INTRODUCTION:

METHODS:   
*Sample Information:*

Pupillary light reflex trajectories were collected in 101 healthy participants with enrolled in groups of daily, occasional and no cannabis consumption. Daily cannabis consumption was defined as smoking or vaping a cannabis flower product at least one time per day, every day of the week for 30 days prior to enrollment (N = 33); occasional consumption was defined as smoking or vaping cannabis flower product on at least one day but no more than two day per week in the 30 days prior to enrollment (N=36); and no cannabis consumption was defined as not having used cannabis in the month prior to enrollment (N=32). Videos of the pupillary light reflex test were recorded prior and post cannabis consumption on the study visit date and processed using task-specific video segmentation techniques (Steinhart Thesis), to create a frame-level trajectory of percent change from baseline values of pupil size for each eye on each participant at time point (prior and post consumption). After video segmentation and pre-processing, 88 post consumption trajectories of the right eye were collected, and after removing one outlier and matching to pre-consumption a total of 84 participants were used in this analysis.

In this sample of 84 participants, there were 29 non-users, 30 occasional and 25 daily users. Participants ranged in age from 25.1 to 45.3 years with an average of 32 years (sd = 5.02); an average BMI of 25.4 kg/m2 (sd. 4.41); and approximately 58% male (N = 49). Time between cannabis consumption and post testing varied from 53 – 84 minutes with a median of 62 minutes. Participants in the no use category were allowed to rest with their eyes closed for approximately equal time as allowed for cannabis consumers to use cannabis.

*Functional Data Analysis*

Functional data analysis (FDA) is a field of statistics that models curves or trajectories of information without extracting pre-defined specific features. It allows examination of differences in the patterns of the curves as it relates to an outcome, and how the patterns of the curves differ based on individual characteristics. Two methods of FDA were used in this analysis (1) scalar-on-function regression (SoFR) and (2) function-on-scalar regression (FoSR). In SoFR, an outcome, such as cannabis consumption status, is regressed on the trajectories to find differences in the trajectories that are associated with the outcome. However, in FoSR the trajectories are regressed on covariates such cannabis use frequency to determine how the trajectories differ by the covariate. In this analysis, a SoFR model was used to determine the subtle differences in the pupillary light reflex that discriminate between cannabis users versus non-users, while the FoSR models were used to distinguish trajectory patterns that are associated with cannabis use frequency. Additionally, due to the variability in the time from cannabis consumption to the post test, a FoSR model was used to explain differences in trajectories due to cannabis use frequency and time differences in wait time between cannabis use and testing.

*Prediction Analysis*

Two separate logistic regression model were used to predict cannabis user and not users. The first model used single value summaries of the trajectory data which included: (a) minimal constriction, the magnitude of peak decrease as a percentage of the pre-illumination diameter; (b) AUC, the magnitude of rebound dilation after the point of minimal constriction; and (c) slope (Steinhart thesis). The second model used the prediction from the SoFR model, which assessed information from the full trajectory of the pupillary light reflex during the post test. Receiver operating curves (ROCs) for each model were used to assess the accuracy of the models with area under the curve.

RESULTS:

DISCUSSION: