

Supplementary Figure 1, related to Figure 1: A novel task for assessment of single individual forelimb movements. **A)** Number of lever presses/minute. **B)** Number of performed sequences/minute. **C)** Fano Factor of the number of presses/sequence **D)** Fano Factor of the average velocity of lever press. Details on Supplementary table 2.

Supplementary Figure 2, related to Figure 1: A novel task for assessment of single individual forelimb movements. **A)** Frames corresponding to the moment of lever press were identified for 5 specific session of the training schedule (Training days – T6, T8, T13 and T18 and Performance session – P23). Sixteen (16) randomly selected frames corresponding to 16 lever presses were subsampled and visually inspected to assess the use of the correct forelimb. Data from one example animal is provided. **B)** Data from the 8 mice is summarized. In the last sessions near all presses (97.66% +- 2.34) were performed by the correct forelimb.

Supplementary Figure 3, related to Figure 2, 3 and 4: Mice perform the task using either the ipsi and contralateral forelimbs. Behavioral results from a group of 6 mice. Data from sessions included in analysis in Figure 2 and Figure 3. Statistical details on Supplementary Table 2. **A)** Total number of presses/session, **B)** % of sequences composed by more than one lever press - Inset % non isolated lever presses **C)** Number of Presses/Sequence. **D)** Histogram of the distribution of number of presses/sequence for ipsi and contralateral movements for one example animal (left) and for all animals across one day (right). **E)** Number of Rewards/Session **F)** % of rewarded Sequences. **G)** InterPress Intervals. **H)** Histogram of the distribution of IPIs for ipsi and contralateral movements for one example animal (left) and for all animals across one day (right) **I)** Fano Factor of InterPress Intervals **J)** Number of sequences performed/minute **K)** Number of rewards obtained/minute.

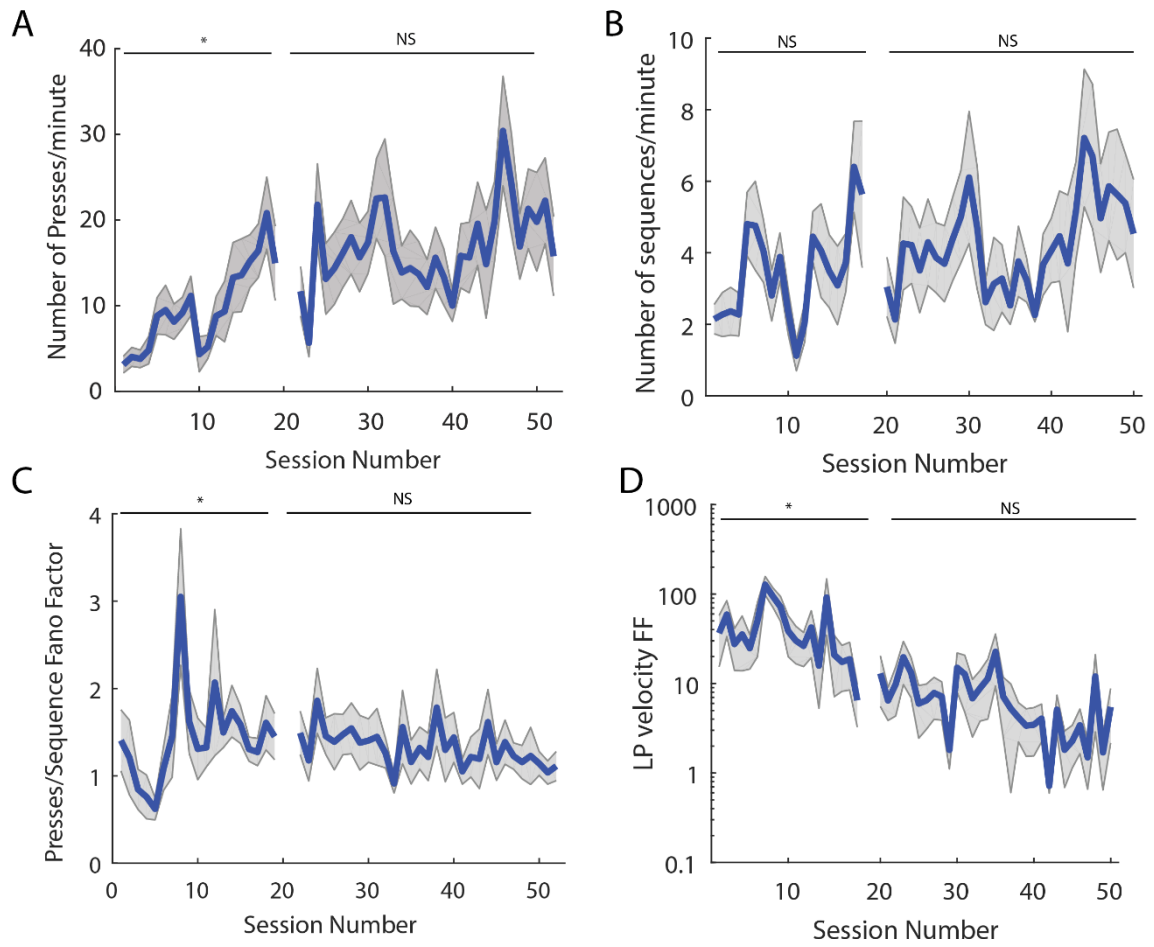
Supplementary Figure 4, related to Figure 2: Neurons are more commonly modulated by only one event (movement or reward) than the two events (Left: 51,47 \pm 5.83 vs. 4.86 \pm 2.34, $t=7.7248$, $df=5$, $p<0.001$; Right: 62,84 \pm 12,50 vs 5.22 \pm 1.86, $t=4.2413$, $df=5$, $p=0.0082$)

Supplementary Figure 5, related to Figure 2: Activity before movement onset is more common than during execution **A)** Number of neurons whose modulation started before movement sequence initiation (compare with Figure 2) and during sequence execution. Two-way repeated-measures ANOVA; main effect before/after $F(1,5)=20.25$, $p=0.0064$; main effect side $F(1,5)=0.9812$, $p=0.3674$; interaction effect $F(1,5)=0.003$, $P=0.9598$ **B)** Example of matched ROIs aligned to first lever press when action is performed by contralateral and ipsilateral forelimb.

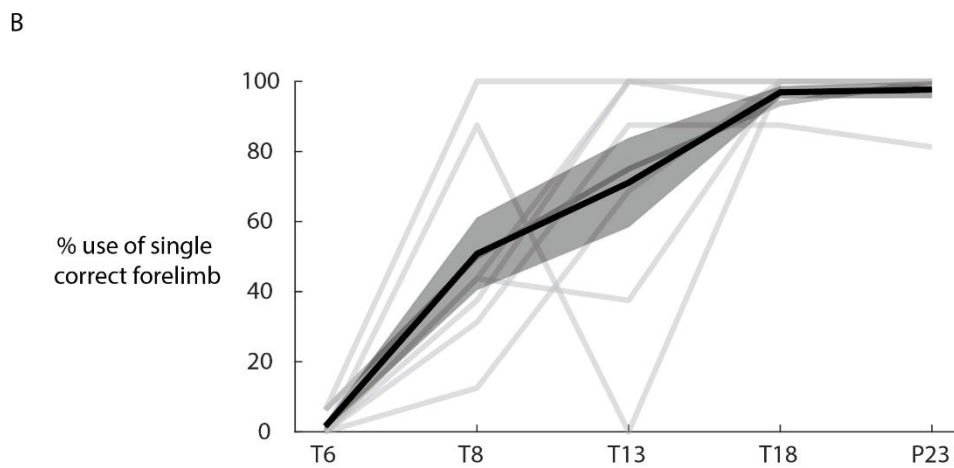
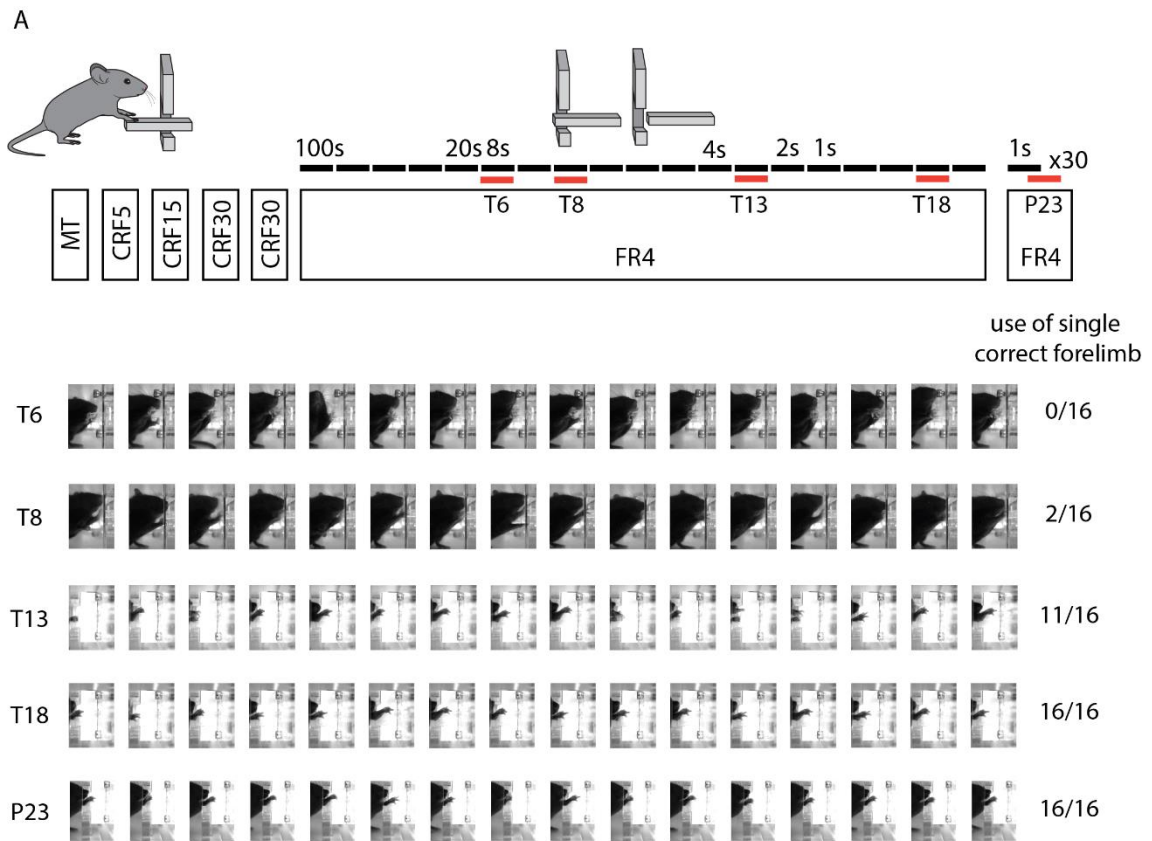
Supplementary Figure 6, related to Figure 4: Overlap between reward-modulated neurons and movement initiation neurons is minimal and lower than expected by random allocation. Monte Carlo simulations (10,000 samples) were used to generate a distribution of the number of overlapping neurons for first press and reward, assuming random assignment. Red line denote the lower margin of the one-sided 95% confidence interval of this simulation (upper limit is $+\infty$). Dashed line represents the number of overlapping neurons found in our experiments.

Supplementary Figure 7, related to Figure 5: Mice still solve the task using the forelimb contralateral to 6-OHDA lesion. **A)** Still images from randomly selected lever presses of an example 6-OHDA treated mouse. Sixteen (16) randomly selected lever presses are used as an example in the 4 conditions (ipsi/contralateral forelimb and before/after 6-OHDA lesion). The mouse used the experiment-intended forelimb in all situations. **B)** For each condition and each animal 16 stills from randomly selected lever presses were visually inspected to assess the use of the correct. Two mice performed

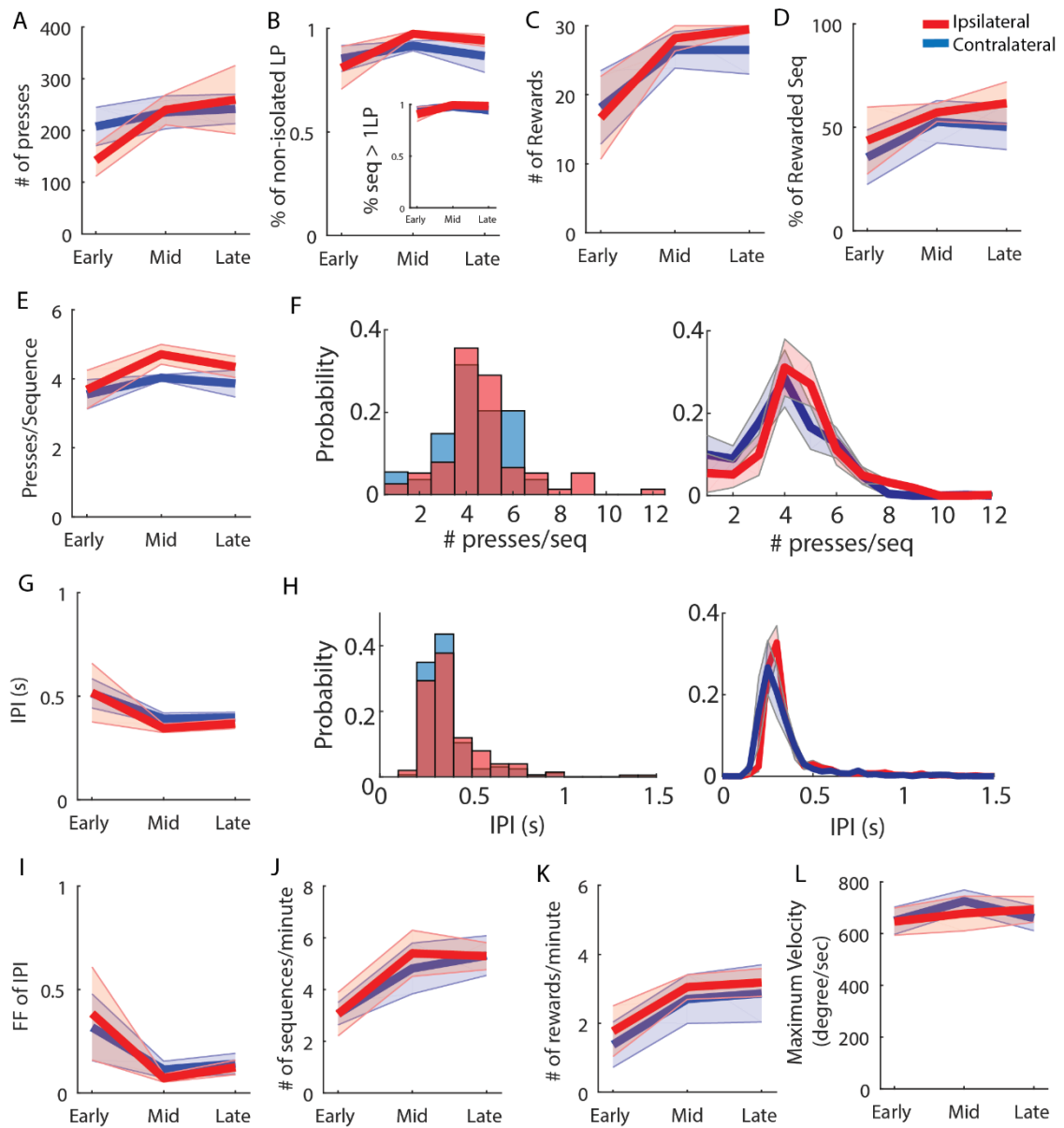
1/16 (6.25%) of the inspected lever presses/condition with the incorrect forelimb (one 6-OHDA treated mouse in the contralateral forelimb after lesion and one saline treated mouse in the ipsilateral forelimb before). Percent of usage of the correct forelimb did not significantly change after 6-OHDA lesion (Contra: 100% \pm 0% to 99.21% \pm 0.78; Ipsi: 100% \pm 0 to 100% \pm 0) or saline injection (Contra: 100% \pm 0% to 100% \pm 0; Ipsi: 98.96% \pm 0.90 to 100% \pm 0). **C)** The two situations with incorrect forelimb used are represented on the right images. An example of the same mouse using the correct forelimb is provided for comparison (left).



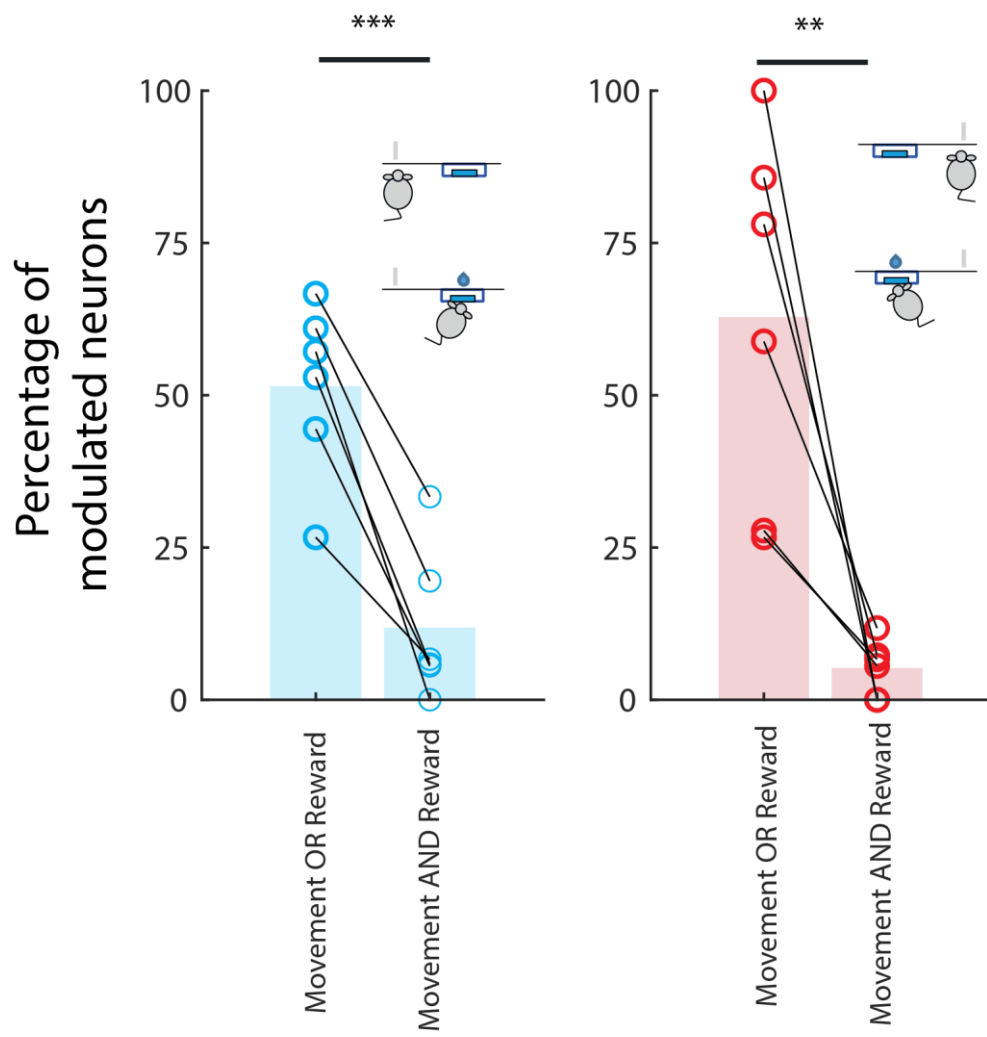
Supplementary Figure 1, related to Figure 1



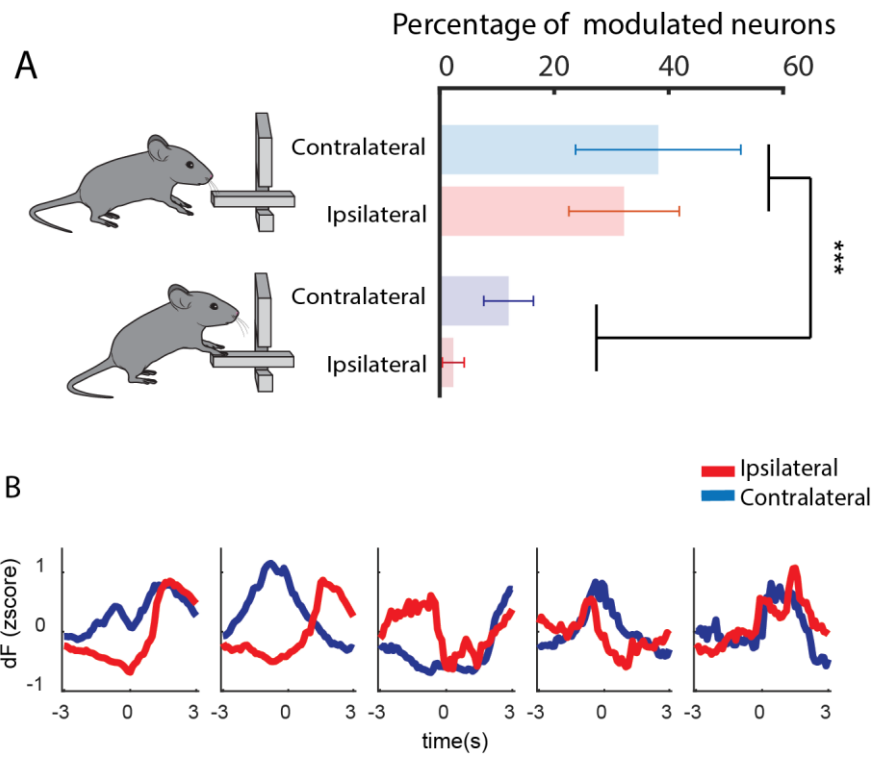
Supplementary Figure 2, related to Figure 1



Supplementary Figure 3, related to Figure 2, 3 and 4

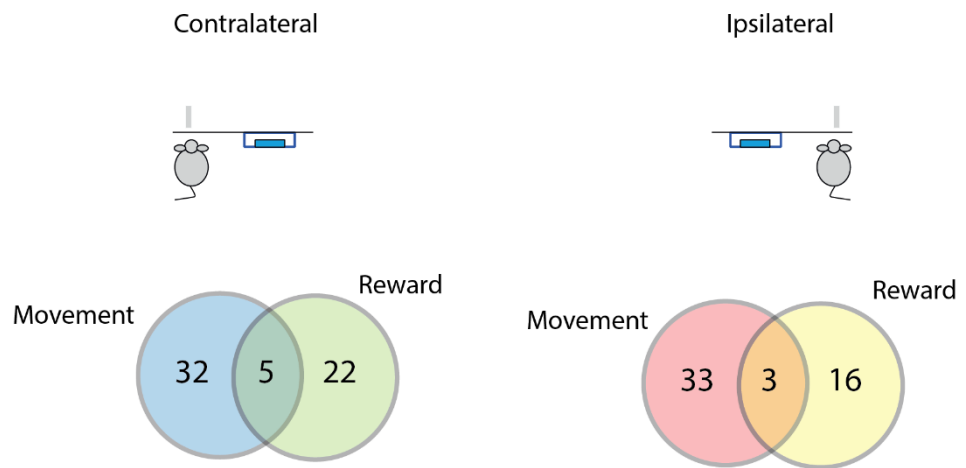


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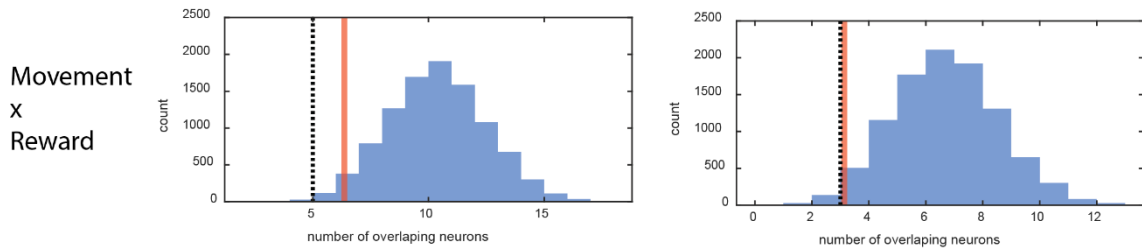


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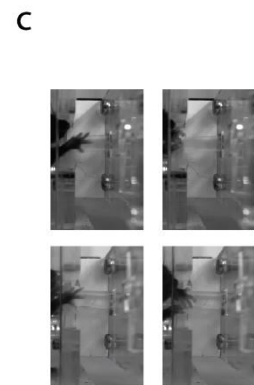
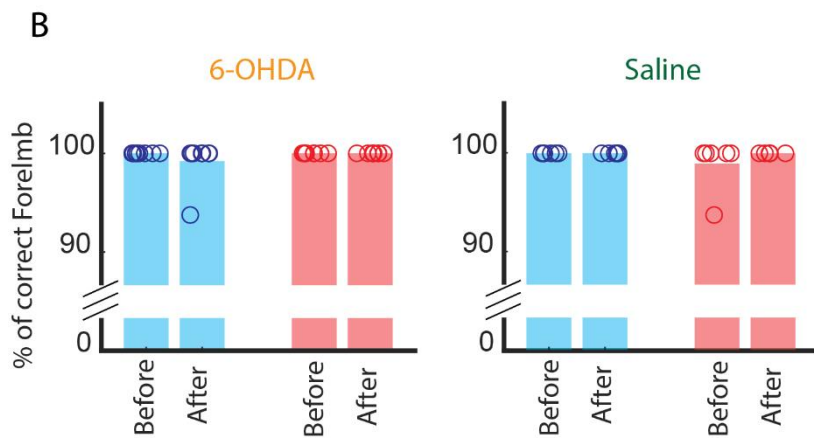
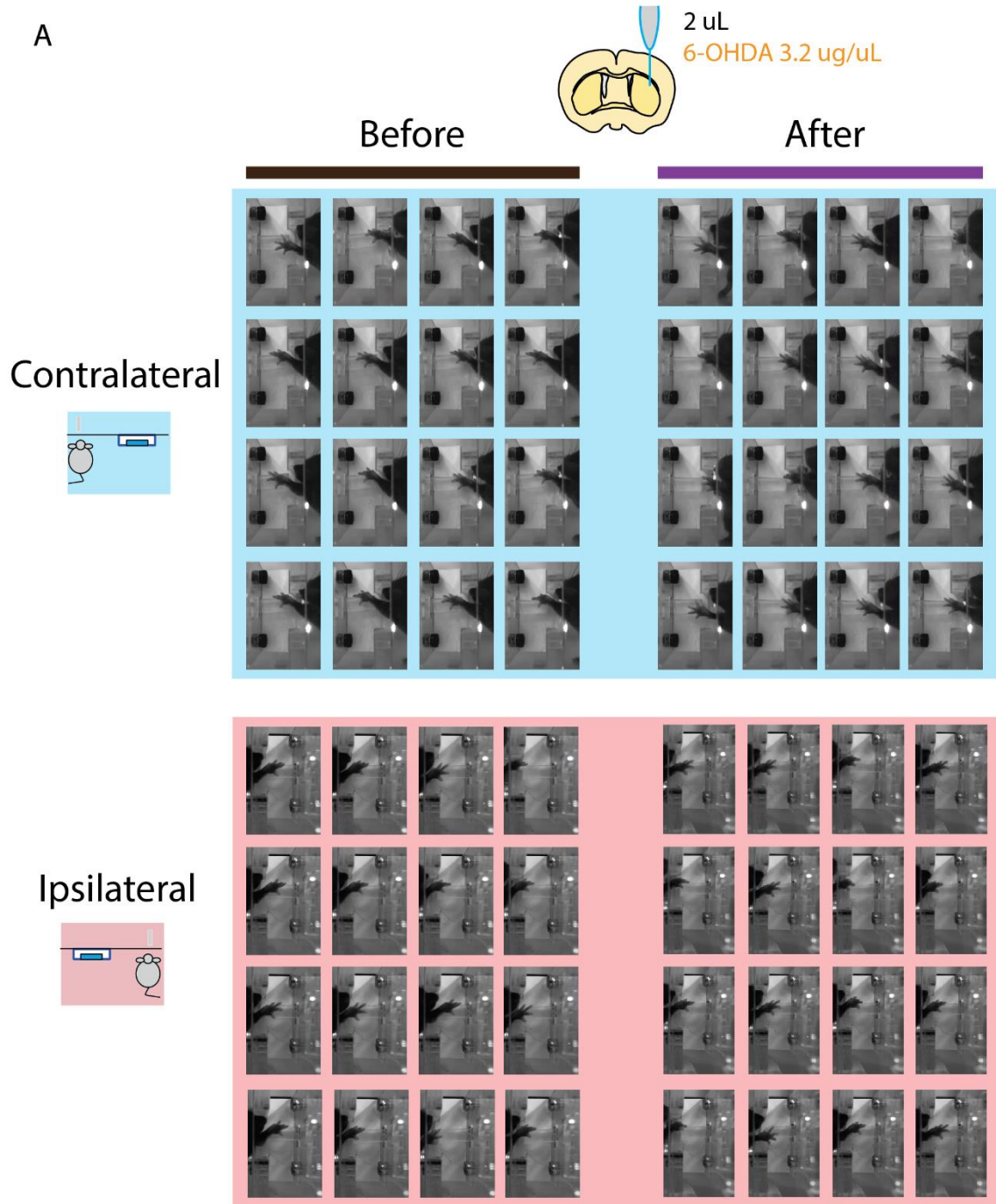
A



B



Supplementary Figure 6, related to Figure 4



Supplementary Figure 7, related to Figure 5

Supplementary Movie 1, related to Figure 1. Mice learn to perform sequences of Lever Pressing with only one forepaw. Simultaneous display of the top and side camera on real time. The animal develops a stereotyped behavior going from the magazine to the lever, pressing a few times and then returning to consume the reinforce.

Supplementary Movie 2, related to Figure 1. Mice learn to perform sequences of Lever Pressing with only one forepaw. Low-speed video (x0.2) of press sequences present in Supplementary Movie 1.

Supplementary Table 1: Detailed statistical analysis

Fig	Sample size (n)	Statistical tests	Value
1B	Wild-type (n=8)	One-way repeated measures ANOVA	Learning: ** F (3,563, 24,94) = 4,514 p=0.0086
			Performance: F (4,955, 34,68) = 1,174 p=0.3415
1C	Wild-type (n=8)	Mixed Effects	Learning: **** F (19, 102) = 8,643, p<0.0001 Learning Inset: **** F (19, 102) = 9,299, p<0.0001
			Learning: F (29, 191) = 1,077, p=0.3686 Learning Inset: F (29, 191) = 1,172, p=0.2610
1D	Wild-type (n=8)	Mixed Effect	F (49, 297) = 4,038, p<0.0001
1E	Wild-type (n=8)	Mixed Effect	L: **** F (19, 109) = 3,269 p<0.0001
			P: F (29, 195) = 1,151, p=0.2817
		One sample t-test (vs. 4)	t7=0.8947, p=0.4007
1I	Wild-type (n=8)	Mixed Effect	L: ** F (19, 106) = 2,148, p=0.0075
			P: F (29, 193) = 0.9681, p=0.5179
		One sample t-test (vs. 1/3)	t7=0.1401, p=0.8926
1J	Wild-type (n=8)	Mixed Effect	L: F (19, 107) = 0.7995, p=0.7031
			F (29, 194) = 0.9138, p=0.5971
1K	Wild-type (n=8)	Mixed Effect	L: **** F (19, 107) = 3,520. p<0.0001
			P: F (29, 194) = 0.8456, p=0.8456
2J	% of Positively modulated neurons (n=6)	Paired t-test	t=0.928, df=5, p=0.8021
2K	Positively	Unpaired t-test	t=3,808, df=68, **** p<0.0001

	modulated neurons: Contra: n=37 Ipsi: n=33		
3A	Positively modulated neurons. Contra: n=37: Ipsi: n=33	Paired t-test	Contra: **** t=4,4930. df=36, p<0.0001 Ipsi: t=0.7195, df=32, p=0.4771
3B	ROIs correlation n=114	Paired t-test	**** t=14,66, df=113, p<0.0001
3C1	Low Vigor trials, n=19 High Vigor trials, n=42	Unpaired t-test	* t=2.411, df=59, p=0.0190
3C2	Low Vigor trials, n=18 High Vigor trials, n=36	Unpaired t-test	* t=2.572, df=52, p=0.0130
3C3	Low Vigor trials, n=21 High Vigor trials, n=26	Unpaired t-test	** t=2.990. df=45, p=0.0045
3C4	Low Vigor trials, n=72 High Vigor trials, n=90	Unpaired t-test	*** t=3.250. df=160. p=0.0014
3D	Vigor modulated neurons.	Fisher Exact test	Contra: n=8/37: Ipsi: n=3/33; p=0.1960 Positive: Contra: n=5/37: Ipsi: n=2/33; p=0.4342 Negative: Contra: n=3/37: Ipsi: n=1/33; p=0.6165
3E	Positively modulated neurons. Contra: n=37: Ipsi: n=33	Paired t-test	* Contra: t=2.3095, df=36, p=0.02680 Ipsi: t=1.1997, df=32, p=0.2390
4C	% of Positively modulated neurons (n=6)	Paired t-test	t=0.2668, df=5, p=0.8003
4F Left	% of Positively modulated neurons (n=6)	Paired t-test	t=0.1010. df=5, p=0.9235
4F	Positively	Unpaired t-test	t=0.7189, df=44, p=0.4760

Right	modulated neurons Contra: n=27 Ipsi: n=19		
4G Left	% of Positively modulated neurons (n=6)	Paired t-test	t=0.2251, df=5, p=0.8308
4G Right	Positively modulated neurons Contra: n=12 Ipsi: n=22	Unpaired t-test	** t=3,3153 , df=32, p=0.0035
5C left	Presses/sequence (n=8)	Repeated measures two-way ANOVA	**** Time: F (1, 7) = 68.90 P<0.0001 Forelimb: F (1, 7) = 4.704 p=0.0667 * Time x Forelimb: F (1, 7) = 11,11 p=0.0125 Sidak's multiple comparison test *** Contralateral p=0.0005 Ipsilateral p=0.1380
5C right	Normalized presses/sequence (n=8)	Paired t-test	** t=3,759, df=7 p=0.0071
		One sample t-test	**** Contralateral: t=11.07, df=7 p<0.0001 Ipsilateral: t=2.281, df=7 p=0.0565
5D left	Presses/sequence (n=6)	Repeated measures two-way ANOVA	* Time: F (1, 5) = 7.704 p=0.0391 Forelimb: F (1, 5) = 2.007 p=0.2157 Time x Forelimb: F (1, 5) = 0.01041 p=0.9227
5D right	Normalized presses/sequence (n=6)	Paired t-test	t=0.4441, df=5, p=0.6755
5E left	% of Long sequences (n=8)	Repeated measures two-way ANOVA	*** Time: F (1, 7) = 30.12 p=0.0009 Forelimb: F (1, 7) = 2.087 p=0.1918 *** Time x Forelimb: F (1, 7) = 32.45 p=0.0007 Sidak's multiple comparison test *** Contralateral p=0.0003 Ipsilateral p=0.9725
5E right	Change in long sequences (n=8)	Paired t-test	** t=4,126, df=7 p=0.0044
		One sample t-test	**** Contralateral: t=15,46, df=7 p<0.0001 Ipsilateral: t=0.2100. df=7 p=0.8397
5F left	% of Long sequences (n=6)	Repeated measures two-way ANOVA	Time: F (1, 5) = 4.911 p=0.0775 Forelimb: F (1, 5) = 0.8281 p=0.4046 Time x Forelimb: F (1, 5) = 0.003268 p=0.9566
5F	Change in long	Paired t-test	t=0.5099, df=5 p=0.6319

right	sequences (n=6)		
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Supplementary Table 2: Related to Supplementary Figure 1

Fig	Sample size (n)	Statistical tests	Value
A	Wild-type (n=8)	Repeated Measures ANOVA	* L: F (2,443, 17,10) = 4.001, p=0.0311 P: F (3,999, 27,99) = 2.042, P=0.1156
B	Wild-type (n=8)	Repeated Measures ANOVA	L: F (3,302, 23,11) = 2.349, P=0.0939 P: F (3,561, 24,93) = 1.984 P=0.1340
C	Wild-type (n=8)	Mixed Effect	* L: F (19, 115) = 1.882, p=0.0219 P: F (29, 194) = 1.333, p=0.1308
D	Wild-type (n=8)	Mixed Effect	* L: F (19, 115) = 1.733, p=0.0402 P: F (29, 194) = 1.044, p=0.4116

Supplementary Table 3, Related to Supplementary Figure 2: Repeated-measures, 2 way ANOVA. Groups are composed of 6 mice, performing on 2 sides across 3 sessions.

	Session	Side	Session x Side
A: Number of Presses	F(2,10) = 1.330 p=0.3075	F(1,5)=0.2092 p=0.6666	F(2,10)=1.290 p=0.3175
B: % of non-isolated Presses	F(2,10) = 1.032 p=0.3914	F(1,5)=0.03333 p=0.8623	F(2,10)=1.094 p=0.3719
B: % of Seq > 1 (inset)	F(2,10) = 1.219 p=0.3358	F(1,5)=0.3852 p=0.5620	F(2,10)=0.8604 p=0.4521
C: Number of Rewards	F(2,10) = 6.091 p=0.0186	F(1,5)=0.05358 p=0.8261	F(2,10)=0.2880 p=0.7558
D: % of Rewarded Sequences	F(2,10) = 2.179 p=0.1640	F(1,5)=0.3660 p=0.5716	F(2,10)=0.07044 p=0.9324
E: Presses/Sequence	F(2,10) = 1.985 p=0.1880	F(1,5)=2.919 p=0.1483	F(2,10)=0.4165 p=0.6703
G: IPI	F(2,10) = 2.009 p=0.1847	F(1,5)=0.3257 p=0.5929	F(2,10)=0.4805 p=0.6320
I: IPI fano factor	F(2,10) = 1.513 p=0.2667	F(1,5)=0.004525 p=0.9490	F(2,10)=0.9085 p=0.4340
J: Number of Sequences/minute	F(2,10) = 3.992 p=0.0532	F(1,5)=0.08217 p=0.7859	F(2,10)=0.1292 p=0.8803
K: Number of Rewards/minute	F(2,10) = 3.912 p=0.0556	F(1,5)=0.2349 p=0.6484	F(2,10)=0.001934 p=0.9981
L: Maximum Press Speed	F(2,10) = 4.075 p=0.0508	F(1,5)=0.03228 p=0.8645	F(2,10)=0.6672 p=0.5346