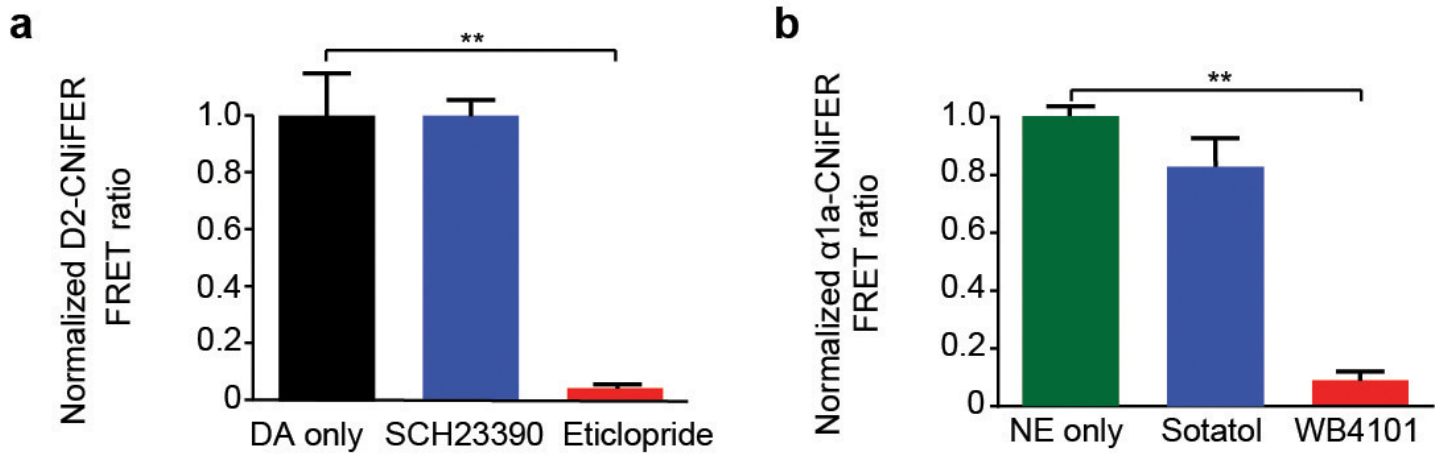
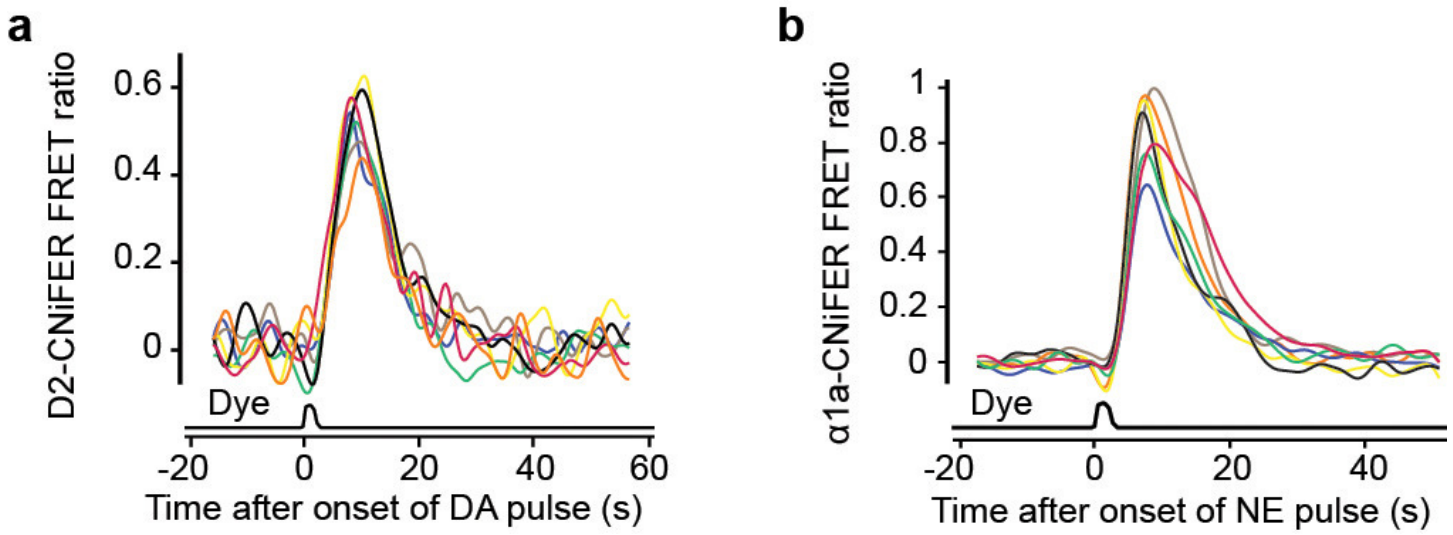



**Supplementary Figure 1**

**Selectivity of D2 and $\alpha_{1A}$ CNiFERs characterized *in vitro*.**

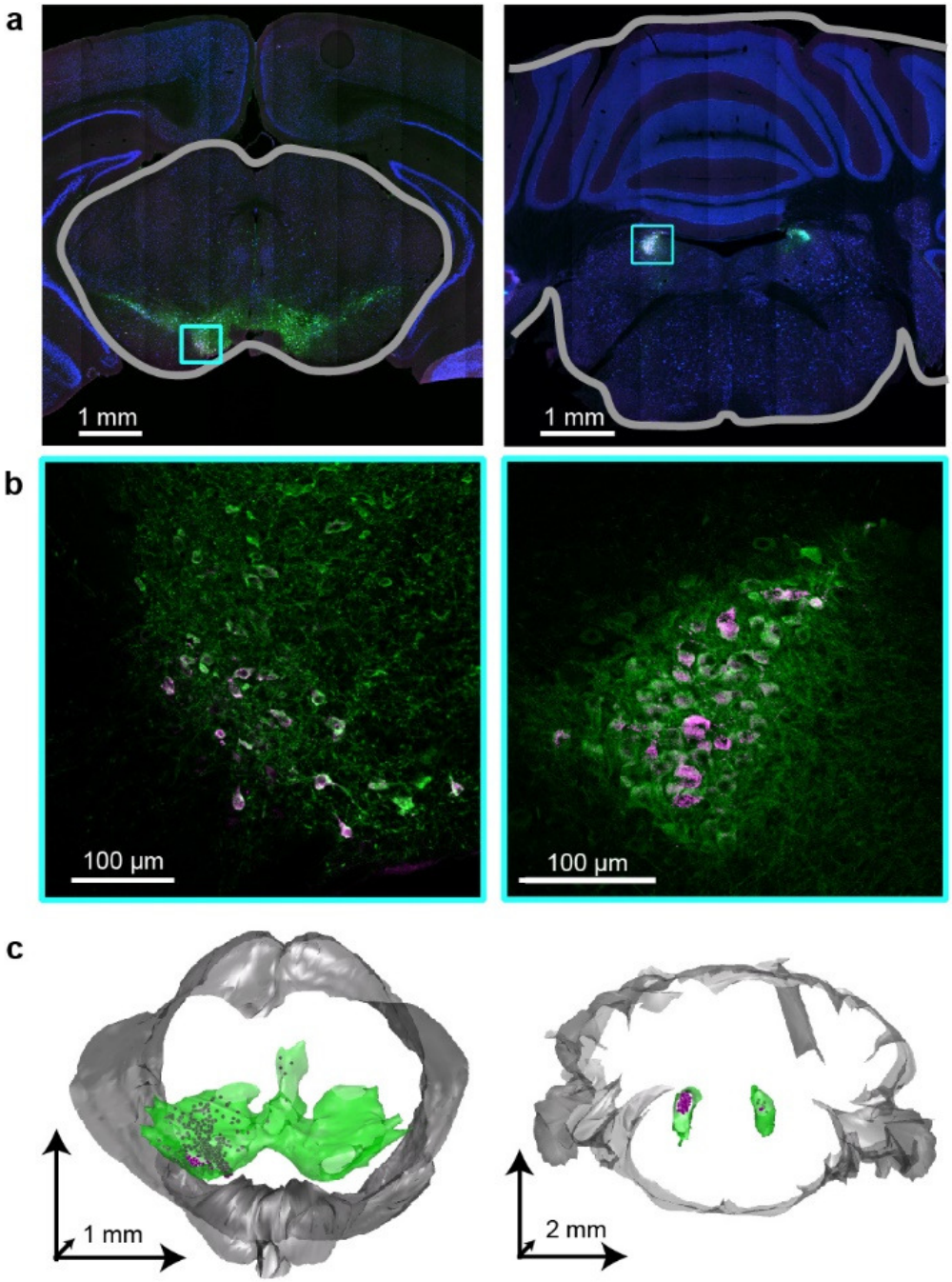
**(a)** D2-CNiFER FRET response to 20 nM DA alone or in the presence of D1-receptor antagonist SCH 23390 (100nM, blue, n = 5; p = 0.89, t-test) or D2-receptor antagonist eticlopride (50nM, red, n = 5, p = 0.0003, t-test). **(b)** $\alpha_{1A}$-CNiFER response to 50 nM NE alone or in the presence of β-adrenergic receptor antagonist sotatol (5 μM, blue, n = 4; p = 0.17, t-test), or $\alpha_{1A}$-receptor antagonist WB4101 (50 nM, red, n = 4, p = 0.0001, t-test). CNiFER response to agonist alone normalized to one, ** $p < 0.001$.




**Supplementary Figure 2**

***In vitro* characterization of CNiFERs to repeated pulses of agonist**.

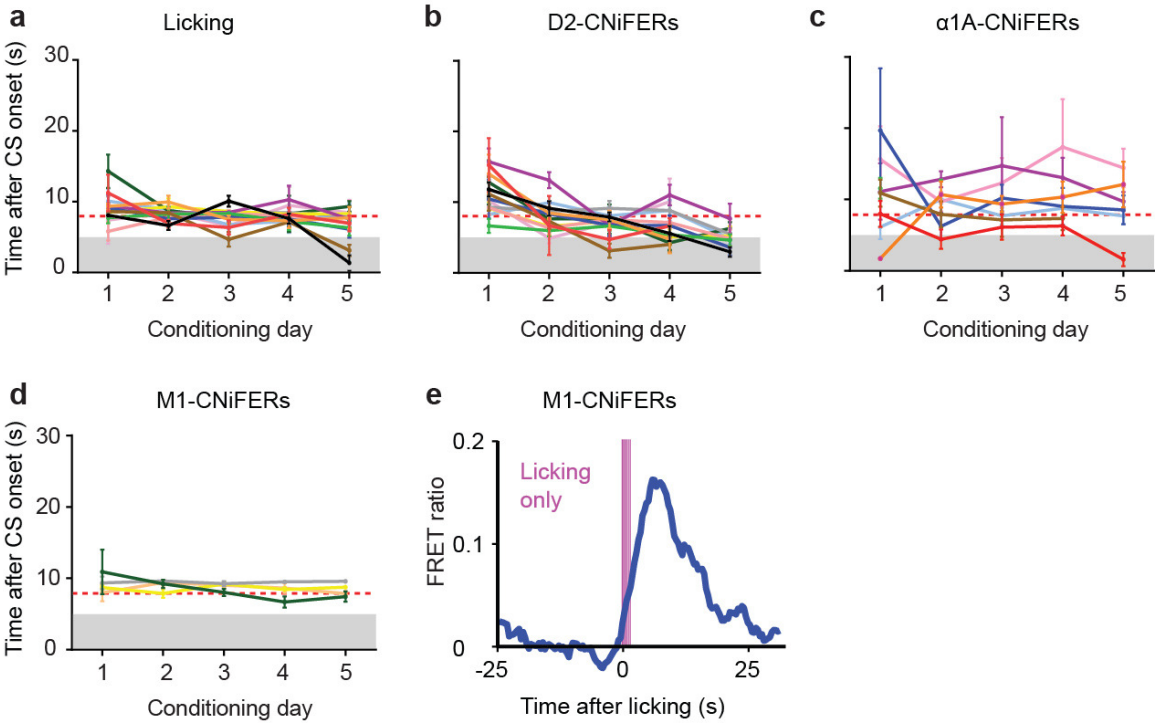
**(a)** Single-trial response of seven individual D2 CNiFERs and **(b)** seven individual $\alpha_{1A}$ CNiFERs to a single 2.5 s pulse of 100 nM DA (left) or 100 nM NE (right).




**Supplementary Figure 3**

**Identification of dopaminergic and noradrenergic projections to frontal cortex**.

**(a)** Immunostaining for tyrosine hydroxylase (green), Fluorogold™ tracer (magenta) injected ~ 200 µm deep into frontal cortex (+1.5 mm A/P, +1.5 mm M/L), and NeuroTrace®, a Nissl stain that labels neurons (blue). Coronal sections including substantia nigra (SN) (left, A/P -3.5 mm) or locus coeruleus (LC) (right, A/P -5.6 mm). **(b)** Co-labeling of tyrosine hydroxylase (green) and Fluorogold™ (magenta) in SN (left) or LC (right), magnified from cyan boxes in (a). **(c)** Position of co-labeled cell bodies in SN (left) or LC (right) indicated by magenta dots imposed on three-dimensional reconstructions as outlined by grey in (a).




**Supplementary Figure 4**

**Individual mouse FRET onset times plotted as a function of conditioning day**.

Error bars represent standard error (n = 13). **(a)** Licking onset times during conditioning trials (CS, grey bar; US, dashed red line) across five days of conditioning. **(b)** D2-CNiFER FRET response onset times during conditioning. FRET onset times are measured relative to CS onset (n = 13). **(c)** $\alpha_{1A}$-CNIFER onset times during conditioning (n = 7). **(d)** M1-CNiFER onset times during conditioning (n = 4). **(e)** Example of M1-CNiFER FRET response in a trial where the animal engaged in high frequency licking but there was no CS or US presentation.