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Mason Kadem
Western University

Shelley Cross-Mellor Ph.D.
Western University

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Mason Kadem* and Dr. Shelley Cross-Mellor

Activation of the immune system results in release of cytokines that affect memory retrieval and induces a general "sickness behavior" as depicted by decreased appetite, locomotor activity, and motivation to exert effort. Lipopolysaccharide (LPS) delivery has been commonly used to study effects of immune system activation in rats using study paradigms that assess changes in motivational behavior. Food-motivated behaviors are driven by positive reinforcement tasks, which rely on adequate memory retrieval to acquire the sought award. Previous studies determined that LPS has a negative impact on food-motivated behavior as depicted by decreased bar pressing frequency, a quantifiable parameter for operationally defining positive reinforcement. However, previous studies did not consider the role of LPS on locomotor activity on the portrayed decreased bar pressing frequency. Therefore, this study will evaluate the role of LPS administration and dose on positive reinforcement retention (through bar pressing for food release) in rats compared to NaCl treated control rats, and whether LPS has an effect on locomotor activity. It was hypothesized that an immune response via LPS delivery will affect memory retrieval in rats in the form of positive reinforcement tasks (lower bar-pressing frequencies), decreased locomotor activity via lower vertical and horizontal movements when compared to control rats. It was found that LPS-treated rats exhibit decreased locomotor activity, and bar pressing frequency compared to control rats, indicating that the decreased desire to exert effort may explain why LPS negatively impacts positive reinforcement retention.

Activation of the immune system results in several behavioral changes known as "sickness behavior", which includes diminished cognitive functioning, memory retrieval, and a decreased appetite (Larson, 2002). Specifically, increased production of inflammatory cytokines, as a result of immune system activation, have been shown to decrease memory retrieval (Woods et al., 2007) and affect food-motivated behavior (Kent, Bret-Dibat, Kelley, & Dantzer, 1996). Food-motivated behavior is reliant upon sufficient memory retrieval. Thus, decreased appetite exhibited during "sickness behavior" post-immune system activation may also highlight decrements in memory retrieval capacity. Lipopolysaccharide (LPS), a glycolipid found in the outer membrane of Gram negative bacteria, is typically administered in studies

* This study was conducted as part of a lab assignment in Psychology 3285 under the supervision of Dr. Shelley Cross-Mellor. Dr. Cross-Mellor proposed the design of the study, and performed some of the key methodological interventions, including, but not limited to the conception of study and statistical analysis of pooled data. Francis Boon (course animal technician) was responsible for injecting animals, animal care as well as the baseline measures. Students in the course were responsible for collecting and sharing data relevant to the training and testing of animals and for the parameters discussed herein (i.e., locomotion, # bar presses, rate of responding, latency to first response). The data were pooled and analyzed by Dr. Cross-Mellor. Each student was then responsible for writing his/her own introduction to the paper, methods, results section and discussion. The authors acknowledge the important contributions of Francis Boon and the other students in the course to the collection of data, but take sole responsibility for all other ideas as expressed in this paper. For inquiries regarding the article, please e-mail the main author at *mason.kadem@uwo.ca*.

investigating effects of immune system activation as LPS delivery has been shown to increase production and release of inflammatory cytokines. To this end, food-motivated behavior dysfunction, that accompanies LPS-induced activation of the immune system, may further indicate deficits in memory retrieval capabilities.

Lipopolysaccharide-treated rats have shown decreased consumption of food (Larson & Dunn, 2001; Larson, 2002); however, findings were interpreted as an indication of depressive tendencies (Yirmiya, 1996) and/or a decrease in reward seeking behavior (Shen, Connor, Nolan, Kelly, & Leonard, 1999). Specifically, these studies indicated that LPS-treated rats exhibit non-pleasure seeking behaviors, anhedonia (Larson, 2002), indicative of a reduced sensitivity to reward (Shen et al., 1999; Yirmiya, 1996). In one study, LPS-treated rats exhibited depressive-like behaviors, which were verified by removal of this behavior when LPS-treated rats were concurrently treated with antidepressants. In the indicated study, the LPS-treated rats decreased consumption of sugar-water solution and also exhibited decreased sexual behavior (Yirmiya, 1996). While these non-pleasure seeking behaviors may be explained by a general apathetic mood towards reward, another plausible explanation for these behaviors may also be a lack of motivation to acquire the reward.

Fifty years ago (1965), Neal Miller observed that rats treated with endotoxin (i.e., LPS) certainly had decreased bar pressing tendencies associated with food-motivated behavior; however, these same rats, when placed in a rotating drum, increased bar pressing frequency as bar pressing resulted in brief rest periods of rotation in the drum (Larson & Dunn, 2001). This and more recent studies (Larson & Dunn, 2001; Larson, 2002) indicate LPS-treated rats in food-motivated behavior using positive reinforcement study paradigms may be impelled by a strong opposition to effort exertion, rather than a mere loss of appetite or a general desensitization to reward.

Food-motivated behavior is quantified by using study paradigms that measure operant conditioning behavior through positive-reinforcement tasks, as in the bar-pressing mechanism in the rodent model (Babbini, Gaiardi, & Bartoletti, 1972). In this model, rats learn to press on a bar and food is subsequently released. In this context, the bar-pressing maneuver relies on memory retrieval, as the act of bar-pressing results in food reward. Thus, while bar pressing has primarily been used as a means to measure a food-motivated behavior in the context of positive reinforcement and reward-seeking, bar pressing can also identify memory retrieval skills. As previously mentioned, LPS-treated rats exhibit a decreased appetite, and a general tendency to refrain from reward-seeking (in the form of food intake). In accordance with Miller's study in 1965, LPS-treated rats exhibit decreased locomotor activity (Engeland, Kavaliers, & Ossenkopp, 2003). However, previous studies did not investigate the role of LPS on positive reinforcement (an indicator for memory retrieval) in a bar pressing study paradigm, and whether LPS-induced lack of locomotor activity had a role in the hypothesized differential responses to positive reinforcement exhibited between LPS-treated rats and control rats.

Thus, this study will evaluate the effect of LPS administration in rats on bar pressing as a means to assess memory retrieval changes that may result with LPS treatment compared to saline-treated rats (control). Food-motivated behavior, a form of operant conditioning which relies on memory retrieval, will be operationally defined by bar pressing frequency. The aforementioned general lack of motivation for effort exertion which accompanies LPS treatment will be accounted for by measuring movement-based parameters, such as vertical and horizontal movement, and assessing how

LPS affects bouts of movement when compared to saline-treated controls. Additionally, there exists a relationship between LPS dose and degree of "sickness behaviors" like loss of appetite, anhedonia, and a general lack of motivation to exert effort (Bassi et al., 2012). Thus, the effect of LPS dose (low versus high) on bar pressing will also be investigated. It is hypothesized that using a food-motivated behavior study paradigm which implements a positive reinforcement task such as bar-pressing, immune suppression via LPS delivery will affect memory retrieval in rats in the form of positive reinforcement tasks, when compared to negative controls (NaCl-treated). Specifically, it is hypothesized that LPS-treated rats will exhibit lower bar-pressing frequencies, and lower vertical and horizontal movements when compared to control rats. Additionally, the decrements in bar pressing and horizontal and vertical movements will be dependent on LPS dose, in that higher LPS dose will result in lower bar pressing and bi-directional movement.

Method

Animals

Twenty-four male Long Evans rats (Charles River, Quebec, Canada), weighing 200-225 g, were housed in pairs in polypropylene cages. The colony room was maintained at 21 ± 1 ºC with a 12-h light/dark schedule (lights on at 0700h). Rats were adopted food deprivation schedule and were maintained at 90% of pre-deprivation body weight. All testing was with accordance to guidelines set out by the Canadian Council on Animal Care (CCAC), and approved by Western's monitoring system.

Apparatus

Operant tests were conducted in a chamber (43 cm X 35 cm X 30 cm) made of plywood with a clear Plexiglas front panel. Inside the chamber, there was a retractable level beside the food pellet dispenser, which was designed to provide reinforcement for every bar press (FR-1). Positive reinforcement was operationally defined by measuring parameters associated with bar pressing (i.e., bar press frequency, response rate, latency to first response, and pre- and post-bar press responses).

Drugs and Procedure

Rats were injected (intraperitoneal [i.p.]) with either 50 ug/kg (low dose) or 200 ug/kg (high dose) LPS derived from *Escherichia coli* 0111:B4, L-2630 (Sigma, St. Louis, MO) that was dissolved in 0.9% saline. Injections were given 90 minutes prior to testing. Rats received a habituation session to familiarize themselves with eating a reinforcing food (food pellets – Test Diet purified rodent table 5TUL). Thereafter, rats received daily training sessions one week prior to the test day. The training session included the rat first being placed in the testing chamber, and the researchers would reinforce every time the rat got close to the bar (by providing food pellets). Thereafter, reinforcement would cease, and the rats were then reinforced only when the rat sniffed or touched the bar, then only when the rat pressed on the bar. This resulted in the rats associating bar pressing with food pellet, using positive operant conditioning. Rats received two baseline test sessions, in box for 12 minutes and number of bar presses monitored on two consecutive days before test day. Prior to the test session on test day, rats were treated with a drug injection, 90 minutes prior to placement in operant chamber for 12 minutes. Thereafter, the following was assessed: locomotion (i.e., horizontal and vertical movements), number of bar presses and corresponding response rate, and latency to first response.

Data Analysis

Repeated measures analysis of variance (ANOVA) was completed for horizontal movements, vertical movements, response rate,

and pre- and post- responses. A one-way ANOVA was completed for latency to first response. In all cases the significance level of alpha was 0.05. Pearson correlations were used to assess inter-rater reliability rater 1 and rater 2 for horizontal movement and vertical movement. Between-subjects factors for horizontal movements, vertical movements, response rate, latency to first response, and pre- and post-responses were assessed based on the type of drug treatment received (at three levels: NaCl Controls, Low Dose LPS, High Dose LPS). Within-subjects factor was time for horizontal movements, vertical movements, and response rate, and the within-subjects factor for pre- and post-responses was number of days. Results are expressed as mean ± standard error of the mean (S.E.M), unless stated otherwise. The researchers were blinded during testing.

Results

Inter-rater observations were strongly correlated, with a Pearson correlation of $r(142) = .86$ and $r(142) = .89$, $p < .05$, for horizontal movement and vertical movement, respectively; therefore analysis was solely completed based on observations made by rater 1.

Horizontal Movements

ANOVA analysis revealed a significant main effect of both group ($F(2, 21) = 4.775$, $p=.020$) and time ($F(5, 105) = 23.38$, $p < .001$) as well as an interaction effect for both group and time ($F(10, 105) = 2.385$, $p = .014$). Horizontal movements across time for NaCl controls, Low Dose LPS (50ug/kg) and High Dose LPS (200 ug/kg) across time are depicted in *Figure 1*. The effect of group on horizontal movements indicates that rats treated with a high dose of LPS had less horizontal movements than both Low Dose LPS-treated rats and NaCl control rats within the first 2 minutes of observation. However, after this first observation, all rat groups exhibited similar levels of horizontal movements with time (Figure 1). The effect of time on horizontal movements is indicated by change in horizontal movement with time. Specifically, High Dose LPS rats had stable number of horizontal movements with time (zero slope, Figure 1), while both the Low Dose LPS and NaCl Control groups had a steep decrease in horizontal movements from the 2nd to the 4th minute (large negative slope), and thereafter followed the same stable non-changing pattern of horizontal movements with time as that shown by High LPS rats (Figure 1). The group and time interaction effect indicates that depending on their group assignment (NaCl Control, Low Dose LPS, High Dose LPS), the rats exhibited a different number of horizontal movements with time. Specifically, both Low Dose LPS-treated and NaCl-treated rats exhibited a negative and linear relationship (negative slope; Figure 1) from two to four minutes as exhibited by a steep and negative slope, while High Dose LPS-treated rats did not exhibit a relationship horizontal movements and time (zero slope; Figure 1).

Vertical Movements

ANOVA analysis revealed a significant main effect of both group ($F(2, 21) = 7.056$, $p = .005$), and Time ($F(5, 105) = 15.833$, $p < .001$), as well as an interaction effect for both group and trial ($F(10, 105) = 2.164$, $p = .026$).Vertical movements across time for NaCl controls, Low Dose LPS (50ug/kg) and High Dose LPS (200 ug/kg) are depicted in *Figure 2.* The effect of group on vertical movements is present due to the finding that rats treated with a high dose of LPS had less vertical movements than both Low Dose LPS-treated rats and NaCl control rats within the first two minutes of observation. However, after this first observation, both Low and High Dose treated rat groups exhibited similar level of vertical movements from four to six minutes, and Low Dose LPS treated rats behaved similarly to NaCl Control rats from

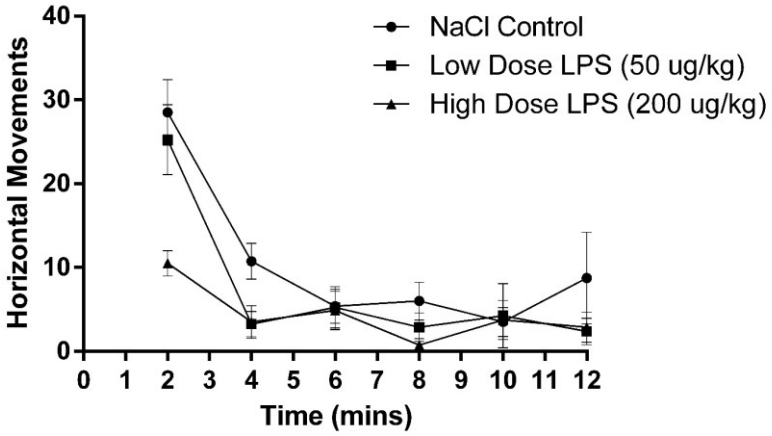

Figure 1. Horizontal movement across time for NaCl-treated, Low Dose LPS-treated, and High Dose LPS-treated rats. Mean + (S.E.M) number of horizontal movements exhibited by three treatment groups, NaCl Control (*n*=8), Low Dose LPS (n=8), and High Dose LPS (*n*=8), across time. High Dose LPS-treated rats had less horizontal movements than both Low Dose LPS-treated rats and NaCl control rats within the first two minutes, followed by similar levels of horizontal movements with time for all groups. NaCl Control and Low Dose LPS rats had a rapid and steep decrease in horizontal movements in the first two minutes (steep, negative slope), compared to the stable non-changing (zero slope) number of movements exhibited by High Dose LPS rats for all observations.

eight to 12 minutes, whereas High Dose LPS treated rats had lower vertical movements in the eight to 12 minutes (Figure 2). The effect of time on vertical movements is indicated by High Dose LPS having less vertical movements with progression of time (negative slope; Figure 2), while both the Low Dose LPS and NaCl Control groups only had decrease in vertical movements from two to four minutes, followed by a stable and non-changing (zero slope; Figure 2) number of vertical movements with the progression of time (from four to 12 minutes). The group and time interaction effect indicates that depending on their group assignment (NaCl Control, Low Dose LPS, High Dose LPS), the rats exhibited a different number of vertical movements with the progression of time (the groups did not exhibit the same slope for vertical movement as a function of time). Specifically, NaCl Control rats had a rapid decrease in vertical movements with the progression of time (as exhibited by a steep negative slope) from two to six minutes, followed by a stable and non-changing (zero slope) number of vertical movements with time. Conversely, the Low Dose LPS-treated rats also exhibited a rapid decrease in vertical movements with progression of time; however, this only occurred during the two to four minute range (as indicated by a steep negative slope). Finally, High Dose LPS-treated rats also exhibited a decrease in vertical movements with progression of time, however the decrease in vertical movements was not as apparent as that seen by the other two groups in the two to six minute ranges. The number of vertical movements elicited by the High Dose LPS-treated rats continued to decrease with time (even after the 6-minute mark) rather than level off like the other two groups (Figure 2).

Response Rate

ANOVA analysis revealed a significant main effect of both group ($F(2, 21) = 16.359$, $p < .001$), and time ($F(5, 105) = 4.896$, $p < .001$).

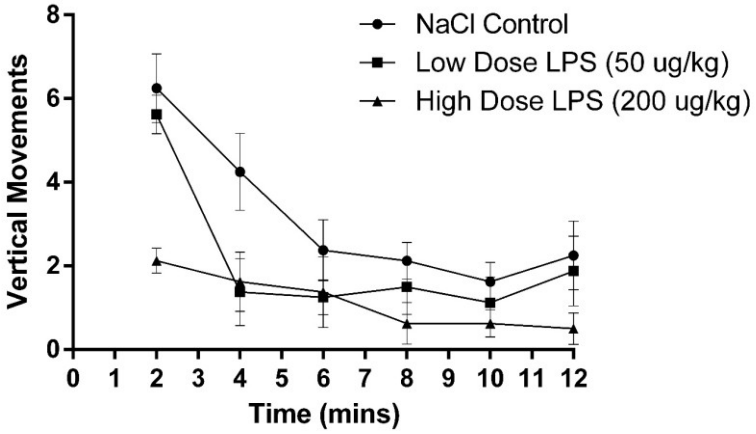

Figure 2. Vertical movement across time for NaCl-treated, Low Dose LPS-treated, and High Dose LPS-treated rats. Mean + (S.E.M) number of vertical movements exhibited by three treatment groups, NaCl Control (*n*=8), Low Dose LPS (*n*=8), and High Dose LPS (*n*=8), across time. High Dose LPS-treated rats had less vertical movements than both Low Dose LPS-treated rats and NaCl control rats within the first six minutes, followed by similar levels of vertical movements with time for all groups. NaCl Control had a rapid and steep decrease vertical movements in the first six minutes (steep, negative slope), as did Low Dose LPS treated rats for the first two minutes. This is in contrast with High Dose LPS treated rats that also decreased vertical movements with time although at a less rapid rate (negative, and less steep slope compared to other groups).

An interaction effect of group and time was not found. Response rates for NaCl controls, Low Dose LPS (50ug/kg) and High Dose LPS (200 ug/kg) across time are depicted in *Figure 3*. The effect of group on response rate is present due to the finding that rats treated with a Low Dose of LPS had less bar presses than the NaCl Control, and the High Dose LPS group had less bar presses than both the Low Dose LPS and the NaCl Control groups (Figure 3), for all observation time points. The effect of time on bar presses is exhibited by a decrease in number of bar presses exhibited by the NaCl Control group from the six to eight minute time frame, while the LPS treated groups did not exhibit a change in bar presses with time. The group and time interaction effects were not found due to all three groups exhibiting the same stable and non-changing relationship with time, as the number of bar presses produced in each group did not vary with the progression of time (zero slope; Figure 3).

Latency to First Response

One-way ANOVA analysis showed a significant main effect of group on latency to first response ($F(2, 21) = 5.425$, $p = .013$). Latency to first response for NaCl controls, Low Dose LPS (50 ug/kg) and High Dose LPS (200 ug/kg) are depicted in *Figure 4.* High Dose LPS treated rats exhibited a greater latency to first response when compared to both the NaCl Control and the Low Dose LPS treated rat groups (Figure 4), while NaCl Control and Low Dose LPS-treated rat groups did not differ from one another and exhibited relatively lower latency to first response.

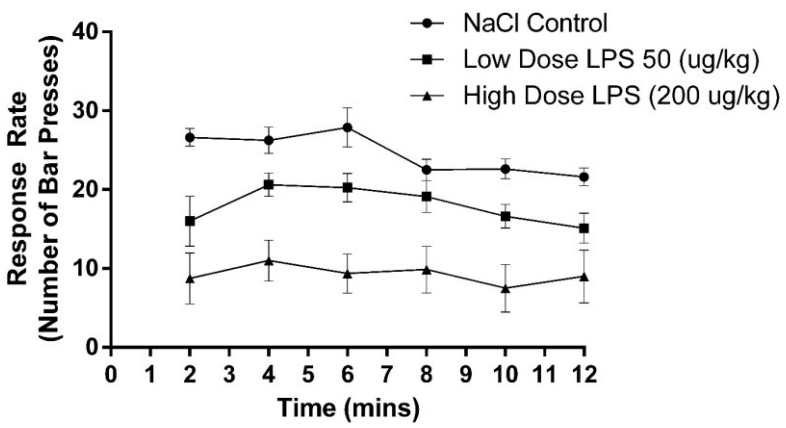

Figure 3. Response rate across time for NaCl-treated, Low Dose LPS-treated, and High Dose LPS-treated rats. Mean + (S.E.M) response rate (number of bar presses) exhibited by three treatment groups, NaCl Control (*n*=8), Low Dose LPS (*n*=8), and High Dose LPS (*n*=8), across time. High Dose LPS-treated rats had lower response rates than both Low Dose LPS-treated rats and NaCl control rats across all time points. All groups exhibited a stable response rate across time (slow change in response rate with time), and NaCl Control rats had a mild decrease in response rate from the 6rd to the 7th minute observation.

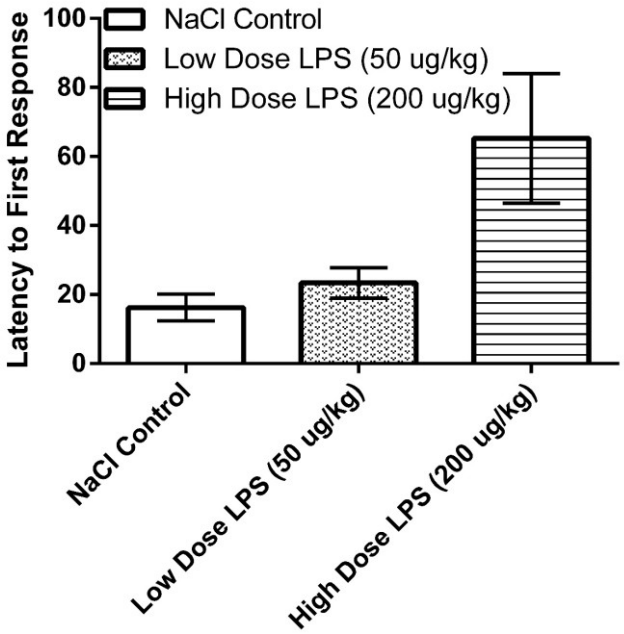

Figure 4. Latency to first response for NaCl-treated, Low Dose LPS-treated, and High Dose LPS-treated rats. Mean + (S.E.M) latency to first response exhibited by three treatment groups, NaCl Control (*n*=8), Low Dose LPS (*n*=8), and High Dose LPS (*n*=8). High Dose LPS-treated rats had greater latency to first response than both Low Dose LPS-treated rats and NaCl control rats. NaCl Control and Low Dose LPS treated rats had similar latency to first response.

Pre- and Post-Responding

ANOVA analysis revealed a significant main effect of both group ($F(2, 21) = 15.352$, $p<.001$), and Day ($F(1, 21) = 11.007$, $p < .003$), as well as an interaction effect for both group and day ($F(2, 21) = 7.731$, $p = .003$). Pre- and post-responses (total number of bar presses on both days) for NaCl controls, Low Dose LPS (50 ug/kg) and High Dose LPS (200 ug/kg) across the two days (baseline day and test day) are depicted in *Figure 5*. The effect of group on pre- and post-responding is present as exhibited when rats treated with a high dose of LPS had fewer bar presses in the post-responding trial (test day) than both the NaCl Control and the Low Dose LPS groups, although bar presses in the pre-responding trial (baseline responses) were similar across all groups. The effect of day on pre- and post-responding bar presses indicates that both Low Dose LPS and High Dose LPS rats exhibited a decrease in bar presses on the post-responding day (test day). The group and time interaction effect indicates that depending on their group assignment (NaCl Control, Low Dose LPS, High Dose LPS), the rats exhibited a different number of Bar Press responses on the Pre- and Post-Days. Specifically, NaCl Control rats had similar bar press responses on both pre- and post-days, while both Low Dose LPS and High Dose LPS treated rats had a decrease in bar presses in the post-day, with High Dose LPS exhibiting the greatest decrease in bar presses in the post-day (Figure 5).

Discussion

The overall finding in this study was that immune activation via LPS delivery impairs retention of positive reinforcement behaviors in a food-motivated study paradigm using bar pressing as a means of operant conditioning. Specifically, the salient findings in this study are: 1) rats given LPS injections exhibited less bar pressing frequency (response rate) and took more time to initially respond to bar pressing (latency to first response) when compared to control rats; 2) rats given LPS injections had a lower total number of bar presses on test day when compared to controls; 3) LPS-treated rats exhibited lower locomotor activity levels when compared to control rats; and 4) there was a dose-dependent effect of LPS on bar pressing tendency, where a higher dose of LPS delivery resulted in lower bar pressing. The findings from this study are consistent with others that show LPS negatively impacts locomotor activity in rats (Engeland et al., 2003). As well, the finding that "sickness behavior" as characterized by appetite changes and anhedonia (lack of reward-seeking), and is LPS dose-dependent, is also consistent with previous findings (Bassi et al., 2012).

Previous studies that investigated effects of LPS treatment on memory retrieval and spatial learning in rats using the Morris Water Maze showed conflicting findings where LPS did not elicit changes in behaviors that were indicative of spatial learning (Cunningham & Sanderson, 2008), and other studies where LPS did affect these behaviors when compared to control rats (Arai, Matsuki, Ikegaya, & Nishiyama, 2001). In studies using the Morris Water Maze, locomotor activity did not differ between LPS-treated and control rats (Huang et al., 2010), whereas locomotor activity was significantly decreased in LPS-treated rats from the study herein. The key difference between the Morris Water Maze study paradigm and the bar pressing positive enforcement paradigm used in the study herein is that the Morris Water Maze focuses on behaviors resulting from negative reinforcement, whereas bar pressing assesses positive reinforcement tendencies.

In the Morris Water Maze, rats are subject to an adverse situation (water) and are seeking the target platform in order to refrain from being submerged in water (Morris, 1984). In the bar

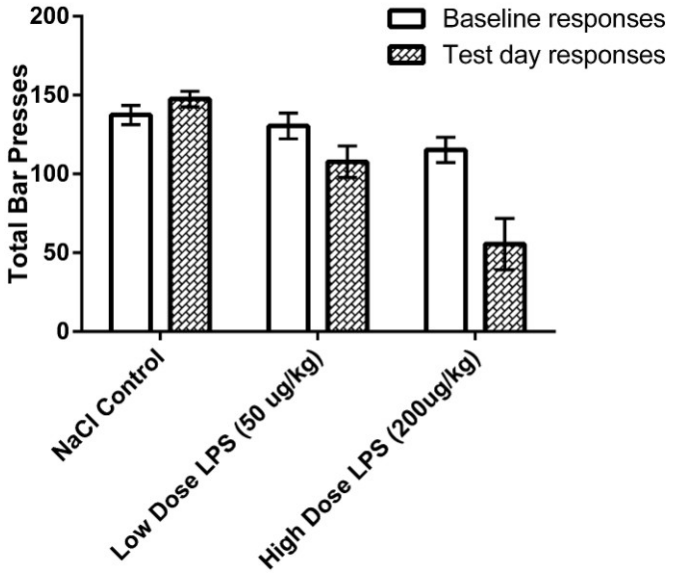

Figure 5. Total bar presses at baseline and on testing day for NaCl-treated, Low Dose LPS-treated, and High Dose LPS-treated rats. Mean + (S.E.M) total bar presses during observations during baseline responses and testing day, exhibited by three treatment groups, NaCl Control (*n*=8), Low Dose LPS (*n*=8), and High Dose LPS (*n*=8). High Dose LPS-treated rats had lower total number of bar presses on test day compared to both Low Dose LPS-treated rats and NaCl control rats. All groups had similar baseline total bar pressing values, and NaCl and Low Dose LPS groups had negligible changes in total bar pressing on test day compared to their baseline bar pressing.

pressing paradigm, rats are not subject to an adverse situation, and instead have to be motivated to seek the reward (i.e., food), and be willing to exert effort to seek the reward (Wilson, MacLaren, & Winn, 2009). In the aforementioned rotating drum experiment conducted by Neal Miller in 1964 where LPS-treated rats exhibited lower bar pressing frequency compared to control rats, and had similar, if not higher, bar pressing frequency when the same LPS-treated rats were placed in a rotating drum and bar pressing resulted in cessation of drum rotation (Larson & Dunn, 2001). The portion of the 1964 Miller study where LPS-treated rats exhibit lower bar pressing frequency than control rats (when not in the rotating drum) is analogous to the studydesign herein. Specifically, the decreased bar-pressing frequency highlights that LPS-treated rats are less inclined to pursue reward-seeking behaviors as exhibited by positive reinforcement bar-pressing. However, the portion of the Miller study where LPS-treated rats exhibit similar if not higher bar-pressing when placed in the rotating drum is analogous to the Morris Water Maze paradigm where rats are placed in an adverse situation (i.e., rotating drum or water submersion) and are motivated by tendencies to avoid negative scenarios. These key differences in study paradigms highlight that LPS-treated rats lose the ability to retain positive reinforcement behavior, while retain the ability to avoid negative scenarios.

An apparent limitation to this study is controlling for baseline levels of memory retrieval capabilities for LPS-treated rats, which are independent of LPS-induced decrements in locomotor activity. The effect of LPS on locomotor activity was accounted for by measuring horizontal and vertical movements, as

a lack of locomotor activity might explain the decreased positive reinforcement retention behaviors exhibited by LPS-treated rats. Similarly, the effect of LPS on memory retrieval should have also been accounted for in order to test whether LPS-induced rats have impaired memory that would impact positive reinforcement tasks such as bar pressing. Another limitation to this study is the duration of LPS incubation. In this study, LPS was used to elicit activation of the immune system under short-term observations. These observations may not capture the full effect of LPS on the immune system, and consequential effect(s) on food-motivated behavior and reward-seeking, as a longer observation window may have been required.

Immune system activation via LPS delivery in rats has been shown to elicit "sickness behavior" (Larson & Dunn, 2001). The findings in the present study highlight characterizing traits in LPS-treated rats that are indicative of "sickness behavior", such as decreased bar pressing frequency, higher latency to first response, lower total bar pressing on test day, and decreased level of movement when compared to control rats. Moreover, "sickness behavior" attributes were exacerbated with higher doses of LPS, which is also in accordance with previous findings (Bassi et al., 2012). One of the questions investigated in this study was whether LPS-treated rats did not pursue bar pressing due to a lack of reward-seeking positive reinforcement behavior, or whether they simply did not want to exert the required effort to obtain the reward, as previous studies have shown decreased locomotor activity with LPS treatment in rats (Engeland et al., 2003). Certainly, in this study, LPS-treated rats exhibited decreased horizontal and vertical movements when compared to control rats. Therefore, although LPS-treated rats may have impaired memory retrieval as exhibited by lower positive reinforcement tendencies shown by decreased bar pressing (when compared to control rats), LPS may have a large enough role on decreasing locomotor activity which may account for these differences in responses between control and LPS treatment. In summation, LPS had a negative effect on positive reinforcement retention in rats using the bar pressing study paradigm, and these effects may be explained by a general lack of effort exertion (i.e., decreased locomotor activity) experienced by rats during LPS treatment.

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