

Supplemental Table 5. Effect of smoked cannabis and alcohol (EtOH) on neurocognitive function: laboratory studies

Task	THC Dose	EtOH (g/kg or target BAC)	N	Age (years) Mean±SD, [Range]	Cannabis History	Measure	Time (h) After THC	Outcome: THC only	Outcome: EtOH only	Outcome: Combination	Relative to	Ref.
Free recall	Two 0% or 3.6% THC joints; 4 puffs/joint spaced by 2 h	0 or 0.6 [M]/0.5 [F]	14	24.5, [21-34]	≥1x/Month; 10/14: >100 lifetime occasions	# Words recalled	~1.25-1.5 <sup>b</sup>	No effect	-2.7 (6.6 vs. 9.3)	No interaction	Before dosing	(56)
Time Estimation	Two 0% or 3.6% THC joints; 4 puffs/joint spaced by 2 h	0 or 0.6 [M]/0.5 [F]	14	24.5, [21-34]	≥1x/Month; 10/14: >100 lifetime occasions	Respond at estimated time targets	~1.25 <sup>b</sup>	Under-estimation	Over-estimation	Interaction: canceled effect	Placebo	(56)
SST	400 µg/kg (~28 mg)	0%, 0.05%, 0.07%	21	23.2±8.4, [19-38]	≥4 Days/week	Stop RT	1-3	No effect	Increased	No interaction	Before THC; placebo alcohol	(63)
Standing Steadiness	Two 0% or 3.6% THC joints; 4 puffs/joint spaced by 2 h	0 or 0.6 [M]/0.5 [F]	14	24.5, [21-34]	≥1x/Month; 10/14: >100 lifetime occasions	Time (sec) before foot down in OLS	~1.25-1.5 <sup>b</sup>	No effect	-11.8 sec (45.9 vs. 57.7 sec)	No interaction	Before dosing	(56)
Equilibrium	0, 1.75% (~16 mg)THC, 3.3% THC (~30 mg)	0, 0.25, 0.5	12	24±3 [21-45]	2-21 Days in past month	Sway/ Composite Equilibrium	~0.25 <sup>a</sup>	Decreased	No effect	No interaction	THC alone	(65)
DSST	Two 0% or 3.6% THC joints; 4 puffs/joint spaced by 2 h	0 or 0.6 [M]/0.5 [F]	14	24.5, [21-34]	≥1x/Month; 10/14: >100 lifetime occasions	# Attempted	~1.25-1.5 <sup>b</sup>	No effect	Decreased	No interaction	Before dosing	(56)

Task	THC Dose	EtOH (g/kg or target BAC)	N	Age (years) Mean±SD, [Range]	Cannabis History	Measure	Time (h) After THC	Outcome: THC only	Outcome: EtOH only	Outcome: Combination	Relative to	Ref.
DSST	Two 0% or 3.6% THC joints; 4 puffs/joint spaced by 2 h	0 or 0.6 [M]/0.5 [F]	14	24.5, [21-34]	≥1x/Month; 10/14: >100 lifetime occasions	# Correct	~1.25-1.5 <sup>b</sup>	No effect	-6.5 (37.4 vs. 43.9)	No interaction	Before dosing	(56)
DSST	Two 0% or 3.6% THC joints; 4 puffs/joint spaced by 2 h	0 or 0.6 [M]/0.5 [F]	14	24.5, [21-34]	≥1x/Month; 10/14: >100 lifetime occasions	% Correct	~1.25-1.5 <sup>b</sup>	-4.8% (91.3% vs. 96.1%)	-5.4% (91.1% vs. 96.5%)	No interaction	Before dosing	(56)
Logical Reasoning	Two 0% or 3.6% THC joints; 4 puffs/joint spaced by 2 h	0 or 0.6 [M]/0.5 [F]	14	24.5, [21-34]	≥1x/Month; 10/14: >100 lifetime occasions	True/False statements	~1.25-1.5 <sup>b</sup>	No effect	No effect	No interaction	Before dosing	(56)
Tower of London	400 µg/kg (~28 mg)	0%, 0.05%, 0.07%	21	23.2±8.4, [19-38]	≥4 Days/week	# Correct decisions	1.17-3.17	No effect	No effect	No interaction	Before THC; placebo alcohol	(63)
Tower of London	400 µg/kg (~28 mg)	0%, 0.05%, 0.07%	21	23.2±8.4, [19-38]	≥4 Days/week	RT	1.17-3.17	No effect	No effect	No interaction	Before THC; placebo alcohol	(63)
CTT	400 µg/kg (~28 mg)	0%, 0.05%, 0.07%	21	23.2±8.4, [19-38]	≥4 Days/week	λ <sub>c</sub>	0.3-3.3	No effect	Decreased	No interaction	Before THC; placebo alcohol	(63)

Task	THC Dose	EtOH (g/kg or target BAC)	N	Age (years) Mean±SD, [Range]	Cannabis History	Measure	Time (h) After THC	Outcome: THC only	Outcome: EtOH only	Outcome: Combination	Relative to	Ref.
DAT	Two 0% or 3.6% THC joints; 4 puffs/joint spaced by 2 h	0 or 0.6 [M]/0.5 [F]	14	24.5, [21-34]	≥1x/Month; 10/14: >100 lifetime occasions	Response to primary target: hit rate	~1.25-1.5 <sup>b</sup>	No effect	No effect	No interaction	Before THC	(56)
DAT	Two 0% or 3.6% THC joints; 4 puffs/joint spaced by 2 h	0 or 0.6 [M]/0.5 [F]	14	24.5, [21-34]	≥1x/Month; 10/14: >100 lifetime occasions	Response to primary target: RT	~1.25-1.5 <sup>b</sup>	No effect	No effect	No interaction	Before THC	(56)
DAT	Two 0% or 3.6% THC joints; 4 puffs/joint spaced by 2 h	0 or 0.6 [M]/0.5 [F]	14	24.5, [21-34]	≥1x/Month; 10/14: >100 lifetime occasions	# False alarm responses	~1.25-1.5 <sup>b</sup>	+0.7 (1.6 vs. 0.9)	No effect	No interaction	Before dosing	(56)
DAT	Two 0% or 3.6% THC joints; 4 puffs/joint spaced by 2 h	0 or 0.6 [M]/0.5 [F]	14	24.5, [21-34]	≥1x/Month; 10/14: >100 lifetime occasions	# Errors estimating # of secondary targets	~1.25-1.5 <sup>b</sup>	No effect	+0.6 (1.6 vs. 1.0)	No interaction	Before dosing	(56)
DAT	0, 13 mg	0, 0.05%	12	26.1 [24-29]	1-4x/Month	# Exercises completed	0.25	No effect	Decreased	Decreased	Placebo	(3)
DAT	0, 13 mg	0, 0.05%	12	26.1 [24-29]	1-4x/Month	% Success in arithmetic task	0.25	Decreased	No effect	No interaction	Placebo	(3)
DAT	0, 13 mg	0, 0.05%	12	26.1 [24-29]	1-4x/Month	# Exercises with no response	0.25	Increased	Increased	Increased	Placebo	(3)

Task	THC Dose	EtOH (g/kg or target BAC)	N	Age (years) Mean±SD, [Range]	Cannabis History	Measure	Time (h) After THC	Outcome: THC only	Outcome: EtOH only	Outcome: Combination	Relative to	Ref.
DAT	0, 13 mg	0, 0.05%	12	26.1 [24-29]	1-4x/Month	RT to secondary task	0.25	Slightly increased	Slightly increased	No interaction	Placebo	(3)
DAT	0, 13 mg	0, 0.05%	12	26.1 [24-29]	1-4x/Month	False alarm responses	0.25	Slightly increased	Slightly increased	Increased; Interaction: greatest effect after combination	Placebo	(3)
DAT	0, 13 mg	0, 0.05%	12	26.1 [24-29]	1-4x/Month	# Exercises completed	1.25	No effect	No effect	Decreased; Interaction: alcohol effects persisted to second trial when combined w/ THC	Placebo	(3)
DAT	0, 13 mg	0, 0.05%	12	26.1 [24-29]	1-4x/Month	% Success in arithmetic task	1.25	Decreased; smaller effect than 1st trial	No effect	No interaction	Placebo	(3)
DAT	0, 13 mg	0, 0.05%	12	26.1 [24-29]	1-4x/Month	# Exercises with no response	1.25	No effect	No effect	Increased; Interaction: effects persisted to second trial w/combination, time effect p=0.06	Placebo	(3)
DAT	0, 13 mg	0, 0.05%	12	26.1 [24-29]	1-4x/Month	RT to secondary task	1.25	No effect	No effect	Slightly increased	Placebo	(3)

Task	THC Dose	EtOH (g/kg or target BAC)	N	Age (years) Mean±SD, [Range]	Cannabis History	Measure	Time (h) After THC	Outcome: THC only	Outcome: EtOH only	Outcome: Combination	Relative to	Ref.
DAT	0, 13 mg	0, 0.05%	12	26.1 [24-29]	1-4x/ month	False alarm responses	1.25	Slightly increased	No effect	Increased; Interaction: greatest effect after combination; persisted to second trial	Placebo	(3)
DAT	400 µg/kg (~28 mg)	0%, 0.05%, 0.07%	21	23.2±8.4, [19-38]	≥4 Days/week	# Control losses	0.5-2.5	Increased	Increased	Increased; Interaction: [statistical] combination produced greatest impairment	Before THC; placebo alcohol	(63)
DAT	400 µg/kg (~28 mg)	0%, 0.05%, 0.07%	21	23.2±8.4, [19-38]	≥4 Days/week	# Correct detections on secondary task	0.5-2.5	Decreased	Decreased	No interaction	Before THC; placebo alcohol	(63)
DAT	400 µg/kg (~28 mg)	0%, 0.05%, 0.07%	21	23.2±8.4, [19-38]	≥4 Days/week	RT	0.5-2.5	Increased	Increased	No interaction	Before THC; placebo alcohol	(63)
DAT	400 µg/kg (~28 mg)	0%, 0.05%, 0.07%	21	23.2±8.4, [19-38]	≥4 Days/week	Tracking error	0.5-2.5	No effect	Increased	No interaction	Before THC; placebo alcohol	(63)

<sup>a</sup>Denotes time after smoking initiated

<sup>b</sup>Denotes time after smoking completed

Abbreviations: THC:  $\Delta^9$ -tetrahydrocannabinol; EtOH: ethanol (alcohol); BAC: blood alcohol content; SD: standard deviation; SST: stop signal task; RT: reaction time; DSST: digit symbol substitution test; CTT: critical tracking task; DAT: divided attention task