

Supplemental Table 4. Cannabis and alcohol effects on simulated and on-road driving

| Measure | Measured by | THC Dose | Dose EtOH (g/kg or target BAC) | N | Age (years) Mean±SD, [Range] | Cannabis History | Time (min) after THC dose | Drive Length/ Time | Outcome: THC only | Outcome: EtOH only | Outcome: Combination | Ref. |
|------------------|----------------------|--|--------------------------------|--------------|------------------------------|-----------------------|---------------------------|----------------------|---|--------------------|--------------------------------------|------|
| <i>Simulator</i> | | | | | | | | | | | | |
| RT | Brake latency | 0, 8, 12, 16 mg Δ ¹ -THC (ate cake) | 0.095% | 8 M | 21-29 | 3 Naïve; all ≤1x/week | >105 | 10 min | Med, High THC ↑ 16, 66% | ↑ 44% | Not dosed together | (64) |
| RT | Brake latency | 0, 1.77, 3.95%; 10 puffs | -- | 10 | 21-45 | ≥Weekly, <daily | Random test battery order | ≤3.5 km | High THC ↑ 0.054 sec (p<0.10) | -- | -- | (57) |
| RT | Brake latency | 0, 1.75, 3.33%; 10 puffs | 0, 0.25, 0.5 | 12 | 21-45 | 2-21 of past 30 days | 25 ^a | 10 min | ns | ↑ ~0.06-0.07 sec | No interaction: ↑ ns from EtOH alone | (65) |
| RT | RT to secondary task | 0, 13, 17 mg | 0, 0.5 | 14 | 26.1 ± 1.3 | 1-4x/ Month | 30 | 54.5 km ^c | Low THC ↑ High THC ↑ more than Low THC | ↑ Same as Low THC | Not dosed together | (10) |
| RT | Incursion avoidance | 0, 22.9 mg | -- | 50 M 35 F | 18-31 | 1-10x/ Month | ~15 ^b | ~15 min | ns | -- | -- | (55) |
| RT | Sign detection | 0, 19, 38 mg | 0, 0.4, 0.6 | 47 | 18-21, 25-40 | Not specified | 5 ^b | 6.6 km | High THC ↑ 0.051 sec | ns | No interaction | (53) |

| Measure | Measured by | THC Dose | Dose EtOH (g/kg or target BAC) | N | Age (years) Mean±SD, [Range] | Cannabis History | Time (min) after THC dose | Drive Length/ Time | Outcome: THC only | Outcome: EtOH only | Outcome: Combination | Ref. |
|---------------------|------------------|--------------|--------------------------------|--------------|------------------------------|------------------|---------------------------|-----------------------------|---|-----------------------|--|------|
| Maintain Headway | Mean Headway (m) | 0, 19, 38 mg | 0, 0.4, 0.6 | 47 | 18-21, 25-40 | Not specified | 5 ^b | 6.6 km | Low, High THC ↑ 8.76, 16.76 | ns | No interaction | (53) |
| Headway Variability | SD Headway (m) | 0, 19, 38 mg | 0, 0.4, 0.6 | 47 | 18-21, 25-40 | Not specified | 5 ^b | 6.6 km | Low, High THC ↑ 4.29, 7.78 | ns | No interaction | (53) |
| Road Tracking | SDLP | 0, 13, 17 mg | 0, 0.5 | 14 | 26.1 ± 1.3 | 1-4x/ Month | 30 | 54.5 km ^c | Low & High THC ↑ | ns | Not dosed together | (10) |
| Road Tracking | SDLP | 0, 22.9 mg | -- | 50 M 35 F | 18-31 | 1-10x/ Month | ~15 ^b | ~15 min | ns | -- | -- | (55) |
| Road Tracking | SDLP (cm) | 0, 19, 38 mg | 0, 0.4, 0.6 | 47 | 18-21, 25-40 | Not specified | 5 ^b | 6.6 km | Low, High THC ↑ 4, 7; Low-High difference ns | Low, High EtOH ↑ 5, 5 | No interaction | (53) |
| Road Tracking | SDLP | 0, 13 mg | 0.05% | 12 | 24-29 | 1-4x/ Month | 30 | 37.7 km, rural ^d | ns | ns | THC+EtOH ↑ relative to placebo, THC only, & alcohol only | (3) |

| Measure | Measured by | THC Dose | Dose EtOH (g/kg or target BAC) | N | Age (years) Mean±SD, [Range] | Cannabis History | Time (min) after THC dose | Drive Length/ Time | Outcome: THC only | Outcome: EtOH only | Outcome: Combination | Ref. |
|---------------|--|------------------------------------|--------------------------------|--------------|------------------------------|--------------------|---------------------------|----------------------|--|--------------------|----------------------|------|
| Road Tracking | # Cones knocked over | 0, 1.77, 3.95% 10 | -- | 10 | 21-45 | ≥Weekly, <daily | Random test battery order | Not given | ns | -- | -- | (57) |
| Tracking | % Time in lane | 0, 16.5, 45.7 mg; 20 mg dronabinol | -- | 8 M | 22-30 | Occasional smokers | 60-330 ^b | Not given | Low, High THC & dronabinol impaired | -- | -- | (60) |
| Road Tracking | “Straddled line” variables (lane division & center division) | 0, 14, 52 mg | -- | 40 | 21-35 | Not given | 30, 80 ^b | Not given | Low, High THC impaired, only at 2 nd drive (t=80 min) | -- | -- | (66) |
| Speed | Mean speed | 0, 1.77, 3.95%; 10 puffs | -- | 10 | 21-45 | ≥Weekly, <daily | Random test battery order | Not given | ns | -- | -- | (57) |
| Speed | Mean speed | 0, 13, 17 mg | 0, 0.5 | 14 | 26.1 ± 1.3 | 1-4x/ Month | 30 | 54.5 km ^c | Low & High THC ↓, dose-dependent | ↑ | Not dosed together | (10) |
| Speed | Mean speed | 0, 22.9 mg | -- | 50 M 35 F | 18-31 | 1-10x/ Month | ~15 ^b | ~15 min | THC ↓ only during multi-tasking (PASAT) | -- | -- | (55) |

| Measure | Measured by | THC Dose | Dose EtOH (g/kg or target BAC) | N | Age (years) Mean±SD, [Range] | Cannabis History | Time (min) after THC dose | Drive Length/ Time | Outcome: THC only | Outcome: EtOH only | Outcome: Combination | Ref. |
|-------------------|-------------------|--|--------------------------------|--------------|------------------------------|-----------------------|---------------------------|-----------------------------|-----------------------|------------------------|--|------|
| Speed | Mean speed (km/h) | 0, 19, 38 mg | 0, 0.4, 0.6 | 47 | 18-21, 25-40 | Not specified | 5 ^b | 6.6 km | High THC ↓ 0.97 | Low EtOH ↑ 0.72 | No interaction | (53) |
| Speed | Mean speed | 0, 13 mg | 0.05% | 12 | 24-29 | 1-4x/ Month | 30 | 37.7 km, rural ^d | THC ↓ | ↑ Relative to THC only | THC+ EtOH ↑, borderline-significant relative to THC only | (3) |
| Speed variability | SD speed | 0, 8, 12, 16 mg Δ ¹ -THC (ate cake) | 0.095% | 8 M | 21-29 | 3 Naïve; all ≤1x/week | >105 | 10 min | High THC ↑ ~110% | ns | Not dosed together | (64) |
| Speed variability | SD speed | 0, 1.77, 3.95%; 10 puffs | -- | 10 | 21-45 | ≥Weekly, <daily | Random test battery order | Not given | ns | -- | -- | (57) |
| Speed variability | SD speed | 0, 13, 17 mg | 0, 0.5 | 14 | 26.1 ± 1.3 | 1-4x/ Month | 30 | 54.5 km ^c | High THC ↑ | ns | Not dosed together | (10) |
| Speed variability | SD speed | 0, 22.9 mg | -- | 50 M 35 F | 18-31 | 1-10x/ Month | ~15 C | ~15 min | ns | -- | -- | (55) |
| Speed variability | SD speed (km/h) | 0, 19, 38 mg | 0, 0.4, 0.6 | 47 | 18-21, 25-40 | Not specified | 5 C | 6.6 km | High THC ↑ 0.62 | Low EtOH ↑ 0.44 | No interaction | (53) |
| Speed variability | SD speed | 0, 13 mg | 0.05% | 12 | 24-29 | 1-4x/ Month | 30 | 37.7 km, rural ^d | ns | ns | No interaction | (3) |

| Measure | Measured by | THC Dose | Dose EtOH (g/kg or target BAC) | N | Age (years) Mean±SD, [Range] | Cannabis History | Time (min) after THC dose | Drive Length/ Time | Outcome: THC only | Outcome: EtOH only | Outcome: Combination | Ref. |
|---|---|------------------------------------|--------------------------------|--------------|------------------------------|--------------------|---------------------------|-----------------------------|---|-----------------------|---------------------------|------|
| Impaired Divided Attention | PASAT distracter task during uneventful drive segment | 0, 22.9 mg | -- | 50 M 35 F | 18-31 | 1-10x/ Month | ~15 ^b | 110 sec | Failure to show practice effects seen under placebo | -- | -- | (55) |
| Impaired Divided Attention | Car Following + Sign Detection Tasks | 0, 19, 38 mg | 0, 0.4, 0.6 | 47 | 18-21, 25-40 | Not specified | 5 ^b | 6.6 km | High THC ↑ mean headway & ↑ SD headway | ns | No interaction | (53) |
| Visual Search/ Visual Processing Speed/ Short-term Memory | Road sign pair detection | 0, 16.5, 45.7 mg; 20 mg dronabinol | -- | 8 M | 22-30 | Occasional smokers | 60-330 ^b | Not given | High THC impaired | -- | -- | (60) |
| Collisions | # Collisions | 0, 13, 17 mg | 0, 0.5 | 14 | 26.1 ± 1.3 | 1-4x/ Month | 30 | 54.5 km ^c | Placebo: 2 Low THC: 3 High THC: 6 | Placebo: 2 EtOH: 4 | Not dosed together | (10) |
| Collisions | # Collisions across study | 0, 13 mg | 0.05% | 12 | 24-29 | 1-4x/ Month | 30 | 37.7 km, rural ^d | Placebo: 2 THC: 3 | Placebo: 2 EtOH: 2 | Placebo: 2 THC+EtOH: 5 | (3) |

| Measure | Measured by | THC Dose | Dose EtOH (g/kg or target BAC) | N | Age (years) Mean±SD, [Range] | Cannabis History | Time (min) after THC dose | Drive Length/Time | Outcome: THC only | Outcome: EtOH only | Outcome: Combination | Ref. |
|------------------|---|---|--------------------------------|----|------------------------------|-----------------------|---------------------------|----------------------|---|-----------------------|---------------------------|----------|
| Collisions | # drivers involved in collisions | 0, 13, 17 mg | 0, 0.5 | 14 | 26.1 ± 1.3 | 1-4x/ Month | 30 | 54.5 km ^c | Placebo: 2 Low THC: 3 High THC: 6 | Placebo: 2 EtOH: 3 | Not dosed together | (10) |
| <i>On-Road</i> | | | | | | | | | | | | |
| RT | Mean RT to preceding vehicle's movement | 0, 100, 200, 300 µg/kg (0, ~7, ~14, ~21 mg) | -- | 16 | 21-40 | >1x/ Month; not daily | 45 ^a | 96 km ^e | ns | -- | -- | (59) |
| RT | Mean RT to preceding vehicle's movement | 0, 100, 200 µg/kg (0, ~7, ~14 mg) | 0, 0.04% | 18 | 21-40 | >1x/ Month; not daily | 30, 75 ^a | 80 km ^f | ns | ns | High THC+EtOH ↑ 36% | (59, 67) |
| Maintain Headway | Mean Headway (m) | 0, 100, 200, 300 µg/kg (0, ~7, ~14, ~21 mg) | -- | 16 | 21-40 | >1x/ Month; not daily | 45 ^a | 96 km ^e | Low, Med, High THC ↑ 8, 6, 2 | -- | -- | (59) |
| Maintain Headway | Mean Headway (m) | 0, 100, 200 µg/kg (0, ~7, ~14 mg) | 0, 0.04% | 18 | 21-40 | >1x/ Month; not daily | 30, 75 ^a | 80 km ^f | ns | ns | No interaction | (59, 67) |

| Measure | Measured by | THC Dose | Dose EtOH (g/kg or target BAC) | N | Age (years) Mean±SD, [Range] | Cannabis History | Time (min) after THC dose | Drive Length/ Time | Outcome: THC only | Outcome: EtOH only | Outcome: Combination | Ref. |
|---------------------|------------------|---|--------------------------------|----|------------------------------|-----------------------|---------------------------|--------------------|---|--------------------|---|----------|
| Headway Variability | SD Headway (m) | 0, 100, 200 µg/kg (0, ~7, ~14 mg) | 0, 0.04% | 18 | 21-40 | >1x/ Month; not daily | 30, 75 ^a | 80 km ^f | Low, High THC ↑ 2.9, 3.8 | ↑ 0.9 | Low, High THC+EtOH ↑ 2.5, 3 | (59, 67) |
| Road Tracking | SDLP | 0, 100, 200, 300 µg/kg (0, ~7, ~14, ~21 mg) | -- | 24 | 21-40 | >1x/ Month; not daily | 40, 100 ^a | 22 km | Low, Med, High THC ↑, both drives | -- | -- | (59) |
| Road Tracking | SDLP (cm) | 0, 100, 200, 300 µg/kg (0, ~7, ~14, ~21 mg) | -- | 16 | 21-40 | >1x/ Month; not daily | 45 ^a | 96 km ^e | Med, High THC ↑ 1.7, 2.9 | -- | -- | (59) |
| Road Tracking | SDLP (cm) | 0, 100, 200 µg/kg (0, ~7, ~14 mg) | 0, 0.04% | 18 | 21-40 | >1x/ Month; not daily | 30, 75 ^a | 80 km ^f | Low, High THC ↑ 2.7 (minor), 3.5 moderate | ↑ 2.2 (minor) | Low, High THC+EtOH ↑ 5.3, 8.5 (severe) | (59, 67) |
| Road Tracking | Time Out of Lane | 0, 100, 200 µg/kg (0, ~7, ~14 mg) | 0, 0.04% | 18 | 21-40 | >1x/ Month; not daily | 30, 75 ^a | 80 km ^f | ns | ns | Low, High THC+EtOH ↑ to >0.6%, to ~1.1% | (59, 67) |

| Measure | Measured by | THC Dose | Dose EtOH (g/kg or target BAC) | N | Age (years) Mean±SD, [Range] | Cannabis History | Time (min) after THC dose | Drive Length/ Time | Outcome: THC only | Outcome: EtOH only | Outcome: Combination | Ref. |
|---------------------------|--------------------------------------|---|--------------------------------|----|------------------------------|-----------------------|----------------------------------|--------------------|-------------------|--------------------|----------------------|------|
| Speed | Mean speed | 0, 100, 200, 300 µg/kg (0, ~7, ~14, ~21 mg) | -- | 24 | 21-40 | >1x/ Month; not daily | 40, 100 ^a | 22 km | ns | -- | -- | (59) |
| Speed | Mean speed | 0, 100, 200, 300 µg/kg (0, ~7, ~14, ~21 mg) | -- | 16 | 21-40 | >1x/ Month; not daily | 45 ^a | 96 km ^c | ns | -- | -- | (59) |
| Speed variability | SD speed | 0, 100, 200, 300 µg/kg (0, ~7, ~14, ~21 mg) | -- | 24 | 21-40 | >1x/ Month; not daily | 40, 100 ^a | 22 km | ns | -- | -- | (59) |
| Speed variability | SD speed | 0, 100, 200, 300 µg/kg (0, ~7, ~14, ~21 mg) | -- | 16 | 21-40 | >1x/ Month; not daily | 45 ^a | 96 km ^c | ns | -- | -- | (59) |
| Visual Search/ Processing | Search for traffic at inter-sections | 0, 100 µg/kg (0, ~7 mg) | 0, 0.05% (reached 0.04%) | 16 | 21-40 | >1x/ Month; not daily | 25 ^a /15 ^c | 40-45 min | ns | ns | ↓ 3% | (4) |

^aDenotes times after smoking initiated

^bDenotes times after smoking completed

^cMostly-straight road, maintain 55 mph: 17.2 km; downhill winding road, limit 45 mph: 12.7 km; follow behind a lead car: 11.6 km; 4 unexpected events, limit 55 mph: 13.0 km

^dMonotonic road with 5 unexpected events: 14.8 km; sharp curves, limit 45 mph, foggy with unexpected events: 12.1 km; downhill, limit 45 mph, moderate & sharp curves, 2 unexpected events: 10.8 km

^eCar following: 16 km; road tracking: 64 km; 2nd car following, 16 km

^fCar following: 40 km (~25 min); road tracking: 40 km (~25 min)

Abbreviations: THC: Δ^9 -tetrahydrocannabinol; BAC: blood alcohol content (%); SD: standard deviation; RT: reaction time; ns: not significant; SDLP: standard deviation of lateral position; PASAT: Paced Auditory Serial Additions Test