

2018

Anorexic and Forgetting Effects of Lipopolysaccharide on Positive Reinforcement in Rats

Mahdieh Varvani Farahani
Western University, mvarvani@uwo.ca

Follow this and additional works at: https://ir.lib.uwo.ca/undergradawards_2018

 Part of the [Psychology Commons](#)

Recommended Citation

Varvani Farahani, Mahdieh, "Anorexic and Forgetting Effects of Lipopolysaccharide on Positive Reinforcement in Rats" (2018). *2018 Undergraduate Awards*. 17.
https://ir.lib.uwo.ca/undergradawards_2018/17

Anorexic and forgetting effects of lipopolysaccharide on positive reinforcement in rats

Abstract

It is widely demonstrated that lipopolysaccharide (LPS), a gram-negative bacteria derived endotoxin, induces symptoms that present similar to a stress response, commonly referred to as 'sickness behaviours'. The purpose of this study was to examine the effects of LPS on learnt food motivated behaviours in rats by analyzing bar pressing behaviours in a Skinner box under an FR-1 schedule. 23 male Long Evans rats were injected with either 200 µg/kg LPS ($n = 8$), 1 mg/kg of scopolamine hydrobromide (a known memory blocker; $n = 7$), or a saline control injection ($n = 8$). Prior to injection, rats were taught through shaping techniques that bar pressing resulted in reward in the form of food pellets. Baseline and test day measures of bar pressing were taken and compared. Bar pressing behaviours analyzed included locomotor activity, number of bar presses, rate of responding, and latency to first response during a 14 min session (2 min time bins). ANOVA was conducted to examine the trends. As expected, LPS rats performed significantly worse on learnt food motivated tasks than control rats, with decreased locomotion, decreased bar pressing, a slower rate of responding, and an increased latency to first response. These findings suggest LPS disrupts learnt food motivated behaviours. Implications lie in potential cytokine monitoring of the anti-psychotic drug induced weight gain seen in the treatment of schizophrenia. Future studies might look into distinguishing LPS induced memory impairment from the anorexic effects of LPS.

Anorexic and forgetting effects of lipopolysaccharide on positive reinforcement in rats

Lipopolysaccharide (LPS), a component of the outer membrane of gram-negative bacteria, is an active endotoxin that stimulates the neuroimmune and neuroendocrine systems (Arai, Matsuki, Ikegaya, & Nishiyama, 2001). Administration of LPS activates the immune system and results in the release of pro-inflammatory cytokines, including interleukin (IL)-1 β , IL-6, and TNF (Kent, Bret-Dibat, Kelley, & Dantzer, 1996; Arai et al., 2001; Sparkman, Martin, Calvert, & Boehm, 2005). LPS typically induces behavioural symptoms that present similar to a stress response, often referred to as 'sickness behaviours'. These behaviours include fever, fatigue, reduced locomotor and exploratory activity, and decreased motivation to engage in usual activities, including feeding, drinking, and social activities (Kent et al., 1996; Shaw, Commins, & O'Mara, 2001; Kinoshita, Cohn, Costa-Pinto, & de Sá-Rocha, 2009). Furthermore, there is overwhelming evidence that LPS and IL-1 β disrupt learning and memory consolidation by interrupting hippocampal long-term potentiation (Vereker, Campbell, Roche, McEntee, & Lynch, 2000; Jo, Park, Lee, Jung, & Lee, 2001).

Disruption of a learnt behaviour, such as bar pressing, can be used as a means of studying sickness behaviours. This paradigm requires that food restricted rats be trained to press a bar for positive food reinforcement. This is a reliable and easily quantifiable measure of motivational fluctuations and has been demonstrated in previous research to be a sensitive index of sickness (Babbini, Gaiardi, & Bartoletti, 1972; Gellert & Sparber, 1977). One particular study conducted by Kent et al. (1996) examined the effects of bilateral microinfusions of IL-1 β to the ventral medial hypothalamus (VMH) of food restricted rats. The VMH is one of two areas of the hypothalamus implicated in the control of food intake, with the lateral hypothalamic area (LHA) being the second. Kent et al. found that IL-1 β injections resulted in a significant decrease in food-

motivated behaviours in rats. Their findings support the notion that IL-1 β induces changes in neuronal activity that result in the suppression of glucose sensitive neurons and the increased activity of glucose responsive neurons (Kuriyama, Hori, Mori, & Nakashima, 1990).

In another study, Plata-Salaman, Oomura, and Kai (1988) further highlighted the importance of hypothalamic regions in the regulation of food intake. They suggested that one of the mechanisms by which IL-1 β and tumour necrosis factor (TNF) suppress food intake involves the inhibition of glucose-sensitive neurons in the LHA. In their study, Plata-Salaman et al. found that intracerebroventricular microinfusions of IL-1 β and TNF in the third ventricle suppressed food intake in rats. Furthermore, reduced water intake was also observed, but it was recognized to be a direct result of suppressed food intake, as water intake immediately recovered to preinfusion levels postinfusion, and no lasting effects were shown. With this rationale, the current study only analyzes food seeking behaviours, as water intake is not expected to be independently affected by immune stimulation.

With regards to the effects of LPS on memory and learnt behaviours, Sparkman, Kohman, Garcia, and Boehm (2005) found that mice treated with LPS showed impaired learning in a two-way active avoidance conditioning task. They observed significantly fewer avoidance responses, and less efficient behaviour in LPS induced mice rather than control mice. Their results suggested that LPS induced animals displayed a weakened association between the unconditioned stimulus and the conditioned stimulus. The current study will attempt to replicate these findings in a positive reinforcement food-motivated task in a rat population. In the current study, rats are expected to exhibit a decreased association between the pressing of the lever and rewarded food pellets once treated with LPS. It is expected that this decreased association will be

observed through a decreased rate and amount of bar pressing, and an increased latency to first response.

Similarly, Kranjac, McLinden, Deodati, Papini, and Chumley (2012) investigated the effects of LPS on memory consolidation in a contextual fear conditioning paradigm. As expected, the LPS injection impaired memory consolidation processes and disrupted learnt behaviours in the conditioning paradigm. The current study aims to connect these findings to the established LPS induced anorexic effects in rats (Kent et al., 1996), and provide further insight into the effects of LPS on positive reinforcement. It is expected that LPS injected rats display impaired memory through an increased latency to first response.

The link between stress and a disruption in learnt behaviours, particularly behaviours that are food motivated, is widely accepted. It follows that the behavioural effects of LPS on animal subjects has been shown to present similar to a stress response. Thus, the current study aims to further explore the effects of immune stimulation on learnt food motivated behaviours, by analyzing the bar pressing behaviours of positively reinforced LPS rats. The aforementioned analysis will pay specific attention to locomotion (horizontal and vertical movements), the total number of bar presses, the rate of responding, and the latency to first response exhibited in rats. Furthermore, an acetylcholine antagonist, scopolamine hydrobromide, is used as a positive control, given its well establish effects as a memory 'blocker' (Ohno, Yamamoto, Kobayashi, & Watanabe, 1993; Hodges, Lindner, Hogan, Jones, & Markus, 2009), and saline injections will be given to control rats in place of immune stimulants and memory blockers.

The current study predicts that LPS will have significant negative effects on memory, and food motivated behaviours in rats. Specifically, LPS injected rats are expected to show sickness

behaviours, as if in response to stress, and display decreased locomotion, decreased total bar presses, a slower rate of responding, and an increased latency to first response.

Method

Subjects

Twenty-three male Long Evans rats from Charles River, Quebec, weighing between 375 and 400 grams, were housed in pairs in polypropylene cages in a colony room (21 ± 1 °C). Rats were habituated to a food deprivation schedule that maintained them at 90% of pre-deprivation weight for one week prior to any testing. Subjects were on a 12:12 light/dark cycle, with lights turning on at 07:00 hr. Rats were divided into three condition groups: LPS ($n = 8$), scopolamine ($n = 7$), and saline control ($n = 8$). All rats were handled and tested in accordance with X's and X's guidelines.

Apparatus

Operant testing was carried out in plywood chambers (43 cm X 35 cm X 30 cm) designed like a standard Skinner box, with a clear Plexiglas front panel to allow for experimental observation, and a retractable lever beside the food pellet dispenser designed to provide reinforcement for every bar press under a fixed-ratio (FR-1) schedule. Lines were drawn in the chambers to divide the floor into six equal squares, and used to vertically dissect the box. The divisions created were used to guide behavioural assessment of the rats' locomotor activity. Number of reinforcements (food pellets rewarded to rats by experimenter) and responses (food pellets rewarded to rats in response to bar presses) were recorded by the apparatus.

Procedure

Drug Treatment. Rats were injected with 1 ml/kg solutions of either 200 µg/kg LPS (from *Escherichia coli* 0111:B4, L-2630; Sigma, St. Louis, MO) dissolved in 0.9% saline, 1

mg/kg of scopolamine hydrobromide (Sigma, St. Louis, MO) dissolved in 0.9% saline, or a control injection of the 0.9% saline vehicle. All injections were administered intraperitoneally. LPS and saline injections were given 2 hr prior to behavioural testing, whereas scopolamine was given 20 min prior to behavioural testing.

Behavioural Testing. Subjects were randomly assigned to one of three treatment conditions: LPS (200 μ g/kg; $n = 8$), scopolamine (1 mg/kg; $n = 7$), or saline control ($n = 8$). Rats received habituation sessions where they were placed in the box, and food pellets (Test Diet purified rodent table 5TUL) were available in the hopper to familiarize them with eating the reinforcer. Rats then received five daily training sessions one week prior to the test day. These training sessions consisted of shaping techniques conducted by the experimenter, where rats were rewarded for successive approximations towards the target behaviour. Small acts that indicated they were on the right path were rewarded by food pellets. Once it was clear rats learned a behaviour, reward for that behaviour was suspended and reward was only given in response to a more substantial behaviour. This was continued until the rats had clearly learnt that bar pressing resulted in reward. Rats received one baseline test session on the Saturday before test day, during which they were in the box for 14 min, divided into seven 2 min time bins, and the number of bar presses was monitored. Rats were injected with their respective drugs either 2 hr (LPS, saline) or 20 min (scopolamine) prior to placement in the operant chamber for 14 min (analyzed in seven 2 min time bins). Experimenters were blind to the rats' conditions. Rats were assessed on their locomotion, number of bar presses, rate of responding, and latency to first response. Horizontal movements were defined as the movement of both a rat's front paws across a single line, or across a diagonal. Anytime the rat's front two paws were off the floor of the box and the rat's snout was above the vertical dissection line constituted as a vertical movement. The

rats' rate of responding was recorded as the number of bar presses per time bin. The latency to first response was measured as the time it took, in seconds, for the rats to bar press for the first time after being placed in the box.

Results

Inter-rater reliabilities between raters one and two were calculated using a Pearson correlation. The two raters' data on horizontal movements and vertical movements were strongly correlated, $r(61) = .96$, and $r(61) = .92$, respectively. Therefore, all of the remaining analysis used only one rater's data. A 3×7 mixed design analysis of variance (ANOVA) was conducted to test the effects of immune stimulation on positive reinforcement in rats, with specific interest in horizontal movements, vertical movements, and rate of bar pressing. The between-subjects factor of treatment condition had three levels: LPS, scopolamine, and control, and the within-subjects factor of time bin had seven levels: time bins 1 through 7. A 3×2 mixed design ANOVA was conducted to test the effects of immune stimulation on bar pressing activity. The between-subjects factor of treatment condition had three levels: LPS, scopolamine, and control, and the within-subjects factor of day had two levels: baseline, and test. A one-way ANOVA was conducted to assess the effects of immune stimulation on latency to first response, with a between-subjects factor of treatment condition that had three levels: LPS, scopolamine, and control. An alpha level of .05 was used for all statistical tests.

A significant main effect of condition was found, such that LPS rats exhibited the least number of horizontal movements, followed by scopolamine rats, and control rats displayed the most horizontal movements, $F(2, 20) = 3.90, p = .037$. Furthermore, horizontal movements significantly decreased over time for all rats, $F(6, 120) = 22.72, p < .001$. A significant interaction was found between condition and time, as LPS rats displayed the least decline in

horizontal movements over time, when compared to scopolamine and control rats, $F(12, 120) = 2.32, p = .011$. These trends can all be seen in Figure 1.

LPS and scopolamine rats displayed significantly less vertical movements when compared to control rats, $F(2, 20) = 7.06, p = .005$. There was a significant decrease in vertical movements over time observed in all rats, $F(6, 120) = 15.83, p < .001$. Additionally, a significant interaction between time and condition was found, such that LPS rats displayed the least decline in vertical movements relative to scopolamine and saline control rats, $F(12, 120) = 2.16, p = .026$ (Figure 2).

A significant main effect emerged as LPS rats responded at a higher rate than scopolamine rats, but a lower rate than control rats, $F(2, 20) = 5.76, p = .01$. Furthermore, rate of responding significantly decreased over time for all rats, $F(6, 120) = 14.21, p < .001$. Referring to Figure 3, a significant interaction was displayed between condition and time, such that LPS rats displayed the greatest decline over time in their response rate as opposed to scopolamine and control rats, $F(12, 120) = 2.39, p = .008$.

Rats displayed a significant main effect of treatment condition on latency to first response, $F(2, 20) = 6.83, p = .005$. As seen in Figure 4, LPS rats displayed greater and lower latencies than control rats and scopolamine rats, respectively.

Lastly, a significant main effect of condition was found on the total number of responses on baseline and test days, $F(2, 20) = 24.53, p < .001$. LPS rats responded more than scopolamine rats but less than control rats on the test day. There was a significant main effect of day, such that a general decrease in responses from baseline to test day was observed, $F(1, 20) = 17.68, p < .001$. However, when analyzing the interaction effect, LPS and scopolamine rats displayed a

decrease in total responses from baseline to test day, whereas control rats performed similarly on both days, $F(2, 20) = 10.29, p = .001$ (Figure 5).

Discussion

As expected, these results suggest that LPS induced rats displayed a significant decrease in food-motivated behaviour. LPS rats exhibited less locomotor activity than scopolamine and control rats, as they made less horizontal and vertical movements. LPS rats demonstrated a significant reduction in responding when compared to control rats, although they still responded more than scopolamine rats. There was a clear disruption in the operantly conditioned food motivated behaviours of the LPS rats, as they displayed increased latency to first response when compared to control rats. However, LPS rats still displayed less latency to first response than scopolamine rats. Furthermore, when comparing the rats' food-motivated behaviour pre and post LPS injection, rats demonstrated induced anorexia effects as there was a significant reduction in responses, as opposed to control rats.

The effects of LPS as an active endotoxin has been widely accepted to present similar to a stress response in animals and result in 'sickness behaviours' (Shaw et al., 2001; Kinoshita et al., 2009). In a study conducted by Plata-Salaman (1994), the effects of centrally administered IL-1 β on the feeding behaviours of rats maintained ad libitum were examined using a computerized behavioural monitoring system. Plata-Salaman found that eating rate decreased in IL-1 β treated rats, alongside reductions in their meal size and duration. Additionally, the depression in food seeking behaviours observed was accompanied by a decrease in locomotor activity, similar to the present study. Although this study did not consider the memory impairment effects of immune stimulation, their findings regarding the depression in food seeking behaviours displayed in immune stimulated rats are congruent with the present study.

Similarly, a study conducted by Bret-Dibat, Bluthe, Kent, Kelley, and Dantzer (1995) examined the effects of LPS and IL-1 β on food motivated behaviours. Food restricted mice were trained to repeatedly poke their noses to receive a food reward at a ratio of 20 pokes per pellet. They found that LPS and IL-1 β injections in mice resulted in decreased food motivated behaviours; the number of nose pokes made to obtain a food pellet significantly diminished. The findings of the current study demonstrate similar anorexic effects of LPS, as the number of bar presses observed significantly decreased in response to the LPS treatment.

The present study also found that rats displayed other sickness behaviours commonly exhibited in LPS treated animals. Decreased locomotion was observed, indicating that rats were fatigued, or had no motivation for exploratory behaviour. Also, they exhibited an increase in latency to first response. This suggests that LPS treatments resulted in memory impairment in the rats. Anaeigoudari et al. (2015) found similar results when examining the effects of LPS on memory and learning in a passive avoidance test. Rats were trained to avoid a dark compartment, in which they had learnt they would be shocked. LPS treated rats displayed significant deficits in memory; they exhibited decreased latency to enter the dark compartment on test day when compared to the control group. Although the methodology of Anaeigoudari et al. is not identical to the present study, LPS rats displayed a disruption in their learnt behaviour following operant conditioning analogous to the increased latency to bar press observed in LPS rats in the current study.

One of the limitations of the present study lies in testing sessions only consisting of a single 14 minute trial. Findings would be more concrete if rats were observed when regaining their motivation to seek food as the effects of LPS diminished, similar to the study conducted by Kent et al. (1996). They tested the anorexic effects of LPS on rats at 1, 2, 4, 8, and 24 hr after

injection. The anorexic effects of LPS had diminished by 24 hr postinjection. Furthermore, Kent et al. found that maximal anorexic effects of IL-1 β are observed 1 hr after intraperitoneal administration. Perhaps the latency period prior to the presentation of LPS effects was overestimated in the current study. However, it would be incorrect to make this assumption without taking into consideration that the current study injected rats with LPS, whereas Kent et al. injected rats with IL-1 β , which has different temporal effects (Turrin et al., 2001).

Furthermore, the current study did not tease apart the individual effects of LPS on learnt behaviours and food motivated behaviours. Rats were observed to show a decline in learnt food motivated behaviours with no means of untangling whether that decline was a result of LPS induced impaired memory, or the anorexic effects of LPS induced sickness behaviours. Given the overwhelming evidence suggesting there are both anorexic and forgetting effects of LPS (Kent et al., 1996; Shaw et al., 2001; Kinoshita et al., 2009; Vereker et al., 2000), it is expected that the diminished learnt food motivated behaviours observed were a result of the combination of both factors. Future studies might look at distinguishing between these two variables, and investigating their individual effects on positive reinforcement, in addition to their interactive effects.

Despite the study's limitations, these findings have noteworthy implications on the physiological role cytokines play in weight regulation. During fat accumulation, adipose tissues secrete various immune factors, including inflammatory cytokines (Fontana, 2009). Consequently, similar to the anorexic effects of LPS observed in the present study, the released cytokines suppress feeding behaviours. In normal weight regulation, cytokines are released to maintain homeostatic balance, and once the required caloric restriction is achieved, the production of inflammatory cytokines is reduced (Fonseka, Müller, & Kennedy, 2016).

However, this process has been found to be disrupted by the long-term treatment of schizophrenia via anti-psychotics (APs). Administration of APs to treat schizophrenia has been found to increase the expression of anti-inflammatory mediators and reduce pro-inflammatory markers, including IL-1 β (Drzyzga, Obuchowicz, Marcinowska, & Herman, 2006; Meyer, Schwarz, & Muller, 2011; Kronfol & Remick, 2000). This disruption in pro-inflammatory adipose signalling induced by APs favours irregular and unhealthy fat accumulation in patients. Thus, the anorexic effects of LPS observed in the current study have implications on the routine clinical monitoring, and even perhaps treatment, of anti-psychotic induced weight gain (Fonseka et al., 2016). Further studies might examine the interactions between pro-inflammatory cytokines (specifically LPS induced IL-1 β) and anti-psychotics, in order to identify a range of plasma levels distinguishing healthy and pathological cytokine concentrations in patients being treated with APs.

In conclusion, the current study found that immune stimulation via LPS injections had significant negative effects on memory and food seeking behaviours in rats. These findings were congruent with the previous literature on the effects of neuroimmune stimulation via the release of pro-inflammatory cytokines. Future studies might extend these findings to find a means of monitoring AP induced weight gain with the help of the anorexic effects of LPS, and its resulting caloric restriction. Another avenue of future research might include the untangling of memory impairments and decreased food motivated behaviours in rats treated with LPS.

References

- Anaeigoudari, A., Shafei, M. N., Soukhtanloo, M., Sadeghnia, H. R., Reisi, P., Beheshti, F., . . . Hosseini, M. (2015). Lipopolysaccharide-induced memory impairment in rats is preventable using 7-nitroindazole. *Arquivos De Neuro-Psiquiatria*, *73*(9), 784–790.
- Arai, K., Matsuki, N., Ikegaya, Y., & Nishiyama, N. (2001). Deterioration of spatial learning performances in lipopolysaccharide-treated mice. *The Japanese Journal of Pharmacology*, *87*, 195–201.
- Babbini, M., Gaiardi, M., & Bartoletti, M. (1972). Changes in operant behavior as an index of a withdrawal state from morphine in rats. *Psychonomic Science*, *29*(3), 142–144.
- Bret-Dibat, J., Bluthé, R., Kent, S., Kelley, K. W., & Dantzer, R. (1995). Lipopolysaccharide and interleukin-1 depress food-motivated behavior in mice by a vagal-mediated mechanism. *Brain, Behavior, and Immunity*, *9*(3), 242–246.
- Drzyzga, L., Obuchowicz, E., Marcinowska, A., & Herman, Z. S. (2006). Cytokines in schizophrenia and the effects of antipsychotic drugs. *Brain, Behavior, and Immunity*, *20*, 532–545.
- Fonseka, T. M., Müller, D. J., & Kennedy, S. H. (2016). Inflammatory Cytokines and Antipsychotic-Induced Weight Gain: Review and Clinical Implications. *Molecular Neuropsychiatry*, *2*, 1–14.
- Fontana, L. (2009). Neuroendocrine factors in the regulation of inflammation: excessive adiposity and calorie restriction. *Experimental Gerontology*, *44*, 41–45.

- Gellert, V. F., & Sparber, S. B. (1977). A comparison of the effects of naloxone upon body weight loss and suppression of fixed-ratio operant behavior in morphine-dependent rats. *The Journal of Pharmacology and Experimental Therapeutics*, *201*(1), 44–54.
- Hodges, D. B., Lindner, M. D., Hogan, J. B., Jones, K. M., & Markus, E. J. (2009). Scopolamine induced deficits in a battery of rat cognitive tests: comparisons of sensitivity and specificity. *Behavioural Pharmacology*, *20*, 237–251.
- Jo, J. H., Park, E. J., Lee, J. K., Jung, M. W., & Lee, C. J. (2001). Lipopolysaccharide inhibits induction of long-term potentiation and depression in the rat hippocampal CA1 area. *European Journal of Pharmacology*, *422*, 69–76.
- Kent, S., Bret-Dibat, J., Kelley, K. W., & Dantzer, R. (1996). Mechanisms of sickness-induced decreases in food-motivated behavior. *Neuroscience and Biobehavioral Reviews*, *20*(1), 171–175.
- Kinoshita, D., Cohn, D. W., Costa-Pinto, F. A., & de Sá-Rocha, L. C. (2009). Behavioral effects of LPS in adult, middle-aged and aged mice. *Physiology & Behavior*, *96*(2), 328–332.
- Kranjac, D., McLinden, K. A., Deodati, L. E., Papini, M. R., Chumley, M. J., & Boehm, G. W. (2012). Peripheral bacterial endotoxin administration triggers both memory consolidation and reconsolidation deficits in mice. *Brain, Behavior, and Immunity*, *26*(1), 109–121.
- Kronfol, Z., & Remick, D. G. (2000). Cytokines and the brain: implications for clinical psychiatry. *The American Journal of Psychiatry*, *157*, 683–694.
- Kuriyama, K., Hori, T., Mori, T., & Nakashima, T. (1990). Actions of interferon- α and interleukin-1 β on the glucose-responsive neurons in the ventromedial hypothalamus. *Brain Research Bulletin*, *24*(6), 803–810.

- Meyer, U., Schwarz, M. J., & Muller, N. (2011). Inflammatory processes in schizophrenia: a promising neuroimmunological target for the treatment of negative/cognitive symptoms and beyond. *Pharmacology & Therapeutics*, *132*, 96–110.
- Ohno, M., Yamamoto, T., Kobayashi, M., & Watanabe, S. (1993). Impairment of working memory induced by scopolamine in rats with noradrenergic DSP-4 lesions. *European Journal of Pharmacology*, *238*, 117–120.
- Plata-Salamán, C. R. (1994). Meal patterns in response to the intracerebroventricular administration of interleukin-1 β in rats. *Physiology & Behavior*, *55*(4), 727–733.
- Plata-Salamán, C. R., Oomura, Y., & Kai, Y. (1988). Tumor necrosis factor and interleukin-1 β : suppression of food intake by direct action in the central nervous system. *Brain Research*, *448*(1), 106–114.
- Shaw, K. N., Commins, S., & O'Mara, S. M. (2001). Lipopolysaccharide causes deficits in spatial learning in the watermaze but not in BDNF expression in the rat dentate gyrus. *Brain Research Reviews*, *124*, 47–54.
- Sparkman, N. A., Martin, L. A., Calvert, W. S., & Boehm, G. W. (2005). Effects of intraperitoneal lipopolysaccharide on Morris maze performance in year-old and 2-month-old female C57BL/6J mice. *Behavioural Brain Research*, *159*(1), 145–151.
- Sparkman, N. L., Kohman, R. A., Garcia, A. K., & Boehm, G. W. (2005). Peripheral lipopolysaccharide administration impairs two-way active avoidance conditioning in C57BL/6J mice. *Physiology & Behavior*, *85*(3), 278–288.
- Turrin, N. P., Gayle, D., Ilyin, S. E., Flynn, M. C., Langhans, W., Schwartz, G. J., & Plata-Salamán, C. R. (2001). Pro-inflammatory and anti-inflammatory cytokine mRNA

induction in the periphery and brain following intraperitoneal administration of bacterial lipopolysaccharide. *Brain Research Bulletin*, 54(4), 443–453.

Vereker, E., Campbell, V., Roche, E., McEntee, E., & Lynch, M. A. (2000). Lipopolysaccharide inhibits long term potentiation in the rat dentate gyrus by activating caspase-1. *The Journal of Biological Chemistry*, 275(34), 26252–8.

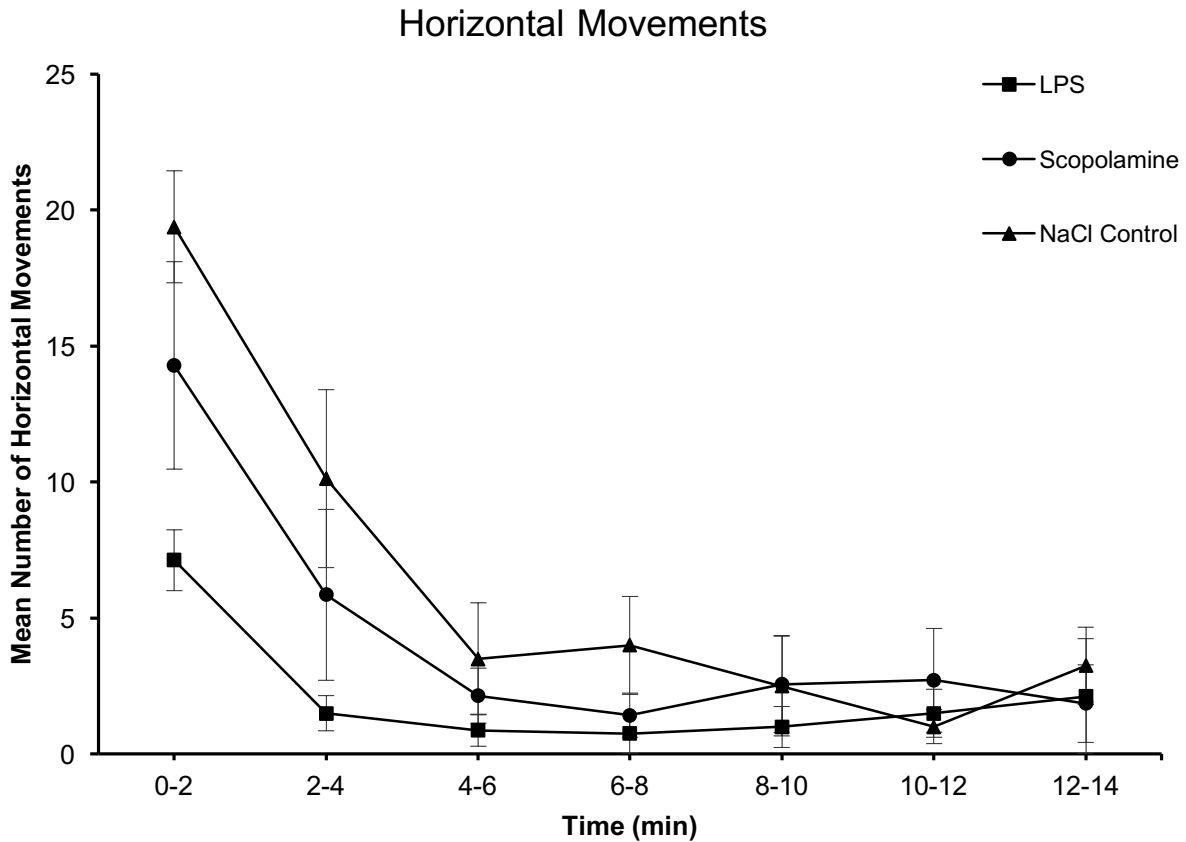


Figure 1. Mean horizontal movements (\pm SEM) observed in 23 rats following injection of 200 $\mu\text{g}/\text{kg}$ lipopolysaccharide (LPS; $n = 8$), 1 mg/kg of scopolamine hydrobromide ($n = 7$), or NaCl control ($n = 8$). LPS rats displayed significantly less horizontal movements than scopolamine and control rats, and the number of horizontal movements displayed by all rats significantly decreased over time. A significant interaction between treatment and time was demonstrated as LPS rats exhibited the least decline in horizontal movements over time compared to scopolamine and control rats.

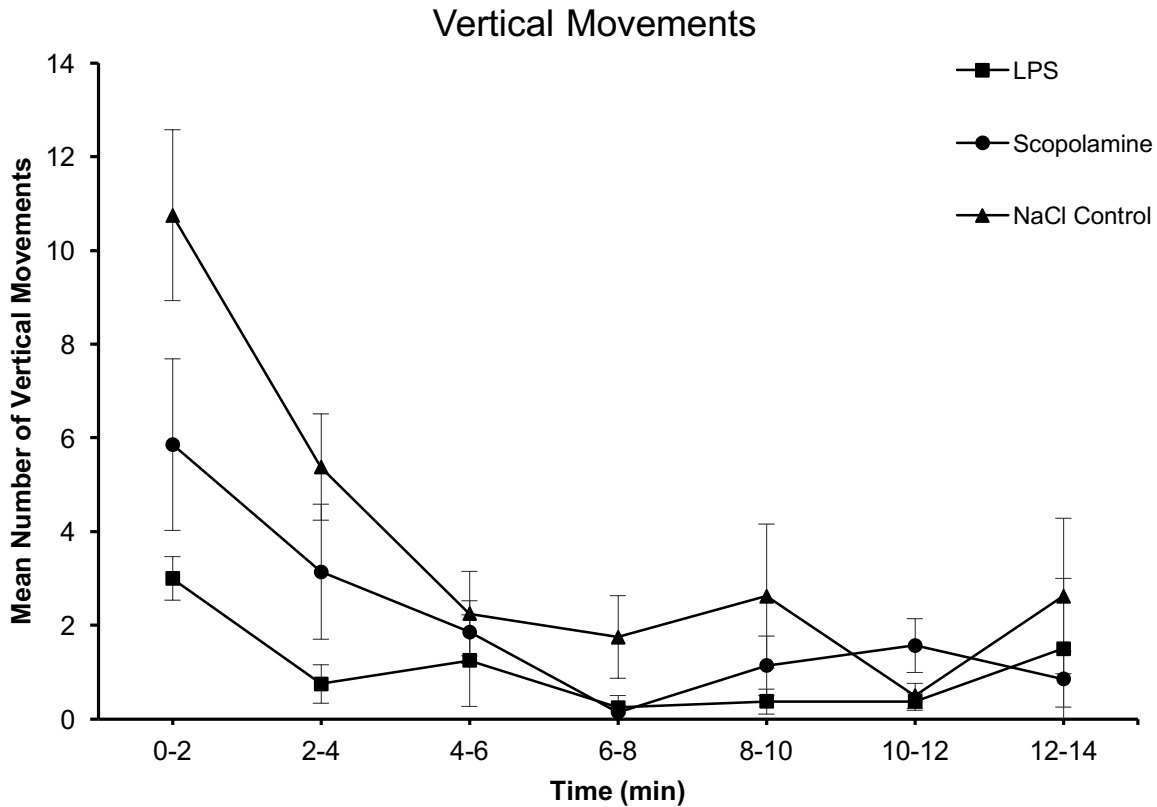


Figure 2. Mean vertical movements (\pm SEM) observed in 23 rats following injection of 200 $\mu\text{g}/\text{kg}$ lipopolysaccharide (LPS; $n = 8$), 1 mg/kg of scopolamine hydrobromide ($n = 7$), or NaCl control ($n = 8$). LPS and scopolamine rats displayed significantly less vertical movements than control rats, and vertical movements significantly decreased over time for all rats. A significant interaction between time and condition was found, such that LPS rats displayed the least decline in vertical movements over time compared to scopolamine and saline control rats.

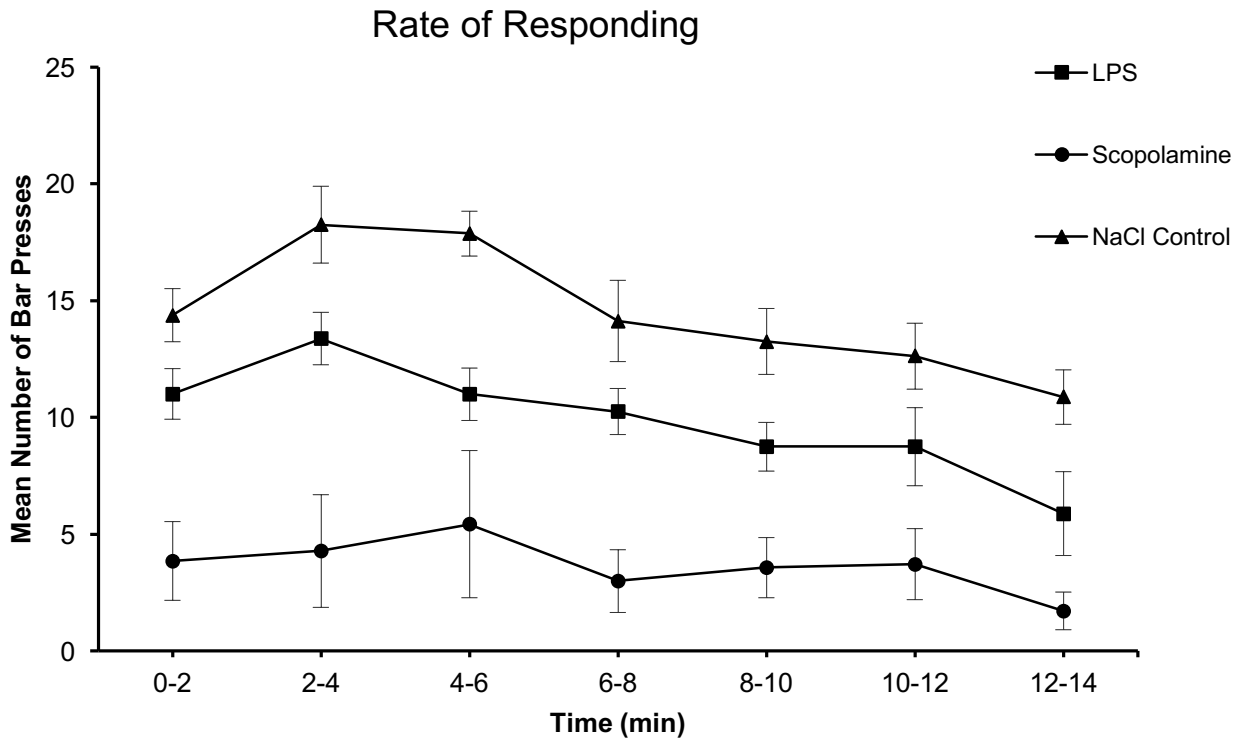


Figure 3. Mean response rate (\pm SEM) observed in 23 rats following injection of 200 $\mu\text{g}/\text{kg}$ lipopolysaccharide (LPS; $n = 8$), 1 mg/kg of scopolamine hydrobromide ($n = 7$), or NaCl control ($n = 8$). LPS rats responded at a higher and lower rate than scopolamine and control rats, respectively. Response rate significantly decreased over time for all rats. A significant interaction between treatment and time was demonstrated as LPS rats displayed the greatest decline over time in their response rate compared to scopolamine and control rats.

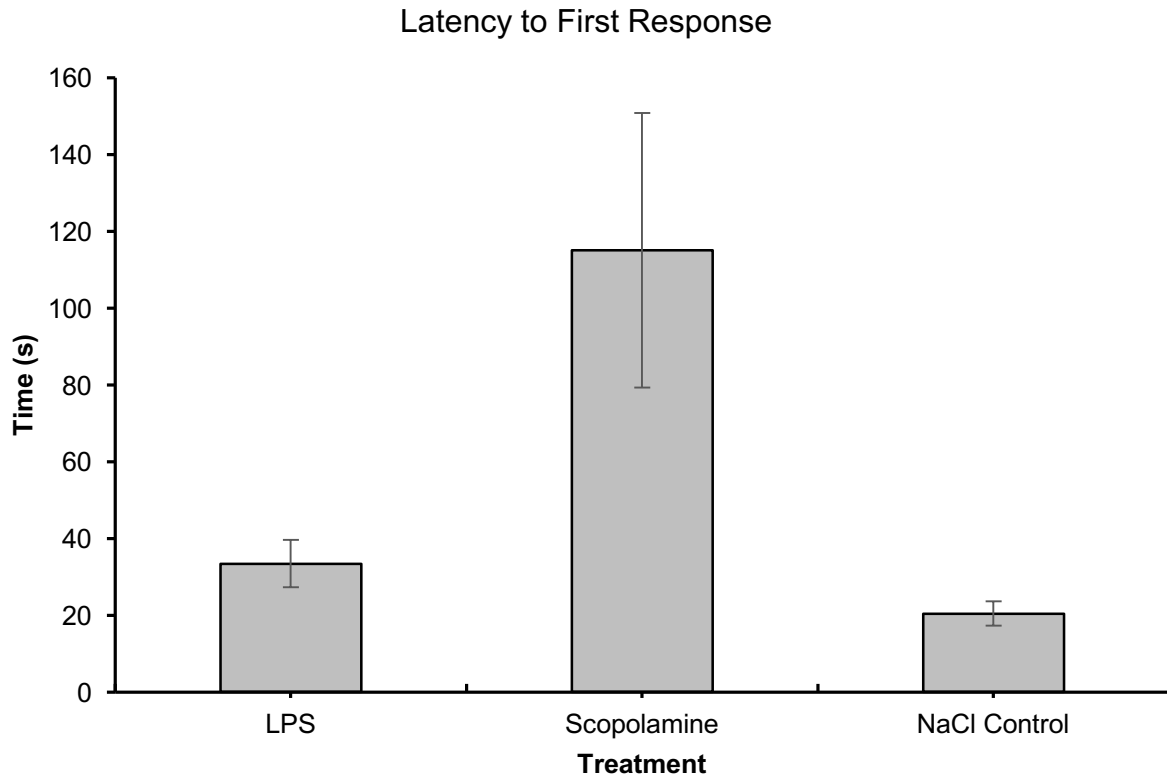


Figure 4. Mean latency to first response (\pm SEM) recorded in 23 rats following injection of 200 μ g/kg lipopolysaccharide (LPS; $n = 8$), 1 mg/kg of scopolamine hydrobromide ($n = 7$), or NaCl control ($n = 8$). LPS rats displayed significantly greater and lower latencies than control and scopolamine rats, respectively.

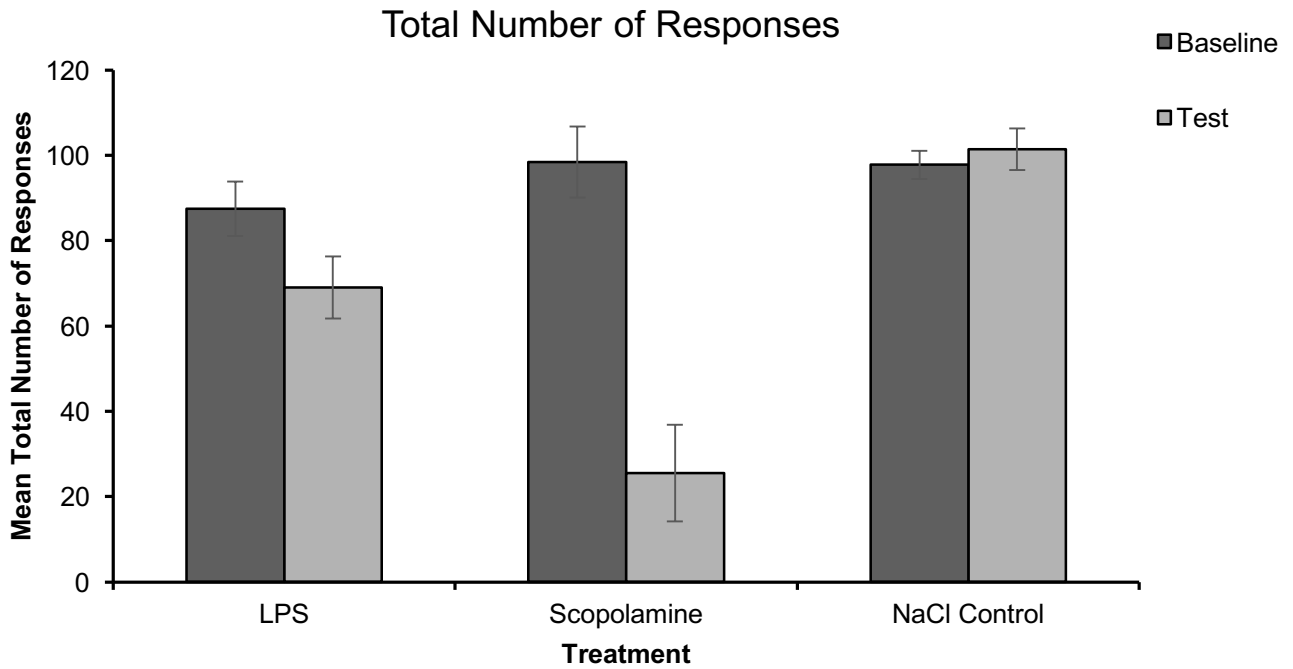


Figure 5. Mean responding in baseline and test days (\pm SEM) recorded in 23 rats following injection of 200 μ g/kg lipopolysaccharide (LPS; $n = 8$), 1 mg/kg of scopolamine hydrobromide ($n = 7$), or NaCl control ($n = 8$). LPS rats responded significantly more and less than scopolamine and control rats, respectively. There was a significant decrease in responding from baseline to test trials for all rats. A significant interaction between treatment and time was seen as LPS and scopolamine rats displayed decreased responses from baseline to test trials, whereas control rats did not.