

# Supplementary Note 6: Detailed statistical document of article figures (v 174)

Atanu Giri

October 11, 2023

## Contents

<b>1</b>	<b>Figure 2</b>	<b>3</b>
1.1	Figure 2a: Control Approach rate (FvM)	3
1.2	Figure 2b: Control Effect of cost on Approach rate (FvM)	3
1.3	Figure 2c: Bayesian analysis of cost	4
1.4	Figure 2d: Control Distance traveled (FvM)	4
1.5	Figure 2e: Control Number of high sp. runs (FvM)	4
1.6	Figure 2f: Control Approach time (FvM)	5
1.7	Figure 2g: Control Prop. of trial out. all reward zones (FvM)	5
1.8	Figure 2h: Control Number of stopping points (FvM)	6
<b>2</b>	<b>Figure 3</b>	<b>6</b>
2.1	Figure 3e: $Ca^{2+}$ activity vs utility	6
2.2	Figure 3f: $Ca^{2+}$ activity at low cost	6
2.3	Figure 3g: $Ca^{2+}$ activity at high cost	7
2.4	Figure 3h: $Ca^{2+}$ activity low cost vs high cost	7
<b>3</b>	<b>Figure 5</b>	<b>7</b>
3.1	Figure 5a: FD vs Control Approach rate	7
3.2	Figure 5b: FD Approach rate at low cost	7
3.3	Figure 5b: FD Approach rate at high cost	8
3.4	Figure 5c: Approach time (FD vs Control)	8
3.5	Figure 5d: Prop. of trial out. all reward zones (FD vs Control)	8
3.6	Figure 5e: Number of stopping points (FD vs Control)	9
3.7	Figure 5f: Number of high sp. runs (FD vs Control)	9
3.8	Figure 5g: Distance traveled (FD vs Control)	9
<b>4</b>	<b>Figure 6</b>	<b>10</b>
4.1	Figure 6a. Approach rate (Control vs Self admin. Oxy)	10
4.2	Figure 6b. Distance traveled (Control vs Self admin. Oxy)	10
4.3	Figure 6c. Number of high speed runs (Control vs Self admin. Oxy)	10
4.4	Figure 6d. Approach time (Control vs Self admin. Oxy)	10
4.5	Figure 6e. Proportion of trials outside all reward zone (Control vs Self admin. Oxy)	10
4.6	Figure 6f. Number of stopping points (Control vs Self admin. Oxy)	10
4.7	Figure 6g. Approach rate (Control vs Abstinence)	10
4.8	Figure 6h. Distance traveled (Control vs Abstinence)	10
4.9	Figure 6i. Number of high speed runs (Control vs Abstinence)	10
4.10	Figure 6j. Approach time (Control vs Abstinence)	11
4.11	Figure 6k. Proportion of trials outside all reward zone (Control vs Abstinence)	11
4.12	Figure 6l. Number of stopping points (Control vs Abstinence)	11
4.13	Figure 6m: Self admin oxycodone Approach rate (FvM)	11
4.14	Figure 6n: Self admin oxycodone Distance traveled (FvM)	12
4.15	Figure 6o: Self admin oxycodone Number of high sp. runs	14

4.16	Figure 6p: Abstinence Approach rate (FvM)	16
4.17	Figure 6q: Abstinence Distance traveled (FvM)	17
4.18	Figure 6r: Abstinence Number of high sp. runs	19
4.19	Figure 6s: Fraction of Sigmoid (Control vs Self admin vs Abstinence)	20
<b>5</b>	<b>Supplemental Figure 1</b>	<b>20</b>
5.1	Figure S.1l: Average time to learn task (FvM)	20
<b>6</b>	<b>Supplemental Figure 2</b>	<b>20</b>
6.1	Figure S.2i: Control Distance traveled, approach only (FvM)	20
6.2	Figure S.2j: Control Number of stopping points, approach only (FvM)	21
6.3	Figure S.2k: Control Number of high sp. runs, approach only (FvM)	21
6.4	Figure S.2l: Control Prop. of trial out. all reward zones, approach only (FvM)	22
6.5	Figure S.2m: Control Number of high sp. runs, reject only (FvM)	22
6.6	Figure S.2n: Control Distance traveled, reject only (FvM)	23
6.7	Figure S.2o: Control Number of stopping points, reject only (FvM)	23
6.8	Figure S.2p: Control Prop. of trial out. all reward zones, reject only (FvM)	24
<b>7</b>	<b>Supplemental Figure 4</b>	<b>24</b>
7.1	Figure S.4d: Shape comparison of psychometric function	24
<b>8</b>	<b>Supplemental Figure 5</b>	<b>24</b>
8.1	Figure S.5a: Control vs FD Distance traveled, approach only	24
8.2	Figure S.5b: Control vs FD Number of stopping points, approach only	24
8.3	Figure S.5c: Control vs FD Number of high speed runs, approach only	25
8.4	Figure S.5d: Control vs FD Proportion of trials outside all reward zone, approach only	25
8.5	Figure S.5e: Control vs FD Distance traveled, reject only	25
8.6	Figure S.5f: Control vs FD Number of stopping points, reject only	25
8.7	Figure S.5g: Control vs FD Number of high speed runs, reject only	25
8.8	Figure S.5h: Control vs FD Proportion of trials outside all reward zone, reject only	25
8.9	Figure S.5i: FD Approach rate (FvM)	25
8.10	Figure S.5j: FD Distance traveled (FvM)	26
8.11	Figure S.5k: FD Number of stopping points (FvM)	28
8.12	Figure S.5l: FD Number of high sp. runs (FvM)	30
8.13	Figure S.5m: FD Prop. of trial out. all reward zones (FvM)	31
8.14	Figure S.5p(left): Distance cluster vs Individual probabilities	33
8.15	Figure S.5p(left): Stop cluster vs Individual probabilities	33
<b>9</b>	<b>Supplemental Figure 6</b>	<b>33</b>
9.1	Figure S.6a: Self admin oxycodone Approach time (FvM)	33
9.2	Figure S.6b: Self admin oxycodone Prop. of trial out. all reward zones (FvM)	34
9.3	Figure S.6c: Self admin oxycodone Number of stopping points (FvM)	36
9.4	Figure S.6d: Abstinence Approach time (FvM)	38
9.5	Figure S.6e: Abstinence Prop. of trial out. all reward zones (FvM)	39
9.6	Figure S.6f: Abstinence Number of stopping points (FvM)	41
9.7	Figure S.6h: Oxycodone I.V. vs Fraction of sigmoid	42
<b>10</b>	<b>Supplemental Figure 7</b>	<b>42</b>
10.1	Figure S.7b: Initial task Approach rate (FvM)	42
10.2	Figure S.7c: Late task Approach rate (FvM)	44
10.3	Figure S.7d: Initial task Approach time (FvM)	45
10.4	Figure S.7e: Late task Approach time (FvM)	47
10.5	Figure S.7f: Initial task Number of high sp. runs (FvM)	48
10.6	Figure S.7g: Late task Number of high sp. runs (FvM)	50
10.7	Figure S.7h: Initial task Distance traveled (FvM)	51
10.8	Figure S.7i: Late task Distance traveled (FvM)	53
10.9	Figure S.7j: Fraction of sigmoid (Control vs Alcohol)	54
10.10	Figure S.7n: Euclidean distance vs Probability	55

A repeated measures analysis of variance (ANOVA) was conducted using the MATLAB `ranova` function to examine the effects of within-subject factors, such as sucrose concentration, and between-subject factors, including gender and experimental conditions (control vs food deprivation). Additionally, pairwise comparisons were conducted to further explore the differences between groups using a post-hoc analysis, specifically the Tukey's honestly significant difference method, implemented with the MATLAB `multcompare` function. To assess the between-subject differences, a two-sample Kolmogorov-Smirnov test was also employed with the MATLAB `kstest2` function.

3-way ANOVA is used investigate main effects of each of the three factors (e.g., sucrose concentration, gender, treatment groups) and any potential interactions between them. This means examining whether each factor individually has a significant effect on the dependent variable and whether there are combined effects due to interactions between the factors.

## 1 Figure 2

### 1.1 Figure 2a: Control Approach rate (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 12, Male N = 11).

Effect of concentration: d.f. = 3,  $F = 118.5268$ ,  $p = 7.3397\text{e-}26$ .

Effect of gender: d.f. = 1,  $F = 3.8265$ ,  $p = 0.0639$ .

`kstest2` results:  $h=0$ ,  $p=8.2894\text{e-}02$ ,  $ks2stat=0.2557$  (overall gender difference)

Post-hoc analysis:

$$0.5\% : p = 0.5994, \quad 2\% : p = 0.0203, \quad 5\% : p = 0.1014, \quad 9\% : p = 0.5338.$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 :  $h = 0$ ,  $p = 0.3032$ ,  $ks2stat = 0.3788$*

*RStest : Conc1 :  $h = 0$ ,  $p = 0.4049$*

*KStest2 : Conc2 :  $h = 1$ ,  $p = 0.0087$ ,  $ks2stat = 0.6439$*

*RStest : Conc2 :  $h = 1$ ,  $p = 0.0187$*

*KStest2 : Conc3 :  $h = 0$ ,  $p = 0.2812$ ,  $ks2stat = 0.3864$*

*RStest : Conc3 :  $h = 0$ ,  $p = 0.1314$*

*KStest2 : Conc4 :  $h = 0$ ,  $p = 0.9465$ ,  $ks2stat = 0.2045$*

*RStest : Conc4 :  $h = 0$ ,  $p = 0.5156$*

### 1.2 Figure 2b: Control Effect of cost on Approach rate (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 12, Male N = 11).

p-value for concentration:  $2.061\text{e-}10$ .

p-value for gender:  $0.15301$ .

`kstest2` results:  $h=0$ ,  $p=9.9819\text{e-}02$ ,  $ks2stat=0.2481$  (overall gender difference)

Post-hoc analysis:

$$240lux : 1.8263\text{e} - 01, \quad 260lux : 5.1534\text{e} - 02, \quad 290lux : 8.8968\text{e} - 01, \quad 320lux : 3.7194\text{e} - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.5833, ks2stat = 0.3030$   
 $RStest : Conc1 : h = 0, p = 0.2815$   
 $KStest2 : Conc2 : h = 0, p = 0.2407, ks2stat = 0.4015$   
 $RStest : Conc2 : h = 0, p = 0.0602$   
 $KStest2 : Conc3 : h = 0, p = 0.6484, ks2stat = 0.2879$   
 $RStest : Conc3 : h = 0, p = 1.0000$   
 $KStest2 : Conc4 : h = 0, p = 0.7136, ks2stat = 0.2727$   
 $RStest : Conc4 : h = 0, p = 0.4235$

### 1.3 Figure 2c: Bayesian analysis of cost

Statistical significance was determined using **Statistical Package for the Social Sciences (SPSS)** package (F = 12, M = 9)

p-value for concentration: <0.0001.

Sex differences across all concentrations  $p = 0.8$ .

Post-hoc analysis:

$15Lux\% : p = 0.000627,$   $240Lux\% : p = 0.0000893,$   $260Lux\% : p = 0.0000658,$   
 $290Lux\% : p = 0.2045,$   $320Lux\% : p = 0.405.$

### 1.4 Figure 2d: Control Distance traveled (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 12, Male N = 11).

Effect of concentration: d.f. = 3, F = 2.2699,  $p = 8.9008e-02$ .

Effect of gender: d.f. = 1, F = 11.8146,  $p = 0.0025$ .

kstest2 results:  $h=1, p=9.4199e-06, ks2stat=0.5019$  (overall gender difference)

Post-hoc analysis:

$0.5\% : 1.2707e - 03,$   $2\% : 1.1033e - 02,$   $5\% : 3.5299e - 03,$   $9\% : 8.9459e - 03$

KStest2 and wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 1, p = 0.0258, ks2stat = 0.5758$   
 $RStest : Conc1 : h = 1, p = 0.0051, zval = 2.8003$   
 $KStest2 : Conc2 : h = 1, p = 0.0361, ks2stat = 0.5530$   
 $RStest : Conc2 : h = 1, p = 0.0151, zval = 2.4311$   
 $KStest2 : Conc3 : h = 1, p = 0.0230, ks2stat = 0.5833$   
 $RStest : Conc3 : h = 1, p = 0.0051, zval = 2.8003$   
 $KStest2 : Conc4 : h = 1, p = 0.0361, ks2stat = 0.5530$   
 $RStest : Conc4 : h = 1, p = 0.0062, zval = 2.7388$

### 1.5 Figure 2e: Control Number of high sp. runs (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 12, Male N = 11).

Effect of concentration: d.f. = 3, F = 23.4392,  $p = 2.6239e-10$ .

Effect of gender: d.f. = 1, F = 12.8352,  $p = 0.0018$ .

kstest2 results:  $h=1, p=3.0470e-05, ks2stat=0.4773$  (overall gender difference)

Post-hoc analysis:

$$0.5\% : 1.6629e - 04, \quad 2\% : 2.5835e - 03, \quad 5\% : 5.1037e - 03, \quad 9\% : 6.0776e - 02$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$\begin{aligned} KStest2 : Conc1 : h = 1, p = 0.0003, ks2stat = 0.8258 \\ RStest : Conc1 : h = 1, p = 0.0006, zval = -3.4158 \\ KStest2 : Conc2 : h = 1, p = 0.0059, ks2stat = 0.6667 \\ RStest : Conc2 : h = 1, p = 0.0042, zval = -2.8619 \\ KStest2 : Conc3 : h = 1, p = 0.0323, ks2stat = 0.5606 \\ RStest : Conc3 : h = 1, p = 0.0106, zval = -2.5541 \\ KStest2 : Conc4 : h = 0, p = 0.1213, ks2stat = 0.4621 \\ RStest : Conc4 : h = 0, p = 0.1481, zval = -1.4463 \end{aligned}$$

## 1.6 Figure 2f: Control Approach time (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 12, Male N = 11).

Effect of concentration: d.f. = 3, F = 6.4355, p = 7.8859e-04.

Effect of gender: d.f. = 1, F = 0.6365, p = 0.4348.

kstest2 results: h=0, p=3.1096e-01, ks2stat=0.1986 (overall gender difference)

Post-hoc analysis:

$$0.5\% : 8.9816e - 01, \quad 2\% : 4.5069e - 01, \quad 5\% : 5.3396e - 01, \quad 9\% : 5.9227e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$\begin{aligned} KStest2 : Conc1 : h = 0, p = 0.7358, ks2stat = 0.2727 \\ RStest : Conc1 : h = 0, p = 0.6458, zval = -0.4597 \\ KStest2 : Conc2 : h = 0, p = 0.4896, ks2stat = 0.3333 \\ RStest : Conc2 : h = 0, p = 0.6682, zval = -0.4286 \\ KStest2 : Conc3 : h = 0, p = 0.8286, ks2stat = 0.2500 \\ RStest : Conc3 : h = 0, p = 0.7169, zval = -0.3627 \\ KStest2 : Conc4 : h = 0, p = 0.7136, ks2stat = 0.2727 \\ RStest : Conc4 : h = 0, p = 0.7350, zval = -0.3385 \end{aligned}$$

## 1.7 Figure 2g: Control Prop. of trial out. all reward zones (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 12, Male N = 11).

Effect of concentration: d.f. = 3, F = 14.3852, p = 3.0392e-07.

Effect of gender: d.f. = 1, F = 1.5082, p = 0.2330.

kstest2 results: h=0, p=3.3508e-01, ks2stat=0.1913 (overall gender difference)

Post-hoc analysis:

$$0.5\% : 2.6980e - 01, \quad 2\% : 7.5679e - 01, \quad 5\% : 8.5789e - 02, \quad 9\% : 3.0110e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.8067, ks2stat = 0.2500$   
 $RStest : Conc1 : h = 0, p = 0.4044, zval = 0.8338$   
 $KStest2 : Conc2 : h = 0, p = 0.9982, ks2stat = 0.1515$   
 $RStest : Conc2 : h = 0, p = 0.8292, zval = 0.2157$   
 $KStest2 : Conc3 : h = 0, p = 0.1006, ks2stat = 0.4773$   
 $RStest : Conc3 : h = 1, p = 0.0483, zval = 1.9743$   
 $KStest2 : Conc4 : h = 0, p = 0.4595, ks2stat = 0.3333$   
 $RStest : Conc4 : h = 0, p = 0.4219, zval = 0.8031$

## 1.8 Figure 2h: Control Number of stopping points (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 12, Male N = 11).

Effect of concentration: d.f. = 3, F = 0.0544, p = 9.8312e-01.

Effect of gender: d.f. = 1, F = 2.1682, p = 0.1557.

kstest2 results: h=1, p=2.5533e-05, ks2stat=0.4811 (overall gender difference)

Post-hoc analysis:

0.5% :  $7.9690e - 02$ , 2% :  $2.5673e - 01$ , 5% :  $1.4691e - 01$ , 9% :  $2.0322e - 01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 1, p = 0.0067, ks2stat = 0.6591$   
 $RStest : Conc1 : h = 1, p = 0.0028, zval = -2.9850$   
 $KStest2 : Conc2 : h = 0, p = 0.2604, ks2stat = 0.3939$   
 $RStest : Conc2 : h = 0, p = 0.1029, zval = -1.6310$   
 $KStest2 : Conc3 : h = 1, p = 0.0323, ks2stat = 0.5606$   
 $RStest : Conc3 : h = 1, p = 0.0289, zval = -2.1849$   
 $KStest2 : Conc4 : h = 0, p = 0.0915, ks2stat = 0.4848$   
 $RStest : Conc4 : h = 0, p = 0.0905, zval = -1.6925$

## 2 Figure 3

### 2.1 Figure 3e: $Ca^{2+}$ activity vs utility

Statistical significance was determined by one-way analysis of variance. (group 1 = 60, group 2 = 61, group 3 = 58, group 4 = 64, group 5 = 22, group 6 = 22, group 7 = 25, group 8 = 18)

p-value for significance of difference between the groups (utility): 0.0429.

Post-hoc analysis by Tukey's HSD method:

No group difference is statistically significant.

### 2.2 Figure 3f: $Ca^{2+}$ activity at low cost

Statistical significance was determined by one-way analysis of variance. (group 1 = 60, group 2 = 61, group 3 = 58, group 4 = 64)

p-value for significance of difference between the groups (concentration): 0.9599.

Post-hoc analysis by Tukey's HSD method:

No group difference is statistically significant.

### 2.3 Figure 3g: $Ca^{2+}$ activity at high cost

Statistical significance was determined by one-way analysis of variance. (group 1 = 22, group 2 = 22, group 3 = 25, group 4 = 18)  
p-value for significance of difference between the groups (concentration): 0.5523.

Post-hoc analysis by Tukey's HSD method:

No group difference is statistically significant.

### 2.4 Figure 3h: $Ca^{2+}$ activity low cost vs high cost

Statistical significance was determined by one-way analysis of variance. (group 1 = 243, group 2 = 87)  
p-value for significance of difference between the groups (concentration): 0.0012.

## 3 Figure 5

### 3.1 Figure 5a: FD vs Control Approach rate

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 22, FD N = 22).  
Effect of concentration: d.f. = 3, F = 281.8850, p = 1.0842e-55.  
Effect of Condition: d.f. = 1, F = 19.0789, p = 0.0001. kstest2 results: h=1, p=1.0816e-02, ks2stat=0.2386 (overall difference in Control vs FD)

Post-hoc analysis:

$$0.5\% : 6.8154e - 01, \quad 2\% : 5.2118e - 01, \quad 5\% : 5.0500e - 04, \quad 9\% : 4.8848e - 03$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$KStest2 : Conc1 : h = 0, p = 0.1746, ks2stat = 0.3182$$

$$RStest : Conc1 : h = 0, p = 0.3038, zval = 1.0283$$

$$KStest2 : Conc2 : h = 0, p = 0.3320, ks2stat = 0.2727$$

$$RStest : Conc2 : h = 0, p = 0.3820, zval = 0.8743$$

$$KStest2 : Conc3 : h = 1, p = 0.0138, ks2stat = 0.4545$$

$$RStest : Conc3 : h = 1, p = 0.0011, zval = -3.2659$$

$$KStest2 : Conc4 : h = 1, p = 0.0000, ks2stat = 0.6818$$

$$RStest : Conc4 : h = 1, p = 0.0003, zval = -3.6583$$

### 3.2 Figure 5b: FD Approach rate at low cost

Statistical significance was determined using SPSS software package (F = 12, M = 9)  
p-value for gender: p<0.001)  
p-value for acceptance rate: 0.723

### 3.3 Figure 5b: FD Approach rate at high cost

Statistical significance was determined using **SPSS** software package (F = 12, M = 10)  
p-value for gender: 0.873)  
p-value for acceptance rate: 0.018

### 3.4 Figure 5c: Approach time (FD vs Control)

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 22, FD N = 22).

Effect of concentration: d.f. = 3, F = 20.1324, p = 6.3645e-10.

Effect of Condition: d.f. = 1, F = 1.7659, p = 0.1946.

kstest2 results: h=0, p=3.5436e-01, ks2stat=0.1435 (overall difference in Control vs FD)

Post-hoc analysis:

$$0.5\% : 1.0418e - 02, \quad 2\% : 3.2611e - 01, \quad 5\% : 7.3375e - 01, \quad 9\% : 1.0336e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$KStest2 : Conc1 : h = 0, p = 0.0647, ks2stat = 0.4286$$

$$RStest : Conc1 : h = 1, p = 0.0127, zval = -2.4921$$

$$KStest2 : Conc2 : h = 1, p = 0.0395, ks2stat = 0.4286$$

$$RStest : Conc2 : h = 0, p = 0.0883, zval = -1.7044$$

$$KStest2 : Conc3 : h = 0, p = 0.7388, ks2stat = 0.1991$$

$$RStest : Conc3 : h = 0, p = 0.6885, zval = 0.4009$$

$$KStest2 : Conc4 : h = 0, p = 0.3320, ks2stat = 0.2727$$

$$RStest : Conc4 : h = 0, p = 0.1625, zval = 1.3966$$

### 3.5 Figure 5d: Prop. of trial out. all reward zones (FD vs Control)

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 22, FD N = 22).

Effect of concentration: d.f. = 3, F = 51.5773, p = 8.1104e-22.

Effect of Condition: d.f. = 1, F = 2.5126, p = 0.1204.

kstest2 results: h=1, p=1.7572e-02, ks2stat=0.2273 (overall difference in Control vs FD)

Post-hoc analysis:

$$0.5\% : 5.6817e - 03, \quad 2\% : 1.9624e - 02, \quad 5\% : 5.4119e - 01, \quad 9\% : 7.4789e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$KStest2 : Conc1 : h = 1, p = 0.0049, ks2stat = 0.5000$$

$$RStest : Conc1 : h = 1, p = 0.0068, zval = -2.7047$$

$$KStest2 : Conc2 : h = 1, p = 0.0356, ks2stat = 0.4091$$

$$RStest : Conc2 : h = 1, p = 0.0186, zval = -2.3536$$

$$KStest2 : Conc3 : h = 0, p = 0.3320, ks2stat = 0.2727$$

$$RStest : Conc3 : h = 0, p = 0.2485, zval = 1.1541$$

$$KStest2 : Conc4 : h = 0, p = 0.3320, ks2stat = 0.2727$$

$$RStest : Conc4 : h = 0, p = 0.9156, zval = -0.1059$$



### 3.6 Figure 5e: Number of stopping points (FD vs Control)

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 22, FD N = 22).

Effect of concentration: d.f. = 3, F = 1.2986, p = 2.7791e-01.

Effect of Condition: d.f. = 1, F = 4.3492, p = 0.0431.

kstest2 results: h=1, p=7.5537e-08, ks2stat=0.4318 (overall difference in Control vs FD)

Post-hoc analysis:

$$0.5\% : 3.9999e - 02, \quad 2\% : 3.3272e - 02, \quad 5\% : 5.5036e - 02, \quad 9\% : 5.9155e - 02$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$KStest2 : Conc1 : h = 1, p = 0.0001, ks2stat = 0.6364$$

$$RStest : Conc1 : h = 1, p = 0.0003, zval = 3.6265$$

$$KStest2 : Conc2 : h = 1, p = 0.0138, ks2stat = 0.4545$$

$$RStest : Conc2 : h = 1, p = 0.0028, zval = 2.9928$$

$$KStest2 : Conc3 : h = 0, p = 0.0828, ks2stat = 0.3636$$

$$RStest : Conc3 : h = 1, p = 0.0109, zval = 2.5468$$

$$KStest2 : Conc4 : h = 1, p = 0.0138, ks2stat = 0.4545$$

$$RStest : Conc4 : h = 1, p = 0.0032, zval = 2.9458$$

### 3.7 Figure 5f: Number of high sp. runs (FD vs Control)

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 22, FD N = 22).

Effect of concentration: d.f. = 3, F = 45.2054, p = 6.6926e-20.

Effect of Condition: d.f. = 1, F = 5.4125, p = 0.0249.

kstest2 results: h=1, p=1.0816e-02, ks2stat=0.2386 (overall difference in Control vs FD)

Post-hoc analysis:

$$0.5\% : 7.3584e - 04, \quad 2\% : 1.0250e - 01, \quad 5\% : 2.0052e - 01, \quad 9\% : 1.2278e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$KStest2 : Conc1 : h = 1, p = 0.0015, ks2stat = 0.5455$$

$$RStest : Conc1 : h = 1, p = 0.0012, zval = 3.2275$$

$$KStest2 : Conc2 : h = 0, p = 0.0828, ks2stat = 0.3636$$

$$RStest : Conc2 : h = 0, p = 0.0689, zval = 1.8191$$

$$KStest2 : Conc3 : h = 0, p = 0.3320, ks2stat = 0.2727$$

$$RStest : Conc3 : h = 0, p = 0.4455, zval = 0.7629$$

$$KStest2 : Conc4 : h = 0, p = 0.1746, ks2stat = 0.3182$$

$$RStest : Conc4 : h = 0, p = 0.1424, zval = 1.4670$$

### 3.8 Figure 5g: Distance traveled (FD vs Control)

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 22, FD N = 22).

Effect of concentration: d.f. = 3, F = 12.6199, p = 2.8777e-07.

Effect of Condition: d.f. = 1, F = 11.2464, p = 0.0017.

kstest2 results: h=1, p=7.5537e-08, ks2stat=0.4318 (overall difference in Control vs FD)

Post-hoc analysis:

0.5% :  $3.7073e - 04$ , 2% :  $7.5759e - 04$ , 5% :  $3.3233e - 02$ , 9% :  $1.3234e - 02$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 :  $h = 1, p = 0.0015, ks2stat = 0.5455$*

*RStest : Conc1 :  $h = 1, p = 0.0008, zval = -3.3683$*

*KStest2 : Conc2 :  $h = 1, p = 0.0356, ks2stat = 0.4091$*

*RStest : Conc2 :  $h = 1, p = 0.0028, zval = -2.9928$*

*KStest2 : Conc3 :  $h = 1, p = 0.0138, ks2stat = 0.4545$*

*RStest : Conc3 :  $h = 1, p = 0.0151, zval = -2.4294$*

*KStest2 : Conc4 :  $h = 1, p = 0.0356, ks2stat = 0.4091$*

*RStest : Conc4 :  $h = 1, p = 0.0151, zval = -2.4294$*

## 4 Figure 6

### 4.1 Figure 6a. Approach rate (Control vs Self admin. Oxy)

Effect of condition: d.f. = 1,  $F = 2.7873$ ,  $p = 0.1051$

kstest2 results:  $h=1$ ,  $p=0.0049$ ,  $ks2stat=0.3196$

### 4.2 Figure 6b. Distance traveled (Control vs Self admin. Oxy)

Effect of condition: d.f. = 1,  $F = 0.0121$ ,  $p = 0.9132$ .

### 4.3 Figure 6c. Number of high speed runs (Control vs Self admin. Oxy)

Effect of condition: d.f. = 1,  $F = 0.0015$ ,  $p = 0.9698$ .

### 4.4 Figure 6d. Approach time (Control vs Self admin. Oxy)

Effect of condition: d.f. = 1,  $F = 1.3040$ ,  $p = 0.2628$ .

### 4.5 Figure 6e. Proportion of trials outside all reward zone (Control vs Self admin. Oxy)

Effect of condition: d.f. = 1,  $F = 0.1051$ ,  $p = 0.7480$ .

### 4.6 Figure 6f. Number of stopping points (Control vs Self admin. Oxy)

Effect of condition: d.f. = 1,  $F = 0.5075$ ,  $p = 0.4816$ .

### 4.7 Figure 6g. Approach rate (Control vs Abstinence)

Effect of condition: d.f. = 1,  $F = 6.1129$ ,  $p = 0.0187$ .

kstest2 results:  $h=1$ ,  $p=0.0000$ ,  $ks2stat=0.4257$

### 4.8 Figure 6h. Distance traveled (Control vs Abstinence)

Effect of condition: d.f. = 1,  $F = 4.3279$ ,  $p = 0.0453$ .

### 4.9 Figure 6i. Number of high speed runs (Control vs Abstinence)

Effect of condition: d.f. = 1,  $F = 0.6038$ ,  $p = 0.4427$ .

#### 4.10 Figure 6j. Approach time (Control vs Abstinence)

Effect of condition: d.f. = 1,  $F = 0.1133$ ,  $p = 0.7387$ .

#### 4.11 Figure 6k. Proportion of trials outside all reward zone (Control vs Abstinence)

Effect of condition: d.f. = 1,  $F = 1.0138$ ,  $p = 0.3213$ .

#### 4.12 Figure 6l. Number of stopping points (Control vs Abstinence)

Effect of condition: d.f. = 1,  $F = 1.9581$ ,  $p = 0.1710$ .

#### 4.13 Figure 6m: Self admin oxycodone Approach rate (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female  $N = 5$ , Male  $N = 5$ ).

Effect of concentration: d.f. = 3,  $F = 3.2073$ ,  $p = 4.1083e-02$ .

Effect of gender: d.f. = 1,  $F = 0.0521$ ,  $p = 0.8251$ .

kstest2 results:  $h=0$ ,  $p=7.7095e-01$ ,  $ks2stat=0.2000$  (overall gender difference)

Post-hoc analysis:

$$0.5\% : 8.0968e - 01, \quad 2\% : 2.1173e - 01, \quad 5\% : 4.2256e - 01, \quad 9\% : 2.2622e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$KStest2 : Conc1 : h = 0, p = 0.6974, ks2stat = 0.4000$$

$$RStest : Conc1 : h = 0, p = 0.6429$$

$$KStest2 : Conc2 : h = 0, p = 0.2090, ks2stat = 0.6000$$

$$RStest : Conc2 : h = 0, p = 0.2063$$

$$KStest2 : Conc3 : h = 0, p = 0.6974, ks2stat = 0.4000$$

$$RStest : Conc3 : h = 0, p = 0.6349$$

$$KStest2 : Conc4 : h = 0, p = 0.6974, ks2stat = 0.4000$$

$$RStest : Conc4 : h = 0, p = 0.3016$$

#### Control vs Self admin. Oxy

##### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control  $N = 12$ , Self admin. Oxy  $N = 5$ ).

p-value for Control vs Self admin. Oxy of female: 0.052962.

kstest2 results:  $h=0$ ,  $p=5.1949e-02$ ,  $ks2stat=0.3458$

Post-hoc analysis:

$$0.5\% : 4.0723e - 04, \quad 2\% : 3.0385e - 01, \quad 5\% : 8.8902e - 02, \quad 9\% : 1.2880e - 05$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 1, p = 0.0089, ks2stat = 0.8000$   
 $RStest : Conc1 : h = 1, p = 0.0039$   
 $KStest2 : Conc2 : h = 0, p = 0.5074, ks2stat = 0.4000$   
 $RStest : Conc2 : h = 0, p = 0.7757$   
 $KStest2 : Conc3 : h = 0, p = 0.1545, ks2stat = 0.5500$   
 $RStest : Conc3 : h = 0, p = 0.1296$   
 $KStest2 : Conc4 : h = 1, p = 0.0004, ks2stat = 1.0000$   
 $RStest : Conc4 : h = 1, p = 0.0003$

#### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, Self admin. Oxy N = 5).

p-value for Control vs Self admin. Oxy of male: 0.74837.

kstest2 results: h=0, p=5.2181e-02, ks2stat=0.3500

Post-hoc analysis:

0.5% :  $1.1302e - 02$ , 2% :  $5.2769e - 04$ , 5% :  $3.4051e - 01$ , 9% :  $7.5302e - 05$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 1, p = 0.0313, ks2stat = 0.7091$   
 $RStest : Conc1 : h = 1, p = 0.0124$   
 $KStest2 : Conc2 : h = 1, p = 0.0079, ks2stat = 0.8182$   
 $RStest : Conc2 : h = 1, p = 0.0018$   
 $KStest2 : Conc3 : h = 0, p = 0.2005, ks2stat = 0.5273$   
 $RStest : Conc3 : h = 0, p = 0.3608$   
 $KStest2 : Conc4 : h = 1, p = 0.0005, ks2stat = 1.0000$   
 $RStest : Conc4 : h = 1, p = 0.0005$

#### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	0.0122	1	0	0.0122	0.6013	0.4396
Condition	0.0762	1	0	0.0762	3.7568	0.055
Concentration	3.0662	3	0	1.0221	50.3587	0
Gender*Condition	0.0379	1	0	0.0379	1.8658	0.1745
Gender*Concentration	0.1742	3	0	0.0581	2.8615	0.0398
Condition*Concentration	1.3945	3	0	0.4648	22.9026	0
Error	2.4152	119	0	0.0203	NaN	NaN
Total	9.9283	131	0	NaN	NaN	NaN

KS test for the effect of condition: h = 1, p = 0.0049, KS statistic = 0.3196.

#### 4.14 Figure 6n: Self admin oxycodone Distance traveled (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 5, Male N = 5).

Effect of concentration: d.f. = 3, F = 0.8971, p = 4.5703e-01.

Effect of gender: d.f. = 1, F = 4.6420, p = 0.0633.

kstest2 results: h=1, p=7.2529e-04, ks2stat=0.6000 (overall gender difference)

Post-hoc analysis:

0.5% :  $1.7344e - 01$ , 2% :  $9.6526e - 02$ , 5% :  $5.1225e - 02$ , 9% :  $4.6853e - 02$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 0, p = 0.2090, ks2stat = 0.6000*

*RStest : Conc1 : h = 0, p = 0.2222*

*KStest2 : Conc2 : h = 0, p = 0.2090, ks2stat = 0.6000*

*RStest : Conc2 : h = 0, p = 0.0952*

*KStest2 : Conc3 : h = 1, p = 0.0361, ks2stat = 0.8000*

*RStest : Conc3 : h = 0, p = 0.0556*

*KStest2 : Conc4 : h = 0, p = 0.2090, ks2stat = 0.6000*

*RStest : Conc4 : h = 0, p = 0.0952*

### **Control vs Self admin. Oxy**

#### **Female:**

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, Self admin. Oxy N = 5).

p-value for Control vs Self admin. Oxy of female: 0.044575.

kstest2 results: h=1, p=7.5094e-04, ks2stat=0.5083

Post-hoc analysis:

0.5% :  $9.0352e - 02$ , 2% :  $3.8910e - 02$ , 5% :  $8.9572e - 02$ , 9% :  $3.1966e - 02$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 0, p = 0.3153, ks2stat = 0.4667*

*RStest : Conc1 : h = 0, p = 0.1946*

*KStest2 : Conc2 : h = 0, p = 0.0950, ks2stat = 0.6000*

*RStest : Conc2 : h = 0, p = 0.1037*

*KStest2 : Conc3 : h = 0, p = 0.2086, ks2stat = 0.5167*

*RStest : Conc3 : h = 0, p = 0.0818*

*KStest2 : Conc4 : h = 0, p = 0.0671, ks2stat = 0.6333*

*RStest : Conc4 : h = 1, p = 0.0365*

#### **Male:**

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, Self admin. Oxy N = 5).

p-value for Control vs Self admin. Oxy of male: 0.0032032.

kstest2 results: h=1, p=6.9107e-06, ks2stat=0.6500

Post-hoc analysis:

0.5% :  $5.9931e - 03$ , 2% :  $2.1350e - 02$ , 5% :  $1.3194e - 03$ , 9% :  $9.8642e - 03$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 1, p = 0.0313, ks2stat = 0.7091$   
 $RStest : Conc1 : h = 1, p = 0.0275$   
 $KStest2 : Conc2 : h = 0, p = 0.0703, ks2stat = 0.6364$   
 $RStest : Conc2 : h = 0, p = 0.0517$   
 $KStest2 : Conc3 : h = 1, p = 0.0252, ks2stat = 0.7273$   
 $RStest : Conc3 : h = 1, p = 0.0087$   
 $KStest2 : Conc4 : h = 0, p = 0.0848, ks2stat = 0.6182$   
 $RStest : Conc4 : h = 1, p = 0.0275$

### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	0.0155	1	0	0.0155	0.0742	0.7858
Condition	0.033	1	0	0.033	0.1576	0.6921
Concentration	0.2361	3	0	0.0787	0.376	0.7705
Gender*Condition	10.5047	1	0	10.5047	50.1828	0
Gender*Concentration	0.313	3	0	0.1043	0.4985	0.684
Condition*Concentration	0.1143	3	0	0.0381	0.182	0.9084
Error	24.91	119	0	0.2093	NaN	NaN
Total	37.6947	131	0	NaN	NaN	NaN

#### 4.15 Figure 60: Self admin oxycodone Number of high sp. runs

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 5, Male N = 5).

Effect of concentration: d.f. = 3, F = 0.5993, p = 6.2169e-01.

Effect of gender: d.f. = 1, F = 3.7946, p = 0.0873.

kstest2 results: h=1, p=8.1617e-03, ks2stat=0.5000 (overall gender difference)

Post-hoc analysis:

0.5% :  $1.9249e - 01$ , 2% :  $1.3288e - 01$ , 5% :  $5.9820e - 02$ , 9% :  $5.9578e - 02$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.6974, ks2stat = 0.4000$   
 $RStest : Conc1 : h = 0, p = 0.2222$   
 $KStest2 : Conc2 : h = 0, p = 0.6974, ks2stat = 0.4000$   
 $RStest : Conc2 : h = 0, p = 0.2222$   
 $KStest2 : Conc3 : h = 0, p = 0.2090, ks2stat = 0.6000$   
 $RStest : Conc3 : h = 0, p = 0.0952$   
 $KStest2 : Conc4 : h = 0, p = 0.2090, ks2stat = 0.6000$   
 $RStest : Conc4 : h = 0, p = 0.0952$

#### Control vs Self admin. Oxy

##### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, Self admin. Oxy N = 5).

p-value for Control vs Self admin. Oxy of female: 0.026023.

kstest2 results: h=1, p=1.3666e-02, ks2stat=0.4042

Post-hoc analysis:

0.5% :  $2.8828e - 02$ , 2% :  $2.3955e - 02$ , 5% :  $8.6383e - 02$ , 9% :  $6.4387e - 02$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 0, p = 0.2086, ks2stat = 0.5167*  
*RStest : Conc1 : h = 0, p = 0.1296*  
*KStest2 : Conc2 : h = 0, p = 0.2406, ks2stat = 0.5000*  
*RStest : Conc2 : h = 0, p = 0.0637*  
*KStest2 : Conc3 : h = 0, p = 0.2086, ks2stat = 0.5167*  
*RStest : Conc3 : h = 0, p = 0.2786*  
*KStest2 : Conc4 : h = 0, p = 0.5074, ks2stat = 0.4000*  
*RStest : Conc4 : h = 0, p = 0.3284*

### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, Self admin. Oxy N = 5).

p-value for Control vs Self admin. Oxy of male: 0.0071297.

kstest2 results: h=1, p=1.6397e-05, ks2stat=0.6273

Post-hoc analysis:

0.5% :  $1.6520e - 02$ , 2% :  $1.9696e - 02$ , 5% :  $2.7185e - 03$ , 9% :  $1.8464e - 02$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 1, p = 0.0313, ks2stat = 0.7091*  
*RStest : Conc1 : h = 0, p = 0.0687*  
*KStest2 : Conc2 : h = 0, p = 0.1019, ks2stat = 0.6000*  
*RStest : Conc2 : h = 1, p = 0.0380*  
*KStest2 : Conc3 : h = 1, p = 0.0252, ks2stat = 0.7273*  
*RStest : Conc3 : h = 1, p = 0.0055*  
*KStest2 : Conc4 : h = 0, p = 0.0848, ks2stat = 0.6182*  
*RStest : Conc4 : h = 1, p = 0.0380*

### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	63.1409	1	0	63.1409	3.463	0.0652
Condition	0.0162	1	0	0.0162	0.0009	0.9763
Concentration	100.3972	3	0	33.4657	1.8354	0.1444
Gender*Condition	906.117	1	0	906.117	49.6964	0
Gender*Concentration	26.2414	3	0	8.7471	0.4797	0.697
Condition*Concentration	48.6865	3	0	16.2288	0.8901	0.4485
Error	2169.7317	119	0	18.233	NaN	NaN
Total	3345.3199	131	0	NaN	NaN	NaN

#### 4.16 Figure 6p: Abstinence Approach rate (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 6, Male N = 6).

Effect of concentration: d.f. = 3, F = 19.9665, p = 2.6307e-07.

Effect of gender: d.f. = 1, F = 0.2008, p = 0.6637.

kstest2 results: h=0, p=6.2161e-01, ks2stat=0.2083 (overall gender difference)

Post-hoc analysis:

$$0.5\% : 7.5735e - 01, \quad 2\% : 3.7013e - 01, \quad 5\% : 8.0930e - 01, \quad 9\% : 6.4244e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$KStest2 : Conc1 : h = 0, p = 0.8096, ks2stat = 0.3333$$

$$RStest : Conc1 : h = 0, p = 1.0000$$

$$KStest2 : Conc2 : h = 0, p = 0.3180, ks2stat = 0.5000$$

$$RStest : Conc2 : h = 0, p = 0.3095$$

$$KStest2 : Conc3 : h = 0, p = 0.8096, ks2stat = 0.3333$$

$$RStest : Conc3 : h = 0, p = 0.8182$$

$$KStest2 : Conc4 : h = 0, p = 0.3180, ks2stat = 0.5000$$

$$RStest : Conc4 : h = 0, p = 0.5887$$

##### Control vs Abstinence

###### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, Abstinence N = 6).

p-value for Control vs initial task of female: 0.18211.

kstest2 results: h=1, p=1.5846e-02, ks2stat=0.3750

Post-hoc analysis:

$$0.5\% : 9.8839e - 05, \quad 2\% : 2.3068e - 04, \quad 5\% : 8.7695e - 01, \quad 9\% : 1.7166e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$KStest2 : Conc1 : h = 1, p = 0.0007, ks2stat = 0.9167$$

$$RStest : Conc1 : h = 1, p = 0.0002$$

$$KStest2 : Conc2 : h = 1, p = 0.0028, ks2stat = 0.8333$$

$$RStest : Conc2 : h = 1, p = 0.0018$$

$$KStest2 : Conc3 : h = 0, p = 0.9290, ks2stat = 0.2500$$

$$RStest : Conc3 : h = 0, p = 0.9636$$

$$KStest2 : Conc4 : h = 0, p = 0.1877, ks2stat = 0.5000$$

$$RStest : Conc4 : h = 0, p = 0.4225$$

###### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, Abstinence N = 6).

p-value for Control vs initial task of male: 0.033933.

kstest2 results: h=1, p=8.7249e-04, ks2stat=0.4811

Post-hoc analysis:

$$0.5\% : 4.0393e - 05, \quad 2\% : 6.3068e - 04, \quad 5\% : 3.1164e - 01, \quad 9\% : 5.9881e - 03$$



KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 1, p = 0.0002, ks2stat = 1.0000$   
 $RStest : Conc1 : h = 1, p = 0.0002$   
 $KStest2 : Conc2 : h = 1, p = 0.0033, ks2stat = 0.8333$   
 $RStest : Conc2 : h = 1, p = 0.0031$   
 $KStest2 : Conc3 : h = 0, p = 0.5232, ks2stat = 0.3788$   
 $RStest : Conc3 : h = 0, p = 0.5249$   
 $KStest2 : Conc4 : h = 1, p = 0.0042, ks2stat = 0.8182$   
 $RStest : Conc4 : h = 1, p = 0.0074$

### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	0.0662	1	0	0.0662	3.0165	0.0848
Condition	0.228	1	0	0.228	10.3954	0.0016
Concentration	5.0851	3	0	1.695	77.2692	0
Gender*Condition	0.0045	1	0	0.0045	0.2061	0.6506
Gender*Concentration	0.0954	3	0	0.0318	1.4503	0.2314
Condition*Concentration	0.7475	3	0	0.2492	11.3581	0
Error	2.786	127	0	0.0219	NaN	NaN
Total	11.0015	139	0	NaN	NaN	NaN

KS test for the effect of condition:  $h = 1, p = 0.0000$ , KS statistic = 0.4257.

### 4.17 Figure 6q: Abstinence Distance traveled (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female  $N = 6$ , Male  $N = 6$ ).

Effect of concentration: d.f. = 3,  $F = 16.2563$ ,  $p = 1.8477e-06$ .

Effect of gender: d.f. = 1,  $F = 1.0727$ ,  $p = 0.3247$ .

kstest2 results:  $h=0, p=2.1598e-01, ks2stat=0.2917$  (overall gender difference)

Post-hoc analysis:

0.5% :  $4.5320e - 01$ , 2% :  $4.5178e - 01$ , 5% :  $3.0428e - 01$ , 9% :  $2.1404e - 01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.8096, ks2stat = 0.3333$   
 $RStest : Conc1 : h = 0, p = 0.4848$   
 $KStest2 : Conc2 : h = 0, p = 0.8096, ks2stat = 0.3333$   
 $RStest : Conc2 : h = 0, p = 0.4848$   
 $KStest2 : Conc3 : h = 0, p = 0.0766, ks2stat = 0.6667$   
 $RStest : Conc3 : h = 0, p = 0.3939$   
 $KStest2 : Conc4 : h = 0, p = 0.3180, ks2stat = 0.5000$   
 $RStest : Conc4 : h = 0, p = 0.2403$

**Control vs Abstinence**  
**Female:**

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, Abstinence N = 6).

p-value for Control vs initial task of female: 0.44479.

kstest2 results: h=0, p=1.0713e-01, ks2stat=0.2917

Post-hoc analysis:

0.5% :  $1.4870e - 01$ , 2% :  $2.5012e - 01$ , 5% :  $9.4955e - 01$ , 9% :  $9.9174e - 01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 0, p = 0.6693, ks2stat = 0.3333*

*RStest : Conc1 : h = 0, p = 0.1797*

*KStest2 : Conc2 : h = 0, p = 0.6693, ks2stat = 0.3333*

*RStest : Conc2 : h = 0, p = 0.3355*

*KStest2 : Conc3 : h = 0, p = 0.1877, ks2stat = 0.5000*

*RStest : Conc3 : h = 0, p = 0.4371*

*KStest2 : Conc4 : h = 0, p = 0.9290, ks2stat = 0.2500*

*RStest : Conc4 : h = 0, p = 0.7503*

### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, Abstinence N = 6).

p-value for Control vs initial task of male: 0.0092961.

kstest2 results: h=1, p=1.2593e-04, ks2stat=0.5379

Post-hoc analysis:

0.5% :  $1.2197e - 03$ , 2% :  $1.8008e - 02$ , 5% :  $2.3136e - 02$ , 9% :  $1.0416e - 01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 1, p = 0.0125, ks2stat = 0.7424*

*RStest : Conc1 : h = 1, p = 0.0071*

*KStest2 : Conc2 : h = 0, p = 0.1997, ks2stat = 0.5000*

*RStest : Conc2 : h = 1, p = 0.0365*

*KStest2 : Conc3 : h = 1, p = 0.0480, ks2stat = 0.6364*

*RStest : Conc3 : h = 0, p = 0.0616*

*KStest2 : Conc4 : h = 1, p = 0.0401, ks2stat = 0.6515*

*RStest : Conc4 : h = 0, p = 0.0616*

### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	5.1572	1	0	5.1572	27.9576	0
Condition	3.9704	1	0	3.9704	21.5238	0
Concentration	2.0282	3	0	0.6761	3.665	0.0142
Gender*Condition	1.0897	1	0	1.0897	5.9071	0.0165
Gender*Concentration	0.1722	3	0	0.0574	0.3112	0.8173
Condition*Concentration	1.1314	3	0	0.3771	2.0444	0.111
Error	23.427	127	0	0.1845	NaN	NaN
Total	38.3866	139	0	NaN	NaN	NaN

#### 4.18 Figure 6r: Abstinence Number of high sp. runs

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 6, Male N = 6).

Effect of concentration: d.f. = 3, F = 6.9387, p = 1.1029e-03.

Effect of gender: d.f. = 1, F = 1.0006, p = 0.3408.

kstest2 results: h=0, p=5.0588e-02, ks2stat=0.3750 (overall gender difference)

Post-hoc analysis:

$$0.5\% : 5.1260e - 01, \quad 2\% : 3.1392e - 01, \quad 5\% : 2.5092e - 01, \quad 9\% : 3.6439e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 0, p = 1.0000, ks2stat = 0.1667*

*RStest : Conc1 : h = 0, p = 0.8182*

*KStest2 : Conc2 : h = 0, p = 0.3180, ks2stat = 0.5000*

*RStest : Conc2 : h = 0, p = 0.2403*

*KStest2 : Conc3 : h = 0, p = 0.3180, ks2stat = 0.5000*

*RStest : Conc3 : h = 0, p = 0.1797*

*KStest2 : Conc4 : h = 1, p = 0.0122, ks2stat = 0.8333*

*RStest : Conc4 : h = 1, p = 0.0411*

##### Control vs Abstinence

###### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, Abstinence N = 6).

p-value for Control vs initial task of female: 0.81023.

kstest2 results: h=0, p=1.0713e-01, ks2stat=0.2917

Post-hoc analysis:

$$0.5\% : 7.6146e - 01, \quad 2\% : 3.6133e - 01, \quad 5\% : 5.3077e - 01, \quad 9\% : 4.9879e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 0, p = 0.9994, ks2stat = 0.1667*

*RStest : Conc1 : h = 0, p = 0.8916*

*KStest2 : Conc2 : h = 0, p = 0.6693, ks2stat = 0.3333*

*RStest : Conc2 : h = 0, p = 0.4371*

*KStest2 : Conc3 : h = 0, p = 0.3842, ks2stat = 0.4167*

*RStest : Conc3 : h = 0, p = 0.5532*

*KStest2 : Conc4 : h = 0, p = 0.0799, ks2stat = 0.5833*

*RStest : Conc4 : h = 0, p = 0.1025*

###### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, Abstinence N = 6).

p-value for Control vs initial task of male: 0.36093.

kstest2 results: h=1, p=6.6954e-03, ks2stat=0.4129

Post-hoc analysis:

$$0.5\% : 8.8333e - 02, \quad 2\% : 6.2386e - 01, \quad 5\% : 1.2699e - 01, \quad 9\% : 5.0279e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 1, p = 0.0125, ks2stat = 0.7424*  
*RStest : Conc1 : h = 1, p = 0.0477*  
*KStest2 : Conc2 : h = 0, p = 0.9495, ks2stat = 0.2424*  
*RStest : Conc2 : h = 0, p = 0.8075*  
*KStest2 : Conc3 : h = 0, p = 0.1106, ks2stat = 0.5606*  
*RStest : Conc3 : h = 0, p = 0.0983*  
*KStest2 : Conc4 : h = 0, p = 0.5232, ks2stat = 0.3788*  
*RStest : Conc4 : h = 0, p = 0.4623*

### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	355.3947	1	0	355.3947	26.0124	0
Condition	41.0987	1	0	41.0987	3.0081	0.0853
Concentration	179.8368	3	0	59.9456	4.3876	0.0057
Gender*Condition	22.2205	1	0	22.2205	1.6264	0.2045
Gender*Concentration	10.9513	3	0	3.6504	0.2672	0.8489
Condition*Concentration	61.1791	3	0	20.393	1.4926	0.2197
Error	1735.1417	127	0	13.6625	NaN	NaN
Total	2545.4129	139	0	NaN	NaN	NaN

#### 4.19 Figure 6s: Fraction of Sigmoid (Control vs Self admin vs Abstinence)

Statistical significance was determined by one-way analysis of variance. (Female Control = 10, Male Control = 10, Female Self admin. Oxy = 5, Male Self admin. Oxy = 5, Female Abstinence = 6, Male Abstinence = 6)

Significance of difference between the groups: d.f. = 5, F = 17.0600, p = 1.2356e-08

Post-hoc analysis by Tukey's HSD method:

*FemaleControlandMaleControl : 0.9862*  
*FemaleControlandFemaleSelfAdmin : 9.5155e - 06*  
*MaleControlandMaleSelfAdmin : 6.2293e - 06*  
*FemaleControlandFemaleAbstinence : 0.0084*  
*MaleControlandMaleSelfAbstinence : 2.9341e - 04*

## 5 Supplemental Figure 1

### 5.1 Figure S.1l: Average time to learn task (FvM)

statistical significance was determined by paired t-test using SPSS software package (F = 12, M = 11). p-value for gender difference: 0.01.

## 6 Supplemental Figure 2

### 6.1 Figure S.2i: Control Distance traveled, approach only (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 12, Male N = 11).

Effect of concentration: d.f. = 3,  $F = 7.9201$ ,  $p = 1.6745e-04$ .  
 Effect of gender: d.f. = 1,  $F = 10.8854$ ,  $p = 0.0038$ .  
 kstest2 results:  $h=1$ ,  $p=7.1912e-04$ ,  $ks2stat=0.4103$  (overall gender difference)

Post-hoc analysis:

$$0.5\% : 1.2870e - 02, \quad 2\% : 2.5797e - 01, \quad 5\% : 2.5247e - 02, \quad 9\% : 1.7835e - 02$$

KStest2 and wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$\begin{aligned} KStest2 : Conc1 : h = 1, p = 0.0121, ks2stat = 0.6364 \\ RStest : Conc1 : h = 1, p = 0.0104 \\ KStest2 : Conc2 : h = 0, p = 0.2270, ks2stat = 0.4167 \\ RStest : Conc2 : h = 0, p = 0.3734 \\ KStest2 : Conc3 : h = 1, p = 0.0452, ks2stat = 0.5500 \\ RStest : Conc3 : h = 1, p = 0.0192 \\ KStest2 : Conc4 : h = 1, p = 0.0289, ks2stat = 0.5682 \\ RStest : Conc4 : h = 1, p = 0.0074 \end{aligned}$$

## 6.2 Figure S.2j: Control Number of stopping points, approach only (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female  $N = 12$ , Male  $N = 11$ ).

Effect of concentration: d.f. = 3,  $F = 5.8431$ ,  $p = 1.4948e-03$ .  
 Effect of gender: d.f. = 1,  $F = 0.5058$ ,  $p = 0.4856$ .  
 kstest2 results:  $h=0$ ,  $p=6.2873e-02$ ,  $ks2stat=0.2710$  (overall gender difference)  
 Post-hoc analysis:

$$0.5\% : 5.8083e - 02 \quad 2\% : 8.8005e - 01, \quad 5\% : 5.5419e - 01, \quad 9\% : 1.6653e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$\begin{aligned} KStest2 : Conc1 : h = 0, p = 0.1473, ks2stat = 0.4545 \\ RStest : Conc1 : h = 0, p = 0.0878 \\ KStest2 : Conc2 : h = 0, p = 0.4896, ks2stat = 0.3333 \\ RStest : Conc2 : h = 0, p = 0.5310 \\ KStest2 : Conc3 : h = 0, p = 0.2689, ks2stat = 0.4000 \\ RStest : Conc3 : h = 0, p = 0.1985 \\ KStest2 : Conc4 : h = 0, p = 0.0915, ks2stat = 0.4848 \\ RStest : Conc4 : h = 0, p = 0.0905 \end{aligned}$$

## 6.3 Figure S.2k: Control Number of high sp. runs, approach only (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female  $N = 12$ , Male  $N = 11$ ).

Effect of concentration: d.f. = 3,  $F = 33.6668$ ,  $p = 1.1834e-12$ .  
 Effect of gender: d.f. = 1,  $F = 1.6147$ ,  $p = 0.2192$ .  
 kstest2 results:  $h=0$ ,  $p=4.3505e-01$ ,  $ks2stat=0.1793$  (overall gender difference)

Post-hoc analysis:

$$0.5\% : 1.9769e - 01, \quad 2\% : 5.3803e - 01, \quad 5\% : 4.1293e - 01, \quad 9\% : 1.8367e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.3744, ks2stat = 0.3636$   
 $RStest : Conc1 : h = 0, p = 0.1486$   
 $KStest2 : Conc2 : h = 0, p = 0.8286, ks2stat = 0.2500$   
 $RStest : Conc2 : h = 0, p = 0.9212$   
 $KStest2 : Conc3 : h = 0, p = 0.4268, ks2stat = 0.3500$   
 $RStest : Conc3 : h = 0, p = 0.1985$   
 $KStest2 : Conc4 : h = 0, p = 0.1328, ks2stat = 0.4545$   
 $RStest : Conc4 : h = 0, p = 0.1661$

#### 6.4 Figure S.2l: Control Prop. of trial out. all reward zones, approach only (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 12, Male N = 11).

Effect of concentration: d.f. = 3, F = 7.3360, p = 3.0532e-04.

Effect of gender: d.f. = 1, F = 0.0233, p = 0.8803.

kstest2 results: h=0, p=7.5063e-01, ks2stat=0.1393 (overall gender difference)

Post-hoc analysis:

0.5% :  $6.6119e - 01$ , 2% :  $4.6695e - 01$ , 5% :  $5.8985e - 01$ , 9% :  $6.5657e - 01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.9852, ks2stat = 0.1818$   
 $RStest : Conc1 : h = 0, p = 0.8422$   
 $KStest2 : Conc2 : h = 0, p = 0.8848, ks2stat = 0.2333$   
 $RStest : Conc2 : h = 0, p = 0.3834$   
 $KStest2 : Conc3 : h = 0, p = 0.5564, ks2stat = 0.3167$   
 $RStest : Conc3 : h = 0, p = 0.4681$   
 $KStest2 : Conc4 : h = 0, p = 0.9610, ks2stat = 0.1970$   
 $RStest : Conc4 : h = 0, p = 0.5588$

#### 6.5 Figure S.2m. Control Number of high sp. runs, reject only (FvM)

Effect of concentration: d.f. = 3, F = 1.7438, p = 1.6766e-01.

Effect of gender: d.f. = 1, F = 12.3666, p = 0.0022.

kstest2 results: h=1, p=4.1576e-07, ks2stat=0.5654 (overall gender difference)

Post-hoc analysis:

0.5% : 0.0003, 2% : 0.0025, 5% : 0.0054, 9% : 0.0742

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 1, p = 0.0003, ks2stat = 0.8258$   
 $RStest : Conc1 : h = 1, p = 0.0006$   
 $KStest2 : Conc2 : h = 1, p = 0.0059, ks2stat = 0.6667$   
 $RStest : Conc2 : h = 1, p = 0.0028$   
 $KStest2 : Conc3 : h = 1, p = 0.0098, ks2stat = 0.6364$   
 $RStest : Conc3 : h = 1, p = 0.0062$   
 $KStest2 : Conc4 : h = 0, p = 0.1902, ks2stat = 0.4333$   
 $RStest : Conc4 : h = 0, p = 0.0806$

## 6.6 Figure S.2n. Control Distance traveled, reject only (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 12, Male N = 11).

Effect of concentration: d.f. = 3, F = 2.7997, p = 4.7581e-02.

Effect of gender: d.f. = 1, F = 7.3378, p = 0.0135.

kstest2 results: h=1, p=2.2098e-04, ks2stat=0.4351 (overall gender difference)

Post-hoc analysis:

0.5% : 0.0048, 2% : 0.0168, 5% : 0.0162, 9% : 0.1742

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 1, p = 0.0289, ks2stat = 0.5682$   
 $RStest : Conc1 : h = 1, p = 0.0074$   
 $KStest2 : Conc2 : h = 1, p = 0.0361, ks2stat = 0.5530$   
 $RStest : Conc2 : h = 1, p = 0.0127$   
 $KStest2 : Conc3 : h = 1, p = 0.0403, ks2stat = 0.5455$   
 $RStest : Conc3 : h = 1, p = 0.0089$   
 $KStest2 : Conc4 : h = 0, p = 0.2270, ks2stat = 0.4167$   
 $RStest : Conc4 : h = 0, p = 0.2766$

## 6.7 Figure S.2o. Control Number of stopping points, reject only (FvM)

Effect of concentration: d.f. = 3, F = 1.4054, p = 2.5002e-01.

Effect of gender: d.f. = 1, F = 1.5795, p = 0.2233.

kstest2 results: h=1, p=2.3013e-04, ks2stat=0.4341 (overall gender difference)

Post-hoc analysis:

0.5% : 0.0987, 2% : 0.2915, 5% : 0.1825, 9% : 0.3455

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 1, p = 0.0289, ks2stat = 0.5682*  
*RStest : Conc1 : h = 1, p = 0.0062*  
*KStest2 : Conc2 : h = 0, p = 0.1006, ks2stat = 0.4773*  
*RStest : Conc2 : h = 0, p = 0.1316*  
*KStest2 : Conc3 : h = 1, p = 0.0361, ks2stat = 0.5530*  
*RStest : Conc3 : h = 1, p = 0.0089*  
*KStest2 : Conc4 : h = 0, p = 0.3162, ks2stat = 0.3833*  
*RStest : Conc4 : h = 0, p = 0.3390*

## 6.8 Figure S.2p. Control Prop. of trial out. all reward zones, reject only (FvM)

Effect of concentration: d.f. = 3, F = 1.0197, p = 3.9035e-01.

Effect of gender: d.f. = 1, F = 1.2575, p = 0.2754.

kstest2 results: h=0, p=6.1613e-02, ks2stat=0.2689 (overall gender difference)

Post-hoc analysis:

0.5% : 0.4147, 2% : 0.7963, 5% : 0.0463, 9% : 0.7952

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 0, p = 0.7136, ks2stat = 0.2727*  
*RStest : Conc1 : h = 0, p = 0.4060*  
*KStest2 : Conc2 : h = 0, p = 0.9094, ks2stat = 0.2197*  
*RStest : Conc2 : h = 0, p = 0.7582*  
*KStest2 : Conc3 : h = 1, p = 0.0289, ks2stat = 0.5682*  
*RStest : Conc3 : h = 1, p = 0.0310*  
*KStest2 : Conc4 : h = 0, p = 0.1582, ks2stat = 0.4500*  
*RStest : Conc4 : h = 0, p = 0.3551*

## 7 Supplemental Figure 4

### 7.1 Figure S.4d: Shape comparison of psychometric function

statistical significance was determined by chi-squared test using **SPSS** software package (F = 12, M = 11).

p-value for Sigmoidal and U-shape for initial 1-3 months: 0.016.

p-value for Sigmoidal and U-shape after a year: 0.0009.

## 8 Supplemental Figure 5

### 8.1 Figure S.5a. Control vs FD Distance traveled, approach only

Effect of condition: d.f. = 1, F = 10.2599, p = 0.0033.

### 8.2 Figure S.5b. Control vs FD Number of stopping points, approach only

Effect of condition: d.f. = 1, F = 5.9745, p = 0.0208.



### 8.3 Figure S.5c. Control vs FD Number of high speed runs, approach only

Effect of condition: d.f. = 1,  $F = 0.6510$ ,  $p = 0.4263$ .

### 8.4 Figure S.5d. Control vs FD Proportion of trials outside all reward zone, approach only

Effect of condition: d.f. = 1,  $F = 3.2717$ ,  $p = 0.0809$ .

### 8.5 Figure S.5e. Control vs FD Distance traveled, reject only

Effect of condition: d.f. = 1,  $F = 17.8994$ ,  $p = 0.0002$ .

### 8.6 Figure S.5f. Control vs FD Number of stopping points, reject only

Effect of condition: d.f. = 1,  $F = 2.2523$ ,  $p = 0.1424$ .

### 8.7 Figure S.5g. Control vs FD Number of high speed runs, reject only

Effect of condition: d.f. = 1,  $F = 9.8747$ ,  $p = 0.0034$ .

### 8.8 Figure S.5h. Control vs FD Proportion of trials outside all reward zone, reject only

Effect of condition: d.f. = 1,  $F = 7.0077$ ,  $p = 0.0121$ .

### 8.9 Figure S.5i: FD Approach rate (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female  $N = 12$ , Male  $N = 10$ ).

Effect of concentration: d.f. = 3,  $F = 182.0357$ ,  $p = 4.3911e-30$ .

Effect of gender: d.f. = 1,  $F = 2.1437$ ,  $p = 0.1587$ .

kstest2 results:  $h=0$ ,  $p=9.3097e-01$ ,  $ks2stat=0.1125$  (overall gender difference)

Post-hoc analysis:

$$0.5\% : 7.8880e - 01, \quad 2\% : 2.2787e - 01, \quad 5\% : 2.6929e - 01, \quad 9\% : 7.6084e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$KStest2 : Conc1 : h = 0, p = 0.9636, ks2stat = 0.2000$$

$$RStest : Conc1 : h = 0, p = 0.5631$$

$$KStest2 : Conc2 : h = 0, p = 0.8286, ks2stat = 0.2500$$

$$RStest : Conc2 : h = 0, p = 0.2840$$

$$KStest2 : Conc3 : h = 0, p = 0.6961, ks2stat = 0.2833$$

$$RStest : Conc3 : h = 0, p = 0.2892$$

$$KStest2 : Conc4 : h = 0, p = 0.8848, ks2stat = 0.2333$$

$$RStest : Conc4 : h = 0, p = 0.8391$$

#### Control vs FD

##### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control  $N = 12$ , FD  $N = 12$ ).

p-value for Control vs FD of female: 0.0042028.

kstest2 results:  $h=1$ ,  $p=2.6487e-02$ ,  $ks2stat=0.2917$

Post-hoc analysis:

$$0.5\% : 6.2877e - 01, \quad 2\% : 4.9942e - 01, \quad 5\% : 9.7466e - 03, \quad 9\% : 4.6536e - 02$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$\begin{aligned} KStest2 : Conc1 : h = 0, p = 0.4333, ks2stat = 0.3333 \\ RStest : Conc1 : h = 0, p = 0.4504 \\ KStest2 : Conc2 : h = 0, p = 0.1862, ks2stat = 0.4167 \\ RStest : Conc2 : h = 0, p = 0.3354 \\ KStest2 : Conc3 : h = 0, p = 0.0656, ks2stat = 0.5000 \\ RStest : Conc3 : h = 1, p = 0.0140 \\ KStest2 : Conc4 : h = 1, p = 0.0002, ks2stat = 0.8333 \\ RStest : Conc4 : h = 1, p = 0.0028 \end{aligned}$$

**Male:**

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, FD N = 10).

p-value for Control vs FD of male: 0.0027308.

kstest2 results: h=0, p=2.9608e-01, ks2stat=0.2068

Post-hoc analysis:

$$0.5\% : 7.4398e - 01, \quad 2\% : 9.6105e - 01, \quad 5\% : 1.0232e - 02, \quad 9\% : 4.9382e - 02$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$\begin{aligned} KStest2 : Conc1 : h = 0, p = 0.2890, ks2stat = 0.4000 \\ RStest : Conc1 : h = 0, p = 0.3734 \\ KStest2 : Conc2 : h = 0, p = 0.9884, ks2stat = 0.1818 \\ RStest : Conc2 : h = 0, p = 0.9716 \\ KStest2 : Conc3 : h = 0, p = 0.0551, ks2stat = 0.5455 \\ RStest : Conc3 : h = 1, p = 0.0166 \\ KStest2 : Conc4 : h = 0, p = 0.0697, ks2stat = 0.5273 \\ RStest : Conc4 : h = 1, p = 0.0301 \end{aligned}$$

**3-way ANOVA Results:**

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	0.0895	1	0	0.0895	4.7591	0.0305
Condition	0.3417	1	0	0.3417	18.158	0
Concentration	18.0205	3	0	6.0068	319.2341	0
Gender*Condition	0.0076	1	0	0.0076	0.4055	0.5251
Gender*Concentration	0.1528	3	0	0.0509	2.707	0.047
Condition*Concentration	0.549	3	0	0.183	9.7255	0
Error	3.1423	167	0	0.0188	NaN	NaN
Total	22.2751	179	0	NaN	NaN	NaN

## 8.10 Figure S.5j: FD Distance traveled (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 12, Male N = 10).

Effect of concentration: d.f. = 3, F = 12.1087, p = 2.6791e-06.

Effect of gender: d.f. = 1, F = 21.4749, p = 0.0002.

kstest2 results: h=1, p=1.3139e-08, ks2stat=0.6375 (overall gender difference)

Post-hoc analysis:

$$0.5\% : 4.0070e - 04, \quad 2\% : 1.4910e - 05, \quad 5\% : 9.2678e - 03, \quad 9\% : 2.5464e - 03$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$KStest2 : Conc1 : h = 1, p = 0.0076, ks2stat = 0.6667$$

$$RStest : Conc1 : h = 1, p = 0.0033$$

$$KStest2 : Conc2 : h = 1, p = 0.0001, ks2stat = 0.9167$$

$$RStest : Conc2 : h = 1, p = 0.0003$$

$$KStest2 : Conc3 : h = 0, p = 0.0567, ks2stat = 0.5333$$

$$RStest : Conc3 : h = 1, p = 0.0229$$

$$KStest2 : Conc4 : h = 1, p = 0.0076, ks2stat = 0.6667$$

$$RStest : Conc4 : h = 1, p = 0.0051$$

### Control vs FD

#### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, FD N = 12).

p-value for Control vs FD of female: 0.0011858.

kstest2 results: h=1, p=1.7074e-05, ks2stat=0.4792

Post-hoc analysis:

$$0.5\% : 5.1267e - 04, \quad 2\% : 4.0099e - 05, \quad 5\% : 1.0567e - 01, \quad 9\% : 1.7728e - 02$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$KStest2 : Conc1 : h = 1, p = 0.0046, ks2stat = 0.6667$$

$$RStest : Conc1 : h = 1, p = 0.0017$$

$$KStest2 : Conc2 : h = 1, p = 0.0009, ks2stat = 0.7500$$

$$RStest : Conc2 : h = 1, p = 0.0005$$

$$KStest2 : Conc3 : h = 0, p = 0.0656, ks2stat = 0.5000$$

$$RStest : Conc3 : h = 0, p = 0.0531$$

$$KStest2 : Conc4 : h = 0, p = 0.0656, ks2stat = 0.5000$$

$$RStest : Conc4 : h = 1, p = 0.0226$$

#### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, FD N = 10).

p-value for Control vs FD of male: 0.016738.

kstest2 results: h=1, p=2.1901e-04, ks2stat=0.4523

Post-hoc analysis:

$$0.5\% : 4.2001e - 03, \quad 2\% : 8.3414e - 02, \quad 5\% : 2.0879e - 02, \quad 9\% : 8.0063e - 02$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 1, p = 0.0198, ks2stat = 0.6182$   
 $RStest : Conc1 : h = 1, p = 0.0067$   
 $KStest2 : Conc2 : h = 0, p = 0.2006, ks2stat = 0.4364$   
 $RStest : Conc2 : h = 0, p = 0.1300$   
 $KStest2 : Conc3 : h = 0, p = 0.0978, ks2stat = 0.5000$   
 $RStest : Conc3 : h = 1, p = 0.0317$   
 $KStest2 : Conc4 : h = 0, p = 0.2205, ks2stat = 0.4273$   
 $RStest : Conc4 : h = 0, p = 0.0845$

### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	27.3951	1	0	27.3951	106.6057	0
Condition	16.098	1	0	16.098	62.6439	0
Concentration	2.7766	3	0	0.9255	3.6016	0.0148
Gender*Condition	1.6504	1	0	1.6504	6.4225	0.0122
Gender*Concentration	0.5568	3	0	0.1856	0.7222	0.5401
Condition*Concentration	1.4535	3	0	0.4845	1.8854	0.134
Error	42.9151	167	0	0.257	NaN	NaN
Total	94.4813	179	0	NaN	NaN	NaN

### 8.11 Figure S.5k: FD Number of stopping points (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 12, Male N = 10).

Effect of concentration: d.f. = 3, F = 3.9968, p = 1.1616e-02.

Effect of gender: d.f. = 1, F = 8.8810, p = 0.0074.

kstest2 results: h=1, p=1.8518e-05, ks2stat=0.5000 (overall gender difference)

Post-hoc analysis:

0.5% :  $1.8703e - 02$ , 2% :  $4.5455e - 04$ , 5% :  $2.3150e - 01$ , 9% :  $1.1937e - 02$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 1, p = 0.0076, ks2stat = 0.6667$   
 $RStest : Conc1 : h = 1, p = 0.0111$   
 $KStest2 : Conc2 : h = 1, p = 0.0003, ks2stat = 0.8333$   
 $RStest : Conc2 : h = 1, p = 0.0014$   
 $KStest2 : Conc3 : h = 0, p = 0.2270, ks2stat = 0.4167$   
 $RStest : Conc3 : h = 0, p = 0.4098$   
 $KStest2 : Conc4 : h = 1, p = 0.0452, ks2stat = 0.5500$   
 $RStest : Conc4 : h = 1, p = 0.0092$

### Control vs FD

#### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, FD N = 12).

p-value for Control vs FD of female: 0.010394.

kstest2 results: h=1, p=4.6080e-05, ks2stat=0.4583

Post-hoc analysis:

0.5% :  $3.0300e - 03$ , 2% :  $7.5065e - 03$ , 5% :  $1.1942e - 01$ , 9% :  $1.3927e - 02$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 1, p = 0.0191, ks2stat = 0.5833*  
*RStest : Conc1 : h = 1, p = 0.0043*  
*KStest2 : Conc2 : h = 1, p = 0.0191, ks2stat = 0.5833*  
*RStest : Conc2 : h = 1, p = 0.0024*  
*KStest2 : Conc3 : h = 0, p = 0.1862, ks2stat = 0.4167*  
*RStest : Conc3 : h = 0, p = 0.2366*  
*KStest2 : Conc4 : h = 0, p = 0.0656, ks2stat = 0.5000*  
*RStest : Conc4 : h = 1, p = 0.0194*

### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, FD N = 10).

p-value for Control vs FD of male: 0.1438.

kstest2 results: h=1, p=4.8245e-06, ks2stat=0.5386

Post-hoc analysis:

0.5% :  $9.9947e - 02$ , 2% :  $1.9939e - 01$ , 5% :  $1.1572e - 01$ , 9% :  $1.9212e - 01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 1, p = 0.0009, ks2stat = 0.8000*  
*RStest : Conc1 : h = 1, p = 0.0022*  
*KStest2 : Conc2 : h = 0, p = 0.0697, ks2stat = 0.5273*  
*RStest : Conc2 : h = 0, p = 0.0725*  
*KStest2 : Conc3 : h = 1, p = 0.0173, ks2stat = 0.6273*  
*RStest : Conc3 : h = 1, p = 0.0028*  
*KStest2 : Conc4 : h = 1, p = 0.0198, ks2stat = 0.6182*  
*RStest : Conc4 : h = 1, p = 0.0448*

### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	290797.7063	1	0	290797.7063	14.1124	0.0002
Condition	403580.2146	1	0	403580.2146	19.5858	0
Concentration	2269.2494	3	0	756.4165	0.0367	0.9906
Gender*Condition	73903.6627	1	0	73903.6627	3.5865	0.06
Gender*Concentration	5914.6548	3	0	1971.5516	0.0957	0.9623
Condition*Concentration	2016.996	3	0	672.332	0.0326	0.9921
Error	3441168.5604	167	0	20605.7998	NaN	NaN
Total	4223019.6835	179	0	NaN	NaN	NaN

## 8.12 Figure S.51: FD Number of high sp. runs (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 12, Male N = 10).

Effect of concentration: d.f. = 3, F = 33.4826, p = 7.6444e-13.

Effect of gender: d.f. = 1, F = 5.9221, p = 0.0245.

kstest2 results: h=1, p=6.8336e-03, ks2stat=0.3500 (overall gender difference)

Post-hoc analysis:

$$0.5\% : 1.1326e - 02, \quad 2\% : 1.2677e - 04, 5\% : 9.3261e - 01, \quad 9\% : 1.6538e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 1, p = 0.0358, ks2stat = 0.5667*

*RStest : Conc1 : h = 1, p = 0.0111*

*KStest2 : Conc2 : h = 1, p = 0.0001, ks2stat = 0.9167*

*RStest : Conc2 : h = 1, p = 0.0003*

*KStest2 : Conc3 : h = 0, p = 0.9989, ks2stat = 0.1500*

*RStest : Conc3 : h = 0, p = 0.9212*

*KStest2 : Conc4 : h = 0, p = 0.5564, ks2stat = 0.3167*

*RStest : Conc4 : h = 0, p = 0.2485*

### Control vs FD

#### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, FD N = 12).

p-value for Control vs FD of female: 0.13035.

kstest2 results: h=0, p=8.3415e-02, ks2stat=0.2500

Post-hoc analysis:

$$0.5\% : 1.5506e - 02, \quad 2\% : 1.7542e - 02, \quad 5\% : 5.6165e - 01, \quad 9\% : 1.9334e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 1, p = 0.0191, ks2stat = 0.5833*

*RStest : Conc1 : h = 1, p = 0.0194*

*KStest2 : Conc2 : h = 1, p = 0.0046, ks2stat = 0.6667*

*RStest : Conc2 : h = 1, p = 0.0102*

*KStest2 : Conc3 : h = 0, p = 0.7864, ks2stat = 0.2500*

*RStest : Conc3 : h = 0, p = 0.5834*

*KStest2 : Conc4 : h = 0, p = 0.4333, ks2stat = 0.3333*

*RStest : Conc4 : h = 0, p = 0.2145*

#### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, FD N = 10).

p-value for Control vs FD of male: 0.025096.

kstest2 results: h=1, p=3.0081e-03, ks2stat=0.3818

Post-hoc analysis:

$$0.5\% : 4.9411e - 04, \quad 2\% : 4.0639e - 01, \quad 5\% : 1.5711e - 02, \quad 9\% : 2.2641e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 1, p = 0.0046, ks2stat = 0.7091$   
 $RStest : Conc1 : h = 1, p = 0.0028$   
 $KStest2 : Conc2 : h = 0, p = 0.5376, ks2stat = 0.3273$   
 $RStest : Conc2 : h = 0, p = 0.3418$   
 $KStest2 : Conc3 : h = 0, p = 0.0551, ks2stat = 0.5455$   
 $RStest : Conc3 : h = 1, p = 0.0448$   
 $KStest2 : Conc4 : h = 0, p = 0.4339, ks2stat = 0.3545$   
 $RStest : Conc4 : h = 0, p = 0.2178$

### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	448.5973	1	0	448.5973	52.871	0
Condition	217.1167	1	0	217.1167	25.589	0
Concentration	476.1899	3	0	158.73	18.7077	0
Gender*Condition	47.5647	1	0	47.5647	5.6059	0.019
Gender*Concentration	29.9264	3	0	9.9755	1.1757	0.3207
Condition*Concentration	41.8773	3	0	13.9591	1.6452	0.1809
Error	1416.9547	167	0	8.4848	NaN	NaN
Total	2703.9688	179	0	NaN	NaN	NaN

### 8.13 Figure S.5m: FD Prop. of trial out. all reward zones (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 12, Male N = 10).

Effect of concentration: d.f. = 3, F = 45.0059, p = 2.3011e-15.

Effect of gender: d.f. = 1, F = 0.7749, p = 0.3892.

kstest2 results: h=0, p=2.6677e-01, ks2stat=0.2083 (overall gender difference)

Post-hoc analysis:

0.5% :  $2.8309e - 01$ , 2% :  $1.3761e - 02$ , 5% :  $8.4288e - 01$ , 9% :  $5.6653e - 01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.4896, ks2stat = 0.3333$   
 $RStest : Conc1 : h = 0, p = 0.3891$   
 $KStest2 : Conc2 : h = 0, p = 0.0567, ks2stat = 0.5333$   
 $RStest : Conc2 : h = 1, p = 0.0149$   
 $KStest2 : Conc3 : h = 0, p = 0.9636, ks2stat = 0.2000$   
 $RStest : Conc3 : h = 0, p = 0.8940$   
 $KStest2 : Conc4 : h = 0, p = 0.3689, ks2stat = 0.3667$   
 $RStest : Conc4 : h = 0, p = 0.5716$

### Control vs FD

#### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, FD N = 12).

p-value for Control vs FD of female: 0.23688.

kstest2 results: h=1, p=4.8054e-02, ks2stat=0.2708

Post-hoc analysis:

0.5% :  $2.8018e - 02$ , 2% :  $8.2300e - 03$ , 5% :  $3.6018e - 01$ , 9% :  $7.4730e - 01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 0, p = 0.1862, ks2stat = 0.4167*  
*RStest : Conc1 : h = 1, p = 0.0399*  
*KStest2 : Conc2 : h = 0, p = 0.0656, ks2stat = 0.5000*  
*RStest : Conc2 : h = 1, p = 0.0163*  
*KStest2 : Conc3 : h = 0, p = 0.1862, ks2stat = 0.4167*  
*RStest : Conc3 : h = 0, p = 0.1651*  
*KStest2 : Conc4 : h = 0, p = 0.7864, ks2stat = 0.2500*  
*RStest : Conc4 : h = 0, p = 0.4510*

### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, FD N = 10).

p-value for Control vs FD of male: 0.19499.

kstest2 results: h=0, p=7.2583e-02, ks2stat=0.2727

Post-hoc analysis:

0.5% :  $5.5760e - 02$ , 2% :  $4.2774e - 01$ , 5% :  $6.6086e - 01$ , 9% :  $2.2116e - 01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 1, p = 0.0227, ks2stat = 0.6091*  
*RStest : Conc1 : h = 1, p = 0.0342*  
*KStest2 : Conc2 : h = 0, p = 0.4339, ks2stat = 0.3545*  
*RStest : Conc2 : h = 0, p = 0.2872*  
*KStest2 : Conc3 : h = 0, p = 0.8603, ks2stat = 0.2455*  
*RStest : Conc3 : h = 0, p = 0.6961*  
*KStest2 : Conc4 : h = 0, p = 0.0876, ks2stat = 0.5091*  
*RStest : Conc4 : h = 0, p = 0.1675*

### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	0.1799	1	0	0.1799	6.1638	0.014
Condition	0.2727	1	0	0.2727	9.3414	0.0026
Concentration	1.7647	3	0	0.5882	20.1509	0
Gender*Condition	0.0005	1	0	0.0005	0.0178	0.8939
Gender*Concentration	0.0584	3	0	0.0195	0.6672	0.5733
Condition*Concentration	0.2834	3	0	0.0945	3.2362	0.0237
Error	4.8749	167	0	0.0292	NaN	NaN
Total	7.4668	179	0	NaN	NaN	NaN



## 8.14 Figure S.5p(left): Distance cluster vs Individual probabilities

Statistical significance was determined by calculating the p-value through a two-sample t-test using MATLAB's ttest2 function. This test was applied to the Euclidean distances derived from the individual rats' probability distributions within distance clusters.

p = 1.0182e-31

## 8.15 Figure S.5p(left): Stop cluster vs Individual probabilities

This test was applied to the Euclidean distances derived from the individual rats' probability distributions within stop clusters.

p = 4.1772e-29

# 9 Supplemental Figure 6

## 9.1 Figure S.6a: Self admin oxycodone Approach time (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 5, Male N = 5).

Effect of concentration: d.f. = 3, F = 2.4534, p = 8.7784e-02.

Effect of gender: d.f. = 1, F = 6.7698, p = 0.0315.

kstest2 results: h=1, p=2.3213e-02, ks2stat=0.4500 (overall gender difference)

Post-hoc analysis:

0.5% : 3.1246e - 03, 2% : 5.8901e - 01, 5% : 3.6169e - 02, 9% : 9.2633e - 01

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 1, p = 0.0038, ks2stat = 1.0000*

*RStest : Conc1 : h = 1, p = 0.0079*

*KStest2 : Conc2 : h = 0, p = 0.9996, ks2stat = 0.2000*

*RStest : Conc2 : h = 0, p = 0.6905*

*KStest2 : Conc3 : h = 1, p = 0.0361, ks2stat = 0.8000*

*RStest : Conc3 : h = 0, p = 0.0556*

*KStest2 : Conc4 : h = 0, p = 0.6974, ks2stat = 0.4000*

*RStest : Conc4 : h = 0, p = 1.0000*

### Control vs Self admin. Oxy

#### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, Self admin. Oxy N = 5).

p-value for Control vs Self admin. Oxy of female: 0.95625.

kstest2 results: h=0, p=8.3454e-01, ks2stat=0.1596

Post-hoc analysis:

0.5% : 2.0591e - 01, 2% : 9.2070e - 01, 5% : 6.9608e - 01, 9% : 1.7620e - 01

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 0, p = 0.1707, ks2stat = 0.5455*  
*RStest : Conc1 : h = 0, p = 0.2674*  
*KStest2 : Conc2 : h = 0, p = 0.9887, ks2stat = 0.2167*  
*RStest : Conc2 : h = 0, p = 0.7990*  
*KStest2 : Conc3 : h = 0, p = 0.4046, ks2stat = 0.4333*  
*RStest : Conc3 : h = 0, p = 0.6461*  
*KStest2 : Conc4 : h = 0, p = 0.5074, ks2stat = 0.4000*  
*RStest : Conc4 : h = 0, p = 0.3284*

#### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, Self admin. Oxy N = 5).

p-value for Control vs Self admin. Oxy of male: 0.11333.

kstest2 results: h=0, p=6.9831e-02, ks2stat=0.3381

Post-hoc analysis:

0.5% :  $2.1225e - 01$ , 2% :  $2.2855e - 01$ , 5% :  $7.6955e - 02$ , 9% :  $5.4354e - 01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 0, p = 0.6450, ks2stat = 0.3636*  
*RStest : Conc1 : h = 0, p = 0.3773*  
*KStest2 : Conc2 : h = 0, p = 0.5402, ks2stat = 0.4000*  
*RStest : Conc2 : h = 0, p = 0.4396*  
*KStest2 : Conc3 : h = 1, p = 0.0388, ks2stat = 0.7000*  
*RStest : Conc3 : h = 0, p = 0.0553*  
*KStest2 : Conc4 : h = 0, p = 0.4648, ks2stat = 0.4182*  
*RStest : Conc4 : h = 0, p = 0.4409*

#### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	23.5048	1	0	23.5048	4.8286	0.03
Condition	8.2571	1	0	8.2571	1.6963	0.1954
Concentration	96.2147	3	0	32.0716	6.5884	0.0004
Gender*Condition	5.0089	1	0	5.0089	1.029	0.3125
Gender*Concentration	10.1859	3	0	3.3953	0.6975	0.5554
Condition*Concentration	21.9818	3	0	7.3273	1.5052	0.2169
Error	564.6711	116	0	4.8679	NaN	NaN
Total	758.4433	128	0	NaN	NaN	NaN

## 9.2 Figure S.6b: Self admin oxycodone Prop. of trial out. all reward zones (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 5, Male N = 5).

Effect of concentration: d.f. = 3, F = 0.5016, p = 6.8473e-01.

Effect of gender: d.f. = 1, F = 2.4942, p = 0.1529.

kstest2 results:  $h=1$ ,  $p=2.3213e-02$ ,  $ks2stat=0.4500$  (overall gender difference)

Post-hoc analysis:

0.5% :  $3.2600e-01$ , 2% :  $1.2515e-01$ , 5% :  $3.5598e-01$ , 9% :  $1.0995e-01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 :  $h = 0, p = 0.2090, ks2stat = 0.6000$*

*RStest : Conc1 :  $h = 0, p = 0.3095$*

*KStest2 : Conc2 :  $h = 0, p = 0.2090, ks2stat = 0.6000$*

*RStest : Conc2 :  $h = 0, p = 0.2222$*

*KStest2 : Conc3 :  $h = 0, p = 0.2090, ks2stat = 0.6000$*

*RStest : Conc3 :  $h = 0, p = 0.3968$*

*KStest2 : Conc4 :  $h = 0, p = 0.2090, ks2stat = 0.6000$*

*RStest : Conc4 :  $h = 0, p = 0.2222$*

### **Control vs Self admin. Oxy**

#### **Female:**

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, Self admin. Oxy N = 5).

p-value for Control vs Self admin. Oxy of female: 0.096217.

kstest2 results:  $h=1$ ,  $p=4.6360e-03$ ,  $ks2stat=0.4458$

Post-hoc analysis:

0.5% :  $2.1543e-01$ , 2% :  $3.5559e-02$ , 5% :  $2.7408e-01$ , 9% :  $2.8956e-01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 :  $h = 0, p = 0.3153, ks2stat = 0.4667$*

*RStest : Conc1 :  $h = 0, p = 0.1542$*

*KStest2 : Conc2 :  $h = 1, p = 0.0259, ks2stat = 0.7167$*

*RStest : Conc2 :  $h = 1, p = 0.0343$*

*KStest2 : Conc3 :  $h = 0, p = 0.7348, ks2stat = 0.3333$*

*RStest : Conc3 :  $h = 0, p = 0.6299$*

*KStest2 : Conc4 :  $h = 0, p = 0.0671, ks2stat = 0.6333$*

*RStest : Conc4 :  $h = 0, p = 0.1503$*

#### **Male:**

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, Self admin. Oxy N = 5).

p-value for Control vs Self admin. Oxy of male: 0.2521.

kstest2 results:  $h=0$ ,  $p=1.3724e-01$ ,  $ks2stat=0.3000$

Post-hoc analysis:

0.5% :  $3.6395e-01$ , 2% :  $5.1022e-01$ , 5% :  $1.7972e-01$ , 9% :  $3.6020e-02$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.7677, ks2stat = 0.3273$   
 $RStest : Conc1 : h = 0, p = 0.7628$   
 $KStest2 : Conc2 : h = 0, p = 0.7072, ks2stat = 0.3455$   
 $RStest : Conc2 : h = 0, p = 0.4592$   
 $KStest2 : Conc3 : h = 0, p = 0.4648, ks2stat = 0.4182$   
 $RStest : Conc3 : h = 0, p = 0.2088$   
 $KStest2 : Conc4 : h = 1, p = 0.0101, ks2stat = 0.8000$   
 $RStest : Conc4 : h = 0, p = 0.0641$

### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	0.0435	1	0	0.0435	1.7476	0.1887
Condition	0.0069	1	0	0.0069	0.2763	0.6001
Concentration	0.1103	3	0	0.0368	1.4758	0.2246
Gender*Condition	0.3152	1	0	0.3152	12.6488	0.0005
Gender*Concentration	0.0352	3	0	0.0117	0.4706	0.7033
Condition*Concentration	0.1621	3	0	0.054	2.1684	0.0953
Error	2.9652	119	0	0.0249	NaN	NaN
Total	3.7529	131	0	NaN	NaN	NaN

### 9.3 Figure S.6c: Self admin oxycodone Number of stopping points (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 5, Male N = 5).

Effect of concentration: d.f. = 3, F = 0.3109, p = 8.1732e-01.

Effect of gender: d.f. = 1, F = 2.9124, p = 0.1263.

kstest2 results: h=1, p=8.1617e-03, ks2stat=0.5000 (overall gender difference)

Post-hoc analysis:

0.5% :  $2.1755e - 01$ , 2% :  $9.1185e - 02$ , 5% :  $1.8516e - 01$ , 9% :  $9.4228e - 02$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.6974, ks2stat = 0.4000$   
 $RStest : Conc1 : h = 0, p = 0.2222$   
 $KStest2 : Conc2 : h = 1, p = 0.0361, ks2stat = 0.8000$   
 $RStest : Conc2 : h = 1, p = 0.0317$   
 $KStest2 : Conc3 : h = 0, p = 0.2090, ks2stat = 0.6000$   
 $RStest : Conc3 : h = 0, p = 0.1508$   
 $KStest2 : Conc4 : h = 0, p = 0.2090, ks2stat = 0.6000$   
 $RStest : Conc4 : h = 0, p = 0.0952$

### Control vs Self admin. Oxy

#### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, Self admin. Oxy N = 5).

p-value for Control vs initial task of female: 0.013864.

kstest2 results: h=1, p=1.6985e-04, ks2stat=0.5542

Post-hoc analysis:

0.5% :  $6.5797e - 03$ , 2% :  $2.4568e - 02$ , 5% :  $3.1498e - 02$ , 9% :  $1.3492e - 02$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 0, p = 0.0950, ks2stat = 0.6000*  
*RStest : Conc1 : h = 1, p = 0.0485*  
*KStest2 : Conc2 : h = 0, p = 0.0671, ks2stat = 0.6333*  
*RStest : Conc2 : h = 1, p = 0.0365*  
*KStest2 : Conc3 : h = 0, p = 0.3153, ks2stat = 0.4667*  
*RStest : Conc3 : h = 0, p = 0.1037*  
*KStest2 : Conc4 : h = 0, p = 0.1545, ks2stat = 0.5500*  
*RStest : Conc4 : h = 0, p = 0.1037*

### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, Self admin. Oxy N = 5).

p-value for Control vs initial task of male: 0.38653.

kstest2 results: h=1, p=4.2681e-03, ks2stat=0.4545

Post-hoc analysis:

0.5% :  $4.9541e - 01$ , 2% :  $3.2649e - 01$ , 5% :  $3.7954e - 01$ , 9% :  $3.6035e - 01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 0, p = 0.1019, ks2stat = 0.6000*  
*RStest : Conc1 : h = 0, p = 0.3196*  
*KStest2 : Conc2 : h = 0, p = 0.2342, ks2stat = 0.5091*  
*RStest : Conc2 : h = 0, p = 0.1451*  
*KStest2 : Conc3 : h = 0, p = 0.2005, ks2stat = 0.5273*  
*RStest : Conc3 : h = 0, p = 0.2212*  
*KStest2 : Conc4 : h = 0, p = 0.1019, ks2stat = 0.6000*  
*RStest : Conc4 : h = 0, p = 0.1451*

### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	63068.0185	1	0	63068.0185	1.5922	0.2095
Condition	79667.9163	1	0	79667.9163	2.0112	0.1588
Concentration	2413.7358	3	0	804.5786	0.0203	0.996
Gender*Condition	794212.3436	1	0	794212.3436	20.0501	0
Gender*Concentration	20606.0544	3	0	6868.6848	0.1734	0.9142
Condition*Concentration	2792.4651	3	0	930.8217	0.0235	0.9951
Error	4713750.3113	119	0	39611.3472	NaN	NaN
Total	5631827.6514	131	0	NaN	NaN	NaN

## 9.4 Figure S.6d: Abstinence Approach time (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 6, Male N = 6).

Effect of concentration: d.f. = 3, F = 8.5277, p = 3.0232e-04.

Effect of gender: d.f. = 1, F = 0.5135, p = 0.4900.

kstest2 results: h=0, p=8.6076e-01, ks2stat=0.1667 (overall gender difference)

Post-hoc analysis:

$$0.5\% : 6.9253e - 01, \quad 2\% : 6.3994e - 01, \quad 5\% : 6.0961e - 01, \quad 9\% : 7.4470e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$KStest2 : Conc1 : h = 0, p = 0.8096, ks2stat = 0.3333$$

$$RStest : Conc1 : h = 0, p = 0.5887$$

$$KStest2 : Conc2 : h = 0, p = 0.8096, ks2stat = 0.3333$$

$$RStest : Conc2 : h = 0, p = 0.6991$$

$$KStest2 : Conc3 : h = 0, p = 0.3180, ks2stat = 0.5000$$

$$RStest : Conc3 : h = 0, p = 0.4848$$

$$KStest2 : Conc4 : h = 0, p = 0.8096, ks2stat = 0.3333$$

$$RStest : Conc4 : h = 0, p = 0.8182$$

### Control vs Abstinence

#### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, Abstinence N = 6).

p-value for Control vs initial task of female: 0.8104.

kstest2 results: h=0, p=5.1065e-01, ks2stat=0.1986

Post-hoc analysis:

$$0.5\% : 9.1448e - 01, \quad 2\% : 8.9431e - 01, \quad 5\% : 7.9708e - 01, \quad 9\% : 6.4577e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$KStest2 : Conc1 : h = 0, p = 0.2971, ks2stat = 0.4545$$

$$RStest : Conc1 : h = 0, p = 0.7325$$

$$KStest2 : Conc2 : h = 0, p = 0.9290, ks2stat = 0.2500$$

$$RStest : Conc2 : h = 0, p = 0.7503$$

$$KStest2 : Conc3 : h = 0, p = 0.9290, ks2stat = 0.2500$$

$$RStest : Conc3 : h = 0, p = 0.8916$$

$$KStest2 : Conc4 : h = 0, p = 0.9290, ks2stat = 0.2500$$

$$RStest : Conc4 : h = 0, p = 0.6820$$

#### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, Abstinence N = 6).

p-value for Control vs initial task of male: 0.8535.

kstest2 results: h=0, p=7.5068e-01, ks2stat=0.1667

Post-hoc analysis:

$$0.5\% : 8.1127e - 01, \quad 2\% : 9.0195e - 01, \quad 5\% : 9.8759e - 01, \quad 9\% : 7.9737e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.7395, ks2stat = 0.3182$   
 $RStest : Conc1 : h = 0, p = 0.4623$   
 $KStest2 : Conc2 : h = 0, p = 0.8163, ks2stat = 0.3000$   
 $RStest : Conc2 : h = 0, p = 0.7925$   
 $KStest2 : Conc3 : h = 0, p = 0.4725, ks2stat = 0.4000$   
 $RStest : Conc3 : h = 0, p = 0.7925$   
 $KStest2 : Conc4 : h = 0, p = 0.2971, ks2stat = 0.4545$   
 $RStest : Conc4 : h = 0, p = 0.6605$

### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	5.7742	1	0	5.7742	1.4499	0.2308
Condition	0.8863	1	0	0.8863	0.2225	0.6379
Concentration	140.1993	3	0	46.7331	11.7345	0
Gender*Condition	0.1205	1	0	0.1205	0.0303	0.8622
Gender*Concentration	2.97	3	0	0.99	0.2486	0.8622
Condition*Concentration	0.9126	3	0	0.3042	0.0764	0.9726
Error	493.8364	124	0	3.9826	NaN	NaN
Total	667.9834	136	0	NaN	NaN	NaN

## 9.5 Figure S.6e: Abstinence Prop. of trial out. all reward zones (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 6, Male N = 6).

Effect of concentration: d.f. = 3, F = 7.6904, p = 5.9005e-04.

Effect of gender: d.f. = 1, F = 2.5630, p = 0.1405.

kstest2 results: h=0, p=2.1598e-01, ks2stat=0.2917 (overall gender difference)

Post-hoc analysis:

0.5% :  $3.2825e - 01$ , 2% :  $4.1626e - 01$ , 5% :  $5.1375e - 02$ , 9% :  $3.6430e - 01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.3180, ks2stat = 0.5000$   
 $RStest : Conc1 : h = 0, p = 0.3939$   
 $KStest2 : Conc2 : h = 0, p = 0.8096, ks2stat = 0.3333$   
 $RStest : Conc2 : h = 0, p = 0.5887$   
 $KStest2 : Conc3 : h = 0, p = 0.0766, ks2stat = 0.6667$   
 $RStest : Conc3 : h = 0, p = 0.0649$   
 $KStest2 : Conc4 : h = 0, p = 0.8096, ks2stat = 0.3333$   
 $RStest : Conc4 : h = 0, p = 0.4848$

### Control vs Abstinence

#### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, Abstinence N = 6).

p-value for Control vs initial task of female: 0.42819.

kstest2 results:  $h=0$ ,  $p=6.9487e-02$ ,  $ks2stat=0.3125$

Post-hoc analysis:

0.5% :  $3.6147e-01$ , 2% :  $8.1315e-01$ , 5% :  $5.1536e-01$ , 9% :  $4.0850e-01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.6693, ks2stat = 0.3333$   
 $RStest : Conc1 : h = 0, p = 0.3731$   
 $KStest2 : Conc2 : h = 0, p = 0.6693, ks2stat = 0.3333$   
 $RStest : Conc2 : h = 0, p = 0.9462$   
 $KStest2 : Conc3 : h = 0, p = 0.1877, ks2stat = 0.5000$   
 $RStest : Conc3 : h = 0, p = 0.2579$   
 $KStest2 : Conc4 : h = 0, p = 0.3842, ks2stat = 0.4167$   
 $RStest : Conc4 : h = 0, p = 0.3704$

### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, Abstinence N = 6).

p-value for Control vs initial task of male: 0.50339.

kstest2 results:  $h=0$ ,  $p=4.1694e-01$ ,  $ks2stat=0.2159$

Post-hoc analysis:

0.5% :  $3.3679e-01$ , 2% :  $8.9578e-01$ , 5% :  $4.9842e-01$ , 9% :  $3.3823e-01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.4722, ks2stat = 0.3939$   
 $RStest : Conc1 : h = 0, p = 0.2455$   
 $KStest2 : Conc2 : h = 0, p = 0.9857, ks2stat = 0.2121$   
 $RStest : Conc2 : h = 0, p = 0.8641$   
 $KStest2 : Conc3 : h = 0, p = 0.1106, ks2stat = 0.5606$   
 $RStest : Conc3 : h = 0, p = 0.1708$   
 $KStest2 : Conc4 : h = 0, p = 0.4722, ks2stat = 0.3939$   
 $RStest : Conc4 : h = 0, p = 0.3108$

### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	0.151	1	0	0.151	7.7287	0.0063
Condition	0.0602	1	0	0.0602	3.0791	0.0817
Concentration	0.4706	3	0	0.1569	8.0279	0.0001
Gender*Condition	0.0002	1	0	0.0002	0.0092	0.9237
Gender*Concentration	0.0293	3	0	0.0098	0.5001	0.6829
Condition*Concentration	0.0196	3	0	0.0065	0.3347	0.8003
Error	2.4814	127	0	0.0195	NaN	NaN
Total	3.3006	139	0	NaN	NaN	NaN



## 9.6 Figure S.6f: Abstinence Number of stopping points (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 6, Male N = 6).

Effect of concentration: d.f. = 3, F = 0.9612, p = 4.2378e-01.

Effect of gender: d.f. = 1, F = 1.1444, p = 0.3099.

kstest2 results: h=1, p=9.3124e-04, ks2stat=0.5417 (overall gender difference)

Post-hoc analysis:

$$0.5\% : 3.2581e - 01, \quad 2\% : 3.9929e - 01, \quad 5\% : 2.7256e - 01, \quad 9\% : 2.6367e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$KStest2 : Conc1 : h = 0, p = 0.0766, ks2stat = 0.6667$$

$$RStest : Conc1 : h = 0, p = 0.1320$$

$$KStest2 : Conc2 : h = 1, p = 0.0122, ks2stat = 0.8333$$

$$RStest : Conc2 : h = 0, p = 0.0649$$

$$KStest2 : Conc3 : h = 0, p = 0.3180, ks2stat = 0.5000$$

$$RStest : Conc3 : h = 0, p = 0.3095$$

$$KStest2 : Conc4 : h = 0, p = 0.3180, ks2stat = 0.5000$$

$$RStest : Conc4 : h = 0, p = 0.2403$$

### Control vs Abstinence

#### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, Abstinence N = 6).

p-value for Control vs initial task of female: 0.23108.

kstest2 results: h=0, p=4.4421e-01, ks2stat=0.2083

Post-hoc analysis:

$$0.5\% : 2.0036e - 01, \quad 2\% : 3.5578e - 01, \quad 5\% : 2.1478e - 01, \quad 9\% : 1.7829e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$KStest2 : Conc1 : h = 0, p = 0.9290, ks2stat = 0.2500$$

$$RStest : Conc1 : h = 0, p = 0.8201$$

$$KStest2 : Conc2 : h = 0, p = 0.6693, ks2stat = 0.3333$$

$$RStest : Conc2 : h = 0, p = 0.8201$$

$$KStest2 : Conc3 : h = 0, p = 0.3842, ks2stat = 0.4167$$

$$RStest : Conc3 : h = 0, p = 0.2129$$

$$KStest2 : Conc4 : h = 0, p = 0.6693, ks2stat = 0.3333$$

$$RStest : Conc4 : h = 0, p = 0.3355$$

#### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, Abstinence N = 6).

p-value for Control vs initial task of male: 0.38794.

kstest2 results: h=1, p=7.4300e-03, ks2stat=0.4091

Post-hoc analysis:

$$0.5\% : 5.3937e - 01, \quad 2\% : 3.3053e - 01, \quad 5\% : 4.3710e - 01, \quad 9\% : 2.8029e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.4238, ks2stat = 0.4091$   
 $RStest : Conc1 : h = 0, p = 0.5908$   
 $KStest2 : Conc2 : h = 0, p = 0.4238, ks2stat = 0.4091$   
 $RStest : Conc2 : h = 0, p = 0.2161$   
 $KStest2 : Conc3 : h = 0, p = 0.4238, ks2stat = 0.4091$   
 $RStest : Conc3 : h = 0, p = 0.5249$   
 $KStest2 : Conc4 : h = 0, p = 0.1106, ks2stat = 0.5606$   
 $RStest : Conc4 : h = 0, p = 0.1215$

### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	581128.0431	1	0	581128.0431	12.7578	0.0005
Condition	352607.5709	1	0	352607.5709	7.7409	0.0062
Concentration	4575.5728	3	0	1525.1909	0.0335	0.9917
Gender*Condition	6646.8434	1	0	6646.8434	0.1459	0.7031
Gender*Concentration	8228.0996	3	0	2742.6999	0.0602	0.9806
Condition*Concentration	5712.0473	3	0	1904.0158	0.0418	0.9886
Error	5784971.7033	127	0	45550.9583	NaN	NaN
Total	6780383.6044	139	0	NaN	NaN	NaN

## 9.7 Figure S.6h: Oxycodone I.V. vs Fraction of sigmoid

Correlation coefficient between amount of oxycodone administered and fraction of sigmoid in all sessions for each animal was determined by MATLAB 'corrcoef' function.

## 10 Supplemental Figure 7

### 10.1 Figure S.7b: Initial task Approach rate (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 12, Male N = 10).

Effect of concentration: d.f. = 3, F = 49.9905, p = 2.5457e-16.

Effect of gender: d.f. = 1, F = 0.5183, p = 0.4799.

kstest2 results: h=0, p=8.0438e-01, ks2stat=0.1333 (overall gender difference)

Post-hoc analysis:

0.5% :  $8.0114e - 01$ , 2% :  $8.8708e - 01$ , 5% :  $5.7254e - 01$ , 9% :  $5.0164e - 01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.8848, ks2stat = 0.2333$   
 $RStest : Conc1 : h = 0, p = 0.8621, zval = 0.1736$   
 $KStest2 : Conc2 : h = 0, p = 1.0000, ks2stat = 0.1167$   
 $RStest : Conc2 : h = 0, p = 1.0000, zval = -0.0000$   
 $KStest2 : Conc3 : h = 0, p = 0.9304, ks2stat = 0.2167$   
 $RStest : Conc3 : h = 0, p = 0.9467, zval = 0.0668$   
 $KStest2 : Conc4 : h = 0, p = 0.8848, ks2stat = 0.2333$   
 $RStest : Conc4 : h = 0, p = 1.0000, zval = -0.0000$

### Control vs Initial Task

#### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, Initial Task N = 12).

p-value for Control vs initial task of female: 0.17699.

kstest2 results: h=0, p=4.8027e-01, ks2stat=0.1667.

Post-hoc analysis:

0.5% :  $4.7801e - 01$ , 2% :  $8.2100e - 01$ , 5% :  $2.6400e - 02$ , 9% :  $9.4445e - 01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.1862, ks2stat = 0.4167$   
 $RStest : Conc1 : h = 0, p = 0.5008$   
 $KStest2 : Conc2 : h = 0, p = 0.0656, ks2stat = 0.5000$   
 $RStest : Conc2 : h = 0, p = 0.3827$   
 $KStest2 : Conc3 : h = 0, p = 0.1862, ks2stat = 0.4167$   
 $RStest : Conc3 : h = 0, p = 0.0526$   
 $KStest2 : Conc4 : h = 0, p = 0.4333, ks2stat = 0.3333$   
 $RStest : Conc4 : h = 0, p = 0.7708$

#### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, Initial Task N = 10).

p-value for Control vs initial task of male: 0.066116.

kstest2 results: h=0, p=6.6144e-01, ks2stat=0.1545

Post-hoc analysis:

0.5% :  $3.4193e - 01$ , 2% :  $2.3440e - 01$ , 5% :  $2.4745e - 02$ , 9% :  $3.3059e - 01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.2890, ks2stat = 0.4000$   
 $RStest : Conc1 : h = 0, p = 0.9153$   
 $KStest2 : Conc2 : h = 0, p = 0.6490, ks2stat = 0.3000$   
 $RStest : Conc2 : h = 0, p = 0.7219$   
 $KStest2 : Conc3 : h = 1, p = 0.0259, ks2stat = 0.6000$   
 $RStest : Conc3 : h = 1, p = 0.0150$   
 $KStest2 : Conc4 : h = 0, p = 0.2890, ks2stat = 0.4000$   
 $RStest : Conc4 : h = 0, p = 0.8039$

### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	0.0929	1	0	0.0929	2.8631	0.0925
Condition	0.1859	1	0	0.1859	5.7305	0.0178
Concentration	13.402	3	0	4.4673	137.6882	0
Gender*Condition	0.0067	1	0	0.0067	0.2063	0.6503
Gender*Concentration	0.0808	3	0	0.0269	0.8303	0.4789
Condition*Concentration	0.4846	3	0	0.1615	4.9791	0.0025
Error	5.4184	167	0	0.0324	NaN	NaN
Total	19.8036	179	0	NaN	NaN	NaN

## 10.2 Figure S.7c: Late task Approach rate (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 10, Male N = 10).

Effect of concentration: d.f. = 3, F = 65.1004, p = 6.1134e-18.

Effect of gender: d.f. = 1, F = 6.0131, p = 0.0246.

kstest2 results: h=0, p=3.6131e-01, ks2stat=0.2000 (overall gender difference)

Post-hoc analysis:

$$0.5\% : 8.8484e - 01, \quad 2\% : 1.0123e - 01, \quad 5\% : 7.5526e - 02, \quad 9\% : 3.3494e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$KStest2 : Conc1 : h = 0, p = 0.9748, ks2stat = 0.2000$$

$$RStest : Conc1 : h = 0, p = 0.5004, zval = 0.6739$$

$$KStest2 : Conc2 : h = 0, p = 0.3129, ks2stat = 0.4000$$

$$RStest : Conc2 : h = 0, p = 0.1315, zval = 1.5083$$

$$KStest2 : Conc3 : h = 0, p = 0.6751, ks2stat = 0.3000$$

$$RStest : Conc3 : h = 0, p = 0.1233, zval = 1.5411$$

$$KStest2 : Conc4 : h = 0, p = 0.9748, ks2stat = 0.2000$$

$$RStest : Conc4 : h = 0, p = 0.4201, zval = 0.8062$$

### Control vs Late Task

#### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, Late Task N = 10).

p-value for Control vs initial task of female: 0.024429.

kstest2 results: h=0, p=2.2658e-01, ks2stat=0.2167.

Post-hoc analysis:

$$0.5\% : 3.7745e - 01, \quad 2\% : 1.4453e - 01, \quad 5\% : 6.0921e - 02, \quad 9\% : 2.1423e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.5564, ks2stat = 0.3167$   
 $RStest : Conc1 : h = 0, p = 0.5960$   
 $KStest2 : Conc2 : h = 0, p = 0.0706, ks2stat = 0.5167$   
 $RStest : Conc2 : h = 0, p = 0.0703$   
 $KStest2 : Conc3 : h = 0, p = 0.1582, ks2stat = 0.4500$   
 $RStest : Conc3 : h = 0, p = 0.0688$   
 $KStest2 : Conc4 : h = 0, p = 0.0873, ks2stat = 0.5000$   
 $RStest : Conc4 : h = 0, p = 0.2595$

#### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, Late Task N = 10).

p-value for Control vs initial task of male: 0.2364.

kstest2 results: h=0, p=3.0854e-01, ks2stat=0.2045

Post-hoc analysis:

0.5% :  $5.0440e - 01$ , 2% :  $4.2998e - 01$ , 5% :  $2.9060e - 01$ , 9% :  $5.8461e - 01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.0978, ks2stat = 0.5000$  $RStest : Conc1 : h = 0, p = 0.3548$  $KStest2 : Conc2 : h = 0, p =$

#### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	0.2624	1	0	0.2624	10.4186	0.0015
Condition	0.1716	1	0	0.1716	6.8126	0.0099
Concentration	13.1391	3	0	4.3797	173.9008	0
Gender*Condition	0.0181	1	0	0.0181	0.7167	0.3985
Gender*Concentration	0.209	3	0	0.0697	2.7663	0.0437
Condition*Concentration	0.1103	3	0	0.0368	1.4593	0.2278
Error	4.0044	159	0	0.0252	NaN	NaN
Total	17.9639	171	0	NaN	NaN	NaN

#### Initial Task vs Late Task:

#### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	0.1824	1	0	0.1824	4.6943	0.0318
Condition	0.0001	1	0	0.0001	0.0013	0.971
Concentration	12.9611	3	0	4.3204	111.1738	0
Gender*Condition	0.0448	1	0	0.0448	1.1539	0.2844
Gender*Concentration	0.085	3	0	0.0283	0.7288	0.5363
Condition*Concentration	0.1284	3	0	0.0428	1.1015	0.3504
Error	6.0235	155	0	0.0389	NaN	NaN
Total	19.5583	167	0	NaN	NaN	NaN

### 10.3 Figure S.7d: Initial task Approach time (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 12, Male N = 10).

Effect of concentration: d.f. = 3,  $F = 3.0746$ ,  $p = 5.4017e-02$ .

Effect of gender: d.f. = 1,  $F = 0.7937$ ,  $p = 0.4073$ .

kstest2 results:  $h=0$ ,  $p=4.6263e-01$ ,  $ks2stat=0.2016$  (overall gender difference)

Post-hoc analysis:

0.5% :  $7.1363e-01$ , 2% :  $7.6787e-01$ , 5% :  $7.5464e-02$ , 9% :  $6.6465e-01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.2141, ks2stat = 0.5000$

$RStest : Conc1 : h = 0, p = 0.3462$

$KStest2 : Conc2 : h = 0, p = 0.3180, ks2stat = 0.5000$

$RStest : Conc2 : h = 0, p = 0.3701$

$KStest2 : Conc3 : h = 1, p = 0.0032, ks2stat = 0.7167$

$RStest : Conc3 : h = 1, p = 0.0192$

$KStest2 : Conc4 : h = 0, p = 0.2503, ks2stat = 0.4545$

$RStest : Conc4 : h = 0, p = 0.5360$

### Control vs Initial Task

#### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, Late Task N = 12).

p-value for Control vs initial task of female: 0.95393.

kstest2 results:  $h=0$ ,  $p=1.0029e-01$ ,  $ks2stat=0.2570$

Post-hoc analysis:

0.5% :  $6.0495e-01$ , 2% :  $7.3330e-02$ , 5% :  $1.0644e-02$ , 9% :  $6.9342e-01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.0876, ks2stat = 0.5091$

$RStest : Conc1 : h = 0, p = 0.5968$

$KStest2 : Conc2 : h = 0, p = 0.0799, ks2stat = 0.5833$

$RStest : Conc2 : h = 1, p = 0.0320$

$KStest2 : Conc3 : h = 0, p = 0.0656, ks2stat = 0.5000$

$RStest : Conc3 : h = 0, p = 0.0606$

$KStest2 : Conc4 : h = 0, p = 0.2812, ks2stat = 0.3864$

$RStest : Conc4 : h = 0, p = 0.3099$

#### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, Late Task N = 10).

p-value for Control vs initial task of male: 0.3337.

kstest2 results:  $h=0$ ,  $p=3.8605e-01$ ,  $ks2stat=0.2110$

Post-hoc analysis:

0.5% :  $7.3182e-01$ , 2% :  $1.6792e-01$ , 5% :  $9.4946e-01$ , 9% :  $6.1620e-01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.2290, ks2stat = 0.4848$   
 $RStest : Conc1 : h = 0, p = 0.2696$   
 $KStest2 : Conc2 : h = 0, p =$

### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	0.0057	1	0	0.0057	0.0008	0.9775
Condition	4.1585	1	0	4.1585	0.5848	0.4457
Concentration	213.9496	3	0	71.3165	10.0285	0
Gender*Condition	9.3398	1	0	9.3398	1.3134	0.2537
Gender*Concentration	27.986	3	0	9.3287	1.3118	0.2729
Condition*Concentration	9.7491	3	0	3.2497	0.457	0.7128
Error	1024.0377	144	0	7.1114	NaN	NaN
Total	1296.7682	156	0	NaN	NaN	NaN

### 10.4 Figure S.7e: Late task Approach time (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 10, Male N = 10).

Effect of concentration: d.f. = 3, F = 1.0838, p = 3.8602e-01.

Effect of gender: d.f. = 1, F = 0.1609, p = 0.7049.

kstest2 results: h=0, p=1.7336e-01, ks2stat=0.2745 (overall gender difference)

Post-hoc analysis:

$$0.5\% : 5.2868e - 01, \quad 2\% : 4.4209e - 01, \quad 5\% : 5.2319e - 01, \quad 9\% : 4.8906e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$KStest2 : Conc1 : h = 1, p = 0.0204, ks2stat = 0.8000$$

$$RStest : Conc1 : h = 1, p = 0.0303$$

$$KStest2 : Conc2 : h = 0, p = 0.5070, ks2stat = 0.4250$$

$$RStest : Conc2 : h = 0, p = 0.2844$$

$$KStest2 : Conc3 : h = 0, p = 0.4892, ks2stat = 0.3556$$

$$RStest : Conc3 : h = 0, p = 0.3562$$

$$KStest2 : Conc4 : h = 0, p = 0.1076, ks2stat = 0.5417$$

$$RStest : Conc4 : h = 1, p = 0.0274$$

### Control vs Late Task

#### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, Late Task N = 10).

p-value for Control vs initial task of female: 0.58585.

kstest2 results: h=0, p=2.9353e-01, ks2stat=0.2134

Post-hoc analysis:

$$0.5\% : 6.6412e - 01, \quad 2\% : 7.3010e - 01, \quad 5\% : 9.4083e - 02, \quad 9\% : 2.9966e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 0, p = 0.2503, ks2stat = 0.4545*  
*RStest : Conc1 : h = 0, p = 0.4111*  
*KStest2 : Conc2 : h = 0, p = 0.9978, ks2stat = 0.1667*  
*RStest : Conc2 : h = 0, p = 0.9692*  
*KStest2 : Conc3 : h = 0, p = 0.1582, ks2stat = 0.4500*  
*RStest : Conc3 : h = 0, p = 0.0698*  
*KStest2 : Conc4 : h = 0, p = 0.8520, ks2stat = 0.2500*  
*RStest : Conc4 : h = 0, p = 1.0000*

#### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, Late Task N = 10).

p-value for Control vs initial task of male: 0.74017.

kstest2 results: h=0, p=2.2511e-01, ks2stat=0.2487

Post-hoc analysis:

0.5% : 6.3673e - 01, 2% : 4.9689e - 01, 5% : 8.2142e - 01, 9% : 5.9077e - 01

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 0, p = 0.1019, ks2stat = 0.6000*  
*RStest : Conc1 : h = 0, p = 0.1149*  
*KStest2 : Conc2 : h = 0, p = 0.5402, ks2stat = 0.4000*  
*RStest : Conc2 : h = 0, p = 0.3710*  
*KStest2 : Conc3 : h = 0, p = 0.4114, ks2stat = 0.3778*  
*RStest : Conc3 : h = 0, p = 0.4470*  
*KStest2 : Conc4 : h = 0, p = 0.2147, ks2stat = 0.4545*  
*RStest : Conc4 : h = 0, p = 0.1518*

#### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	23.2272	1	0	23.2272	4.5491	0.0347
Condition	0.258	1	0	0.258	0.0505	0.8225
Concentration	255.2297	3	0	85.0766	16.6626	0
Gender*Condition	3.2778	1	0	3.2778	0.642	0.4244
Gender*Concentration	28.1551	3	0	9.385	1.8381	0.1431
Condition*Concentration	11.3002	3	0	3.7667	0.7377	0.5313
Error	699.4998	137	0	5.1058	NaN	NaN
Total	1000.7338	149	0	NaN	NaN	NaN

#### 10.5 Figure S.7f: Initial task Number of high sp. runs (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 12, Male N = 10).

Effect of concentration: d.f. = 3, F = 1.8924, p = 1.4050e-01.

Effect of gender: d.f. = 1, F = 0.8500, p = 0.3675.

kstest2 results: h=0, p=1.2139e-01, ks2stat=0.2458 (overall gender difference)



Post-hoc analysis:

0.5% :  $7.7450e - 01$ , 2% :  $9.1269e - 01$ , 5% :  $3.6064e - 03$ , 9% :  $5.6181e - 01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 :  $h = 0, p = 0.9304, ks2stat = 0.2167$*

*RStest : Conc1 :  $h = 0, p = 0.7667$*

*KStest2 : Conc2 :  $h = 0, p = 0.8286, ks2stat = 0.2500$*

*RStest : Conc2 :  $h = 0, p = 0.7667$*

*KStest2 : Conc3 :  $h = 1, p = 0.0101, ks2stat = 0.6500$*

*RStest : Conc3 :  $h = 1, p = 0.0111$*

*KStest2 : Conc4 :  $h = 0, p = 0.1072, ks2stat = 0.4833$*

*RStest : Conc4 :  $h = 0, p = 0.3734$*

### Control vs Initial Task

#### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, Initial Task N = 12).

p-value for Control vs initial task of female: 0.013.

kstest2 results:  $h=1, p=4.8054e-02, ks2stat=0.2708$

Post-hoc analysis:

0.5% :  $8.0719e - 02$ , 2% :  $1.3341e - 02$ , 5% :  $3.6748e - 02$ , 9% :  $7.0275e - 01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 :  $h = 0, p = 0.0656, ks2stat = 0.5000$*

*RStest : Conc1 :  $h = 1, p = 0.0351$*

*KStest2 : Conc2 :  $h = 1, p = 0.0191, ks2stat = 0.5833$*

*RStest : Conc2 :  $h = 1, p = 0.0086$*

*KStest2 : Conc3 :  $h = 0, p = 0.0656, ks2stat = 0.5000$*

*RStest : Conc3 :  $h = 1, p = 0.0262$*

*KStest2 : Conc4 :  $h = 0, p = 0.1862, ks2stat = 0.4167$*

*RStest : Conc4 :  $h = 0, p = 0.5067$*

#### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, Initial Task N = 10).

p-value for Control vs initial task of male: 0.49907.

kstest2 results:  $h=0, p=5.7150e-01, ks2stat=0.1659$

Post-hoc analysis:

0.5% :  $8.6648e - 01$ , 2% :  $7.4849e - 01$ , 5% :  $1.6437e - 02$ , 9% :  $7.9965e - 01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.2646, ks2stat = 0.4091$   
 $RStest : Conc1 : h = 0, p = 0.5035$   
 $KStest2 : Conc2 : h = 0, p = 0.6114, ks2stat = 0.3091$   
 $RStest : Conc2 : h = 0, p = 0.6985$   
 $KStest2 : Conc3 : h = 1, p = 0.0198, ks2stat = 0.6182$   
 $RStest : Conc3 : h = 1, p = 0.0183$   
 $KStest2 : Conc4 : h = 0, p = 0.8290, ks2stat = 0.2545$   
 $RStest : Conc4 : h = 0, p = 0.9719$

### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	380.4236	1	0	380.4236	13.5543	0.0003
Condition	258.1331	1	0	258.1331	9.1971	0.0028
Concentration	336.9166	3	0	112.3055	4.0014	0.0088
Gender*Condition	73.4858	1	0	73.4858	2.6183	0.1075
Gender*Concentration	76.5402	3	0	25.5134	0.909	0.438
Condition*Concentration	88.7222	3	0	29.5741	1.0537	0.3704
Error	4687.1338	167	0	28.0667	NaN	NaN
Total	5899.4658	179	0	NaN	NaN	NaN

## 10.6 Figure S.7g: Late task Number of high sp. runs (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 10, Male N = 10).

Effect of concentration: d.f. = 3, F = 0.5016, p = 6.8275e-01.

Effect of gender: d.f. = 1, F = 1.8180, p = 0.1943.

kstest2 results: h=0, p=1.3925e-01, ks2stat=0.2500 (overall gender difference)

Post-hoc analysis:

0.5% :  $4.4173e - 01$ , 2% :  $1.5443e - 01$ , 5% :  $4.3851e - 01$ , 9% :  $8.8666e - 02$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.3129, ks2stat = 0.4000$   
 $RStest : Conc1 : h = 0, p = 0.3075$   
 $KStest2 : Conc2 : h = 0, p = 0.6751, ks2stat = 0.3000$   
 $RStest : Conc2 : h = 0, p = 0.1620$   
 $KStest2 : Conc3 : h = 0, p = 0.6751, ks2stat = 0.3000$   
 $RStest : Conc3 : h = 0, p = 0.9698$   
 $KStest2 : Conc4 : h = 0, p = 0.1108, ks2stat = 0.5000$   
 $RStest : Conc4 : h = 0, p = 0.0890$

### Control vs Late Task

#### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, Late Task N = 10).

p-value for Control vs late task of female: 0.062741.

kstest2 results: h=0, p=1.6019e-01, ks2stat=0.2333

Post-hoc analysis:

0.5% :  $1.4081e-01$ , 2% :  $8.1374e-03$ , 5% :  $1.3291e-02$ , 9% :  $4.2351e-01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 0, p = 0.6259, ks2stat = 0.3000*  
*RStest : Conc1 : h = 0, p = 0.3390*  
*KStest2 : Conc2 : h = 1, p = 0.0076, ks2stat = 0.6667*  
*RStest : Conc2 : h = 1, p = 0.0062*  
*KStest2 : Conc3 : h = 0, p = 0.1902, ks2stat = 0.4333*  
*RStest : Conc3 : h = 1, p = 0.0321*  
*KStest2 : Conc4 : h = 0, p = 0.2270, ks2stat = 0.4167*  
*RStest : Conc4 : h = 0, p = 0.2485*

### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, Late Task N = 10).

p-value for Control vs late task of male: 0.36436.

kstest2 results: h=0, p=1.1714e-01, ks2stat=0.2523

Post-hoc analysis:

0.5% :  $6.9166e-01$ , 2% :  $5.0927e-02$ , 5% :  $5.4199e-01$ , 9% :  $5.5656e-01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 0, p = 0.2646, ks2stat = 0.4091*  
*RStest : Conc1 : h = 0, p = 0.4597*  
*KStest2 : Conc2 : h = 0, p = 0.0008, ks2stat = 0.9777*  
*RStest : Conc2 : h = 0, p = 0.9777*  
*KStest2 : Conc3 : h = 0, p = 0.967, ks2stat = 0.3619*  
*RStest : Conc3 : h = 0, p = 0.3619*  
*KStest2 : Conc4 : h = 0, p = 0.3619, ks2stat = 0.3619*  
*RStest : Conc4 : h = 0, p = 0.3619*

### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	744.2571	1	0	744.2571	21.8951	0
Condition	306.8216	1	0	306.8216	9.0263	0.0031
Concentration	117.5248	3	0	39.1749	1.1525	0.3298
Gender*Condition	0.0267	1	0	0.0267	0.0008	0.9777
Gender*Concentration	8.8943	3	0	2.9648	0.0872	0.967
Condition*Concentration	109.5021	3	0	36.5007	1.0738	0.3619
Error	5404.726	159	0	33.992	NaN	NaN
Total	6729.4241	171	0	NaN	NaN	NaN

## 10.7 Figure S.7h: Initial task Distance traveled (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 12, Male N = 10).

Effect of concentration: d.f. = 3, F = 2.4366, p = 7.3371e-02.

Effect of gender: d.f. = 1, F = 17.9034, p = 0.0004.

kstest2 results: h=1, p=2.4759e-06, ks2stat=0.5417 (overall gender difference)

Post-hoc analysis:

0.5% :  $1.2714e-02$ , 2% :  $5.9126e-02$ , 5% :  $8.5187e-04$ , 9% :  $1.1225e-03$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 1, p = 0.0220, ks2stat = 0.6000$   
 $RStest : Conc1 : h = 1, p = 0.0092$   
 $KStest2 : Conc2 : h = 0, p = 0.0567, ks2stat = 0.5333$   
 $RStest : Conc2 : h = 0, p = 0.0806$   
 $KStest2 : Conc3 : h = 1, p = 0.0076, ks2stat = 0.6667$   
 $RStest : Conc3 : h = 1, p = 0.0022$   
 $KStest2 : Conc4 : h = 1, p = 0.0076, ks2stat = 0.6667$   
 $RStest : Conc4 : h = 1, p = 0.0041$

### Control vs Initial Task

#### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, Initial Task N = 12).

p-value for Control vs initial task of female: 0.01429.

kstest2 results: h=1, p=4.6080e-05, ks2stat=0.4583

Post-hoc analysis:

0.5% :  $6.7266e - 02$ , 2% :  $1.6070e - 02$ , 5% :  $3.1394e - 01$ , 9% :  $9.0362e - 03$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.0656, ks2stat = 0.5000$   
 $RStest : Conc1 : h = 0, p = 0.0999$   
 $KStest2 : Conc2 : h = 1, p = 0.0191, ks2stat = 0.5833$   
 $RStest : Conc2 : h = 1, p = 0.0304$   
 $KStest2 : Conc3 : h = 0, p = 0.0656, ks2stat = 0.5000$   
 $RStest : Conc3 : h = 0, p = 0.1749$   
 $KStest2 : Conc4 : h = 0, p = 0.0656, ks2stat = 0.5000$   
 $RStest : Conc4 : h = 1, p = 0.0086$

#### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, Initial Task N = 10).

p-value for Control vs initial task of male: 0.013586.

kstest2 results: h=1, p=1.3560e-03, ks2stat=0.4045

Post-hoc analysis:

0.5% :  $1.3573e - 02$ , 2% :  $3.4304e - 02$ , 5% :  $4.5088e - 02$ , 9% :  $5.5697e - 02$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$KStest2 : Conc1 : h = 0, p = 0.0782, ks2stat = 0.5182$   
 $RStest : Conc1 : h = 1, p = 0.0221$   
 $KStest2 : Conc2 : h = 1, p = 0.0259, ks2stat = 0.6000$   
 $RStest : Conc2 : h = 1, p = 0.0265$   
 $KStest2 : Conc3 : h = 0, p = 0.2006, ks2stat = 0.4364$   
 $RStest : Conc3 : h = 0, p = 0.0528$   
 $KStest2 : Conc4 : h = 0, p = 0.2418, ks2stat = 0.4182$   
 $RStest : Conc4 : h = 0, p = 0.1300$

### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	17.7228	1	0	17.7228	75.0599	0
Condition	8.437	1	0	8.437	35.7328	0
Concentration	1.1351	3	0	0.3784	1.6025	0.1907
Gender*Condition	0.0679	1	0	0.0679	0.2874	0.5926
Gender*Concentration	0.6284	3	0	0.2095	0.8872	0.4491
Condition*Concentration	0.6088	3	0	0.2029	0.8595	0.4634
Error	39.4312	167	0	0.2361	NaN	NaN
Total	68.6863	179	0	NaN	NaN	NaN

### 10.8 Figure S.7i: Late task Distance traveled (FvM)

Statistical significance was determined by Repeated measures analysis of variance. (Female N = 10, Male N = 10).

Effect of concentration: d.f. = 3, F = 0.7077, p = 5.5161e-01.

Effect of gender: d.f. = 1, F = 4.6430, p = 0.0450.

kstest2 results: h=1, p=1.0793e-02, ks2stat=0.3500 (overall gender difference)

Post-hoc analysis:

$$0.5\% : 9.3255e - 02, \quad 2\% : 8.9902e - 02, \quad 5\% : 5.4953e - 01, \quad 9\% : 6.7305e - 03$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

$$KStest2 : Conc1 : h = 1, p = 0.0310, ks2stat = 0.6000$$

$$RStest : Conc1 : h = 0, p = 0.0890$$

$$KStest2 : Conc2 : h = 0, p = 0.3129, ks2stat = 0.4000$$

$$RStest : Conc2 : h = 0, p = 0.1212$$

$$KStest2 : Conc3 : h = 0, p = 0.3129, ks2stat = 0.4000$$

$$RStest : Conc3 : h = 0, p = 0.6232$$

$$KStest2 : Conc4 : h = 1, p = 0.0069, ks2stat = 0.7000$$

$$RStest : Conc4 : h = 1, p = 0.0113$$

### Control vs Late Task

#### Female:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 12, Late Task N = 10).

p-value for Control vs late task of female: 0.72859.

kstest2 results: h=0, p=3.6205e-01, ks2stat=0.1917

Post-hoc analysis:

$$0.5\% : 8.6636e - 01, \quad 2\% : 5.2765e - 01, \quad 5\% : 4.3035e - 01, \quad 9\% : 2.4643e - 01$$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 0, p = 0.7647, ks2stat = 0.2667*  
*RStest : Conc1 : h = 0, p = 0.6682*  
*KStest2 : Conc2 : h = 0, p = 0.6259, ks2stat = 0.3000*  
*RStest : Conc2 : h = 0, p = 0.5310*  
*KStest2 : Conc3 : h = 0, p = 0.4896, ks2stat = 0.3333*  
*RStest : Conc3 : h = 0, p = 0.5752*  
*KStest2 : Conc4 : h = 0, p = 0.3689, ks2stat = 0.3667*  
*RStest : Conc4 : h = 0, p = 0.1985*

#### Male:

Statistical significance was determined by Repeated measures analysis of variance. (Control N = 11, Late Task N = 10).

p-value for Control vs late task of male: 0.13682.

kstest2 results: h=1, p=1.1240e-02, ks2stat=0.3409

Post-hoc analysis:

0.5% :  $9.0183e - 02$ , 2% :  $5.1266e - 01$ , 5% :  $9.7800e - 02$ , 9% :  $2.6146e - 01$

KStest2 and Wilcoxon rank sum test Results (complementary to post-hoc analysis)

*KStest2 : Conc1 : h = 0, p = 0.0876, ks2stat = 0.5091*  
*RStest : Conc1 : h = 0, p = 0.0845*  
*KStest2 : Conc2 : h = 0, p = 0.2890, ks2stat = 0.4000*  
*RStest : Conc2 : h = 0, p = 0.5035*  
*KStest2 : Conc3 : h = 0, p = 0.0978, ks2stat = 0.5000*  
*RStest : Conc3 : h = 0, p = 0.2178*  
*KStest2 : Conc4 : h = 0, p = 0.5742, ks2stat = 0.3182*  
*RStest : Conc4 : h = 0, p = 0.4181*

#### 3-way ANOVA Results:

Source	Sum Sq.	d.f.	Singular?	Mean Sq.	F	Prob>F
Gender	10.6559	1	0	10.6559	46.8601	0
Condition	1.0952	1	0	1.0952	4.8163	0.0296
Concentration	0.376	3	0	0.1253	0.5512	0.6481
Gender*Condition	0.3553	1	0	0.3553	1.5624	0.2131
Gender*Concentration	0.2714	3	0	0.0905	0.3978	0.7548
Condition*Concentration	0.1164	3	0	0.0388	0.1706	0.9161
Error	36.1564	159	0	0.2274	NaN	NaN
Total	49.1756	171	0	NaN	NaN	NaN

#### 10.9 Figure S.7j: Fraction of sigmoid (Control vs Alcohol)

Statistical significance was determined by one-way analysis of variance. (Female Control = 10, Male Control = 10, Female Late task = 10, Male Late task = 10)

Significance of difference between the groups: d.f. = 3, F = 2.4814, p = 0.0766.

Post-hoc analysis by Tukey's HSD method:

Female Control and Male Control: 0.8723

Female Control and Female Late task: 0.9123  
Male Control and Male Late task: 0.0579

### **10.10 Figure S.7n: Euclidean distance vs Probability**

Statistical significance was determined by computing the p-value through a two-sample t-test, using MATLAB's `ttest2` function, performed on individual rats' probabilities from the beginning of their experimentation from the end of their experimentation.

$p = 0.012928$