

Supplemental Material

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Evidence that Sedative Effects of Benzodiazepines Involve Unexpected GABA_A Receptor Subtypes: Quantitative Observation Studies in Rhesus Monkeys

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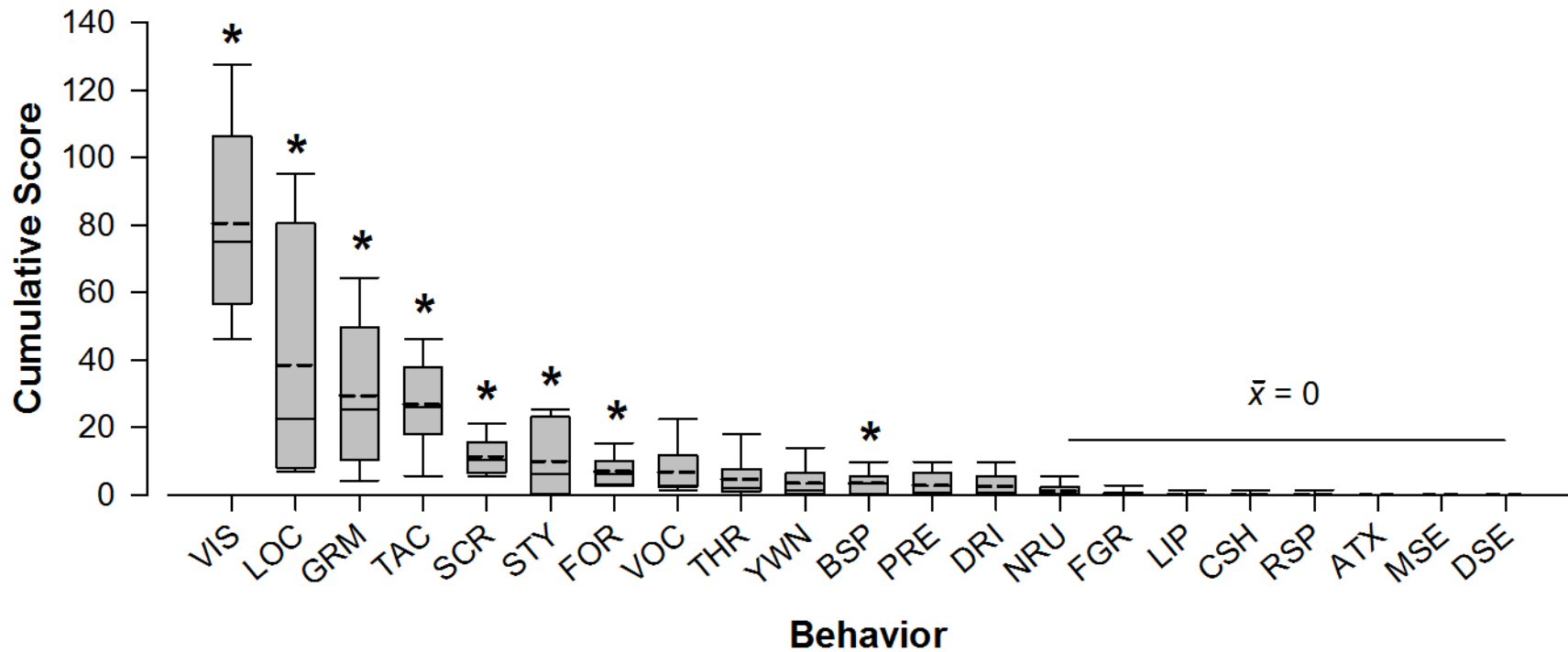


Figure 1. Profile of species-typical behaviors and drug-induced sedative behavior in six adult male and female rhesus macaques. Data were collected during “baseline” tests, which consisted of saline injections or vehicle injections, followed by multiple time points. Data (frequency scores, see Methods) were averaged for two baseline tests and cumulated across the time points. Each box-and-whisker represents the range (error bars), the inter-quartile range (the top and bottom of the box), the median (solid horizontal line), and the mean (dashed horizontal line). Note that * $p > 0.05$, Shapiro-Wilk Normality test (i.e., data sets passed the normality test with W -Statistics > 0.8) and data under the horizontal line did not differ significantly from zero ($\bar{x} = 0$, one-sample t -tests, $p > 0.05$). See Table 1 for definitions of individual behaviors.

Table 1. Analysis of all behavioral categories following multiple doses of the seven test compounds. Significant effects were identified as at least one dose significantly different from vehicle (N=4 monkeys). See Table 1 for identification of abbreviations and definitions.

Compounds	No Change	Increase	Decrease	Increase & Decrease
Alprazolam	LOC, GRM, SCR, STY, FOR, VOC, THR, FGR, YWN, BSP, PRE, DRI, NRU, LIP, CSH, LDR	RSP, MSE, DSE, ATX	VIS, TAC	
Diazepam	LOC, GRM, SCR, STY, FOR, VOC, THR, FGR, YWN, BSP, PRE, DRI, NRU, LIP, CSH, LDR	RSP, MSE, DSE, ATX	VIS, TAC	
Zolpidem	GRM, SCR, STY, FOR, VOC, THR, FGR, YWN, BSP, PRE, DRI, NRU, LIP, RSP, MSE, CSH, LDR	LOC*, DSE, ATX	VIS	TAC
HZ-166	VIS, LOC, GRM, SCR, STY, FOR, LOC, THR, FGR, YWN, BSP, PRE, DRI, NRU, ATX, LIP, CSH, MSE, DSE, LDR	RSP	TAC	
MRK-696	VIS, LOC, GRM, SCR, STY, FOR, LOC, THR, FGR, YWN, BSP, PRE, DRI, NRU, LIP, CSH, MSE, DSE, LDR	RSP, ATX	TAC	
TPA-023B	VIS, LOC, GRM, SCR, STY, FOR, LOC, THR, FGR, YWN, BSP, PRE, DRI, NRU, ATX, LIP, CSH, MSE, DSE, LDR	RSP	TAC	
*LOC was associated with a significant overall main effect of dose (ANOVA) but none of the doses were significantly different from vehicle (Bonferroni t-tests, P>0.05).				