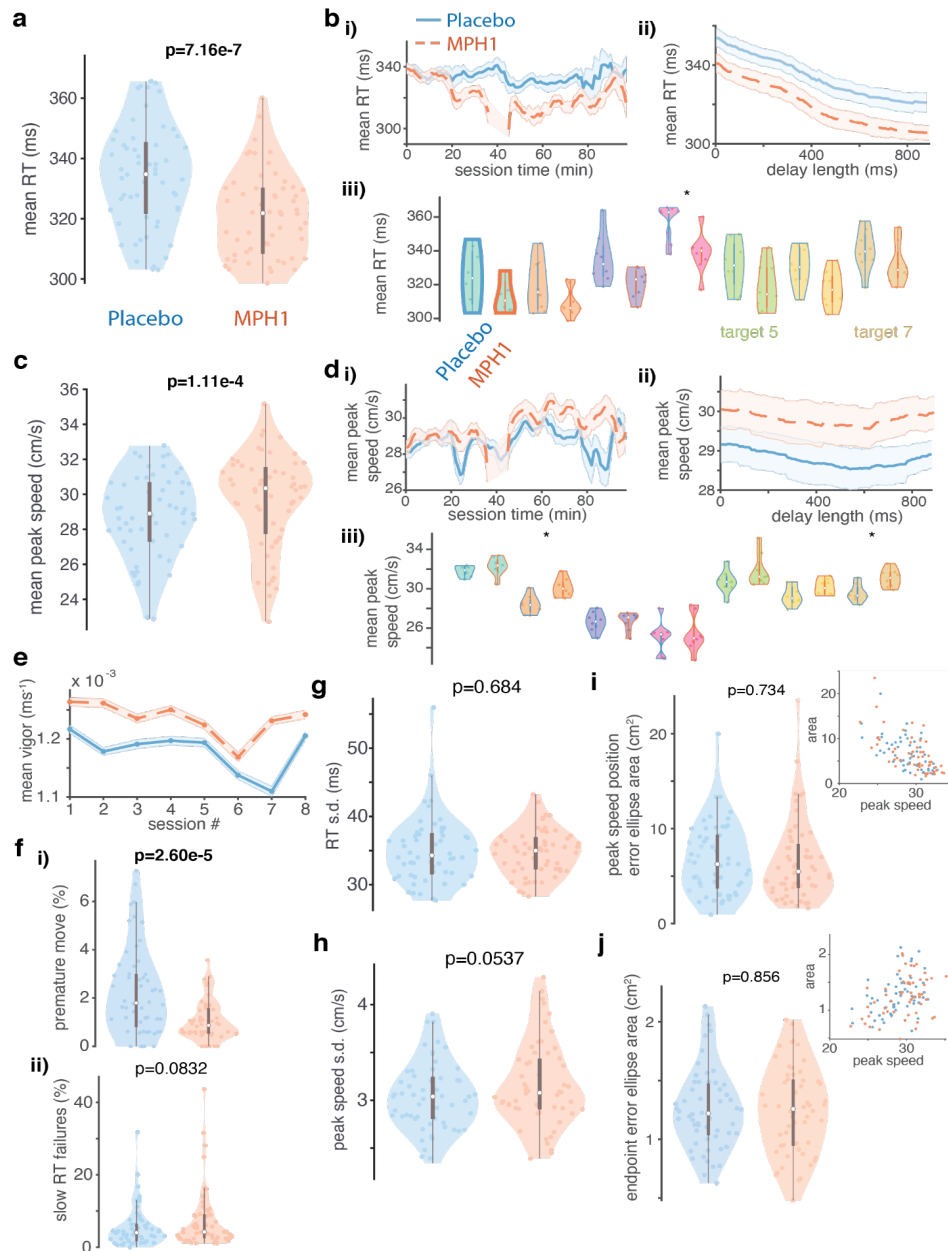


1470 **Supplementary Figure 1: Behavioral effects of MPH for the 4 mg/kg MPH dose in monkey U and associated placebo sessions (“U4” dataset).**

1475 **a) Reaction time distributions across treatments.** Same as Figure 2a, but for U4. **b) RT over elapsed session time, delay, and reach target condition across treatments.** Same as Figure 2b, but for U4. **c) Peak reach speed distributions across treatments.** Same as Figure 2c, but for U4. **d) Peak speed over time, trial count, delay, and reach target condition across treatments.** Same as b, but for peak reach speed. **e) Vigor over sessions by treatment.** Mean per-session vigor (\pm s.e.m.) across all trials for each treatment. Vigor is calculated per trial as the inverse of the sum of the RT and the reach duration^{50,59}. Orange dashed lines: MPH sessions; blue solid lines: placebo sessions. **f) Impulsivity. i) False starts across treatments.** Conventions as in Figure 2a, but for distributions of the per-session, per-target proportion of trials aborted due to premature hand movements (moving during the delay period, or online RT <150ms) in each treatment. **ii) Sluggish starts across treatments.** Same as i, but for per-session, per-target proportion of trials aborted due to online RTs that were too slow. **g) RT variability across treatments.** Same as Figure 3a, but for U4. **h) Peak reach speed variability across treatment conditions.** Same as g, but for distributions of the per-session, per-target standard deviation of the peak reach speed in each treatment. **i) Variability of hand position at the time of peak reach speed across treatments.** Same as Figure 3d, but for U4. **j) Variability of reach endpoint position across treatments.** Same as i, but for distributions of 2D hand positions at the endpoint of each reach.

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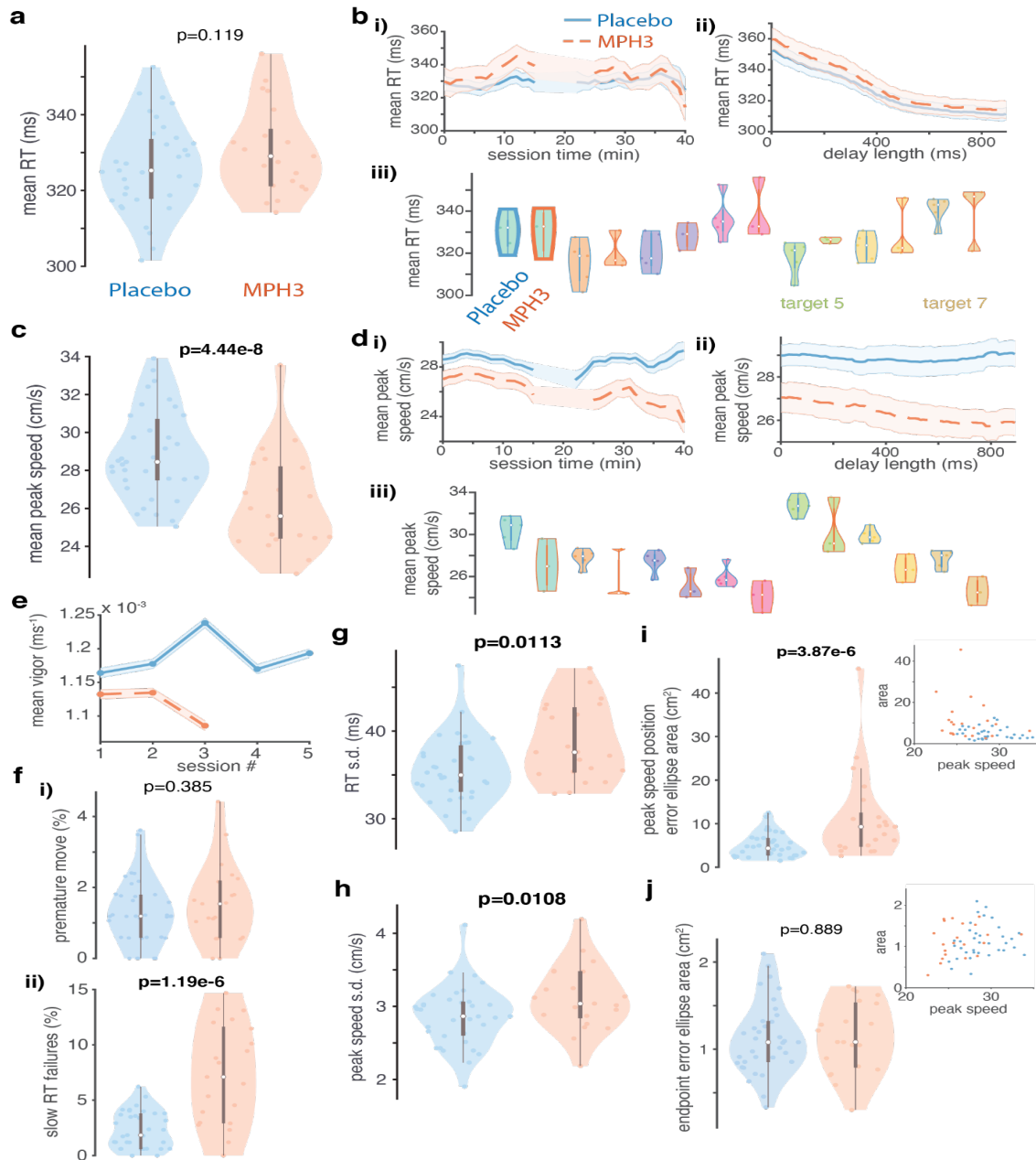
1490

Supplementary Figure 2: Behavioral effects of MPH for the 1.3 mg/kg MPH dose in monkey P and associated placebo sessions ("P1" dataset).

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a) Reaction time distributions across treatments. Same as Figure 2a, but for P1. **b) RT over elapsed session time, delay, and reach target condition across treatments.** Same as Figure 2b, but for P1. **c) Peak reach speed distributions across treatments.** Same as Figure 2c, but for P1. **d) Peak speed over time, trial count, delay, and reach target condition across treatments.** Same as b, but for peak reach speed. **e) Vigor over sessions by treatment.** Same as Supplementary Figure 1e, but for P3. **f) Impulsivity.** **i) False starts across treatments.** Same as Supplementary Figure 1f, but for P3. **ii) Sluggish starts across treatments.** Same as i, but for per-session, per-target proportion of trials aborted due to online RTs that were too slow. **g) RT variability across treatments.** Same as Figure 3a, but for P1. **h) Peak reach speed variability across treatment conditions.** Same as g, but for distributions of the per-session, per-target standard deviation of the peak reach speed in each treatment. **i) Variability of hand position at the time of peak reach speed across treatments.** Same as Figure 3d, but for P1. **j) Variability of reach endpoint position across treatments.** Same as i, but for distributions of 2D hand positions at the endpoint of each reach.

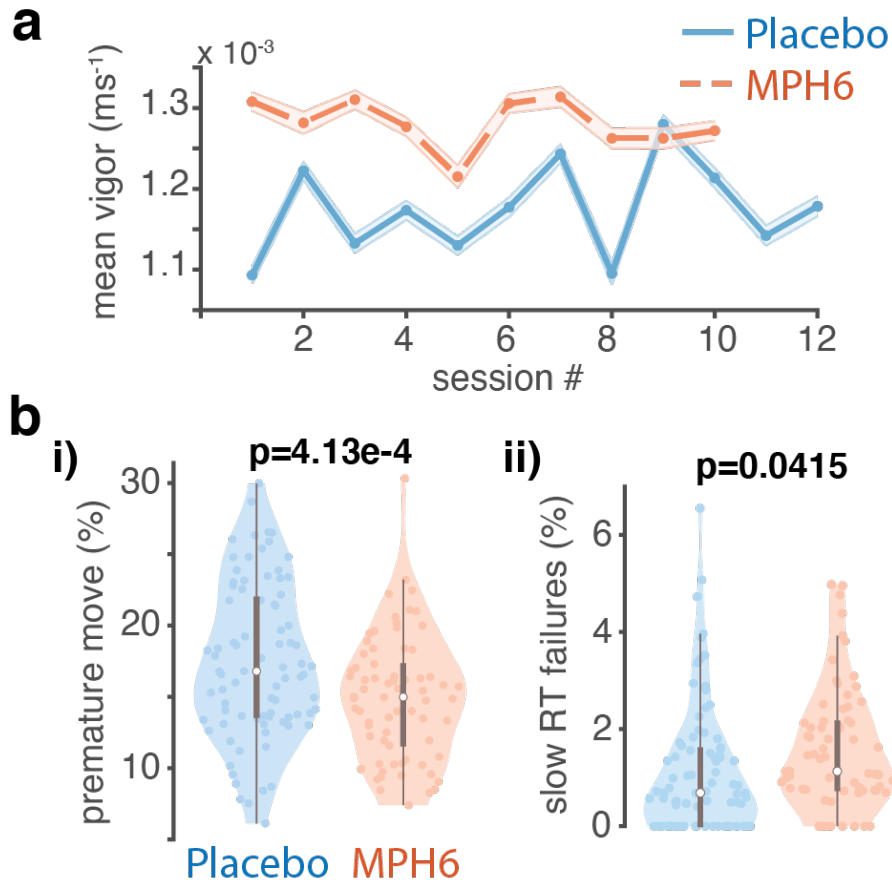
1500



Supplementary Figure 3: Behavioral effects of MPH for the 3 mg/kg MPH dose in monkey P and associated placebo sessions ("P3" dataset).

1505 **a) Reaction time distributions across treatments.** Same as Figure 2a, but for P3. **b) RT over elapsed session time, delay, and reach target condition across treatments.** Same as Figure 2b, but for P3. **c) Peak reach speed distributions across treatments.** Same as Figure 2c, but for P3. **d) Peak speed over time, trial count, delay, and reach target condition across treatments.** Same as b, but for peak reach speed. **e) Vigor over sessions by treatment.** Same as Supplementary Figure 1e, but for P3. **f) Impulsivity.** **i) False starts across treatments.** Same as Supplementary Figure 1f, but for P3. **ii) Sluggish starts across treatments.** Same as i, but for per-session, per-target proportion of trials aborted due to online RTs that were too slow. **g) RT variability across treatments.** Same as Figure 3a, but for P3. **h) Peak reach speed variability across treatment conditions.** Same as g, but for distributions of the per-session, per-target standard deviation of the peak reach speed in each treatment. **i) Variability of hand position at the time of peak reach speed across treatments.** Same as Figure 3d, but for P3. **j) Variability of reach endpoint position across treatments.** Same as i, but for distributions of 2D hand positions at the endpoint of each reach.

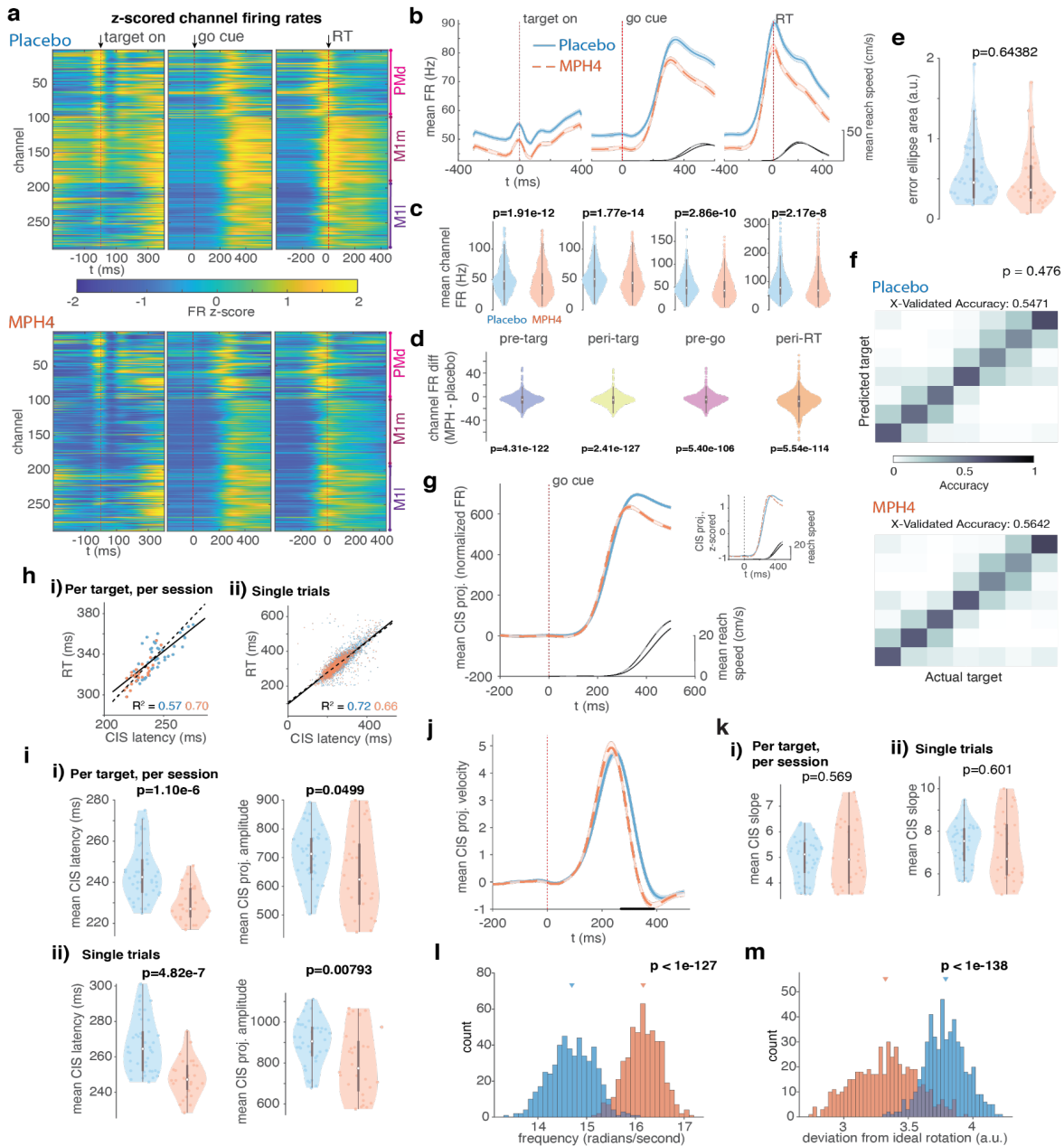
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Supplementary Figure 4: Tolerance and trial outcomes.

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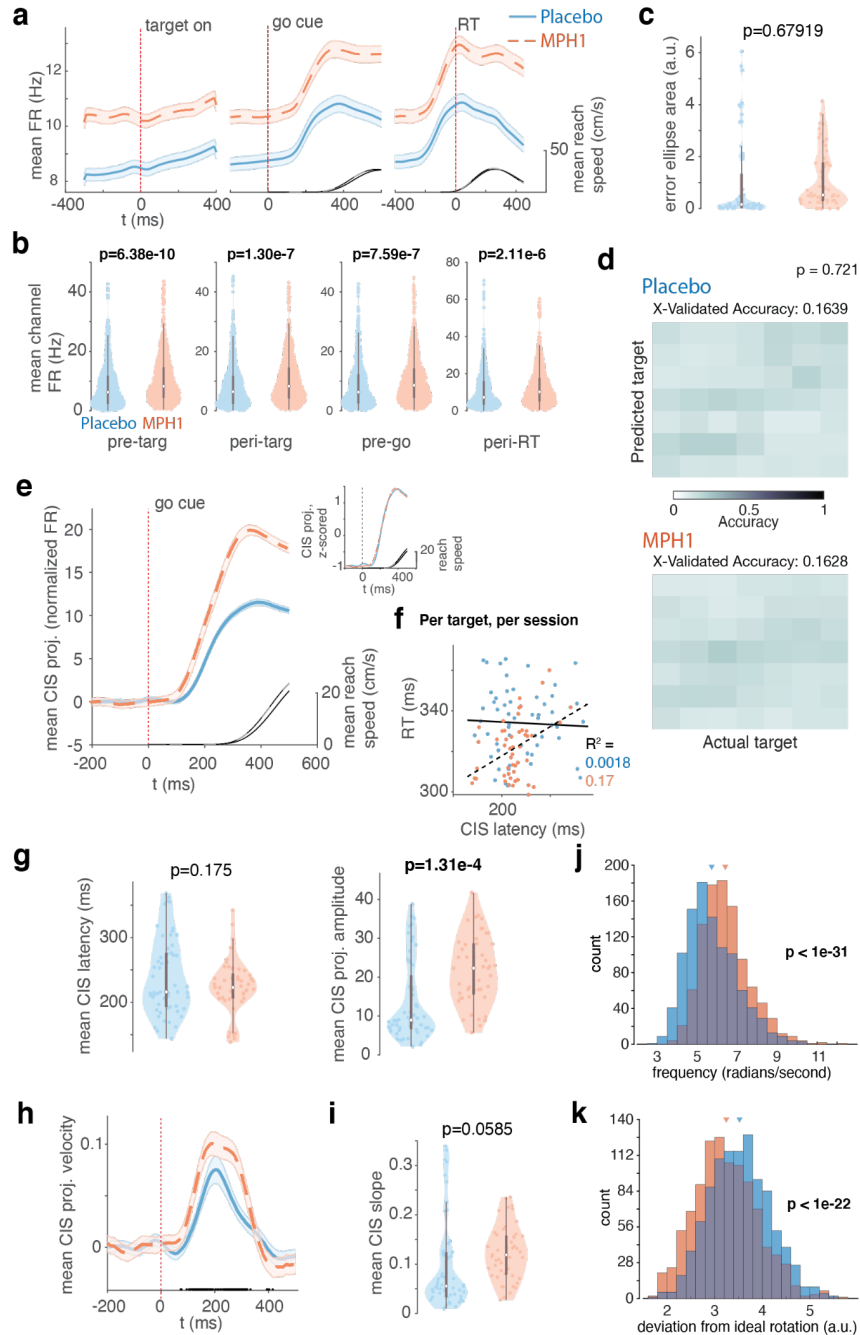
a) Vigor over sessions by treatment. Mean per-session vigor (\pm s.e.m.) across all trials for each treatment. Vigor is calculated per trial as the inverse of the sum of the RT and the reach duration^{50,59}. Orange dashed lines: MPH sessions; blue solid lines: placebo sessions. **b) Impulsivity. i) False starts across treatments.** Conventions as in Figure 2a, but for distributions of the per-session, per-target proportion of trials aborted due to premature hand movements (moving during the delay period, or online RT <150ms) in each treatment. **ii) Sluggish starts across treatments.** Same as i, but for per-session, per-target proportion of trials aborted due to online RTs that were too slow.



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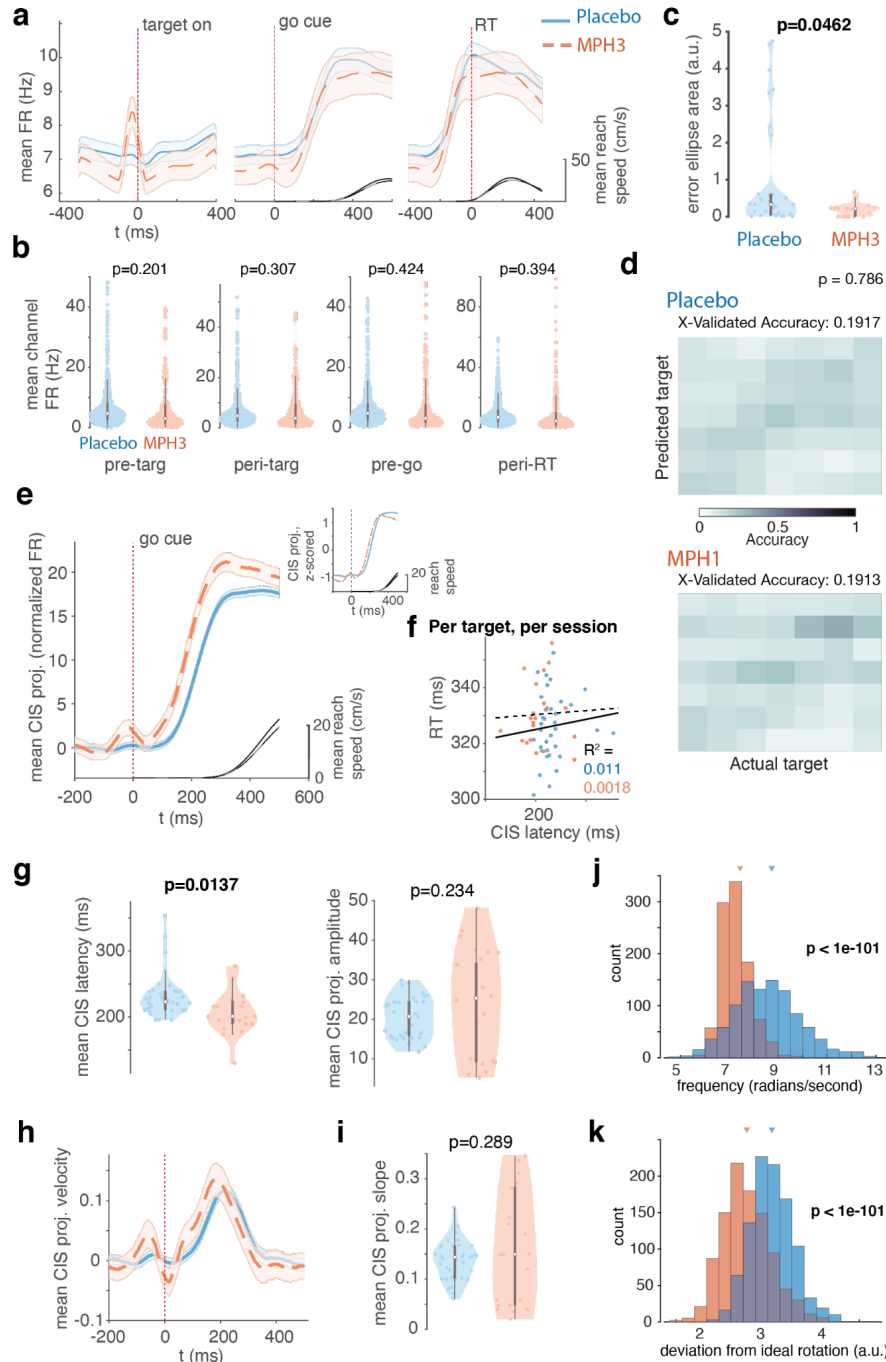
Supplementary Figure 5: Neural effects of MPH for the U4 dataset.

1530 **a-e) FR differences across treatment conditions.** **a)** FR heatmaps, z-scored across treatments. Same as Figure 4a, but for U4.
b) Mean population FR trajectories by treatment. Collapsed across all reach targets and aligned to target onset, go cue, and RT,
 across all channels during MPH vs. placebo sessions. Mean reach speed trajectories are overlaid on the right axes. Dashed lines:
 MPH; solid lines: placebo sessions. **c)** Distribution of mean single-channel PSTH values across all time points in each of four
 1535 **trial epochs.** Same as Figure 4d, but for U4. **d)** Distribution of single-channel mean condition-averaged FR differences by
 treatment. Same as Figure 4d, but for U4. **e)** Distributions (by treatment) of the per-session, per-target variability of the
 preparatory neural state. Same as Figure 5c, but for U4. **f)** Discrete reach target decoding from preparatory activity across
 1540 **treatment conditions.** Same as Figure 5d, but for U4. **g)** Condition-invariant signal (CIS) across treatment conditions. Same
 as Figure 6b, but for U4. **h)** CIS correlation with reaction time (RT). Same as Figure 6c, but for U4. **i)** CIS latency and
 amplitude across treatments. Same as Figure 6d, but for U4. **j)** CIS velocity across treatments. Same as Figure 6e, but for U4.
k) CIS slope across treatments. Same as Figure 6f, but for U4. **l)** Execution-related rotation frequency across treatments.
 Same as Figure 7b, but for U4, with one exception: frequency was calculated from the top 6 dimensions (see Methods). **m)**
 Deviation from ideal rotations across treatments. Same as Figure 7c, but for U4, and with deviation calculated from the top 6
 dimensions as in l.



Supplementary Figure 6: Neural effects of MPH for the P1 dataset.

1545 a) Mean population FR trajectories by treatment. Same as Supplementary Figure 5b, but for P1. b) Distribution of mean
 1550 single-channel PSTH values across all time points in each of four trial epochs. Same as Figure 4d, but for P1. c) Distributions
 (by treatment) of the per-session, per-target variability of the preparatory neural state. Same as Figure 5c, but for P1. d)
 Discrete reach target decoding from preparatory activity across treatment conditions. Same as Figure 5d, but for P1. e)
 Condition-invariant signal (CIS) across treatment conditions. Same as Figure 6b, but for P1. f) CIS correlation with reaction
 time (RT). Same as Figure 6c)i, but for P1. g) CIS latency and amplitude across treatments. Same as Figure 6d)i, but for P1. h)
 CIS velocity across treatments. Same as Figure 6e, but for P1. i) CIS slope across treatments. Same as Figure 6f)i, but for P1.
 j) Execution-related rotation frequency across treatments. Same as Figure 7b, but for P1. k) Deviation from ideal rotations
 across treatments. Same as Figure 7c, but for P1.

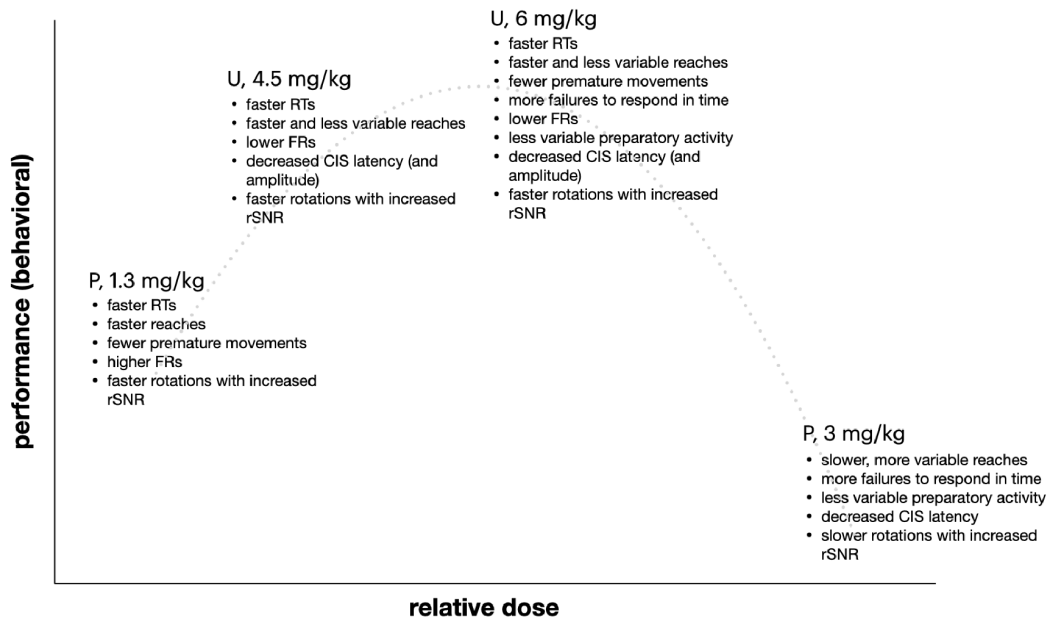


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Supplementary Figure 7: Neural effects of MPH for the P3 dataset.

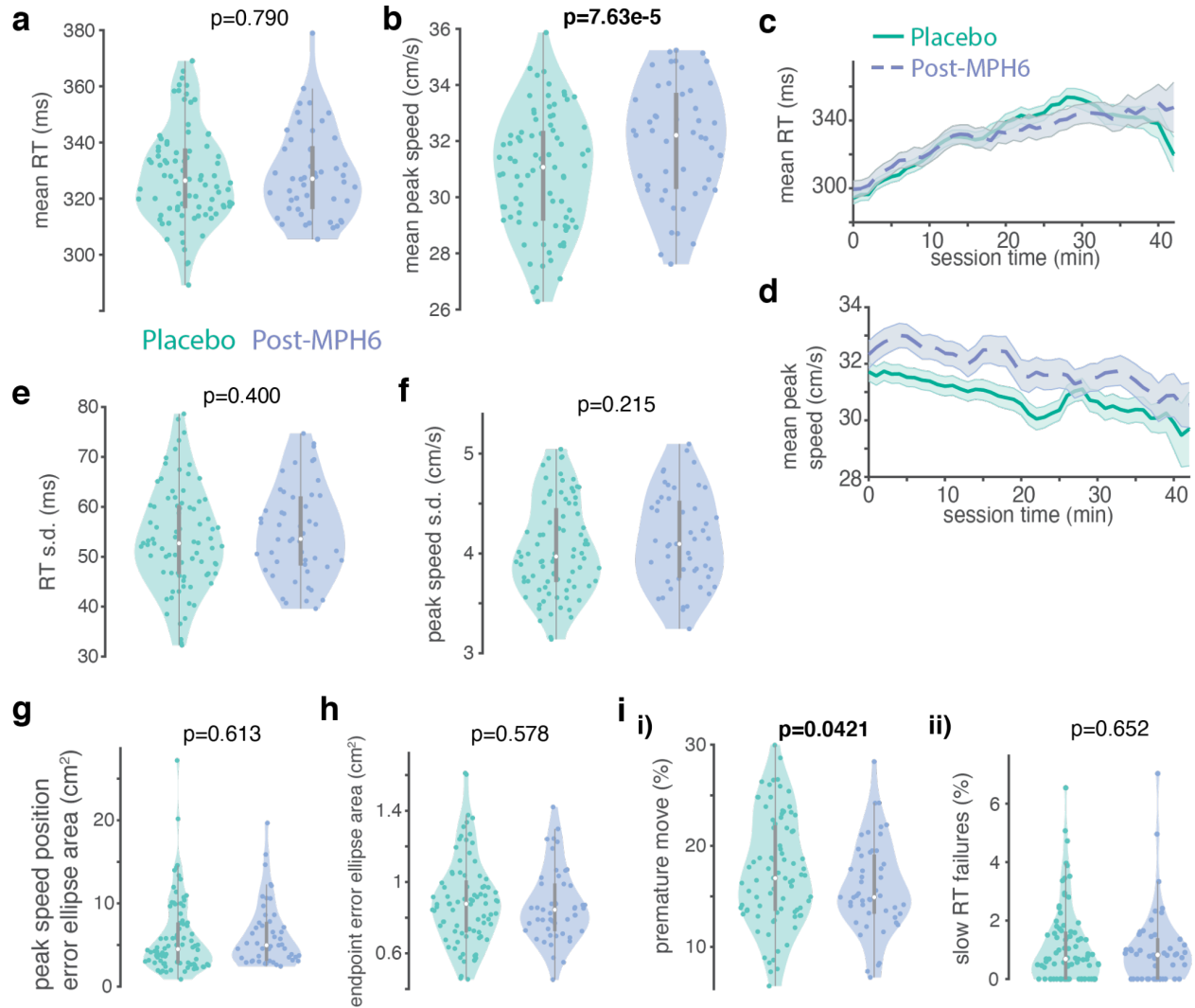
1560 **a) Mean population FR trajectories by treatment.** Same as Supplementary Figure 5b, but for P3. **b) Distribution of mean single-channel PSTH values across all time points in each of four trial epochs.** Same as Figure 4d, but for P3. **c) Distributions (by treatment) of the per-session, per-target variability of the preparatory neural state.** Same as Figure 5c, but for P3. **d) Discrete reach target decoding from preparatory activity across treatment conditions.** Same as Figure 5d, but for P3. **e) Condition-invariant signal (CIS) across treatment conditions.** Same as Figure 6b, but for P3. **f) CIS correlation with reaction time (RT).** Same as Figure 6c)i, but for P3. **g) CIS latency and amplitude across treatments.** Same as Figure 6d)i, but for P3. **h) CIS velocity across treatments.** Same as Figure 6e, but for P3. **i) CIS slope across treatments.** Same as Figure 6f)i, but for P3. **j) Execution-related rotation frequency across treatments.** Same as Figure 7b, but for P3. **k) Deviation from ideal rotations across treatments.** Same as Figure 7c, but for P3.

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Supplementary Figure 8: Postulated inter-subject “inverted-U” dose-response curve for effects of MPH
Summary of behavioral and neural effects by dose and monkey.

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Supplementary Figure 9: Behavioral effects of MPH in monkey U on RT, reach speed, reach variability, and trial outcomes for sessions the day after a 6 mg/kg dose and associated placebo sessions (“post-MPH6” dataset).

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a) Reaction time distributions. Same as Figure 2a, but for post-MPH6. **c) Peak reach speed distributions.** Same as Figure 2c, but for post-MPH6. **c) RT over time.** Same as Figure 2b)i, but for post-MPH. Purple dashed lines: post-MPH6 sessions; green solid lines: placebo sessions. **d) Peak speed over time.** Same as c, but for peak reach speed. **e) RT variability.** Same as Figure 3a, but for post-MPH6. **f) Peak reach speed variability.** Same as e, but for peak reach speed. **g) Variability of hand position at the time of peak reach speed across treatments.** Same as Figure 3d, but for post-MPH6. **h) Variability of reach endpoint position across treatments.** Same as Figure 3e, but for post-MPH6. **i) Impulsivity.** **i) False starts across treatments.** Same as Supplementary Figure 4b)i, but for post-MPH6. **ii) Sluggish starts across treatments.** Same as Supplementary Figure 4b)ii, but for post-MPH6.

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