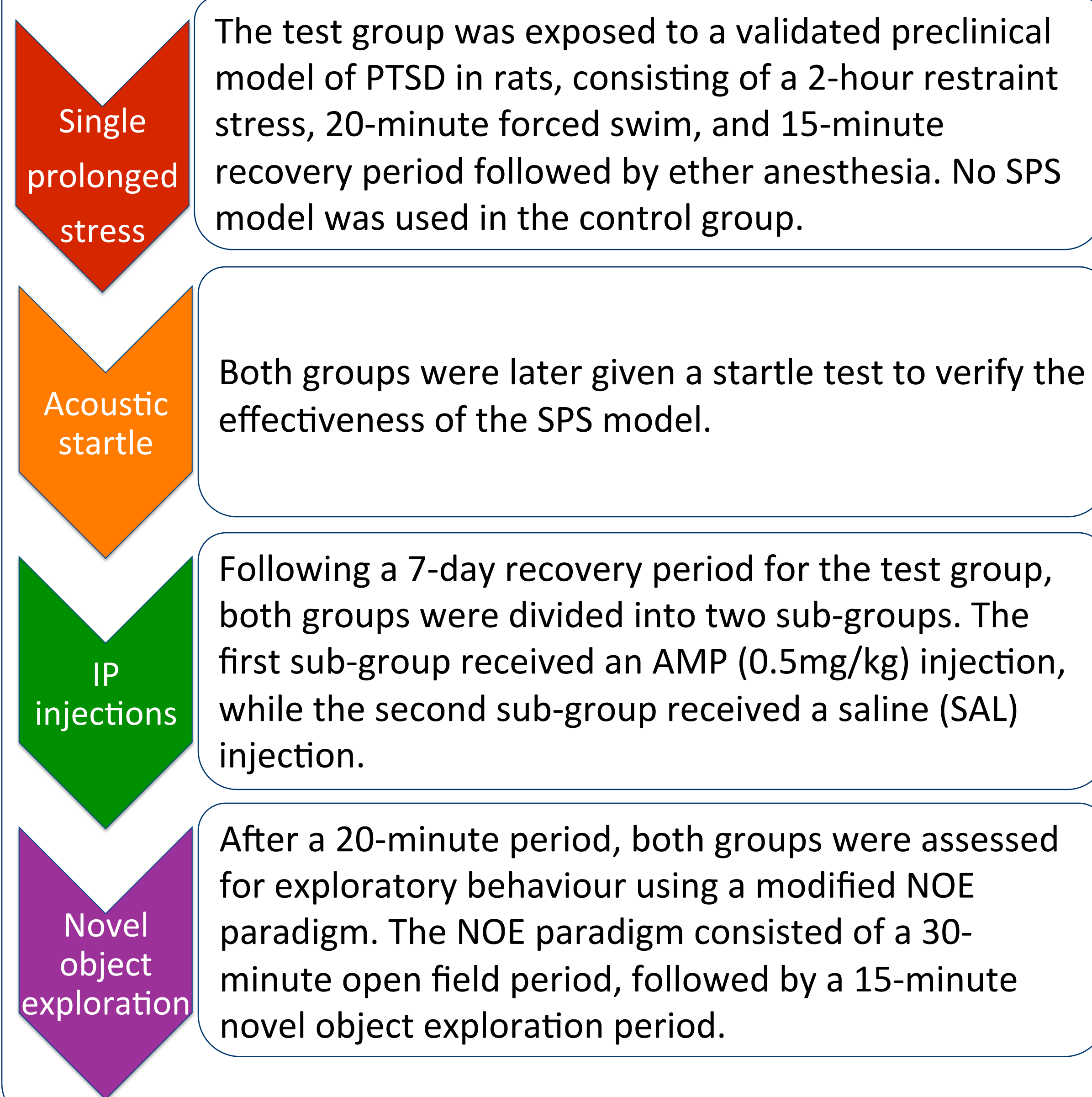


Introduction

Post-traumatic stress disorder (PTSD) is a debilitating disorder that is triggered by direct or indirect exposure to a traumatic stressor. This disorder is highly comorbid with substance use disorders (SUD), suggesting that they both involve similar neuronal mechanisms. Neural modifications found in the mesolimbic dopaminergic pathway have been linked to chronic substance abuse, leading to a distortion in normal reward functioning. In regards to PTSD, the human literature has observed increased blood and urine dopamine (DA) levels; however, there is a lack of research on DA levels in the brain. The current study examines whether PTSD can be related to behavioural alterations linked with the dopaminergic system. To investigate this possible correlation, two groups of 20 male Sprague-Dawley rats were used to explore the effects of exposure to a single prolonged stress (SPS) model and *d*-amphetamine (AMP) injections on exploratory behaviour. Such behaviour was assessed using a modified novel object exploration (NOE) paradigm.



Methodology



Validation

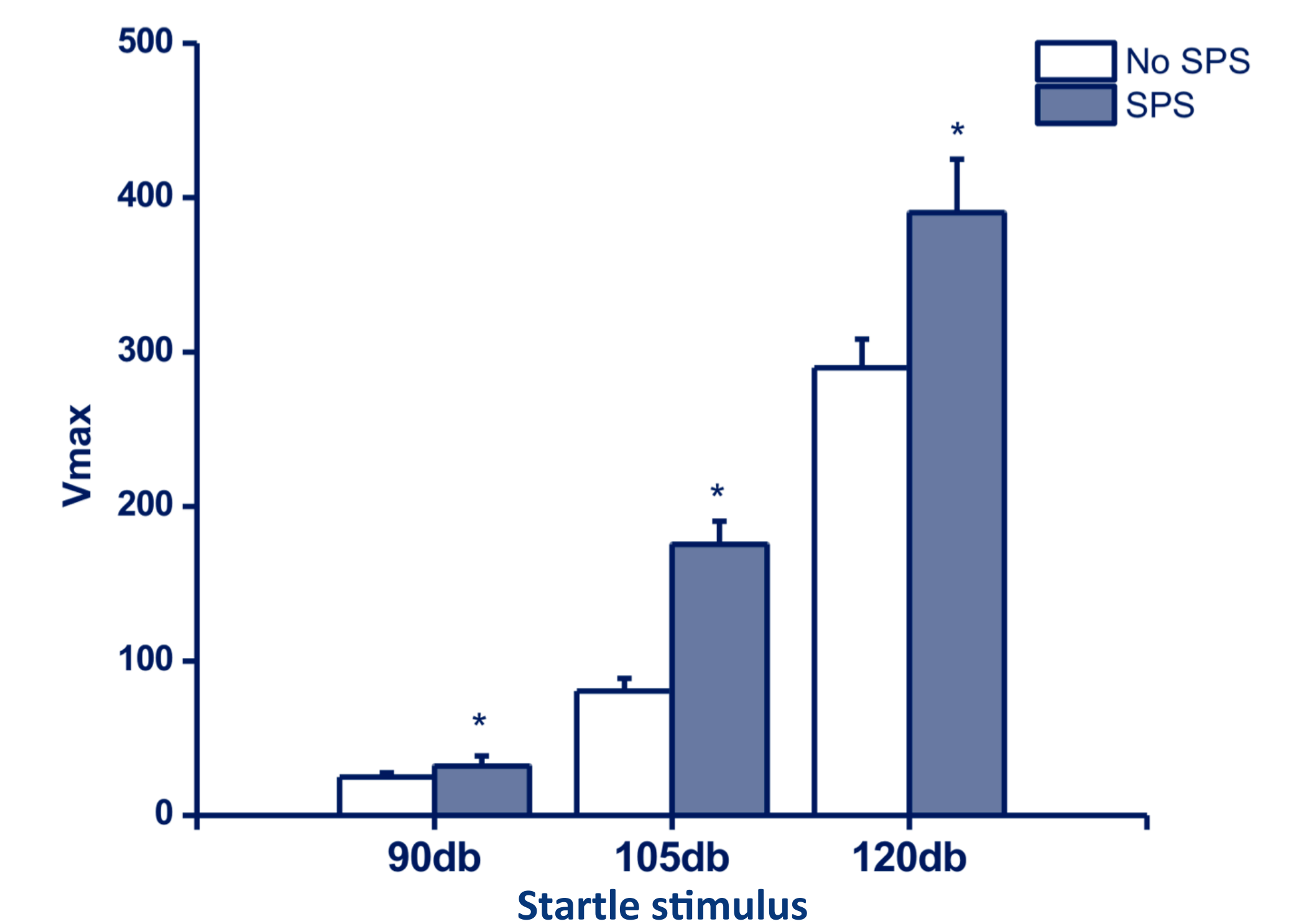


Figure 1. Effect of SPS model exposure on sensorimotor reactivity, as evaluated using acoustic startle responding in first cohort of Sprague-Dawley rats. Values represent the mean (\pm SE) peak response (maximum startle amplitude) averaged over 10 trials ($n = 10$ rats/group).

Results

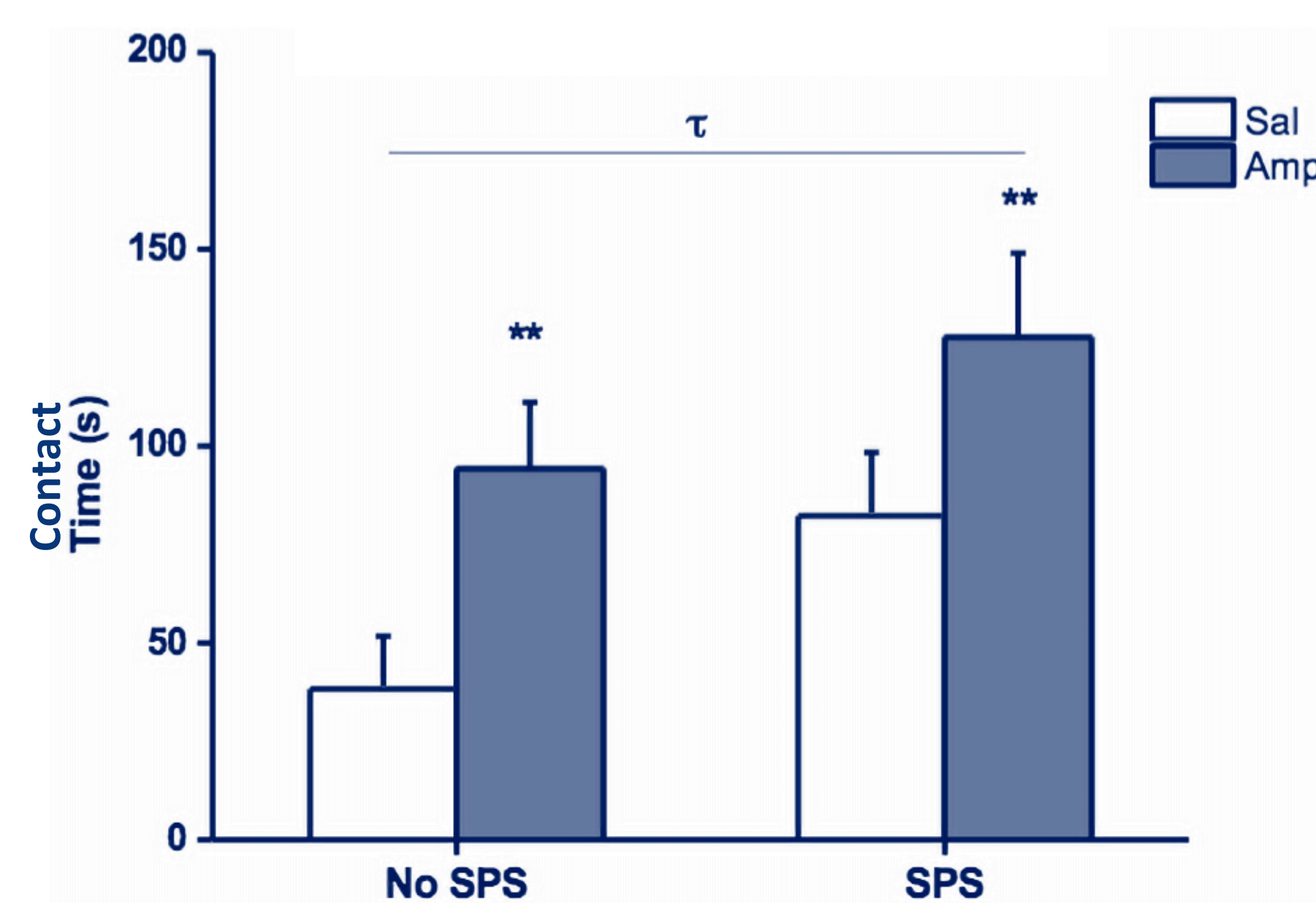


Figure 2. Effect of AMP and SPS exposure on time spent sniffing and touching object during 15-min presentation of novel object. Values represent the mean (\pm SE) contact time ($n = 14-16$ rats/group).

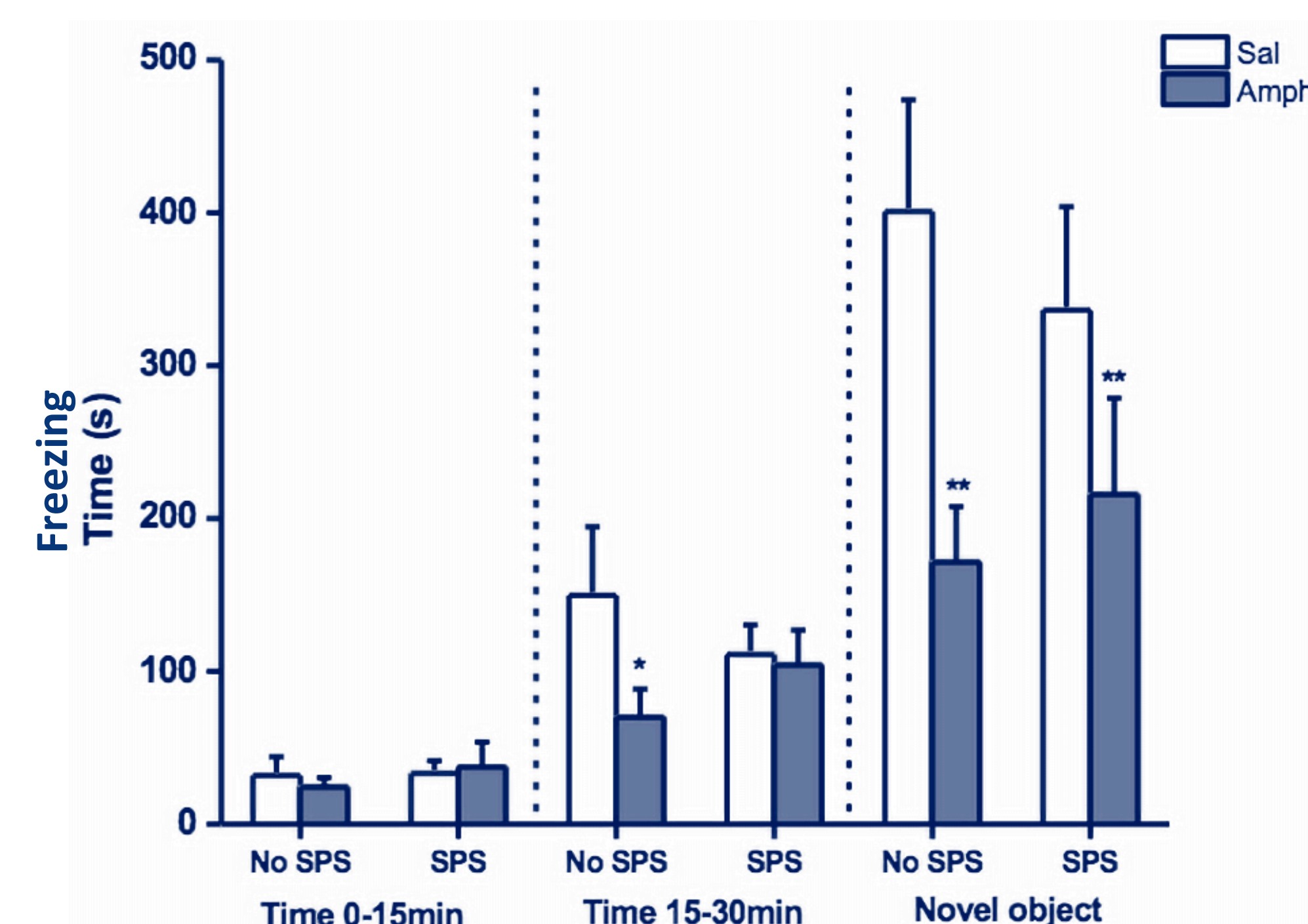


Figure 3. Effect of AMP and SPS exposure on anxiogenic behaviour, as evaluated by freezing behaviour. Values represent the mean (\pm SE) freezing time during each of three time segments ($n = 10$ rats/group).

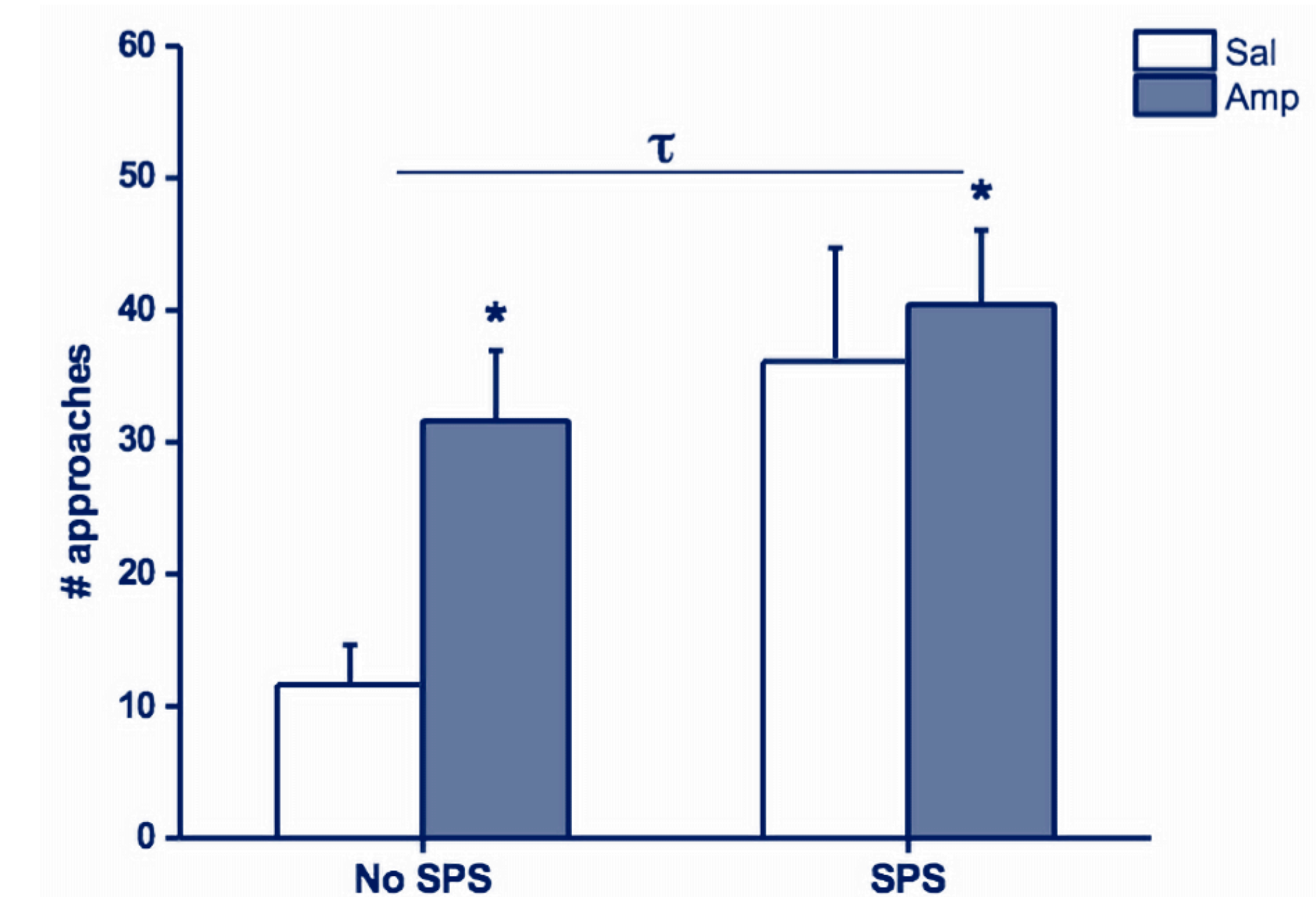


Figure 4. Effect of AMP and SPS exposure on approaches to center of arena during 15-min presentation of novel object. Values represent the mean (\pm SE) number of approaches ($n = 14-16$ rats/group).

Discussion

The exaggerated maximum startle amplitude observed in SPS-exposed rats compared to control rats in Fig 1 demonstrates the validity of SPS as an animal model of PTSD.

In regards to the NOE test, AMP-injected rats had higher contact time ($p < 0.01$) and number of approaches ($p < 0.05$), compared to SAL-injected rats, confirming that AMP increases exploratory behaviours linked to the dopaminergic system (Fig 2 & 4). Similarly, SPS-exposed rats had higher contact time



($p < 0.05$) and number of approaches ($p < 0.05$) when compared to No SPS rats, demonstrating that SPS exposure also increases exploratory behaviours in this paradigm.

Furthermore, during presentation of the novel object, AMP-injected rats froze significantly less than SAL-injected rats (Figure 3), suggesting that AMP has an anxiolytic effect. The AMP effect can be seen to reduce freezing during the 15-30 minute period (in No SPS rats, $p < 0.05$) and the 30-45 minute period (in No SPS and SPS rats, $p < 0.01$).

Conclusion

The results of the current study support the hypothesized link between PTSD and dopamine-related behaviours. SPS exposure was associated with increased novelty-seeking behaviour, as well as cross-sensitization of AMP-related exploratory behaviours. These findings may offer a basis of using stress-induced mesolimbic pathway modifications to explain reduced reward expectation & satisfaction in individuals with PTSD. Although this evidence can be used to shed light on the nature of the interaction between PTSD and SUDs, this interaction must be explored further, especially as it relates to reward system functioning.

Acknowledgements

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