

Eye Blink Rate as a Proxy for Dopamine Function

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Background

- Eye blink rate (EBR) has been hypothesized to be a noninvasive measure of tonic dopamine (DA) in the synapse, where blinks significantly correlate with concentration of DA¹.
- Findings on the accuracy of EBR as a proxy for tonic DA have been generally mixed², which calls into question the validity of this measure as a putative marker of DA function.
- Modafinil, a cognitive enhancer often used to treat narcolepsy, has been found to block DA transporters and acutely increase DA levels in the brain (Figure 1)³.
- In this study, modafinil was administered in three doses to determine whether enhanced DA signaling dose-dependently increases EBR.

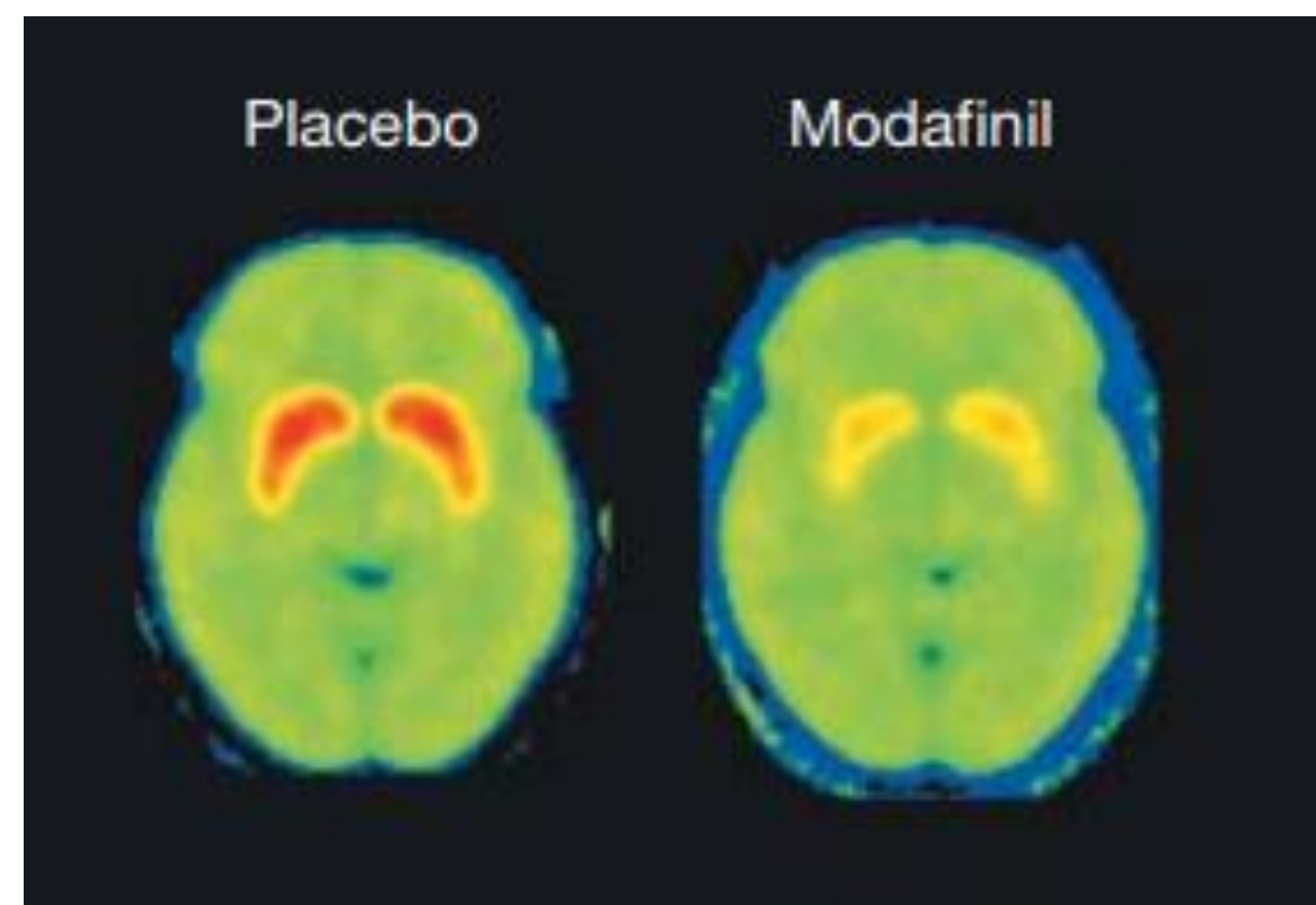


Figure 1. An averaged positron emission tomography image of the striatum showing that DA occupancy is higher for modafinil than placebo (Volkow et al., 2009).

Method

- Thirty subjects were randomly assigned to placebo (0mg), low (100mg), and high (200mg) doses of modafinil in a within-subjects design using a Latin square counterbalancing procedure.
- Blinks were detected from left and right frontal electroencephalography (EEG) electrodes during four minutes of eyes-open baseline recording (Figure 2). EBR was calculated as the number of blinks per minute.
- Blinks were visually counted by two raters who were blind to drug condition. Number of blinks were averaged for cases where interrater reliability was less than 95%.

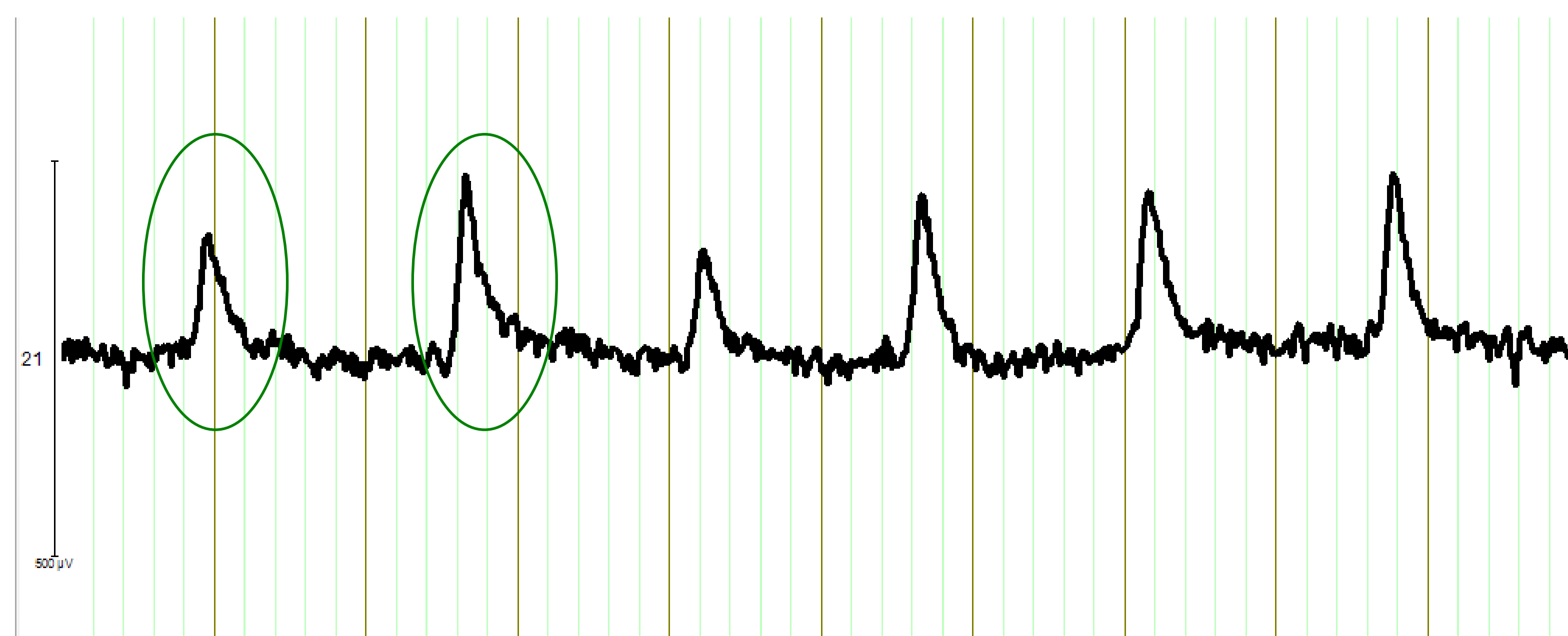


Figure 2. Eye blinks appear in the EEG as positive deflections over frontal eye channels. Six eye blinks can be seen in this example.

Results

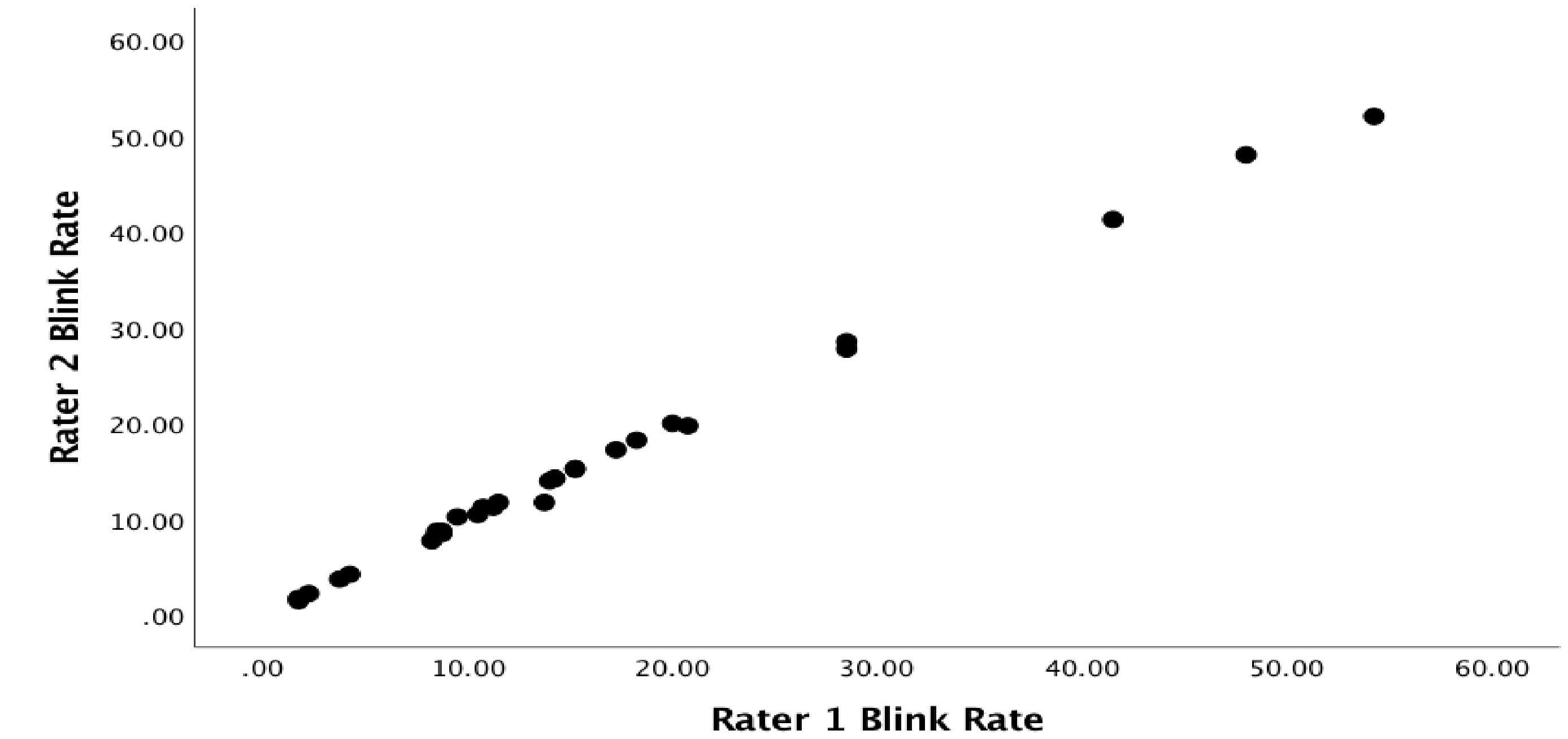


Figure 3. Interrater reliability. Two raters, blinded to drug condition, scored the blinks with an inter-rater reliability of .99.

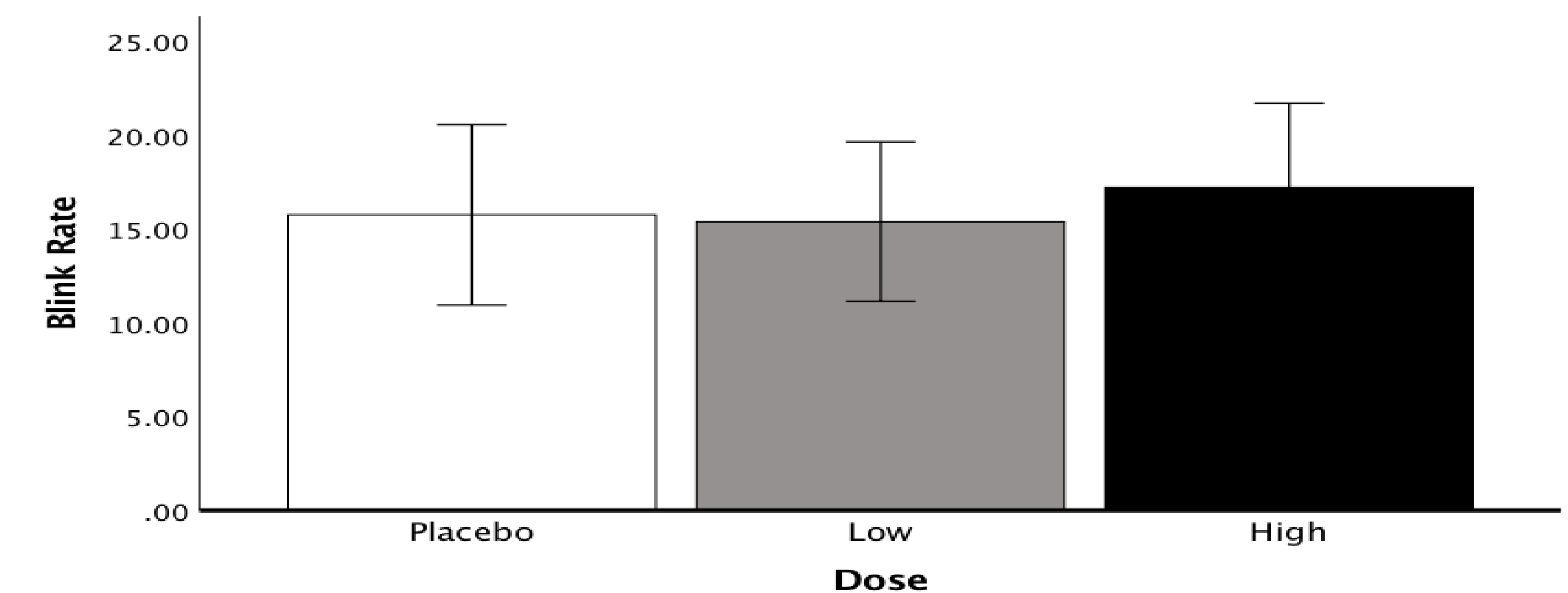


Figure 4. Modafinil did not modulate eye blink rate. Blinks were numerically greater in the high dose (M = 68.3) compared to placebo (M = 62.9) and low (M = 61.5), but the effect did not reach statistical significance ($F(2, 58) = 0.88, p = .42$). Nineteen participants showed more blinks in the high dose than the placebo dose (binomial $p = .051$). On average, participants showed 5.88 more blinks in the high dose than placebo (Cohen's $d = .019, p = .31$). The error bars represent 95% confidence intervals.

Discussion

- Contrary to our hypotheses, modafinil did not significantly increase EBR at any of the administered doses.
- Our findings suggest that EBR may not be as sensitive to dopaminergic modulation as previously hypothesized.
- Given that, on average, eye blinks were greater in the high dose than placebo, it is possible that a higher modafinil dose would have produced an effect. Alternatively, we speculate that more selective DA agonists (e.g., pramipexole) would dose-dependently increase EBR.
- Future research should test other compounds to form conclusions about the validity of EBR as a putative marker for DA function.

References

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2. Jongkees, B. J., & Colzato, L. S. (2016). Spontaneous eye blink rate as predictor of dopamine-related cognitive function: A review. *Neuroscience & Biobehavioral Reviews*, 71, 58-82.
3. Volkow, N. D., Fowler, J. S., Logan, J., Alexoff, D., Zhu, W., Telang, F., ... & Hubbard, B. (2009). Effects of modafinil on dopamine and dopamine transporters in the male human brain: clinical implications. *Jama*, 301(11), 1148-1154.