The effects of nabilone (a synthetic cannabinoid agonist) on funneling illusion and working memory

POSTER:TU655

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BACKGROUND

- Although nabilone has been approved as an anti-emetic medication, it has been applied as an analgesic adjuvant in the management of neuropathic pain and other chronic pain conditions.
- There are limited studies **on the cognitive and psychotomimetic effects** of cannabinoid compounds.
- Therefore, we examined the effects of acute cannabinoid intoxication on working memory (WM), psychosis-like experiences (PLE), and tactile funneling illusion (TFI) following oral doses of nabilone (1-2 mg) administration.
- People integrate multiple stimuli over space and time to form unified percepts of objects and events [1], and alterations in integration have been proposed as being important for a range of clinical disorders that experience alterations in perception [2,3].
- **Tactile Funneling Illusion (TFI)** is an ideal means to test effects of nabilone on both temporal and spatial BWs in the unimodal somatosensory domain
- Two important domains of WM (i.e., Verbal and Spatial) using **digit span and spatial span tasks**

METHODS

❑ **Ethics:** The University of Western Australia Human Research Ethics Committee (RA/4/20/4558).

❑ A randomized, double-blind, counterbalanced, crossover manner

- **Healthy participants (n=32)** completed the TFI test at various delays and distances of separation of stimuli and after receiving nabilone (2-4 mg, PO) or placebo.
- Using three temporal (0, 500, and 750 ms) and five spatial (i.e., 5, 4, 3, 2, 1 cm) conditions **(Figure 1).**
- The primary illusory measures were funneling and errors of localisation (EL).
- **Twenty-eight participants** also completed the WM tests **(digit and spatial span tasks)** across different delay conditions (0, 6, 12, 18 s). (Figure 2).
- **Five psychological scores (**BPRS, MIS, and SAPS) and
- **Three physiological measures** (BP, HR, and temporal body) **(Figure 3).**

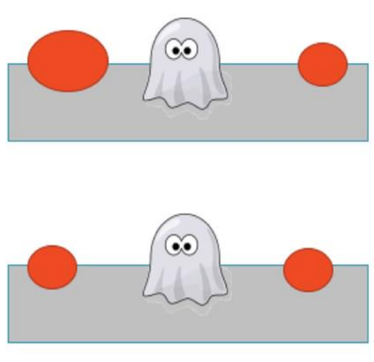

Figure 1: Funneling for the one synchronous and two asynchronous temporal conditions

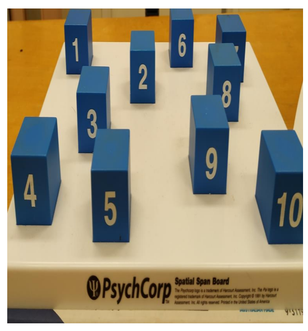

Figure 2: Spatial Span Task

❑ **Statistical analysis:** The statistical analysis was performed using R version 3.6.3

- Repeated measures ANOVAs were used to analyse the data
- Then paired t-tests were used for pairwise comparisons between drug and placebo.
- Wilcoxon rank sum tests with continuity correction were used if the residuals deviated substantially from normality

RESULTS

❑ Nabilone impaired VWM ($p = 0.03$, weak effect size $\eta 2 = 0.02$), and SWM ($p = 0.00016$, $\eta 2 = 0.08$) (see **Figure 6**).

- In addition, there were significant negative correlations between occasions of cannabis use and overall WM averaged scores across drug treatments ($\rho = -0.49$, $p = 0.007$) and under placebo ($\rho = -0.45$, $p = 0.004$).
- The drug effect in the less frequent cannabis users was more pronounced on each WM ($p < 0.01$), while there appeared to be little drug effect in the frequent cannabis users.

❑ There were no main effects of nabilone on illusion (**Figure 4**). However Nabilone decreased funneling in a delay-dependent manner ($p = 0.0016$), whereby funneling was reduced at 0 ms ($p = 0.01$) (**Figure 5**).

- Nabilone also significantly reduced EL in a distance-dependent manner ($p = 0.038$), specifically at 4 cm

❑ Increasing effects of nabilone on the BPRS ($V = 193$, $p = 0.03$) and PAS ($V = 228$, $p = 0.006$), but not on Launay-Slade ($V = 74$, $p = 0.77$), MIS ($V = 136$, $p = 0.69$) and SAPS ($V = 190$, $p = 0.11$).

- However, there was no significant effect of nabilone on the combined scale score ($V = 176$, $p = 0.5$).

❑ There were associations between the overall psychometric scores and funneling under the strongest (0 ms delay) illusion condition, which is dependent on the drug condition (nabilone $\rho = 0.45$, $p = 0.028$).

❑ Psychometric scores were negatively correlated with WM averaged across all delays and both modalities, under placebo ($\rho = -0.41$, $p = 0.04$) (**Figure 7).**

CONCLUSION

- Low doses of synthetic cannabinoid impaired SWM and VWM indicating that exogenous activation of the cannabinoid system influences cognitive performance.
- The results replicated previous findings that schizotypy is correlated with deficits in WM.
- Unlike the effects of dexamphetamine in our previous studies, low activation of the cannabinoid system decreases the illusory perception of funneling, with a narrowing of spatial BWs.
- However, nabilone increased ratings on measures of psychosis-like experiences suggesting that nabilone may render PLE scores and objective illusory assessments.
- In addition, there were positive associations between PLE scores and experience of the funneling illusion that was present for nabilone but not placebo, indicating the potential influence of PLE scores on tactile illusory under drug condition

ACKNOWLEDGMENT

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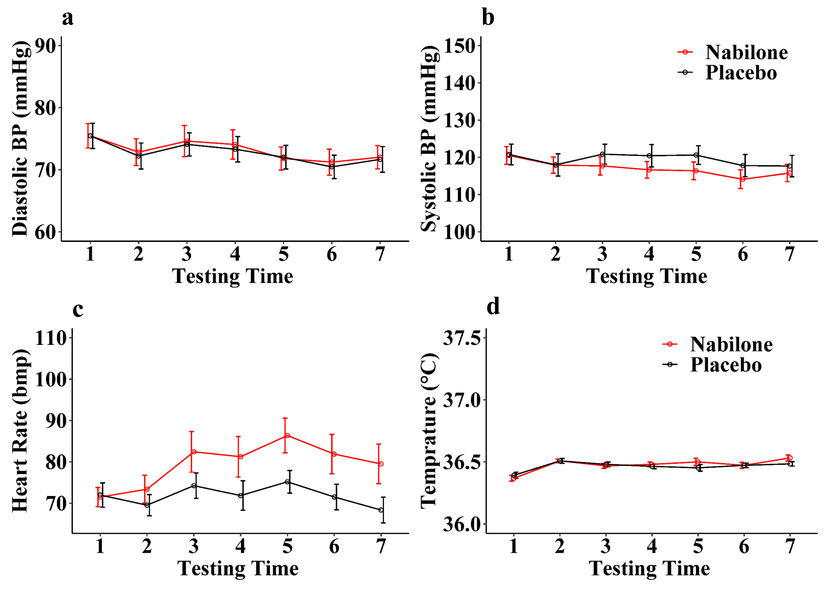

Figure 3: The effect of nabilone (2-4 mg, PO) on diastolic BP (A), systolic BP(B), heart rate (C), and body temperature (D) as a function of time. The seven testing times were 0, 60, 90, 175, 220, 280, and 370 min of post-drug administration. N = 24

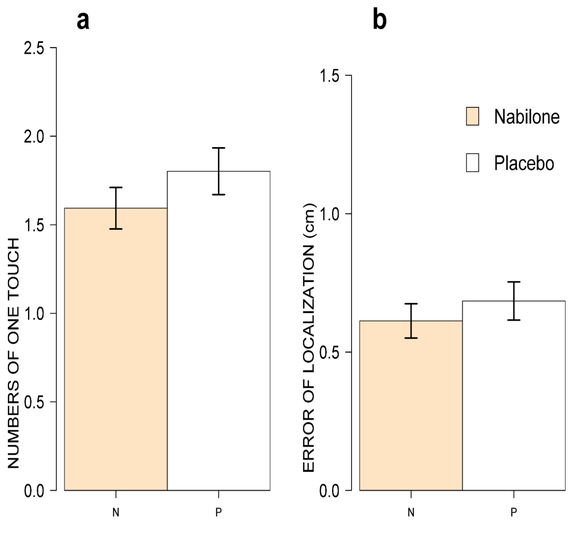

Figure 4: Main effects of nabilone (2-4 mg, PO) on funneling (a) and error of localization (b) averaged across averaged delay and distance condition. There were no significant main effect of nabilone. N = 32

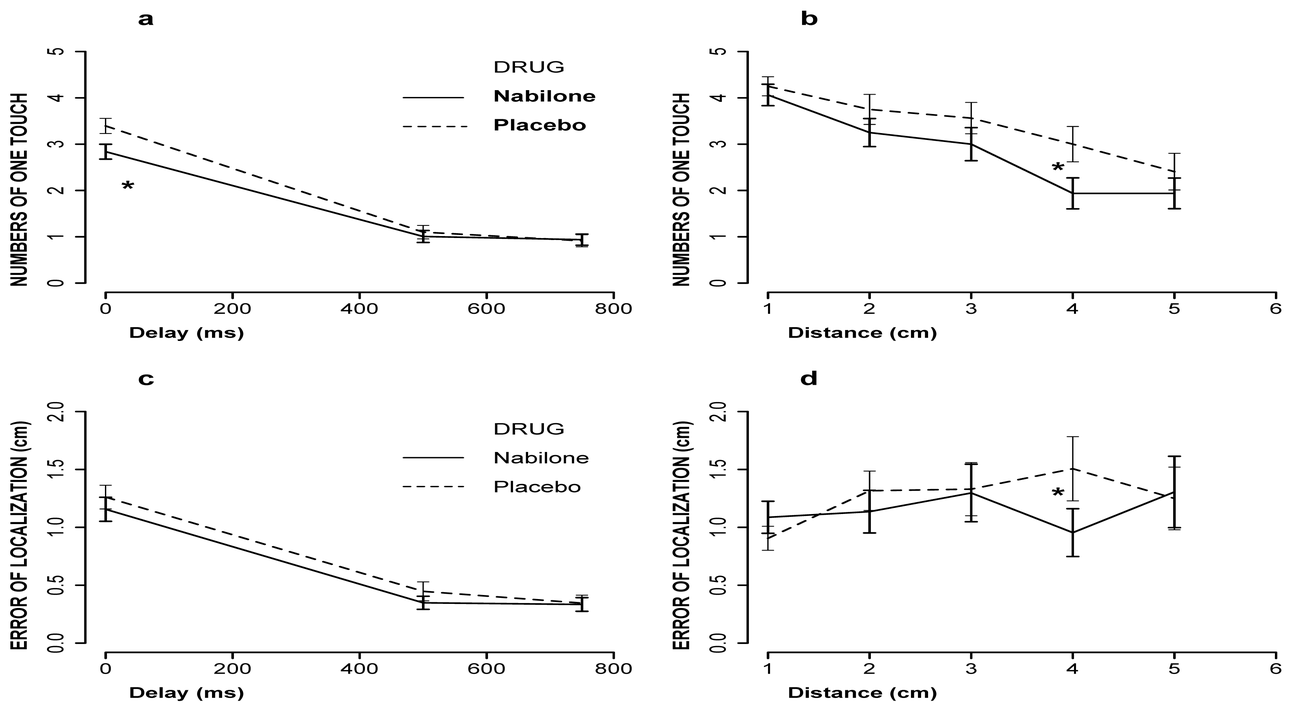

Figure 5: The effect of nabilone (2-4 mg, PO) on funneling (a and b) and EL (c and d). Data are presented as numbers of one touch (single touches felt) as a function of delay (a); numbers of one touch during synchronous delay condition (0 ms) as a function of distance (b); error of localisation as a function of delay (c); error of localisation during 0 ms as a function of distance (d).

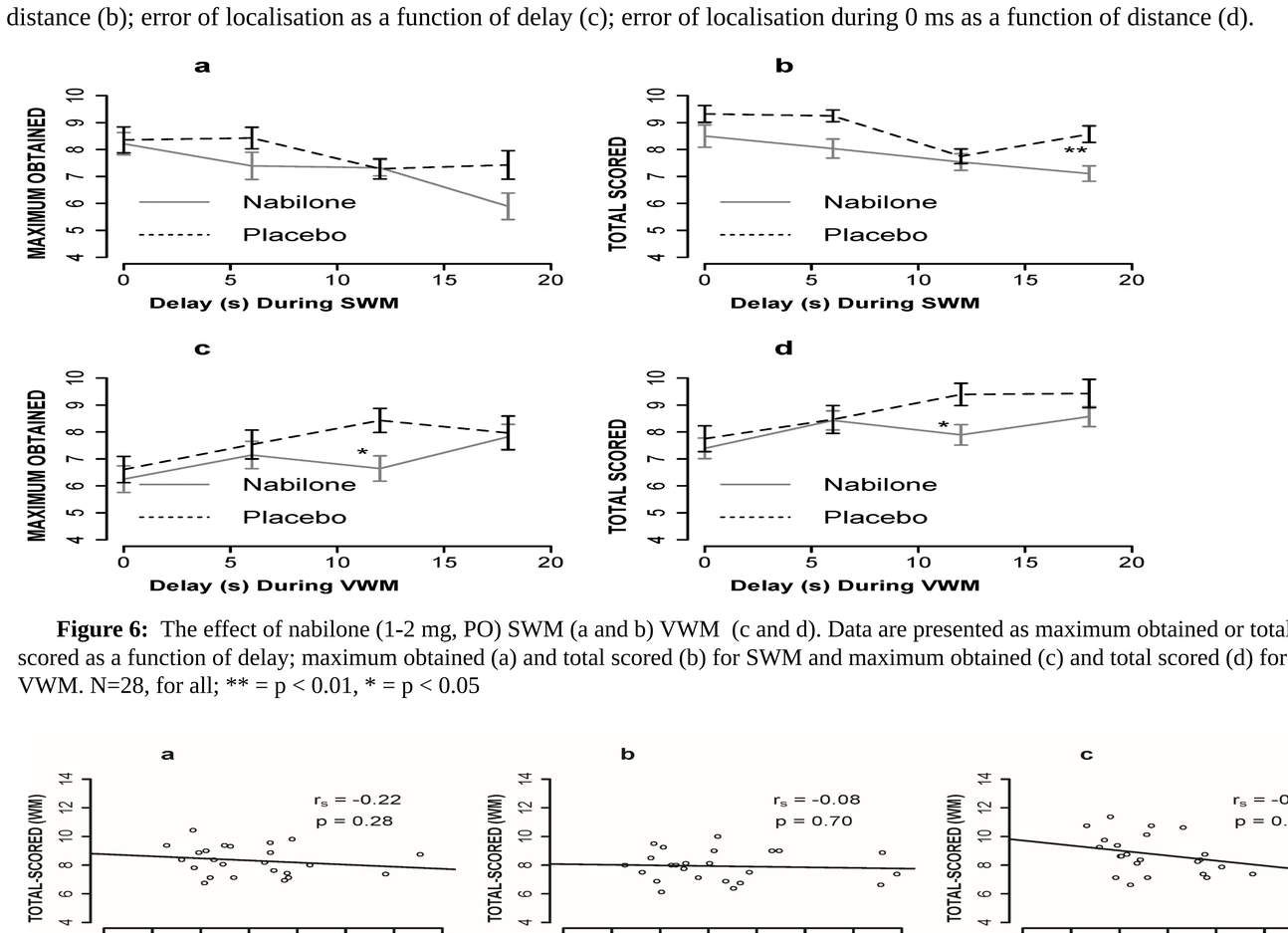

Figure 6: The effect of nabilone (1-2 mg, PO) SWM (a and b) VWM (c and d). Data are presented as maximum obtained or total scored as a function of delay; maximum obtained (a) and total scored (b) for SWM and maximum obtained (c) and total scored (d) for VWM. N=28, for all; ** = $p < 0.01$, * = $p < 0.05$

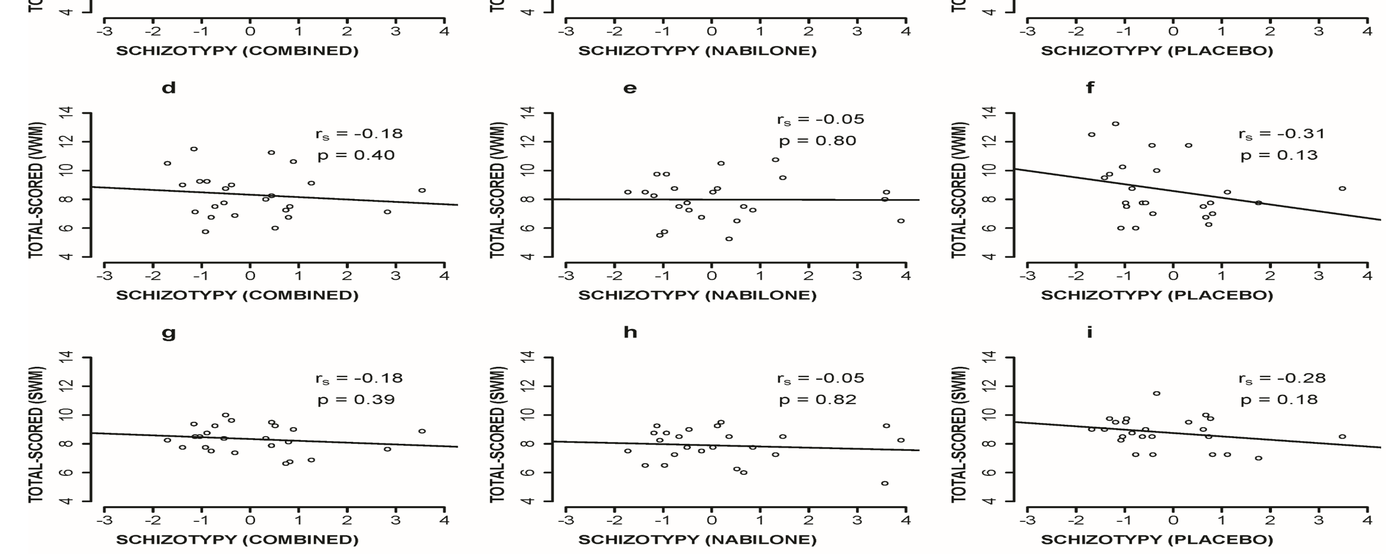

Figure 7: Scatterplot plots of associations between WM (a –c), VWM (d-f) and SWM (g-i), and overall psychometric score. Data are presented as total scored as a function of schizotypy score during combined drugs (a), nabilone (b) and placebo (c) for WM, during combined drugs (d), nabilone (e) and placebo (f) for VWM and averaged scores across drug treatments (g), nabilone (h) and placebo (i) for SWM. There was a significant negative correlation between schizotypy scores and WM during placebo conditions.

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