Supplementary Online Material

Supplementary Methods

The fractional release parameter *f*, was calculated from ln $(F_1/F_2)/\Delta$STIM (Bamford *et al.*, 2004b), where ln is the natural logarithm, F_1 and F_2 are the fluorescent intensities at t_1 and t_2 respectively, and ΔSTIM is the number of stimuli delivered during that period.

Supplementary Figures

Figure S1. Amphetamine reduces in the fractional release of FM1-43 in WT mice at 20 Hz

The mean fractional destaining per cortical stimulus (*f*; see Supplementary Methods) represents another way to examine change in release kinetics from presynaptic terminals. Similar to previous reports (Bamford *et al.*, 2004b), the fractional release of FM1-43 declined with increases in the stimulus frequency (0.221% ± 0.018% at 1 Hz, *f* = 0.026% ± 0.002% at 10 Hz, and *f* = 0.017% ± 0.002% at 20 Hz; $F_{(4,150)} = 25$; $P < 0.001$, ANOVA). As expected, there was little change in fractional destaining at stimulation frequencies above 20 Hz (*f* = 0.008% ± 0.001% at 30 Hz and *f* = 0.007% ± 0.001% at 40 Hz), as any further potential decrement in the fractional release of FM1-43, as a result of increased stimulation frequency, was offset by the corresponding depression in FM1-43 release. Amphetamine also caused a decline in the fractional release of FM1-43 with higher rates of stimulation (decreasing from *f* = 0.204% ± 0.02% at 1 Hz to *f* = 0.021% ± 0.003% at 10 Hz, *f* = 0.010% ± 0.001% at 20 Hz, *f* = 0.007% ± 0.001% at 30 Hz, and to *f* = 0.006% ± 0.001% at 40 Hz; $F_{(4,240)} = 7.08$, $P = 0.001$, ANOVA), but compared to vehicle, produced a significant depression in fractional destaining of FM1-43 only at 20 Hz ($F_{(2,90)} = 25$, ***$P < 0.001$, ANOVA).

Figure S2. Amphetamine filters corticoaccumbal inputs

A, the normal probability plots show individual terminal halftimes, with and without amphetamine. At 1 Hz stimulation frequency, amphetamine had no effect on terminal release. ***B***, at 10 Hz, the destaining kinetics following amphetamine revealed at least 2

terminal subpopulations arising at ~0.5 standard deviations above the median values, showing that dopamine decreased exocytosis and produced a low-pass frequency filter with filtering applied specifically to a subset of terminals with a low probability of release. ***C***, at 20 Hz, amphetamine inhibited release from a greater proportion of slower-destaining terminals, with filtering specific to those terminals with a lower probability of release. ***D***, amphetamine lost its capacity to filter presynaptic terminals at higher stimulation frequencies of 30 Hz and ***E***, 40 Hz.

Figure S3. D1 and D2 dopamine receptors create frequency-dependent subsets of corticoaccumbal terminals

A, normal probability plot comparing individual halftimes of release in slices from WT mice with and without SKF38393 at 1 Hz, ***B***, 10 Hz, and ***C***, 20 Hz. ***D***, normal probability plot comparing individual halftimes of release in slices from WT mice with and without quinpirole (QUIN) at 1 Hz, ***E***, 10 Hz, and ***F***, 20 Hz.

Figure S4. Endocannabinoids promote presynaptic inhibition of all cortical terminals at higher stimulation frequencies

A, normal probability plot comparisons of individual halftimes of release in slices from WT and $CB_1^{-/-}$ mice showed similar distributions at 1 Hz, ***B***, 10 Hz and ***C***, 20 Hz. ***D***, compared to slices from WT mice, higher stimulation frequencies of 30 Hz and ***E***, 40 Hz increased exocytosis from most terminals in $CB_1^{-/-}$ mice.

Figure S5. D1Rs modulate corticoaccumbal terminals with a low-probability of release

A, individual terminal responses to treatments shown in **Fig. 2*A*** demonstrate that either amphetamine or the D1R agonist SKF38393 inhibited exocytosis from terminals with the lowest probability of release. ***B***, analysis of the individual terminal responses for treatments shown in **Fig. 2*C*** demonstrates that either SKF38393 or adenosine inhibited exocytosis from terminals with a low probability of release. ***C***, individual terminal responses for destaining curves shown in **Fig. 2*E*** demonstrate that the NMDAR antagonist APV prevented inhibition by SKF38393, while the CB_1R antagonist AM251 had no effect.

D, the individual terminal responses for the destaining curves shown in **Fig. 2*G*** demonstrates that the AMPAR antagonist NBQX reduced inhibition of low-probability release synapses following SKF38393.

Figure S6. D2Rs modulate terminals with a low probability of release while CB_1Rs more broadly inhibit corticoaccumbal terminals

A, individual terminal responses for the experiments shown in **Fig. 3*A*** demonstrate that both amphetamine and quinpirole inhibited terminals with the lowest probability of release, while the D2R antagonist sulpiride only partially blocked inhibition by amphetamine. ***B***, the individual terminal responses for destaining curves shown in **Fig. 3*C*** show that both D1 and D2 receptor antagonists SCH23390 and sulpiride were required to block inhibition from terminals with a low probability of release. ***C***, individual terminal responses for the experiments shown **Fig. 3*E*** show that the CB_1R agonist WIN55-2,2 (WIN) inhibited a broad population of terminals, the CB_1R antagonist AM251 blocked inhibition by the D2R agonist quinpirole, and AM251 boosted release from most cortical terminals.

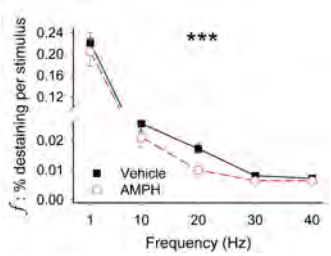
Figure S7. D1Rs excite terminals with a low release probability when glutamate receptors are blocked

A, individual terminal responses for destaining curves in **Fig. 4*A*** show that the D1R agonist SKF38393 boosted exocytosis from terminals with a low probability of release once AMPA, NMDA and mGluRs are blocked by NBQX, APV and MCPG. ***B***, individual terminal responses for destaining curves in **Fig. 4*C*** show that these glutamate antagonists prevented the inhibition of low release probability terminals by the D2R agonist quinpirole and they did not increase FM1-43 destaining beyond control in the presence of quinpirole.

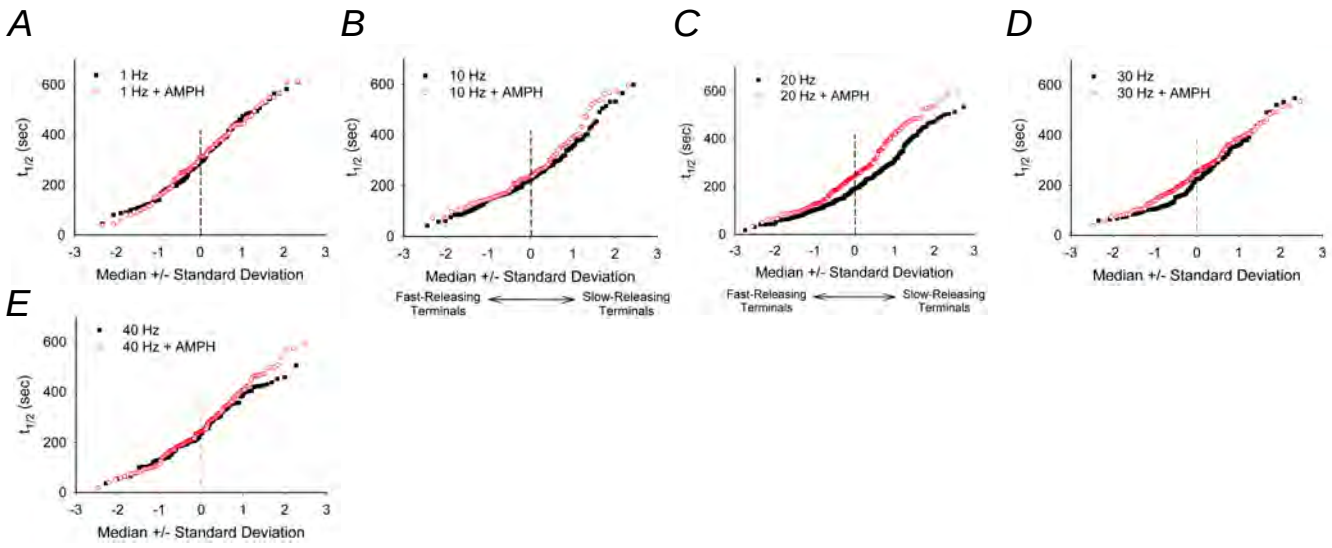
Supplementary References

Bamford NS, Zhang H, Schmitz Y, Wu NP, Cepeda C, Levine MS, Schmauss C, Zakharenko SS, Zablow L & Sulzer D. (2004b). Heterosynaptic dopamine neurotransmission selects sets of corticostriatal terminals. *Neuron* **42,** 653-663.

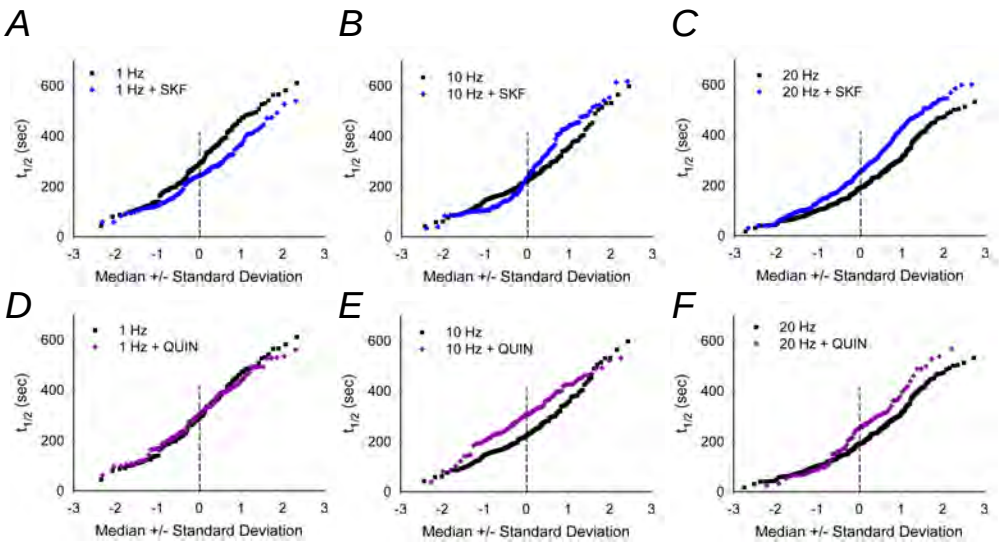
W. Wang and others - Supplemental Figure 1



W. Wang and others - Supplemental Figure 2



W. Wang and others - Supplemental Figure 3



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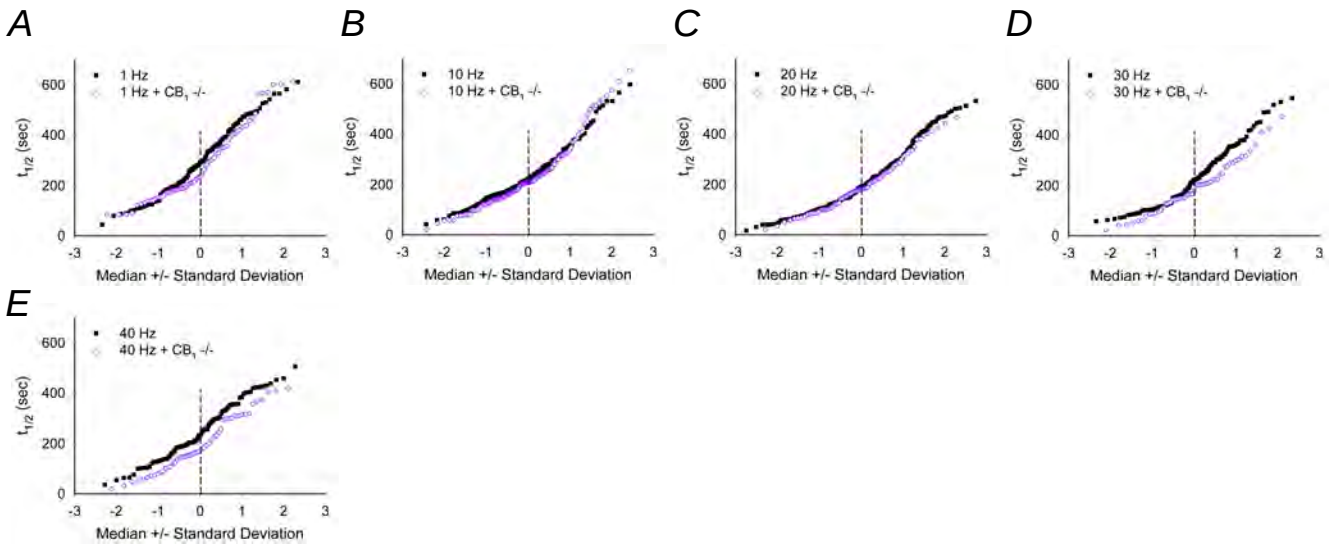
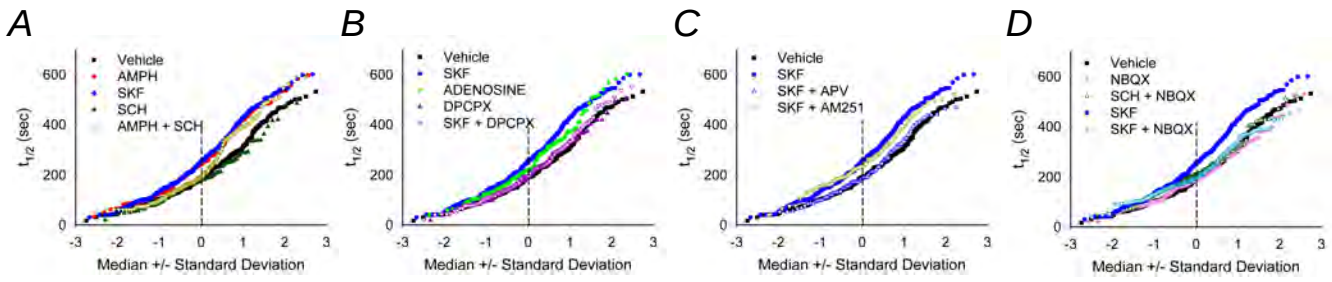
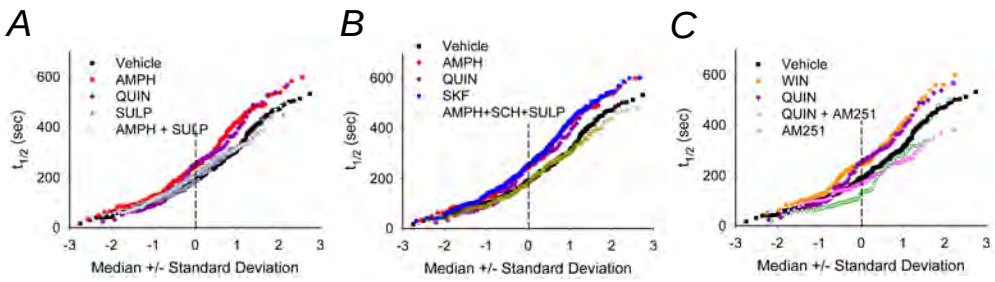


W. Wang and others - Supplemental Figure 5



W. Wang and others - Supplemental Figure 6



W. Wang and others - Supplemental Figure 7