Effect of Parameters on the Caffeine-effect Factor

To illustrate the temporal change of the caffeine-effect factor $g_{PD}(t,c)$ and its sensitivity to changes to the caffeine model parameters (M_0, k_0, z, and k_a), we computed $g_{PD}(t,c)$ as given in Equation 6a for the caffeine condition in study V3 (study condition 6 in Table 1), while considering a ±20% variation in the parameter values. Specifically, to quantify the effect of each parameter, we computed $g_{PD}(t,\mathrm{c})$ by varying that parameter from –20% to +20% of its nominal value, while keeping the other parameters fixed at their nominal values listed in Table 3. Figures S1A and S1B illustrate the corresponding variations of the caffeine-effect factor as a function of time for lapses and mean RT statistics, respectively.

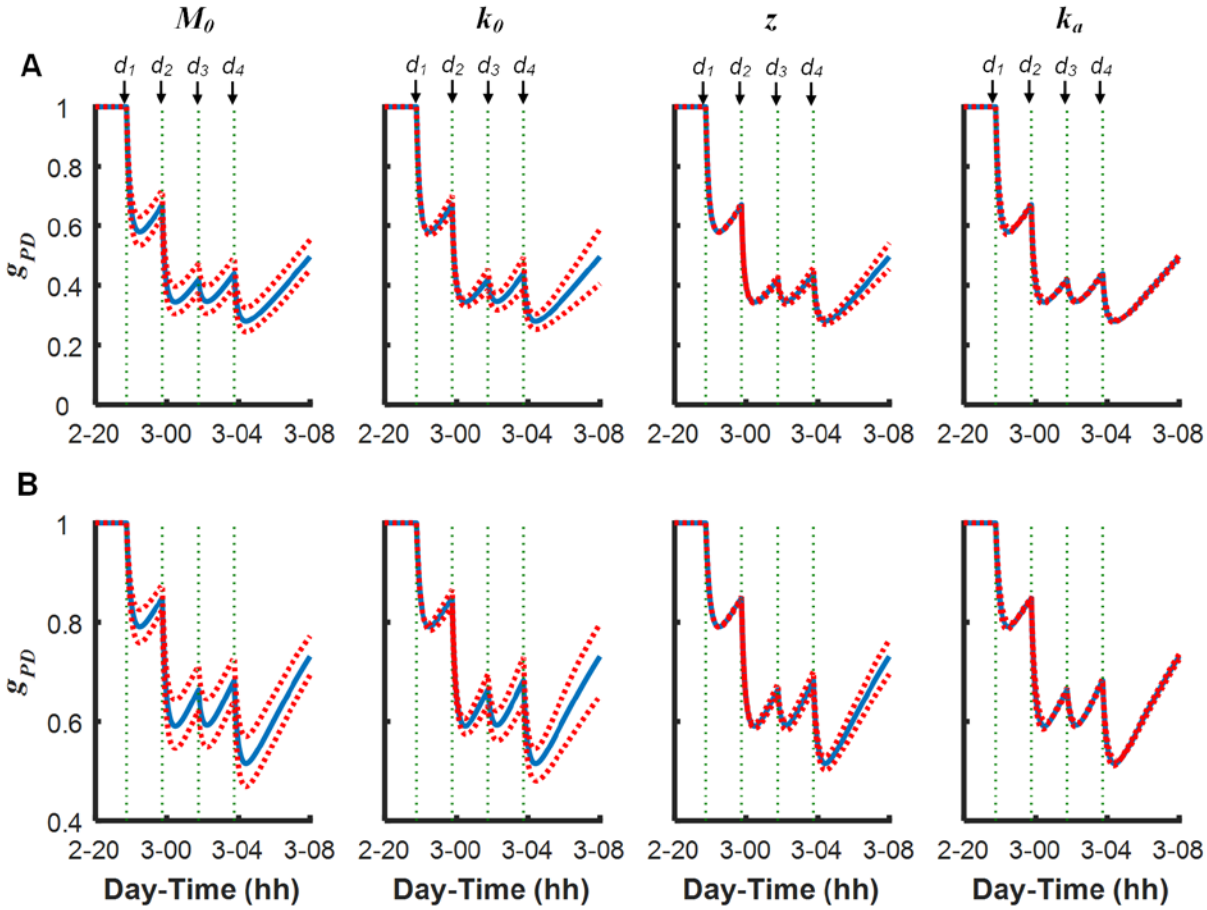

Figure S1. Caffeine-effect factor g_{PD} and the effect of ±20% variation in the caffeine model parameters (M_0, k_0, z, and k_a) on g_{PD} for study condition 6 (Table 1) in study V3 for lapses (panels A) and mean response time (RT) (panels B) statistics. The blue solid lines represent $g_{PD}(t,c)$ for the nominal parameter values specified in Table 3. The red dotted lines represent $g_{PD}(t,c)$ for ±20% variation of each parameter value from its nominal value used throughout the manuscript. The four panels in each row show the effect of varying one parameter at a time, while keeping the remaining three parameters fixed at their nominal values. Thin dotted vertical lines denote caffeine intake (d_1 = 100 mg, d_2 = 200 mg, d_3 = 100 mg, and d_4 = 200 mg).

RMSEs of UMP Predictions for Individual Data

In order to provide a quantitative indication of the accuracy of the UMP group-average model in predicting individual data, we computed the RMSEs between the UMP predictions and individual PVT data for each of the 10 subjects in the placebo and caffeine conditions (study conditions 3 and 4 in Table 1) in study V2. Therefore, we added a constant value δ to the UMP-predicted output for each individual prediction, where δ was computed as the difference between the average measured PVT performance for that individual and the average predicted performance on the first day of TSD/CSR. Additionally, to quantify the benefit of accounting for caffeine effects in the UMP over the original (caffeine-free) UMP, for the caffeine condition, we also computed the RMSE of the caffeine-free UMP for each subject, where the RMSE was computed over the time period following the first caffeine dose. Table S1 lists the RMSEs of the UMP (P_c) and caffeine-free model (P_0) predictions for each subject for both PVT statistics.

As expected, we observed that the individual RMSEs were, on average, larger than the RMSEs obtained on group-averaged data (see Table 4). Nevertheless, consistent with our findings on predictions of group-averaged data, on average, accounting for caffeine effects in the UMP provided significant improvements over a caffeine-free model (36% for lapses and 48% for mean RT). In fact, the UMP was better than the caffeine-free model in 8 of the 10 subjects in study condition 4, with the RMSEs being significantly lower for the UMP compared to the caffeine-free model for both PVT statistics ($P < 0.01$, Wilcoxon paired, two-sided, signed-rank test).

Table S1. Root mean squared errors (RMSEs) of UMP (P_c) and caffeine-free model (P_0) predictions of individual data across study conditions 3 and 4 in *Study V2* for both lapses and mean response time (RT) statistics. Also shown are the average RMSEs over the 10 subjects for each study condition and statistic. RMSEs of UMP that performed better than their corresponding caffeine-free models are in boldface.

Study Condition 3			**Study Condition 4**				
Subject #	**Lapses (#)**	**Mean RT (msec)**	**Subject #**	**Lapses (#)**		**Mean RT (msec)**	
	P_0	P_0		P_c	P_0	P_c	P_0
1	4.4	109	1	6.0	4.6	85	59
2	4.5	57	2	**1.6**	**4.5**	**43**	**124**
3	5.1	57	3	**4.5**	**4.8**	**53**	**127**
4	5.7	82	4	**3.4**	**5.2**	**51**	**111**
5	5.4	124	5	**2.6**	**4.7**	**50**	**123**
6	6.3	89	6	**2.2**	**5.6**	**52**	**133**
7	3.8	113	7	**1.6**	**5.1**	**41**	**102**
8	6.7	91	8	6.3	6.2	96	67
9	8.7	93	9	**1.4**	**5.3**	**31**	**109**
10	6.1	91	10	**4.3**	**6.7**	**53**	**129**
Average	5.7	91	Average	**3.4**	**5.3**	**56**	**108**