

Supplemental Table 1. Overall effect of blood Δ^9 -tetrahydrocannabinol (THC) concentration ($\mu\text{g/L}$), breath alcohol concentration (BrAC, $\text{g}/210\text{L}$), time, and interactions (THC*BrAC, time*THC, time*BrAC, time*THC*BrAC) on subjective effects in 19 healthy, occasional-to-moderate cannabis smokers following controlled vaporized cannabis administration with and without oral alcohol.

| Parameter | b | SE _b | df | t | p | 95% Confidence Interval of b | |
|---------------------------------------|--------|-----------------|-------|------|------------------|------------------------------|-------------|
| | | | | | | Lower Bound | Upper Bound |
| <i>Likert Feel Hungry</i> | | | | | | | |
| Intercept | 0.435 | 0.197 | 32.9 | 2.2 | 0.035 | 0.034 | 0.836 |
| Blood THC | | | 406.9 | -1.6 | 0.103 | | |
| BrAC | | | 433.4 | 0.1 | 0.902 | | |
| Time | 0.473 | 0.046 | 433.9 | 10.4 | <0.001 | 0.384 | 0.563 |
| THC*BrAC | | | 433.2 | 0.9 | 0.379 | | |
| Time*THC | | | 445.2 | 1.3 | 0.210 | | |
| Time*BrAC | | | 433.5 | -0.3 | 0.753 | | |
| Time*THC*BrAC | | | 433.8 | 0.4 | 0.659 | | |
| <i>Likert Shakiness/Tremulousness</i> | | | | | | | |
| Intercept | 0.072 | 0.036 | 140.9 | 2.0 | 0.044 | 0.002 | 0.143 |
| Blood THC | 0.004 | 0.002 | 18.5 | 2.5 | 0.023 | 0.001 | 0.008 |
| BrAC | | | 547.2 | -0.4 | 0.682 | | |
| Time | -0.016 | 0.008 | 547.6 | -2.1 | 0.037 | -0.031 | -0.001 |
| THC*BrAC | | | 549.4 | 0.2 | 0.805 | | |
| Time*THC | | | 550.2 | 1.5 | 0.129 | | |
| Time*BrAC | | | 546.4 | 1.6 | 0.114 | | |
| Time*THC*BrAC | | | 545.4 | -0.2 | 0.846 | | |
| <i>Likert Nausea</i> | | | | | | | |
| Intercept | 0.116 | 0.043 | 36.2 | 2.7 | 0.010 | 0.030 | 0.202 |
| Blood THC | -0.002 | 0.001 | 666.0 | -2.2 | 0.031 | -0.004 | 0.000 |
| BrAC | | | 657.0 | -1.4 | 0.151 | | |
| Time | -0.019 | 0.004 | 657.4 | -4.2 | <0.001 | -0.028 | -0.010 |
| THC*BrAC | | | 658.6 | 0.9 | 0.369 | | |
| Time*THC | 0.005 | 0.002 | 623.2 | 2.5 | 0.011 | 0.001 | 0.008 |
| Time*BrAC | | | 656.6 | 1.8 | 0.067 | | |
| Time*THC*BrAC | | | 659.2 | -0.8 | 0.396 | | |
| <i>Likert Headache</i> | | | | | | | |
| Intercept | 0.172 | 0.057 | 42.4 | 3.0 | 0.004 | 0.057 | 0.286 |
| Blood THC | | | 191.2 | -1.6 | 0.110 | | |
| BrAC | -2.438 | 1.224 | 659.1 | -2.0 | 0.047 | -4.841 | -0.035 |
| Time | | | 659.4 | -0.7 | 0.471 | | |
| THC*BrAC | | | 661.2 | 0.0 | 0.964 | | |
| Time*THC | | | 618.3 | -0.3 | 0.782 | | |
| Time*BrAC | | | 658.8 | -0.1 | 0.891 | | |
| Time*THC*BrAC | | | 659.4 | 1.1 | 0.251 | | |
| <i>Likert Palpitations</i> | | | | | | | |
| Intercept | | | 539.2 | 0.4 | 0.657 | | |
| Blood THC | | | 0.93 | 1.6 | 0.377 | | |
| BrAC | | | 654.8 | 0.4 | 0.698 | | |
| Time | | | 654.9 | -0.4 | 0.662 | | |
| THC*BrAC | | | 654.4 | -1.3 | 0.207 | | |

| | | | | | | | | |
|-----------------------------|---------------|--------|-------|-------|------|--------------|--------|--------|
| | Time*THC | | | 654.5 | 0.0 | 0.981 | | |
| | Time*BrAC | | | 654.8 | -0.3 | 0.728 | | |
| | Time*THC*BrAC | | | 654.4 | 1.6 | 0.115 | | |
| <i>Likert Upset Stomach</i> | | | | | | | | |
| | Intercept | | | 48.6 | 2.0 | 0.057 | | |
| | Blood THC | | | 140.9 | -0.5 | 0.637 | | |
| | BrAC | | | 657.4 | -0.8 | 0.400 | | |
| Time | | -0.008 | 0.004 | 656.8 | -2.3 | 0.019 | -0.015 | -0.001 |
| | THC*BrAC | | | 658.3 | 0.4 | 0.692 | | |
| | Time*THC | | | 671.3 | 1.4 | 0.153 | | |
| | Time*BrAC | | | 656.6 | 0.9 | 0.365 | | |
| | Time*THC*BrAC | | | 657.6 | 0.4 | 0.712 | | |

Data from 19 occasional-to-moderate cannabis smokers who participated in all dosing sessions. Subjective effects were measured by 100 mm visual-analogue scales (VAS) or 5-point Likert scales (Likert) with choices 0≡“none”, 1≡“slight”, 2≡“mild”, 3≡“moderate”, 4≡“severe” after drinking placebo or active alcohol (calculated to produce approximate peak 0.065% BrAC) and inhaling placebo, 2.9% THC, or 6.7% THC vaporized cannabis (500 mg, Volcano® Medic vaporizer).

Linear mixed model results; b is parameter (coefficient) estimate for each factor (negative b indicates the parameter decreases the subjective effect; positive b indicates the parameter increases the overall effect).

Overall equation: [Subjective Effect Result] = Intercept + $b_{\text{Blood THC}} * [\text{THC}]_{\text{blood}}$ + $b_{\text{BrAC}} * \text{BrAC}$ + $b_{\text{Time}} * \text{post-dose time}$ + $b_{\text{THC*BrAC}} * [\text{THC}]_{\text{blood}} * \text{BrAC}$ + $b_{\text{Time*THC}} * \text{post-dose time} * [\text{THC}]_{\text{blood}}$ + $b_{\text{Time*BrAC}} * \text{post-dose time} * \text{BrAC}$ + $b_{\text{Time*THC*BrAC}} * \text{post-dose time} * [\text{THC}]_{\text{blood}} * \text{BrAC}$

^aValues in **bold** are statistically significant (p<0.05); only significant predictors are considered in the final model.

Abbreviations: SE, standard error; df, degrees of freedom; VAS, visual-analogue scale; THC, Δ^9 -tetrahydrocannabinol; BrAC, breath alcohol concentration.

Supplemental Table 2. Overall effect of oral fluid (OF) Δ^9 -tetrahydrocannabinol (THC) concentration ($\mu\text{g/L}$), breath alcohol concentration (BrAC, $\text{g}/210\text{L}$), time, and interactions (THC*BrAC, time*THC, time*BrAC, time*THC*BrAC) on subjective effects beginning 1.4h post-dose in 19 occasional-to-moderate cannabis smokers following controlled vaporized cannabis administration with and without oral alcohol.

| Parameter | b | SE _b | df | t | p ^a | 95% Confidence Interval of b | |
|---------------------------------------|--------|-----------------|--------|-------|------------------|------------------------------|-------------|
| | | | | | | Lower Bound | Upper Bound |
| <i>VAS Anxious</i> | | | | | | | |
| Intercept | 5.332 | 1.102 | 58.09 | 4.84 | <0.001 | 3.127 | 7.537 |
| OF THC | 0.045 | 0.014 | 11.06 | 3.32 | 0.007 | 0.015 | 0.075 |
| BrAC | | | 869.16 | 1.50 | 0.133 | | |
| Time | -0.370 | 0.128 | 866.25 | -2.88 | 0.004 | -0.621 | -0.118 |
| THC*BrAC | | | 861.97 | -1.17 | 0.244 | | |
| Time*THC | | | 821.08 | -0.15 | 0.884 | | |
| Time*BrAC | | | 869.48 | 0.25 | 0.805 | | |
| Time*THC*BrAC | | | 852.98 | -0.78 | 0.433 | | |
| Subject Variance in Intercepts (THC) | 11.928 | 4.245 | | | 0.005 | 5.938 | 23.960 |
| Subject variance in Slopes (THC) | | | | | 0.176 | | |
| ARH1 rho (slope-intercept covariance) | 0.682 | 0.174 | | | <0.000 | 0.191 | 0.900 |
| <i>VAS Good Drug Effect</i> | | | | | | | |
| Intercept | 16.427 | 1.904 | 52.38 | 8.63 | <0.001 | 12.608 | 20.247 |
| OF THC | 0.222 | 0.057 | 7.31 | 3.92 | 0.005 | 0.089 | 0.354 |
| BrAC | 376.67 | 68.01 | 869.93 | 5.54 | <0.001 | 243.18 | 510.15 |
| Time | -2.081 | 0.213 | 864.72 | -9.75 | <0.001 | -2.500 | -1.662 |
| THC*BrAC | -0.698 | 0.299 | 860.75 | -2.33 | 0.020 | -1.285 | -0.111 |
| Time*THC | | | 820.97 | -0.32 | 0.749 | | |
| Time*BrAC | -75.40 | 29.06 | 853.06 | -2.59 | 0.010 | -132.44 | -18.35 |
| Time*THC*BrAC | -0.129 | 0.177 | 861.05 | -0.73 | 0.468 | -0.477 | 0.219 |
| Subject Variance in Intercepts (THC) | 37.956 | 13.375 | | | 0.005 | 19.03 | 75.73 |
| Subject variance in Slopes (THC) | | | | | 0.082 | | |
| ARH1 rho (slope-intercept covariance) | 0.805 | 0.128 | | | <0.001 | 0.381 | 0.950 |
| <i>VAS High</i> | | | | | | | |
| Intercept | 15.33 | 1.80 | 59.87 | 8.53 | <0.001 | 11.73 | 18.92 |
| OF THC | 0.373 | 0.117 | 10.50 | 3.20 | 0.009 | 0.115 | 0.632 |
| BrAC | 296.40 | 66.95 | 854.38 | 4.43 | 0.000 | 164.99 | 427.81 |
| Time | -1.994 | 0.211 | 860.70 | -9.47 | 0.000 | -2.407 | -1.581 |
| THC*BrAC | -0.583 | 0.295 | 858.67 | -1.98 | 0.048 | -1.162 | -0.004 |
| Time*THC | | | 862.55 | -0.55 | 0.580 | | |
| Time*BrAC | -65.08 | 28.50 | 849.15 | -2.28 | 0.023 | -121.02 | -9.15 |
| Time*THC*BrAC | | | 866.18 | -0.26 | 0.794 | | |
| Subject Variance in Intercepts (THC) | 31.076 | 11.110 | | | 0.005 | 15.421 | 62.622 |
| Subject variance in Slopes (THC) | 0.242 | 0.111 | | | 0.030 | 0.098 | 0.597 |
| ARH1 rho (slope-intercept covariance) | 0.555 | 0.186 | | | 0.003 | 0.099 | 0.819 |
| <i>VAS Restless</i> | | | | | | | |
| Intercept | 10.97 | 2.36 | 41.71 | 4.65 | <0.001 | 6.21 | 15.73 |
| OF THC | | | 93.04 | 1.84 | 0.069 | | |
| BrAC | | | 810.57 | -0.29 | 0.770 | | |
| Time | | | 869.52 | 0.16 | 0.871 | | |
| THC*BrAC | | | 819.76 | -0.73 | 0.467 | | |

| | | | | | | | | |
|--|---------------|-------|--------|--------|----------------|--------------|--------|--------|
| | Time*THC | | | 887.55 | -0.38 | 0.704 | | |
| | Time*BrAC | | | 872.48 | 0.57 | 0.566 | | |
| | Time*THC*BrAC | | | 875.57 | 0.03 | 0.977 | | |
| Subject Variance in Intercepts (THC) | 67.08 | 23.06 | | | | 0.004 | 34.20 | 131.59 |
| Subject variance in Slopes (THC) | | | | | | 0.311 | | |
| ARH1 rho (slope-intercept covariance) | | | | | | 0.541 | | |
| <i>VAS Sedated</i> | | | | | | | | |
| Intercept | 17.21 | 3.08 | 29.43 | 5.60 | < 0.001 | 10.92 | 23.50 | |
| | OF THC | | 59.47 | 0.57 | 0.570 | | | |
| | BrAC | | 830.58 | 0.63 | 0.528 | | | |
| Time | -1.26 | 0.24 | 875.41 | -5.16 | < 0.001 | -1.73 | -0.78 | |
| | THC*BrAC | | 831.80 | 0.48 | 0.631 | | | |
| | Time*THC | | 886.81 | 0.58 | 0.563 | | | |
| | Time*BrAC | | 877.81 | 0.71 | 0.478 | | | |
| | Time*THC*BrAC | | 882.50 | -1.75 | 0.081 | | | |
| Subject Variance in Intercepts (THC) | 140.12 | 46.80 | | | | 0.003 | 72.81 | 269.65 |
| Subject variance in Slopes (THC) | | | | | | 0.333 | | |
| ARH1 rho (slope-intercept covariance) | -0.699 | 0.222 | | | | 0.002 | -0.938 | -0.015 |
| <i>VAS Stimulated</i> | | | | | | | | |
| Intercept | 16.37 | 2.05 | 37.02 | 7.97 | < 0.001 | 12.21 | 20.53 | |
| OF THC | 0.219 | 0.075 | 5.10 | 2.93 | 0.032 | 0.028 | 0.411 | |
| BrAC | 222.54 | 61.77 | 840.77 | 3.60 | 0.000 | 101.29 | 343.79 | |
| Time | -1.799 | 0.194 | 855.59 | -9.27 | < 0.001 | -2.180 | -1.418 | |
| | THC*BrAC | | 824.85 | -1.53 | 0.126 | | | |
| | Time*THC | | 840.19 | 0.19 | 0.853 | | | |
| | Time*BrAC | | 827.69 | -1.92 | 0.055 | | | |
| | Time*THC*BrAC | | 833.83 | -1.26 | 0.209 | | | |
| Subject Variance in Intercepts (THC) | 54.51 | 18.57 | | | | 0.003 | 27.96 | 106.28 |
| Subject variance in Slopes (THC) | | | | | | 0.141 | | |
| ARH1 rho (slope-intercept covariance) | 0.564 | 0.176 | | | | 0.001 | 0.133 | 0.816 |
| <i>VAS Stoned</i> | | | | | | | | |
| Intercept | 14.67 | 2.21 | 39.74 | 6.63 | < 0.001 | 10.20 | 19.13 | |
| OF THC | 0.280 | 0.093 | 6.46 | 3.01 | 0.022 | 0.057 | 0.503 | |
| BrAC | 283.22 | 69.37 | 841.69 | 4.08 | < 0.001 | 147.05 | 419.38 | |
| Time | -1.740 | 0.217 | 853.57 | -8.00 | < 0.001 | -2.167 | -1.314 | |
| | THC*BrAC | | 833.62 | -1.63 | 0.102 | | | |
| | Time*THC | | 844.07 | -0.80 | 0.426 | | | |
| Time*BrAC | -76.84 | 29.67 | 834.59 | -2.59 | 0.010 | -135.07 | -18.60 | |
| | Time*THC*BrAC | | 839.33 | -0.68 | 0.499 | | | |
| Subject Variance in Intercepts (THC) | 60.63 | 20.77 | | | | 0.004 | 30.98 | 118.67 |
| Subject variance in Slopes (THC) | | | | | | 0.100 | | |
| ARH1 rho (slope-intercept covariance) | | | | | | 0.615 | | |
| <i>Likert Difficulty Concentrating</i> | | | | | | | | |
| Intercept | 0.514 | 0.092 | 32.69 | 5.57 | < 0.001 | 0.326 | 0.702 | |
| | OF THC | | 6.91 | 2.12 | 0.072 | | | |
| BrAC | 7.86 | 2.55 | 876.67 | 3.08 | 0.002 | 2.86 | 12.87 | |
| Time | -0.052 | 0.008 | 870.90 | -6.46 | < 0.001 | -0.067 | -0.036 | |
| | THC*BrAC | | 850.03 | 0.48 | 0.632 | | | |
| | Time*THC | | 857.74 | 0.79 | 0.432 | | | |

| | | | | | | | | |
|---|---------------|---------|--|--------|-------|------------------|---------|---------|
| | Time*BrAC | | | 863.12 | -1.88 | 0.061 | | |
| | Time*THC*BrAC | | | 852.98 | -0.40 | 0.693 | | |
| Subject Variance in Intercepts (THC) | 0.119 | 0.040 | | | | 0.003 | 0.061 | 0.230 |
| Subject variance in Slopes (THC) | | | | | | 0.147 | | |
| ARH1 rho (slope-intercept covariance) | 0.549 | 0.178 | | | | 0.002 | 0.116 | 0.807 |
| <i>Likert Altered Sense of Time</i> | | | | | | | | |
| Intercept | 0.334 | 0.071 | | 49.98 | 4.68 | <0.001 | 0.191 | 0.478 |
| OF THC | 0.005 | 0.002 | | 12.06 | 2.35 | 0.037 | 0.000 | 0.010 |
| BrAC | 5.605 | 2.503 | | 881.85 | 2.24 | 0.025 | 0.693 | 10.517 |
| Time | -0.044 | 0.008 | | 874.51 | -5.56 | <0.001 | -0.059 | -0.028 |
| | THC*BrAC | | | 875.97 | -1.03 | 0.302 | | |
| | Time*THC | | | 719.54 | 0.24 | 0.807 | | |
| | Time*BrAC | | | 874.10 | -0.95 | 0.343 | | |
| | Time*THC*BrAC | | | 839.79 | -0.10 | 0.919 | | |
| Subject Variance in Intercepts (THC) | 0.055 | 0.019 | | | | 0.004 | 0.028 | 0.109 |
| Subject variance in Slopes (THC) | 0.000 | 0.000 | | | | 0.022 | 0.000 | 0.000 |
| ARH1 rho (slope-intercept covariance) | 0.922 | 0.060 | | | | <0.001 | 0.674 | 0.983 |
| <i>Likert Slowed/Slurred Speech</i> | | | | | | | | |
| Intercept | 0.141 | 0.045 | | 85.37 | 3.14 | 0.002 | 0.052 | 0.230 |
| | OF THC | | | 14.87 | 1.73 | 0.104 | | |
| BrAC | 5.748 | 1.859 | | 875.26 | 3.09 | 0.002 | 2.100 | 9.396 |
| Time | -0.019 | 0.006 | | 875.46 | -3.25 | 0.001 | -0.030 | -0.008 |
| | THC*BrAC | | | 874.56 | 1.18 | 0.239 | | |
| | Time*THC | | | 875.67 | 0.01 | 0.993 | | |
| | Time*BrAC | | | 874.96 | -1.22 | 0.223 | | |
| | Time*THC*BrAC | | | 874.66 | -1.45 | 0.147 | | |
| Subject Variance in Intercepts (THC) | 0.015 | 0.006 | | | | 0.009 | 0.007 | 0.032 |
| Subject variance in Slopes (THC) | 0.00014 | 0.00006 | | | | 0.021 | 0.00006 | 0.00032 |
| ARH1 rho (slope-intercept covariance) | | | | | | -- | | |
| <i>Likert Body Feels Sluggish/Heavy</i> | | | | | | | | |
| Intercept | 0.574 | 0.091 | | 48.11 | 6.32 | <0.001 | 0.391 | 0.757 |
| | OF THC | | | 11.29 | 1.71 | 0.115 | | |
| BrAC | 7.502 | 3.152 | | 881.42 | 2.38 | 0.018 | 1.316 | 13.687 |
| Time | -0.058 | 0.010 | | 874.12 | -5.91 | <0.001 | -0.078 | -0.039 |
| | THC*BrAC | | | 873.41 | -0.20 | 0.842 | | |
| | Time*THC | | | 875.71 | 1.32 | 0.188 | | |
| | Time*BrAC | | | 877.21 | -0.60 | 0.546 | | |
| | Time*THC*BrAC | | | 867.94 | -0.96 | 0.338 | | |
| Subject Variance in Intercepts (THC) | 0.091 | 0.032 | | | | 0.004 | 0.046 | 0.181 |
| Subject variance in Slopes (THC) | | | | | | 0.225 | | |
| ARH1 rho (slope-intercept covariance) | | | | | | 0.386 | | |
| <i>Likert Feel Thirsty</i> | | | | | | | | |
| Intercept | 1.142 | 0.112 | | 48.47 | 10.22 | <0.001 | 0.918 | 1.367 |
| OF THC | 0.004 | 0.001 | | 12.40 | 2.88 | 0.013 | 0.001 | 0.007 |
| | BrAC | | | 880.91 | -0.09 | 0.926 | | |
| Time | -0.128 | 0.012 | | 875.64 | -10.6 | <0.001 | -0.152 | -0.104 |
| | THC*BrAC | | | 878.53 | 0.55 | 0.581 | | |
| Time*THC | 0.001 | 0.000 | | 863.23 | 3.20 | 0.001 | 0.000 | 0.002 |
| Time*BrAC | 5.565 | 1.660 | | 878.88 | 3.35 | 0.001 | 2.307 | 8.822 |

| | | | | | | | |
|--|--------|--------|--------|-------|------------------|--------|--------|
| Time*THC*BrAC | -0.024 | 0.010 | 873.11 | -2.35 | 0.019 | -0.044 | -0.004 |
| Subject Variance in Intercepts (THC) | 0.138 | 0.048 | | | 0.004 | 0.069 | 0.272 |
| Subject variance in Slopes (THC) | | | | | 0.136 | | |
| ARH1 rho (slope-intercept covariance) | 0.598 | 0.256 | | | 0.020 | -0.092 | 0.900 |
| <i>Likert Dizzy</i> | | | | | | | |
| Intercept | 0.082 | 0.027 | 197.43 | 3.01 | 0.003 | 0.028 | 0.135 |
| OF THC | | | 15.59 | 1.43 | 0.174 | | |
| BrAC | 4.408 | 1.277 | 864.60 | 3.45 | 0.001 | 1.902 | 6.914 |
| Time | -0.009 | 0.004 | 863.05 | -2.22 | 0.027 | -0.017 | -0.001 |
| THC*BrAC | | | 875.78 | 0.13 | 0.895 | | |
| Time*THC | | | 782.83 | -0.04 | 0.968 | | |
| Time*BrAC | -1.481 | 0.543 | 864.55 | -2.73 | 0.007 | -2.547 | -0.415 |
| Time*THC*BrAC | | | 860.09 | -0.18 | 0.857 | | |
| Subject Variance in Intercepts (THC) | 0.003 | 0.001 | | | 0.029 | 0.001 | 0.007 |
| Subject variance in Slopes (THC) | 0.0003 | 0.0001 | | | 0.007 | 0.0001 | 0.0005 |
| ARH1 rho (slope-intercept covariance) | | | | | 0.509 | | |
| <i>Likert Dry Mouth or Throat</i> | | | | | | | |
| Intercept | 0.727 | 0.093 | 71.08 | 7.83 | <0.001 | 0.542 | 0.913 |
| OF THC | 0.013 | 0.005 | 9.79 | 2.54 | 0.030 | 0.002 | 0.024 |
| BrAC | | | 863.27 | 1.60 | 0.110 | | |
| Time | -0.084 | 0.011 | 868.02 | -7.33 | <0.001 | -0.107 | -0.062 |
| THC*BrAC | | | 864.66 | 0.47 | 0.637 | | |
| Time*THC | 0.001 | 0.000 | 842.04 | 3.06 | 0.002 | 0.000 | 0.002 |
| Time*BrAC | | | 856.97 | -0.54 | 0.591 | | |
| Time*THC*BrAC | | | 865.39 | -0.98 | 0.326 | | |
| Subject Variance in Intercepts (THC) | 0.074 | 0.027 | | | 0.006 | 0.036 | 0.152 |
| Subject variance in Slopes (THC) | 0.000 | 0.000 | | | 0.039 | 0.000 | 0.001 |
| ARH1 rho (slope-intercept covariance) | 0.628 | 0.169 | | | 0.000 | 0.190 | 0.857 |
| <i>Likert Feel Hungry</i> | | | | | | | |
| Intercept | 1.771 | 0.123 | 57.82 | 14.41 | <0.001 | 1.525 | 2.017 |
| OF THC | | | 896.47 | -1.67 | 0.096 | | |
| BrAC | -14.84 | 4.41 | 882.70 | -3.37 | 0.001 | -23.49 | -6.19 |
| Time | -0.238 | 0.014 | 883.14 | -16.6 | <0.001 | -0.266 | -0.210 |
| THC*BrAC | | | 889.20 | 1.45 | 0.148 | | |
| Time*THC | 0.001 | 0.000 | 899.57 | 2.83 | 0.005 | 0.000 | 0.002 |
| Time*BrAC | 9.144 | 1.944 | 884.02 | 4.70 | <0.001 | 5.328 | 12.959 |
| Time*THC*BrAC | | | 895.64 | -1.88 | 0.060 | | |
| Subject Variance in Intercepts (THC) | 0.150 | 0.053 | | | 0.005 | 0.075 | 0.299 |
| Subject variance in Slopes (THC) | | | | | 0.479 | | |
| ARH1 rho (slope-intercept covariance) | | | | | -- | | |
| <i>Likert Feel Shakiness/Tremulousness</i> | | | | | | | |
| Intercept | | | 810.68 | 1.66 | 0.097 | | |
| OF THC | | | 0.27 | 1.37 | 0.650 | | |
| BrAC | | | 879.36 | -0.38 | 0.702 | | |
| Time | | | 876.77 | -1.45 | 0.149 | | |
| THC*BrAC | | | 878.33 | -1.88 | 0.061 | | |
| Time*THC | | | 878.42 | -0.48 | 0.628 | | |
| Time*BrAC | | | 879.56 | 0.86 | 0.390 | | |
| Time*THC*BrAC | 0.0059 | 0.0027 | 878.26 | 2.14 | 0.033 | 0.0005 | 0.0113 |

| | | | | | | | | |
|---------------------------------------|---------|--------|--------|-------|----------------|--------------|--------|-------|
| Subject Variance in Intercepts (THC) | | | | | | 0.721 | | |
| Subject variance in Slopes (THC) | 0.000 | 0.000 | | | | 0.006 | 0.000 | 0.000 |
| ARH1 rho (slope-intercept covariance) | | | | | | -- | | |
| <i>Likert Nausea</i> | | | | | | | | |
| Intercept | 0.126 | 0.032 | 93.30 | 3.88 | < 0.001 | 0.061 | 0.190 | |
| OF THC | | | 251.26 | 1.01 | 0.315 | | | |
| BrAC | | | 886.90 | -0.82 | 0.414 | | | |
| Time | -0.017 | 0.004 | 884.95 | -3.97 | < 0.001 | -0.026 | -0.009 | |
| THC*BrAC | | | 891.21 | -0.89 | 0.374 | | | |
| Time*THC | | | 896.37 | -0.35 | 0.728 | | | |
| Time*BrAC | | | 886.58 | 0.54 | 0.591 | | | |
| Time*THC*BrAC | | | 890.11 | 1.04 | 0.299 | | | |
| Subject Variance in Intercepts (THC) | 0.007 | 0.003 | | | | 0.009 | 0.004 | 0.016 |
| Subject variance in Slopes (THC) | 0.000 | 0.000 | | | | 0.040 | 0.000 | 0.000 |
| ARH1 rho (slope-intercept covariance) | | | | | | -- | | |
| <i>Likert Headache</i> | | | | | | | | |
| Intercept | 0.168 | 0.056 | 70.65 | 3.01 | 0.004 | 0.057 | 0.280 | |
| OF THC | | | 892.32 | -0.56 | 0.578 | | | |
| BrAC | | | 881.93 | -1.38 | 0.169 | | | |
| Time | | | 882.26 | -1.17 | 0.241 | | | |
| THC*BrAC | | | 892.35 | -0.54 | 0.586 | | | |
| Time*THC | | | 898.44 | 0.85 | 0.393 | | | |
| Time*BrAC | | | 884.07 | 0.30 | 0.761 | | | |
| Time*THC*BrAC | | | 898.61 | 0.60 | 0.549 | | | |
| Subject Variance in Intercepts (THC) | 0.027 | 0.010 | | | | 0.006 | 0.013 | 0.055 |
| Subject variance in Slopes (THC) | | | | | | 0.923 | | |
| ARH1 rho (slope-intercept covariance) | | | | | | -- | | |
| <i>Likert Palpitations</i> | | | | | | | | |
| Intercept | -0.012 | 0.005 | 411.13 | -2.27 | 0.024 | -0.022 | -0.002 | |
| OF THC | | | 7.33 | 1.52 | 0.171 | | | |
| BrAC | 0.819 | 0.268 | 887.10 | 3.06 | 0.002 | 0.294 | 1.345 | |
| Time | 0.0018 | 0.0008 | 889.95 | 2.13 | 0.034 | 0.0001 | 0.0034 | |
| THC*BrAC | | | 883.82 | -1.17 | 0.243 | | | |
| Time*THC | | | 886.13 | -1.31 | 0.192 | | | |
| Time*BrAC | -0.255 | 0.114 | 885.69 | -2.24 | 0.025 | -0.478 | -0.032 | |
| Time*THC*BrAC | | | 884.81 | -0.07 | 0.947 | | | |
| Subject Variance in Intercepts (THC) | | | | | | 0.083 | | |
| Subject variance in Slopes (THC) | 0.000 | 0.000 | | | | 0.004 | 0.000 | 0.000 |
| ARH1 rho (slope-intercept covariance) | | | | | | -- | | |
| <i>Likert Upset Stomach</i> | | | | | | | | |
| Intercept | 0.061 | 0.021 | 173.16 | 2.95 | 0.004 | 0.020 | 0.102 | |
| OF THC | | | 47.87 | 1.37 | 0.177 | | | |
| BrAC | | | 889.33 | -0.61 | 0.540 | | | |
| Time | -0.007 | 0.003 | 886.65 | -2.42 | 0.016 | -0.013 | -0.001 | |
| THC*BrAC | -0.014 | 0.004 | 889.86 | -3.41 | 0.001 | -0.023 | -0.006 | |
| Time*THC | -0.0002 | 0.0001 | 894.36 | -1.97 | 0.0497 | -0.0004 | 0.0000 | |
| Time*BrAC | | | 888.49 | 0.17 | 0.868 | | | |
| Time*THC*BrAC | 0.010 | 0.002 | 888.86 | 4.05 | < 0.001 | 0.005 | 0.015 | |
| Subject Variance in Intercepts | 0.002 | 0.001 | | | | 0.020 | 0.001 | 0.004 |

| (THC) | | | | | |
|---------------------------------------|-------|-------|--------------|-------|-------|
| Subject variance in Slopes (THC) | 0.000 | 0.000 | 0.010 | 0.000 | 0.000 |
| ARHI rho (slope-intercept covariance) | | | -- | | |

Data from 19 occasional-to-moderate cannabis smokers who participated in all dosing sessions, excluding times <1.4h post-dose. Subjective effects were measured by 100 mm visual-analogue scales (VAS) or 5-point Likert scales (Likert) with choices 0≡“none”, 1≡“slight”, 2≡“mild”, 3≡“moderate”, 4≡“severe” after drinking placebo or active alcohol (calculated to produce approximate peak 0.065% BrAC) and inhaling placebo, 2.9% THC, or 6.7% THC vaporized cannabis (500 mg, Volcano® Medic vaporizer).

Linear mixed model results; b is parameter (coefficient) estimate for each factor (negative b indicates the parameter decreases the subjective effect; positive b indicates the parameter increases the overall effect).

Overall equation: [Subjective Effect Result] = Intercept + $b_{OF\ THC} * [THC]_{blood}$ + $b_{BrAC} * BrAC$ + $b_{Time} * post-dose\ time$ + $b_{THC*BrAC} * [THC]_{OF} * BrAC$ + $b_{Time*THC} * post-dose\ time * [THC]_{OF}$ + $b_{Time*BrAC} * post-dose\ time * BrAC$ + $b_{Time*THC*BrAC} * post-dose\ time * [THC]_{OF} * BrAC$

^aValues in **bold** are statistically significant (p<0.05); only significant predictors are considered in the final model.

Abbreviations: SE, standard error; df, degrees of freedom; VAS, visual-analogue scale; THC, Δ⁹-tetrahydrocannabinol; BrAC, breath alcohol concentration.

Supplemental Table 3. Overall effect of oral fluid (OF) Δ^9 -tetrahydrocannabinol (THC) concentration ($\mu\text{g/L}$), breath alcohol concentration (BrAC, $\text{g}/210\text{L}$), time, and interactions (THC*BrAC, time*THC, time*BrAC, time*THC*BrAC) on subjective effects in 19 occasional-to-moderate cannabis smokers following controlled vaporized cannabis administration with and without oral alcohol.

| Parameter | b | SE _b | df | t | p ^a | 95% Confidence Interval of b | |
|---------------------------------------|---------|-----------------|--------|-------|----------------|------------------------------|-------------|
| | | | | | | Lower Bound | Upper Bound |
| <i>VAS Anxious</i> | | | | | | | |
| Intercept | 9.003 | 1.123 | 45.88 | 8.0 | < 0.001 | 6.742 | 11.264 |
| OF THC | | | 6.97 | 0.6 | 0.585 | | |
| BrAC | | | 978.55 | 0.6 | 0.559 | | |
| Time | -0.965 | 0.125 | 970.53 | -7.7 | < 0.001 | -1.210 | -0.719 |
| THC*BrAC | | | 942.52 | 1.0 | 0.322 | | |
| Time*THC | 0.0063 | 0.0025 | 810.20 | 2.5 | 0.011 | 0.0014 | 0.0111 |
| Time*BrAC | | | 974.93 | 0.4 | 0.718 | | |
| Time*THC*BrAC | -0.103 | 0.050 | 876.28 | -2.1 | 0.037 | -0.201 | -0.006 |
| Subject Variance in Intercepts (THC) | 13.890 | 4.984 | | | 0.005 | 6.875 | 28.062 |
| Subject variance in Slopes (THC) | | | | | 0.528 | | |
| ARH1 rho (slope-intercept covariance) | 0.646 | 0.310 | | | 0.037 | -0.268 | 0.948 |
| <i>VAS Good Drug Effect</i> | | | | | | | |
| Intercept | 24.610 | 2.114 | 36.63 | 11.6 | < 0.001 | 20.325 | 28.895 |
| OF THC | 0.0073 | 0.0026 | 10.54 | 2.8 | 0.017 | 0.0016 | 0.0130 |
| BrAC | 264.584 | 39.073 | 990.22 | 6.8 | < 0.001 | 187.909 | 341.259 |
| Time | -3.401 | 0.208 | 987.76 | -16.3 | < 0.001 | -3.809 | -2.992 |
| THC*BrAC | | | 977.73 | 0.4 | 0.687 | | |
| Time*THC | 0.0182 | 0.0040 | 867.47 | 4.5 | < 0.001 | 0.0103 | 0.0260 |
| Time*BrAC | -57.421 | 19.932 | 988.98 | -2.9 | 0.004 | -96.535 | -18.306 |
| Time*THC*BrAC | -0.230 | 0.077 | 937.40 | -3.0 | 0.003 | -0.380 | -0.079 |
| Subject Variance in Intercepts (THC) | 56.978 | 19.796 | | | 0.004 | 28.838 | 112.576 |
| Subject variance in Slopes (THC) | | | | | 0.058 | 0.000 | 0.000 |
| ARH1 rho (slope-intercept covariance) | 0.830 | 0.142 | | | 0.000 | 0.285 | 0.970 |
| <i>VAS High</i> | | | | | | | |
| Intercept | 25.628 | 2.050 | 42.01 | 12.5 | < 0.001 | 21.491 | 29.765 |
| OF THC | 0.0115 | 0.0036 | 11.00 | 3.2 | 0.008 | 0.0037 | 0.0193 |
| BrAC | 195.297 | 40.951 | 991.81 | 4.8 | < 0.001 | 114.935 | 275.658 |
| Time | -3.631 | 0.219 | 988.84 | -16.6 | < 0.001 | -4.060 | -3.201 |
| THC*BrAC | | | 935.55 | -0.5 | 0.620 | | |
| Time*THC | 0.0187 | 0.0041 | 638.56 | 4.5 | < 0.001 | 0.0106 | 0.0268 |
| Time*BrAC | -47.901 | 20.878 | 991.03 | -2.3 | 0.022 | -88.870 | -6.931 |
| Time*THC*BrAC | -0.196 | 0.079 | 787.41 | -2.5 | 0.013 | -0.351 | -0.041 |
| Subject Variance in Intercepts (THC) | 49.024 | 17.353 | | | 0.005 | 24.497 | 98.108 |
| Subject variance in Slopes (THC) | 0.000 | 0.000 | | | 0.037 | 0.000 | 0.001 |
| ARH1 rho (slope-intercept covariance) | 0.923 | 0.070 | | | < 0.001 | 0.596 | 0.987 |
| <i>VAS Restless</i> | | | | | | | |
| Intercept | 12.717 | 2.121 | 33.43 | 6.0 | < 0.001 | 8.405 | 17.029 |
| OF THC | | | 55.54 | 0.0 | 0.982 | | |

| | | | | | | | | |
|--|---------------|--------|--|--------|------|--------------|--------|---------|
| | BrAC | | | 977.92 | -0.2 | 0.821 | | |
| | Time | | | 971.19 | -1.3 | 0.181 | | |
| | THC*BrAC | | | 946.79 | 1.0 | 0.338 | | |
| | Time*THC | | | 994.51 | 1.4 | 0.173 | | |
| | Time*BrAC | | | 965.82 | 0.3 | 0.780 | | |
| | Time*THC*BrAC | | | 995.77 | -1.1 | 0.266 | | |
| Subject Variance in Intercepts (THC) | 60.781 | 20.866 | | | | 0.004 | 31.014 | 119.120 |
| Subject variance in Slopes (THC) | | | | | | 0.312 | | |
| ARH1 rho (slope-intercept covariance) | | | | | | 0.653 | | |

VAS Sedated

| | | | | | | | | |
|--|-----------|--------|---------|------|----------------|--------------|--------|--------|
| Intercept | 18.366 | 2.715 | 27.42 | 6.8 | < 0.001 | 12.799 | 23.933 | |
| | OF THC | | 998.87 | -1.4 | 0.174 | | | |
| | BrAC | | 990.41 | 0.4 | 0.659 | | | |
| Time | -1.448 | 0.208 | 990.22 | -7.0 | < 0.001 | -1.856 | -1.041 | |
| | THC*BrAC | | 994.46 | 1.3 | 0.197 | | | |
| Time*THC | 0.0087 | 0.0041 | 1003.97 | 2.1 | 0.037 | 0.0005 | 0.0168 | |
| | Time*BrAC | | 990.19 | 1.3 | 0.209 | | | |
| Time*THC*BrAC | -0.159 | 0.079 | 1000.95 | -2.0 | 0.044 | -0.313 | -0.004 | |
| Subject Variance in Intercepts (THC) | 18.366 | 2.715 | | | | 0.003 | 12.799 | 23.933 |
| Subject variance in Slopes (THC) | | | -- | -- | -- | | | |
| ARH1 rho (slope-intercept covariance) | | | -- | -- | -- | | | |

VAS Stimulated

| | | | | | | | | |
|--|---------|--------|--------|-------|----------------|----------------|---------|---------|
| Intercept | 23.298 | 2.282 | 29.53 | 10.2 | < 0.001 | 18.634 | 27.962 | |
| | OF THC | | 3.50 | 1.5 | 0.221 | | | |
| BrAC | 226.775 | 35.601 | 945.07 | 6.4 | < 0.001 | 156.910 | 296.641 | |
| Time | -2.930 | 0.188 | 978.90 | -15.6 | < 0.001 | -3.299 | -2.561 | |
| THC*BrAC | 0.044 | 0.016 | 953.00 | 2.7 | 0.006 | 0.012 | 0.076 | |
| Time*THC | 0.0213 | 0.0036 | 936.20 | 5.9 | < 0.001 | 0.0142 | 0.0285 | |
| Time*BrAC | -77.518 | 18.029 | 950.94 | -4.3 | < 0.001 | - | -42.137 | |
| | | | | | | 112.898 | | |
| Time*THC*BrAC | -0.324 | 0.069 | 936.73 | -4.7 | < 0.001 | -0.460 | -0.187 | |
| Subject Variance in Intercepts (THC) | 76.099 | 25.727 | | | | 0.003 | 39.229 | 147.622 |
| Subject variance in Slopes (THC) | | | | | | 0.245 | | |
| ARH1 rho (slope-intercept covariance) | 0.628 | 0.162 | | | | < 0.001 | 0.211 | 0.851 |

VAS Stoned

| | | | | | | | | |
|--|----------|--------|--------|-------|----------------|--------------|---------|---------|
| Intercept | 23.581 | 2.219 | 36.32 | 10.6 | < 0.001 | 19.081 | 28.081 | |
| | OF THC | | 8.10 | 1.1 | 0.300 | | | |
| BrAC | 159.548 | 40.963 | 979.29 | 3.9 | < 0.001 | 79.163 | 239.933 | |
| Time | -3.178 | 0.218 | 984.66 | -14.6 | < 0.001 | -3.605 | -2.751 | |
| | THC*BrAC | | 976.63 | 0.0 | 0.987 | | | |
| Time*THC | 0.0166 | 0.0042 | 975.54 | 3.9 | < 0.001 | 0.0083 | 0.0250 | |
| Time*BrAC | -55.741 | 20.971 | 978.65 | -2.7 | 0.008 | -96.895 | -14.586 | |
| Time*THC*BrAC | -0.212 | 0.081 | 974.10 | -2.6 | 0.009 | -0.370 | -0.053 | |
| Subject Variance in Intercepts (THC) | 63.059 | 21.915 | | | | 0.004 | 31.909 | 124.615 |
| Subject variance in Slopes (THC) | | | | | | 0.097 | | |
| ARH1 rho (slope-intercept covariance) | | | | | | 0.249 | | |

Likert Difficulty Concentrating

| | | | | | | | | |
|--|----------|--------|--------|--------|------|------------------|--------|--------|
| Intercept | | 0.594 | 0.097 | 27.13 | 6.1 | <0.001 | 0.394 | 0.794 |
| | OF THC | | | 8.39 | 1.5 | 0.161 | | |
| BrAC | | 7.252 | 1.376 | 989.34 | 5.3 | <0.001 | 4.552 | 9.953 |
| Time | | -0.064 | 0.007 | 991.00 | -8.8 | <0.001 | -0.078 | -0.050 |
| | THC*BrAC | | | 989.10 | 0.1 | 0.885 | | |
| Time*THC | | 0.0003 | 0.0001 | 981.98 | 2.1 | 0.034 | 0.0000 | 0.0006 |
| Time*BrAC | | -1.560 | 0.701 | 988.02 | -2.2 | 0.026 | -2.937 | -0.184 |
| Time*THC*BrAC | | -0.006 | 0.003 | 980.15 | -2.2 | 0.025 | -0.011 | -0.001 |
| Subject Variance in Intercepts (THC) | | 0.146 | 0.049 | | | 0.003 | 0.076 | 0.281 |
| Subject variance in Slopes (THC) | | | | | | 0.087 | | |
| ARH1 rho (slope-intercept covariance) | | 0.659 | 0.155 | | | <0.001 | 0.247 | 0.869 |

Likert Altered Sense of Time

| | | | | | | | | |
|--|-----------|--------|--------|--------|------|------------------|--------|--------|
| Intercept | | 0.473 | 0.084 | 32.21 | 5.6 | <0.001 | 0.301 | 0.645 |
| | OF THC | | | 10.37 | 1.8 | 0.102 | | |
| BrAC | | 3.087 | 1.421 | 995.32 | 2.2 | 0.030 | 0.297 | 5.876 |
| Time | | -0.066 | 0.008 | 995.52 | -8.7 | <0.001 | -0.081 | -0.051 |
| | THC*BrAC | | | 921.42 | 0.8 | 0.444 | | |
| Time*THC | | 0.0004 | 0.0001 | 524.49 | 2.6 | 0.008 | 0.0001 | 0.0006 |
| | Time*BrAC | | | 995.25 | 0.1 | 0.886 | | |
| Time*THC*BrAC | | -0.007 | 0.003 | 688.97 | -2.6 | 0.010 | -0.012 | -0.002 |
| Subject Variance in Intercepts (THC) | | 0.098 | 0.034 | | | 0.003 | 0.050 | 0.192 |
| Subject variance in Slopes (THC) | | 0.000 | 0.000 | | | 0.034 | 0.000 | 0.000 |
| ARH1 rho (slope-intercept covariance) | | 0.981 | 0.024 | | | <0.001 | 0.776 | 0.999 |

Likert Slowed/Slurred Speech

| | | | | | | | | |
|--|---------------|--------|-------|--------|------|------------------|--------|--------|
| Intercept | | 0.268 | 0.056 | 38.18 | 4.8 | <0.001 | 0.154 | 0.382 |
| | OF THC | | | 18.85 | 1.8 | 0.091 | | |
| BrAC | | 2.907 | 1.065 | 989.38 | 2.7 | 0.006 | 0.816 | 4.997 |
| Time | | -0.038 | 0.006 | 990.28 | -6.7 | <0.001 | -0.049 | -0.027 |
| | THC*BrAC | | | 990.31 | -0.8 | 0.430 | | |
| | Time*THC | | | 992.84 | 0.2 | 0.803 | | |
| | Time*BrAC | | | 989.37 | -0.1 | 0.904 | | |
| | Time*THC*BrAC | | | 991.08 | 0.5 | 0.604 | | |
| Subject Variance in Intercepts (THC) | | | | -- | -- | -- | | |
| Subject variance in Slopes (THC) | | | | -- | -- | -- | | |
| ARH1 rho (slope-intercept covariance) | | | | -- | -- | -- | | |

Likert Body Feels Sluggish/Heavy

| | | | | | | | | |
|---|-----------|---------|--------|---------|------|------------------|---------|--------|
| Intercept | | 0.677 | 0.089 | 33.81 | 7.6 | <0.001 | 0.496 | 0.858 |
| OF THC | | -0.0001 | 0.0000 | 958.74 | -3.4 | 0.001 | -0.0002 | 0.0000 |
| BrAC | | 6.043 | 1.595 | 998.29 | 3.8 | <0.001 | 2.912 | 9.174 |
| Time | | -0.075 | 0.008 | 996.81 | -9.0 | <0.001 | -0.092 | -0.059 |
| THC*BrAC | | 0.002 | 0.001 | 1007.01 | 3.0 | 0.003 | 0.001 | 0.004 |
| Time*THC | | 0.0007 | 0.0002 | 1014.76 | 4.0 | <0.001 | 0.0003 | 0.0010 |
| | Time*BrAC | | | 998.17 | -0.7 | 0.503 | | |
| Time*THC*BrAC | | -0.011 | 0.003 | 1012.50 | -3.4 | 0.001 | -0.017 | -0.005 |
| Subject Variance in Intercepts (THC) | | | | -- | -- | -- | | |
| Subject variance in Slopes (THC) | | | | -- | -- | -- | | |

| | | | | | | | | |
|---------------------------------------|---------------|---------|--------|--------|-------|------------------|----------|----------|
| ARH1 rho (slope-intercept covariance) | | | -- | -- | -- | | | |
| <i>Likert Feel Thirsty</i> | | | | | | | | |
| Intercept | | 1.036 | 0.132 | 82.86 | 7.9 | <0.001 | 0.773 | 1.298 |
| OF THC | | -0.0002 | 0.0001 | 25.13 | -3.0 | 0.006 | -0.00032 | -0.00006 |
| | BrAC | | | 434.92 | -0.7 | 0.455 | | |
| | Time | | | 437.45 | 0.2 | 0.803 | | |
| THC*BrAC | | 0.005 | 0.001 | 411.88 | 4.2 | <0.001 | 0.003 | 0.007 |
| Time*THC | | 0.0015 | 0.0003 | 407.93 | 5.4 | <0.001 | 0.0010 | 0.0021 |
| Time*BrAC | | 5.808 | 1.648 | 430.90 | 3.5 | <0.001 | 2.569 | 9.048 |
| Time*THC*BrAC | | -0.023 | 0.005 | 428.57 | -4.3 | <0.001 | -0.034 | -0.013 |
| Subject Variance in Intercepts (THC) | | 0.122 | 0.050 | | | 0.014 | 0.055 | 0.271 |
| Subject variance in Slopes (THC) | | | | | | 0.299 | | |
| ARH1 rho (slope-intercept covariance) | | | | | | 0.581 | | |
| <i>Likert Dizzy</i> | | | | | | | | |
| Intercept | | 0.180 | 0.032 | 77.56 | 5.6 | <0.001 | 0.117 | 0.244 |
| | OF THC | | | 15.89 | 1.3 | 0.208 | | |
| | BrAC | | | 976.30 | 0.1 | 0.895 | | |
| Time | | -0.024 | 0.004 | 977.01 | -5.7 | <0.001 | -0.032 | -0.016 |
| | THC*BrAC | | | 991.05 | -0.6 | 0.522 | | |
| | Time*THC | | | 925.95 | -0.6 | 0.517 | | |
| | Time*BrAC | | | 979.24 | -0.4 | 0.659 | | |
| | Time*THC*BrAC | | | 969.93 | 0.9 | 0.353 | | |
| Subject Variance in Intercepts (THC) | | 0.008 | 0.003 | | | 0.009 | 0.004 | 0.017 |
| Subject variance in Slopes (THC) | | 0.000 | 0.000 | | | 0.005 | 0.000 | 0.000 |
| ARH1 rho (slope-intercept covariance) | | 0.478 | 0.210 | | | 0.023 | -0.013 | 0.783 |
| <i>Likert Dry Mouth or Throat</i> | | | | | | | | |
| Intercept | | 0.936 | 0.096 | 44.50 | 9.7 | <0.001 | 0.742 | 1.130 |
| | OF THC | | | 5.95 | -1.4 | 0.199 | | |
| | BrAC | | | 994.59 | 1.4 | 0.157 | | |
| Time | | -0.117 | 0.011 | 992.21 | -11.1 | <0.001 | -0.138 | -0.096 |
| THC*BrAC | | 0.003 | 0.001 | 955.85 | 3.5 | 0.001 | 0.001 | 0.005 |
| Time*THC | | 0.0016 | 0.0002 | 827.72 | 7.8 | <0.001 | 0.0012 | 0.0020 |
| | Time*BrAC | | | 994.25 | 1.1 | 0.274 | | |
| Time*THC*BrAC | | -0.020 | 0.004 | 893.64 | -5.1 | <0.001 | -0.028 | -0.012 |
| Subject Variance in Intercepts (THC) | | 0.106 | 0.037 | | | 0.005 | 0.053 | 0.211 |
| Subject variance in Slopes (THC) | | | | | | 0.480 | | |
| ARH1 rho (slope-intercept covariance) | | 0.652 | 0.316 | | | 0.039 | -0.289 | 0.952 |
| <i>Likert Feel Hungry</i> | | | | | | | | |
| Intercept | | 0.398 | 0.199 | 65.02 | 2.0 | 0.050 | 0.000 | 0.796 |
| | OF THC | | | 435.03 | -1.5 | 0.147 | | |
| | BrAC | | | 431.91 | 1.0 | 0.298 | | |
| Time | | 0.498 | 0.040 | 431.36 | 12.6 | <0.001 | 0.420 | 0.576 |
| | THC*BrAC | | | 433.29 | 1.3 | 0.208 | | |
| | Time*THC | | | 439.20 | 1.2 | 0.212 | | |
| | Time*BrAC | | | 431.62 | -0.7 | 0.481 | | |
| | Time*THC*BrAC | | | 437.25 | -0.9 | 0.348 | | |
| Subject Variance in Intercepts | | | | -- | -- | -- | | |

| | | | | | | | | |
|--|---------------------------------------|--|--|----|----|----|--|--|
| | (THC) | | | | | | | |
| | Subject variance in Slopes (THC) | | | -- | -- | -- | | |
| | ARH1 rho (slope-intercept covariance) | | | -- | -- | -- | | |

Likert Feel Shakiness/Tremulousness

| | | | | | | | | |
|------------------|---------------------------------------|--------|-------|--------|------|------------------|--------|--------|
| Intercept | | 0.105 | 0.022 | 241.61 | 4.7 | <0.001 | 0.061 | 0.149 |
| | OF THC | | | 7.36 | 1.5 | 0.164 | | |
| | BrAC | | | 975.85 | -0.8 | 0.396 | | |
| Time | | -0.016 | 0.004 | 977.34 | -4.5 | <0.001 | -0.023 | -0.009 |
| | THC*BrAC | | | 975.86 | -0.2 | 0.854 | | |
| | Time*THC | | | 976.80 | 0.5 | 0.606 | | |
| | Time*BrAC | | | 976.13 | 1.1 | 0.256 | | |
| | Time*THC*BrAC | | | 976.30 | 0.6 | 0.560 | | |
| | Subject Variance in Intercepts (THC) | | | -- | -- | -- | | |
| | Subject variance in Slopes (THC) | | | -- | -- | -- | | |
| | ARH1 rho (slope-intercept covariance) | | | -- | -- | -- | | |

Likert Nausea

| | | | | | | | | |
|------------------|---------------------------------------|--------|-------|---------|------|--------------|--------|--------|
| Intercept | | 0.099 | 0.032 | 46.07 | 3.1 | 0.003 | 0.035 | 0.162 |
| | OF THC | | | 1011.88 | -1.8 | 0.070 | | |
| | BrAC | | | 997.10 | -1.5 | 0.142 | | |
| Time | | -0.014 | 0.003 | 996.65 | -4.1 | 0.000 | -0.020 | -0.007 |
| | THC*BrAC | | | 1005.44 | 1.4 | 0.158 | | |
| | Time*THC | | | 1015.98 | 1.7 | 0.087 | | |
| | Time*BrAC | | | 996.83 | 1.9 | 0.061 | | |
| | Time*THC*BrAC | | | 1015.12 | -1.5 | 0.133 | | |
| | Subject Variance in Intercepts (THC) | -- | -- | -- | -- | -- | -- | -- |
| | Subject variance in Slopes (THC) | -- | -- | -- | -- | -- | -- | -- |
| | ARH1 rho (slope-intercept covariance) | -- | -- | -- | -- | -- | -- | -- |

Likert Headache

| | | | | | | | | |
|------------------|---------------------------------------|-------|-------|---------|------|--------------|-------|-------|
| Intercept | | 0.120 | 0.048 | 45.24 | 2.5 | 0.017 | 0.023 | 0.217 |
| | OF THC | | | 1012.48 | -1.8 | 0.073 | | |
| | BrAC | | | 997.27 | -1.9 | 0.061 | | |
| | Time | | | 996.05 | -0.1 | 0.901 | | |
| | THC*BrAC | | | 1007.83 | 1.3 | 0.200 | | |
| | Time*THC | | | 1009.41 | 1.7 | 0.094 | | |
| | Time*BrAC | | | 997.05 | 0.5 | 0.606 | | |
| | Time*THC*BrAC | | | 1013.23 | -1.1 | 0.255 | | |
| | Subject Variance in Intercepts (THC) | | | -- | -- | -- | | |
| | Subject variance in Slopes (THC) | | | -- | -- | -- | | |
| | ARH1 rho (slope-intercept covariance) | | | -- | -- | -- | | |

Likert Palpitations

| | | | | | | | | |
|------------------|--------|-------|-------|--------|-----|--------------|-------|-------|
| Intercept | | 0.018 | 0.009 | 440.53 | 2.1 | 0.039 | 0.001 | 0.036 |
| | OF THC | | | 3.33 | 1.1 | 0.342 | | |
| | BrAC | | | 994.30 | 1.5 | 0.135 | | |

| | | | | | | | | |
|-----------------------------|---------------------------------------|--------|-------|---------|------|--------------|--------|--------|
| Time | | -0.003 | 0.001 | 987.49 | -2.1 | 0.035 | -0.006 | 0.000 |
| | THC*BrAC | | | 994.68 | 0.1 | 0.900 | | |
| | Time*THC | | | 990.39 | 0.9 | 0.382 | | |
| | Time*BrAC | | | 994.39 | -1.2 | 0.213 | | |
| | Time*THC*BrAC | | | 994.15 | -0.6 | 0.521 | | |
| | Subject Variance in Intercepts (THC) | | | -- | -- | -- | | |
| | Subject variance in Slopes (THC) | | | -- | -- | -- | | |
| | ARH1 rho (slope-intercept covariance) | | | -- | -- | -- | | |
| <i>Likert Upset Stomach</i> | | | | | | | | |
| Intercept | | 0.050 | 0.023 | 48.34 | 2.2 | 0.033 | 0.004 | 0.095 |
| | OF THC | | | 1011.55 | -1.6 | 0.109 | | |
| | BrAC | | | 997.08 | -0.4 | 0.677 | | |
| Time | | -0.007 | 0.003 | 997.06 | -2.7 | 0.007 | -0.012 | -0.002 |
| | THC*BrAC | | | 1005.32 | 0.7 | 0.456 | | |
| | Time*THC | | | 1008.66 | 1.7 | 0.087 | | |
| | Time*BrAC | | | 996.78 | 0.8 | 0.453 | | |
| | Time*THC*BrAC | | | 1012.68 | -0.9 | 0.361 | | |
| | Subject Variance in Intercepts (THC) | | | -- | -- | -- | | |
| | Subject variance in Slopes (THC) | | | -- | -- | -- | | |
| | ARH1 rho (slope-intercept covariance) | | | -- | -- | -- | | |

Data from 19 occasional-to-moderate cannabis smokers who participated in all dosing sessions. Subjective effects were measured by 100 mm visual-analogue scales (VAS) or 5-point Likert scales (Likert) with choices 0≡“none”, 1≡“slight”, 2≡“mild”, 3≡“moderate”, 4≡“severe” after drinking placebo or active alcohol (calculated to produce approximate peak 0.065% BrAC) and inhaling placebo, 2.9% THC, or 6.7% THC vaporized cannabis (500 mg, Volcano[®] Medic vaporizer).

Linear mixed model results; b is parameter (coefficient) estimate for each factor (negative b indicates the parameter decreases the subjective effect; positive b indicates the parameter increases the overall effect).

Overall equation: [Subjective Effect Result] = Intercept + $b_{\text{OF THC}} \cdot [\text{THC}]_{\text{blood}}$ + $b_{\text{BrAC}} \cdot \text{BrAC}$ + $b_{\text{Time}} \cdot \text{post-dose time}$ + $b_{\text{THC} \cdot \text{BrAC}} \cdot [\text{THC}]_{\text{OF}} \cdot \text{BrAC}$ + $b_{\text{Time} \cdot \text{THC}} \cdot \text{post-dose time} \cdot [\text{THC}]_{\text{OF}}$ + $b_{\text{Time} \cdot \text{BrAC}} \cdot \text{post-dose time} \cdot \text{BrAC}$ + $b_{\text{Time} \cdot \text{THC} \cdot \text{BrAC}} \cdot \text{post-dose time} \cdot [\text{THC}]_{\text{OF}} \cdot \text{BrAC}$

^aValues in **bold** are statistically significant (p<0.05); only significant predictors are considered in the final model.

Abbreviations: SE, standard error; df, degrees of freedom; VAS, visual-analogue scale; THC, Δ^9 -tetrahydrocannabinol; BrAC, breath alcohol concentration.

Supplemental Table 4. Median [range] (N) oral fluid (OF)/blood and OF/plasma Δ^9 -tetrahydrocannabinol (THC), 11-nor-9-carboxy-THC (THCCOOH), cannabidiol (CBD) and cannabiniol (CBN) ratios by time point after controlled vaporized cannabis and low-dose oral alcohol to healthy adult occasional-to-moderate cannabis smokers.

| Time Post-Dose (h) | No Alcohol | | | Alcohol | | |
|--------------------|------------------------|-------------------------|------------------------|------------------------|------------------------|------------------------|
| | Placebo | Low 2.9% THC | High 6.7% THC | Placebo | Low 2.9% THC | High 6.7% THC |
| OF/Blood THC | | | | | | |
| -0.8 | 4.0 [0.5-8.2] (5) | 4.9 [3.3-7.1] (3) | 1.6 [1.1-2.2] (2) | 2.2 [0.8-9.0] (3) | 5.2 [1.3-6.4] (4) | 2.6 [2.0-8.3] (3) |
| 0.17 | 2.9 [0.4-10.0] (17) | 19.6 [0.8-840] (19) | 27.1 [1.6-887] (19) | 2.9 [1.4-30.7] (9) | 23.0 [1.9-256] (19) | 16.5 [0.7-723] (19) |
| 1.4 | 1.7 [0.8-7.9] (6) | 15.4 [0.9-225] (18) | 27.8 [1.7-227] (18) | 1.8 [1.2-36.4] (5) | 20.8 [1.5-417] (19) | 26.7 [1.3-444] (19) |
| 2.3 | 1.6 [0.7-8.9] (6) | 18.9 [0.8-133] (17) | 21.5 [0.8-253] (15) | 2.0 [1.8-4.4] (3) | 16.4 [4.0-214] (16) | 24.2 [1.0-452] (16) |
| 3.3 | 1.7 [1.5-2.7] (4) | 15.7 [2.3-110] (12) | 9.6 [0.9-174] (15) | 1.5 [1.3-4.6] (4) | 11.9 [2.8-168] (14) | 33.5 [3.2-203] (13) |
| 6.3 | 0.8 [0.3-1.7] (5) | 3.7 [0.7-15.3] (8) | 7.1 [1.1-15.7] (7) | 1.2 [0.3-1.4] (3) | 4.9 [0.9-31.1] (7) | 8.5 [2.1-55.9] (9) |
| 8.3 | 0.5 [0.3-1.8] (3) | 1.6 [0.7-49.4] (8) | 1.8 [1.3-10.1] (5) | 0.9 [0.3-2.0] (4) | 3.7 [1.2-29.9] (5) | 5.3 [0.8-28.5] (7) |
| OF/Plasma THC | | | | | | |
| -0.8 | 5.1 [0.6-8.2] (6) | 5.9 [3.1-13.2] (5) | 1.4 [1.0-8.4] (4) | 2.5 [0.6-7.7] (5) | 2.5 [0.7-5.5] (5) | 4.8 [1.9-20.1] (4) |
| 0.17 | 1.9 [0.3-7.5] (18) | 15.5 [0.5-505] (19) | 21.0 [1.0-585] (19) | 2.8 [0.4-22.2] (11) | 14.8 [1.5-156] (19) | 11.5 [0.4-463] (19) |
| 1.4 | 1.9 [1.1-6.8] (5) | 11.3 [0.6-159] (18) | 17.6 [1.4-166] (18) | 2.0 [1.1-32.5] (5) | 16.2 [0.9-359] (19) | 18.6 [0.9-319] (19) |
| 2.3 | 1.8 [1.4-6.0] (5) | 13.0 [0.5-90.1] (17) | 15.0 [0.5-144] (16) | 1.5 [1.2-4.9] (5) | 12.5 [2.3-186] (17) | 20.7 [0.8-315] (18) |
| 3.3 | 1.6 [1.3-4.3] (5) | 7.7 [1.2-80.5] (13) | 8.7 [0.7-139] (15) | 1.3 [0.9-1.4] (3) | 9.8 [2.1-188] (17) | 19.7 [0.5-129] (16) |
| 6.3 | 0.9 [0.3-1.2] (6) | 1.8 [0.5-15.3] (7) | 4.3 [0.8-62.2] (11) | 1.2 [0.2-1.3] (4) | 4.6 [0.5-35.0] (10) | 5.7 [0.6-47.7] (10) |
| 8.3 | 0.5 [0.2-1.5] (5) | 1.5 [0.4-33.7] (9) | 4.0 [0.9-46.3] (7) | 0.5 [0.2-0.8] (4) | 2.6 [0.4-21.8] (8) | 4.6 [1.0-20.6] (9) |
| OF/Blood THCCOOH | | | | | | |
| -0.8 | 4.0 [1.5-10.5] (8) | 3.0 [2.5-7.7] (7) | 3.8 [1.2-7.7] (7) | 3.9 [2.1-8.0] (6) | 4.0 [1.8-12.1] (6) | 3.7 [1.9-8.8] (7) |
| 0.17 | 2.5 [1.2-7.9] (6) | 3.2 [2.8-4.2] (7) | 2.8 [0.7-3.8] (8) | 3.8 [2.0-7.0] (7) | 3.6 [1.3-12.5] (8) | 2.9 [0.6-11.6] (9) |
| 1.4 | 3.4 [1.2-9.0] (7) | 2.6 [1.9-9.7] (8) | 3.0 [1.2-8.7] (9) | 4.9 [2.2-8.9] (9) | 4.6 [2.1-17.0] (12) | 4.8 [1.9-20.9] (11) |
| 2.3 | 4.8 [1.4-7.2] (6) | 3.4 [1.8-7.9] (9) | 3.5 [2.4-11.1] (8) | 6.2 [3.2-10.1] (7) | 4.7 [2.6-13.6] (11) | 4.5 [2.2-17.9] (12) |
| 3.3 | 3.1 [1.3-5.7] (6) | 3.2 [2.1-5.6] (10) | 2.8 [1.3-7.2] (10) | 4.7 [2.1-5.8] (7) | 4.3 [2.4-14.3] (10) | 4.4 [1.3-19.6] (9) |
| 6.3 | 3.8 [2.1-5.9] (6) | 4.3 [1.7-11.5] (9) | 3.2 [1.9-5.3] (9) | 4.3 [3.0-13.4] (7) | 4.5 [1.5-12.3] (11) | 3.5 [2.7-9.7] (8) |
| 8.3 | 3.7 [2.8-11.7] (4) | 4.7 [2.0-5.8] (8) | 3.1 [1.5-6.3] (8) | 4.0 [2.1-8.1] (6) | 5.0 [1.5-9.8] (8) | 2.9 [2.2-6.1] (8) |
| OF/Plasma THCCOOH | | | | | | |
| -0.8 | 2.7 [1.0-6.3] | 1.7 [1.2-4.7] | 2.0 [0.7-3.6] | 2.7 [1.5-5.0] | 2.7 [1.1-6.8] | 2.3 [1.7-5.1] |

| | | | | | | |
|---------------|---------------|----------------|-----------------|---------------|----------------|------------------|
| | (8) | (7) | (7) | (7) | (6) | (7) |
| 0.17 | 1.6 [1.0-4.5] | 2.1 [1.7-2.8] | 1.9 [0.5-2.6] | 2.6 [1.6-4.8] | 2.1 [0.8-7.1] | 1.8 [0.4-7.6] |
| | (6) | (7) | (8) | (7) | (8) | (9) |
| 1.4 | 2.7 [0.9-5.7] | 1.8 [1.3-6.6] | 1.9 [0.8-4.3] | 3.2 [1.4-5.9] | 3.2 [1.1-10.6] | 3.5 [1.1-13.3] |
| | (7) | (8) | (9) | (9) | (12) | (11) |
| 2.3 | 3.3 [1.1-4.6] | 2.3 [1.1-4.6] | 2.8 [1.4-5.5] | 3.9 [2.0-7.0] | 3.1 [1.8-8.8] | 3.0 [1.2-11.1] |
| | (6) | (9) | (8) | (7) | (11) | (12) |
| 3.3 | 2.0 [1.0-3.6] | 2.0 [0.9-4.0] | 2.0 [0.7-3.4] | 3.2 [1.2-4.8] | 3.0 [1.6-7.9] | 2.5 [0.8-12.4] |
| | (6) | (10) | (10) | (7) | (10) | (9) |
| 6.3 | 2.5 [1.4-4.0] | 3.5 [1.1-8.3] | 2.0 [1.0-3.4] | 2.8 [2.0-9.3] | 2.8 [1.0-8.8] | 2.4 [1.9-6.4] |
| | (6) | (9) | (9) | (7) | (11) | (8) |
| 8.3 | 2.3 [1.9-7.0] | 3.2 [1.3-3.7] | 1.9 [0.8-4.0] | 2.7 [1.6-5.1] | 3.3 [1.0-5.8] | 2.0 [1.4-3.8] |
| | (5) | (8) | (8) | (6) | (8) | (8) |
| OF/Blood CBD | | | | | | |
| -0.8 | -- | -- | -- | -- | -- | -- |
| 0.17 | | | 45.2 [2.5-183] | | | 32.8 [10.6-1607] |
| | | | (10) | | | (13) |
| 1.4 | -- | -- | -- | -- | -- | -- |
| 2.3 | -- | -- | -- | -- | -- | -- |
| 3.3 | -- | -- | -- | -- | -- | -- |
| 6.3 | -- | -- | -- | -- | -- | -- |
| 8.3 | -- | -- | -- | -- | -- | -- |
| OF/Plasma CBD | | | | | | |
| -0.8 | -- | -- | -- | -- | -- | -- |
| 0.17 | | | 56.5 [2.2-1015] | | | 25.6 [8.6-1060] |
| | | | (12) | | | (16) |
| 1.4 | -- | -- | -- | -- | -- | -- |
| 2.3 | -- | -- | -- | -- | -- | -- |
| 3.3 | -- | -- | -- | -- | -- | -- |
| 6.3 | -- | -- | -- | -- | -- | -- |
| 8.3 | -- | -- | -- | -- | -- | -- |
| OF/Blood CBN | | | | | | |
| -0.8 | -- | -- | -- | -- | -- | -- |
| 0.17 | 1.5 | 20.7 [1.0-173] | 36.7 [2.0-120] | 38.9 | 29.0 [1.4-192] | 28.2 [5.1-947] |
| | (1) | (11) | (9) | (1) | (16) | (14) |
| 1.4 | -- | -- | -- | -- | -- | -- |
| 2.3 | -- | -- | -- | -- | -- | -- |
| 3.3 | -- | -- | -- | -- | -- | -- |
| 6.3 | -- | -- | -- | -- | -- | -- |
| 8.3 | -- | -- | -- | -- | -- | -- |
| OF/Plasma CBN | | | | | | |
| -0.8 | -- | -- | -- | -- | -- | -- |
| 0.17 | 1.3 | 10.3 [0.8-640] | 60.5 [1.7-118] | 43.5 | 29.8 [1.7-166] | 20.2 [5.3-828] |
| | (1) | (14) | (10) | (1) | (15) | (15) |
| 1.4 | -- | -- | -- | -- | -- | -- |
| 2.3 | -- | -- | -- | -- | -- | -- |
| 3.3 | -- | -- | -- | -- | -- | -- |
| 6.3 | -- | -- | -- | -- | -- | -- |
| 8.3 | -- | -- | -- | -- | -- | -- |

Alcohol administration: oral placebo or active alcohol (calculated to produce approximate peak 0.065% BrAC).

Cannabis administration: inhaled placebo, 2.9% THC, or 6.7% THC vaporized cannabis (500 mg, Volcano[®] Medic vaporizer). Data from 19 occasional-to-moderate cannabis smokers who participated in all dosing sessions. N represents number of paired-positive specimens contributing to the result.

Abbreviations: OF, oral fluid; THC, Δ^9 -tetrahydrocannabinol; THCCOOH, 11-nor-9-carboxy-THC; CBD, cannabidiol; CBN, cannabinol.

Supplemental Table 5. (To accompany Figure 3): Regression equations and slope comparisons for (A) oral fluid (OF) Δ^9 -tetrahydrocannabinol (THC) versus blood THC concentration, and (B) OF versus plasma THC concentration after low (2.9% THC) and high (6.7% THC) dose vaporized cannabis administration with and without oral alcohol to 19 healthy, adult occasional-to-moderate cannabis smokers.

A) OF versus Blood THC Figure 3A Regression Equations

| | Low (2.9% THC) | High (6.7% THC) | $p_{\text{high-low}}$ (slopes) |
|--|--|--|---------------------------------------|
| No Alcohol | $y = 34.12x + 104.5$ $R^2 = 0.075, N = 130$ | $y = 43.40x + 85.52$ $R^2 = 0.184, N = 130$ | 0.5123 |
| Alcohol | $y = 34.60x + 40.58$ $R^2 = 0.324, N = 131$ | $y = 80.65x + 210.3$ $R^2 = 0.153, N = 131$ | 0.0866 |
| $p_{\text{alcohol-no alcohol}}$ (slopes) | 0.9646 | 0.0745 | Overall p (slopes, all doses): 0.0171 |

B) OF versus Plasma THC Figure 3B Regression Equations

| | Low (2.9% THC) | High (6.7% THC) | $p_{\text{high-low}}$ (slopes) |
|--|--|--|---------------------------------------|
| No Alcohol | $y = 25.20x + 91.54$ $R^2 = 0.087, N = 130$ | $y = 28.98x + 92.24$ $R^2 = 0.192, N = 130$ | 0.6925 |
| Alcohol | $y = 24.76x + 35.60$ $R^2 = 0.333, N = 131$ | $y = 50.41x + 282.3$ $R^2 = 0.141, N = 131$ | 0.1725 |
| $p_{\text{alcohol-no alcohol}}$ (slopes) | 0.9534 | 0.1183 | Overall p (slopes, all doses): 0.0668 |

N represents number of specimen pairs.