A double-blind, randomized, controlled crossover trial of cannabis in adults with Tourette syndrome

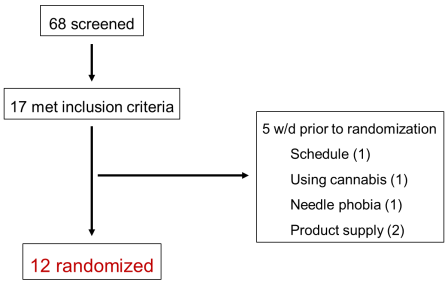
Elia Abi-Jaoude MD, PhD[1,2], Tracy Bhikram PhD[2], Ferdous Parveen MBBS[2], Jody Levenbach PhD C Psych[2], Myriam Lafreniere-Roula PhD[2], Paul Sandor MD[2,3]

[1]The Hospital for Sick Children [2], University Health Network [3]Youthdale Treatment Centers Department of Psychiatry, University of Toronto, Toronto, Ontario, Canada

Cannabis and TS

- Case series (*Sandyk & Awerbuch, 1988; Müller-Vahl et al, 1998; Abi-Jaoude et al, 2017; Thaler et al, 2018; Milosev et al, 2019*)
- Two RCTs (*Müller-Vahl et al, 2002; Müller-Vahl et al, 2003*)
  - Oral THC
  - Findings inconsistent

Participants



- 11 males, 1 female; 38 yo (22-54)
- OCD (7), ADHD (6), anxiety (4), depression (3), ASD (1)
- YGTSS-TTS 28.7 (15-44)
- Concurrent meds – 7 participants: antipsychotic (3), benztropine (2), SSRI (3), bupropion (1), stimulant (2), anticonvulsant (1), benzodiazepine (3), other (4)
- Past cannabis use (3)

3 dropouts

- Adverse event – syncope/seizure (1)
- Unable to draw blood (1)
- Schedule (1)

Objective

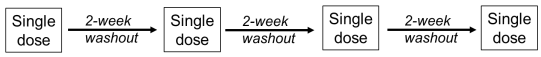
Efficacy and tolerability of three vaporized medical cannabis products and placebo for tics

- Primary efficacy endpoint: MRVTRS
- Secondary efficacy endpoints: PUTS, SUDS, CGI-I
- Correlation with cannabinoid plasma levels
- Tolerability

Analysis

- Nonlinear mixed effects modelling
- Repeated measures
- Adjusted for baseline score
- Treatment order effects
- Correlation with cannabinoid plasma levels
- Adjusted for multiple comparisons

Design



vaporized cannabis, 0.25 g

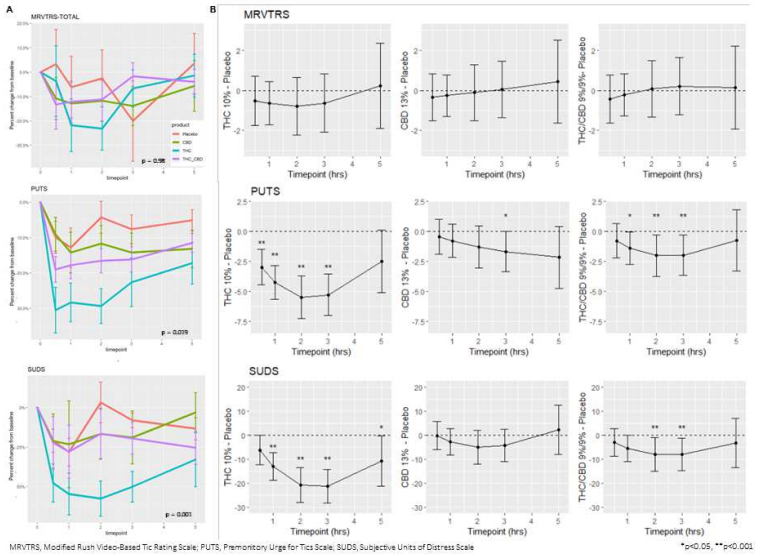
- THC 10%
- THC/CBD 9%/9%
- CBD 13%
- placebo THC <0.3%, CBD <0.3%

Sampling: 0, 0.5, 1, 2, 3, 5 hours

- MRVTRS, PUTS, SUDS
- Blood: THC, OH-THC, COOH-THC, CBD

Results

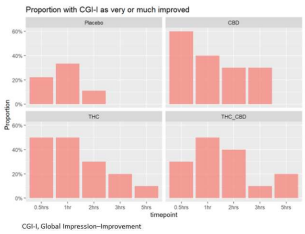
Figure 1. Changes in MRVTRS, PUTS and SUDS scores over the course of 5 hours after administration of cannabis or placebo product. A. Mean and standard error of percent change from baseline is plotted at each time point. B. Contrasts of estimated means for THC 10%, THC/CBD 9%/9%, and CBD 13% versus placebo at timepoints 0.5, 1, 2, 3, and 5 hours after product administration.



MRVTRS, Modified Rush Video-Based Tic Rating Scale; PUTS, Premonitory Urge for Tics Scale; SUDS, Subjective Units of Distress Scale

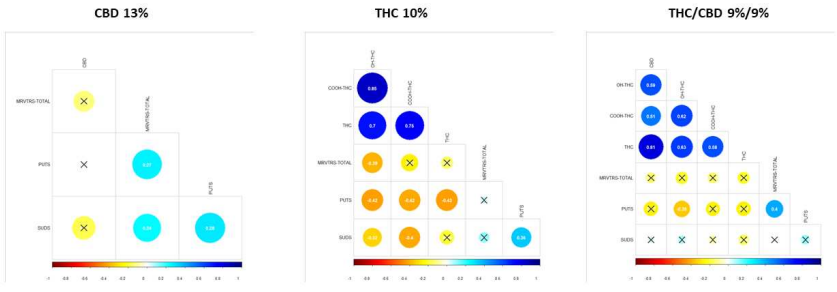
*p<0.05, **p<0.001

Figure 2.
A. Proportion of participants rated as "very much improved" or "much improved" on the CGI-I over the course of 5 hours after administration of cannabis or placebo product.
B. Odds ratio estimates [95% CI] for pairwise contrasts with p-values adjusted with the Tukey method.



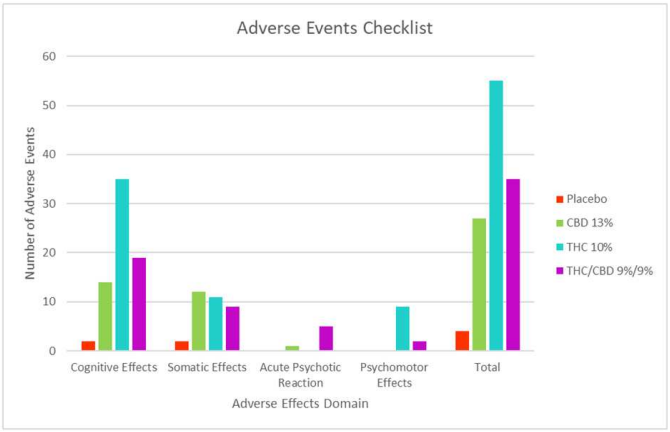
Contrast	OR [95% CI]	P-value
CBD / Placebo	5.114 [0.967,27.038]	0.057
THC / Placebo	7.221 [1.288,40.487]	0.017
THC-CBD / Placebo	4.936 [0.958,25.447]	0.06

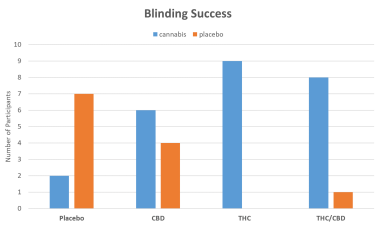
Figure 3. Correlation matrices showing strength (number inside circle), direction (warm colors = negative, cool colors = positive), and significance (p value ≥ 0.05 indicated by X inside circle) of correlations between cannabinoid and metabolite plasma levels with MRVTRS, PUTS, and SUDS scores for each of the cannabis products



MRVTRS, Modified Rush Video-Based Tic Rating Scale; PUTS, Premonitory Urge for Tics Scale; SUDS, Subjective Units of Distress Scale

Figure 4. Number of adverse events reported for each of the cannabis and placebo products based on the adverse events checklist





Conclusions

- No statistically significant difference on MRVTRS
- THC 10% significantly better than placebo on secondary outcomes
- THC and metabolite plasma levels correlated with improvement on all measures
- THC 10% resulted in the most AEs
- This pilot data will inform the design of a larger chronic treatment RCT

Limitations

- Sample size
- Single dose
- Fixed dose
- Delivery
- Blinding

Funding

Tourette Association of America