactive drugs. Finally, the cannabis users in this sample were adolescents and young adults who varied widely in their use history. Future research should be conducted to see whether these results replicate in a sample of cannabis dependent individuals who are older and have a longer duration of heavy and sustained use.

Contributors

Amanda Bolbecker, Ashley Schnakenberg Martin, Brian O'Donnell, Sharlene Newman and William Hetrick were responsible for the overall design and implementation of the study. Deborah Althorp and Behdad Tahayori assisted in computational analysis of the sway data. Leah Moravec and Karen Lorite Gomez were responsible for recruitment, subject assessment, data processing and quality control and assisted with diagnostic determinations. All authors contributed to the writing of the manuscript. All authors have approved the final article.

Conflict of Interest

No conflict declared

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Figure Legends

Figure 1. Exemplar COP sway path plots for an N-CB participant (left) and a CB participant (right) in the ECBC condition.

Figure 2. Rambling and trembling trajectories for the same exemplar participants whose COP path length data can be seen in Figure 1, with the N-CB participant's data on the top and the CB participant's data on the bottom.

Figure 3. Path length data for N-CB group (blue) and CB group (red). Path length was longer in the cannabis group.

Figure 4. Rambling and trembling for ML and AP directions. Panels 4A-4D are arranged similarly, with base-open data presented in the left panel, followed by base-closed on the right. Data for the N-CB group is in blue, and the CB group's data is in red. 4A shows ML rambling, and ML trembling is represented in 4B. Panels 4C-4D show AP rambling and trembling, respectively. The cannabis users overall had increased rambling and trembling, and in both ML and AP trembling, this increase was significant.
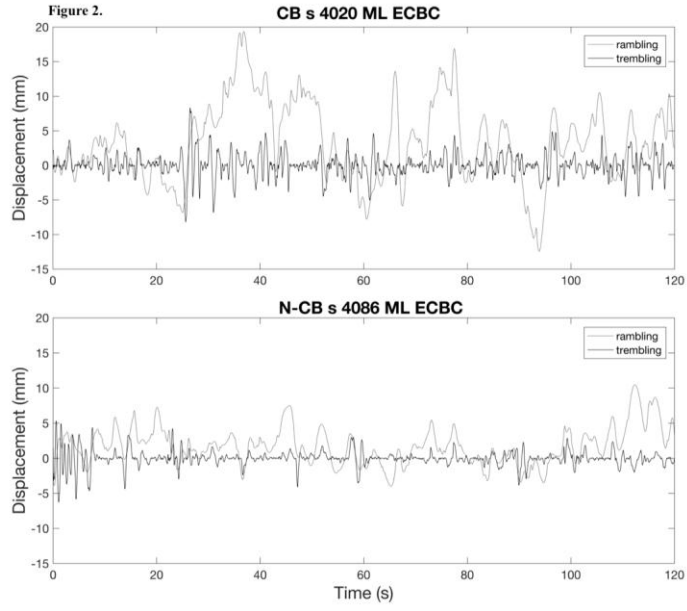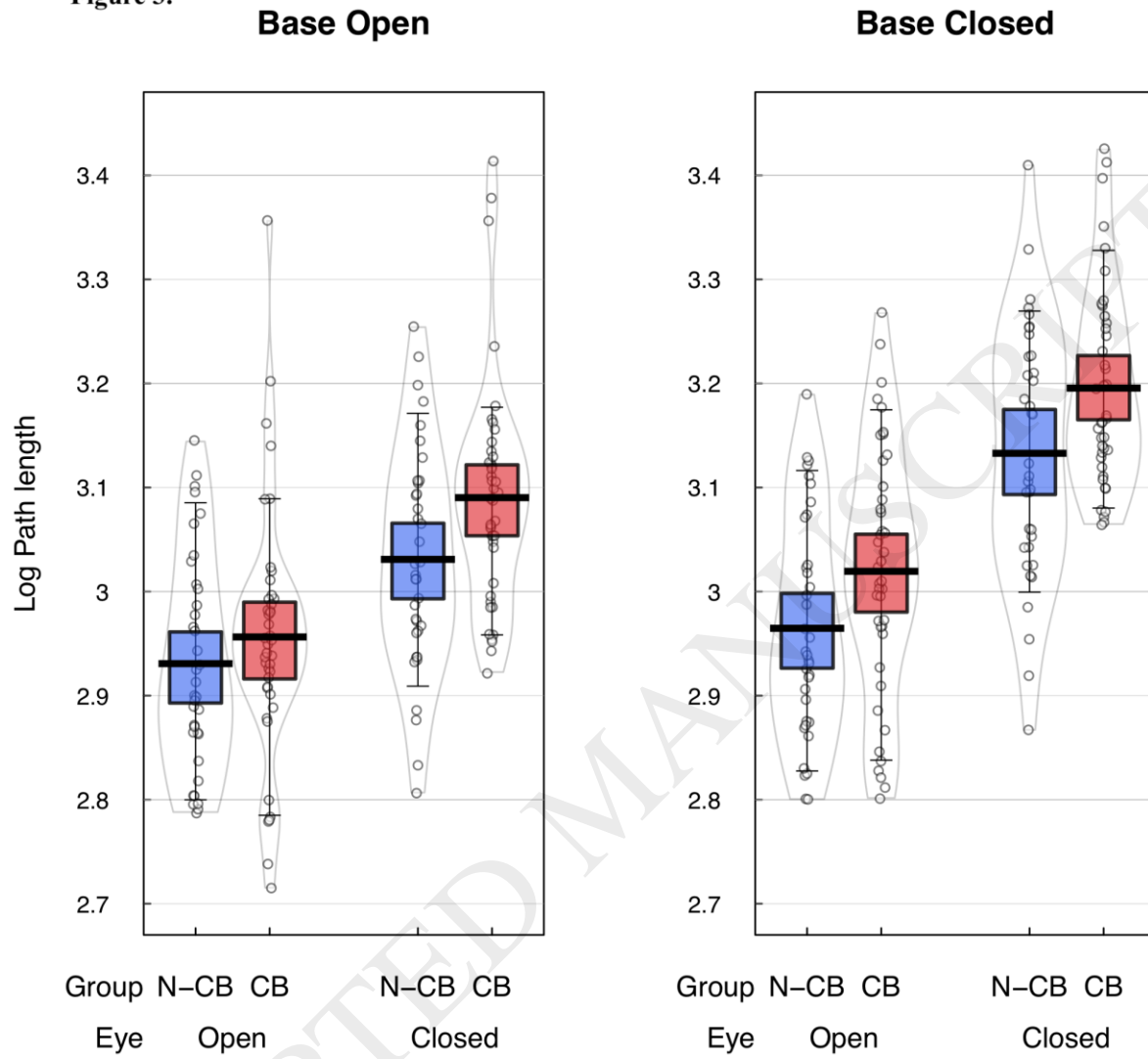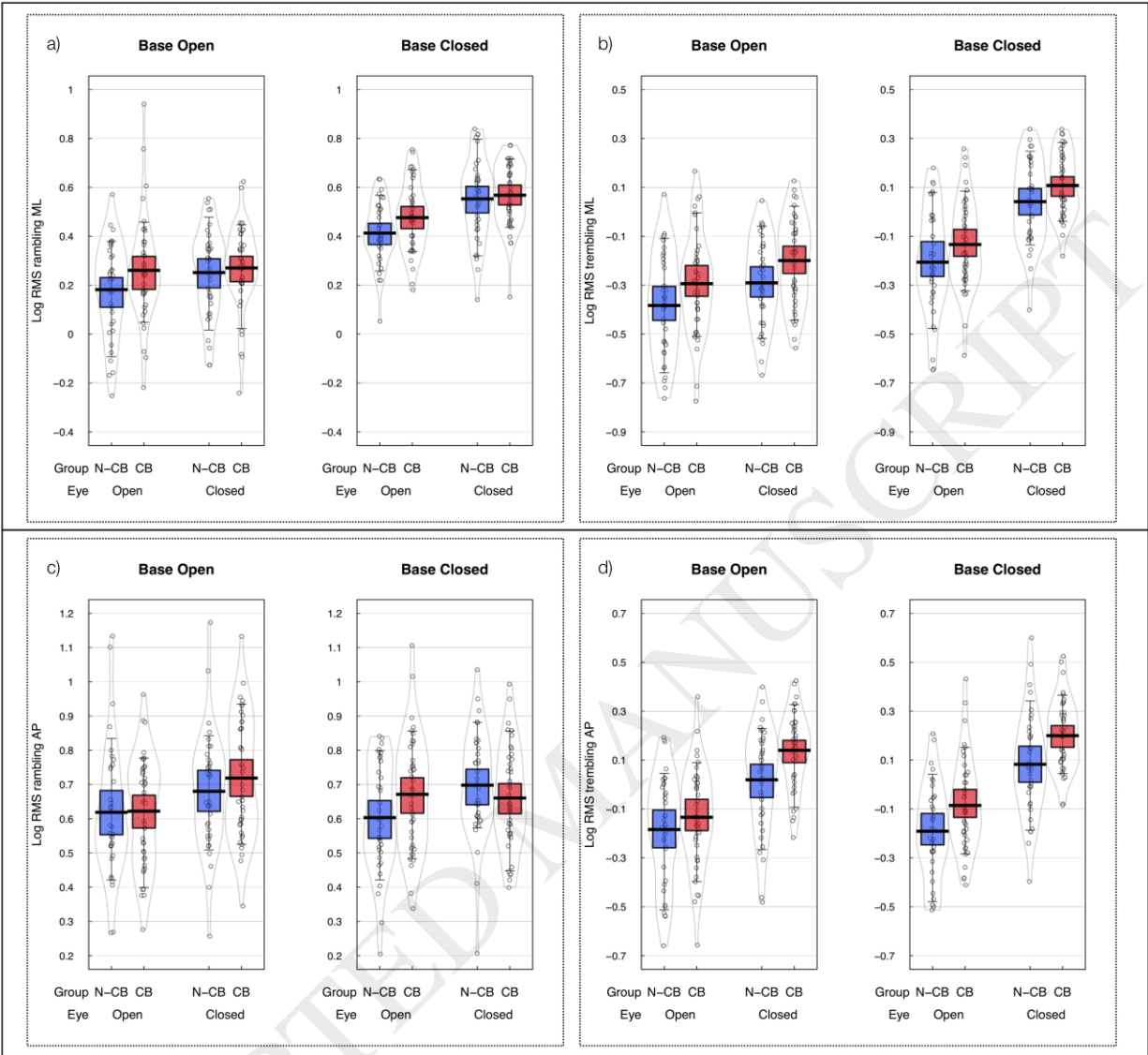

Figure 1.

Figure 2.

Figure 3.

Base Open

Base Closed
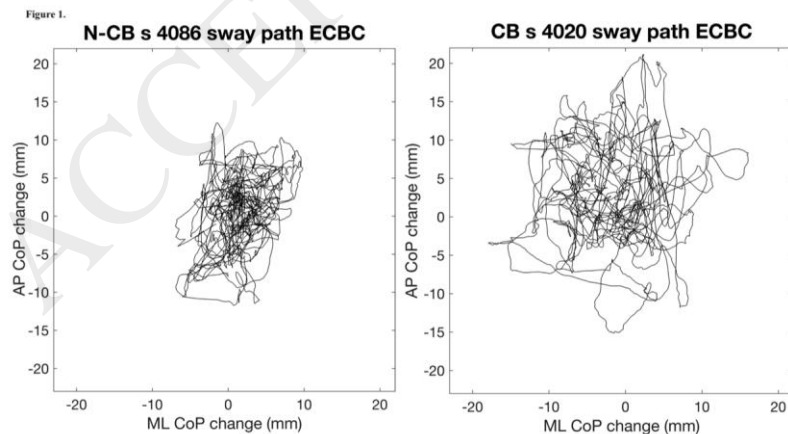
Table 1. Demographic information for N-CB and CB groups.

Demographic variable	N-CB (N=36)	CB (N=42)
Sex	20F, 16M	23F, 19M
Age	M= 22.3 (SD=3.9)	M=21.2 (SD=3.9)
Weight (Kg)	M=71.2 (SD=18.3)	M=73.4 (SD=17.0)
Lifetime Cannabis Uses	M=1.30 (SD=3.35)	M=1423.4 (SD=2231)
Years of Education	M=15.6 (SD=2.5)	M=14.0 (SD=1.9)
WASI IQ Estimate	M=115 (SD=10.2)	M=110 (SD=9.5)