How social activity affects exercise in a rat model of depression proneness

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With depression rising worldwide, finding effective, affordable relief is a pressing global public health need. Social activity and physical activity both function as natural depression remedies, but depression can interfere with these activities. This study explores whether an increase in social activity can simultaneously increase voluntary exercise. If so, a single remedy could potentially yield two benefits. Rats were singly or paired housed to model social activity, and voluntary wheel running was measured. Depression proneness was modeled with Occidental Low-Saccharin-Consuming (LoS) rats; relative to high-saccharin-consuming (HiS) rats, LoS rats are more anxious and vulnerable to stress, both of which are risk factors for depression. Whether LoS rats would benefit more from social housing than HiS rats was of interest. Pair-housing increased wheel running, equally so among LoS and HiS rats. These results suggest that social activity may increase motivation to exercise, regardless of depression proneness.

Keywords: paired housing, social activity, wheel running, physical activity, depression, rats

According to the World Health Organization, depression is one of the leading causes of death and disability globally, with that number expected to rise to the second leading cause by the year 2020 (World Health Organization, 2012). With depression’s capacity to cause great harm to those who suffer from it, learning how to alleviate it becomes especially vital. Evidence-based treatment strategies for depression range from medication to more natural remedies, such as 30 minutes of exercise a day or social support from family and friends (Stanton & Reaburn, 2014; Steger & Kashdan, 2009). Many people diagnosed with depression look to natural remedies because they are affordable and have fewer side effects than prescription medication (Olfson et al., 2006; Simon et al., 2004). However, methods used to alleviate depression are rendered inadequate when the symptoms of depression stop people from using these methods.

One of the best-known and effective ways to help treat mild to moderate depression without medication is regular, vigorous exercise (Dunn et al., 2005; Stanton & Reaburn, 2014). Exercise can be helpful for depression by facilitating the habituation of corticosterone in response to stress; exercised animals that were exposed to stress habituated significantly faster than non-exercised animals (Sasse et al., 2008). This suggests that repeated stress, a factor in developing depression, may be reduced by voluntary exercise. In a new study of how exercise affects mood, individuals who self-reported high tolerance to exercise experienced more positive affect and less negative affect during a physiologically demanding task than did their low tolerance peers (Tempest & Parfitt, 2015). This finding suggests that regular exercise can facilitate mood regulation and thus help keep depression at bay.

However, one of the primary symptoms of depression is the psychomotor agitation or retardation. Many people suffering from Major Depressive Disorder report reduced energy and activity (American Psychiatric Association, 2013), making regular exercise simply out of the question. The symptoms of depression that prevent people from exercising may also prevent them from seeking contact with loved ones. Thus, although a depressed person may crave social contact, symptoms of depression lead to social isolation, which further reduces opportunities for physical activity (American Psychiatric Association, 2013).

Identifying interventions that increase physical activity could be a valuable way of disrupting the...
vicious cycle. Increases in social activity, even with just one person, might alleviate symptoms of depression. This could in turn increase regular exercise, producing a synergistic effect. If alleviating loneliness both improves mood and increases spontaneous motor activity, it becomes a valuable direct and indirect intervention for depression. Potentially, then, we can “kill two birds with one stone” -- increasing social contact to not only alleviate feelings of social isolation but also to strengthen motivation to exercise.

Some practical and ethical limitations to studying depression in humans can be overcome by studying laboratory rats, whose nervous system and basic emotional systems are similar to humans' (Panksepp, 2005). Experimental (e.g. learned helplessness) and dispositional (“Flinders sensitive” rats) rat models of depression have been validated using behavioral and pharmacological methods (Overstreet, 2012). Moreover, exercise alleviates depressive symptoms in rats (Zheng, 2005). Studying laboratory rats therefore is a rigorous experimental means of exploring whether social interventions alter spontaneous exercise.

The present study examined whether rats reunited with a sibling would exercise more than rats that remain single housed. Motivation to exercise was measured as wheel running. Wheel running can be seen as a measure of anxiety, especially in experiments involving food scarcity (Dess et al., 2007). However, wheel running induces positive affect and is positively reinforcing in rats (Smith & Lynch, 2012), and even free-living rodents wheel run when given the opportunity to do so (Meijer & Robbers, 2014). Thus, it is reasonable to assume that among the freely fed rats in the present study, wheel running was spontaneous and affectively positive.

The present study also modeled individual differences in depression proneness with selectively bred rats. Occidental HiS and LoS rats have been selectively bred for more than forty generations on the basis of voluntary saccharin intake, a mixture of artificial sweetener and water (Dess et al., 2013). Selection on the taste phenotype was initiated as a result of several studies that revealed effects of experimental stress on ingestion, including reduced saccharin solution intake. Spontaneously low saccharin intake was hypothesized to be a potential marker for stress vulnerability and associated emotional and energy regulatory processes. Since then, the HiS and LoS rats have been used to study the relationship between emotion and how eating and physical activity are organized and regulated.

Selective pressure on the taste phenotypes was expected to lead to differences in emotionality. Indeed, relative to high saccharin (HiS) rats, low saccharin (LoS) rats are higher in anxiety and stress vulnerability, more sensitive to metabolic challenges, and lower in social status (Dess et al., 2013; Eaton et al., 2012). As predicted, the distinctive HiS and LoS taste phenotypes serve as a marker for individual and social behaviors in these rats. These line differences are not a consequence of prior saccharin intake because in all studies, including the present, the 24-hour two-bottle assessment of the saccharin phenotype is conducted after the experiment is over. The designations of “LoS” and “HiS” then, are properly understood as terms referring to lineage -- the behavior characteristic of parents, grandparents, and earlier ancestors -- and not to the saccharin intake of rats prior to other data collection in a particular study.

In the present study, the two lines were used to see whether the differences in taste phenotype would predict different effects of social housing on voluntary exercising. Because LoS rats are higher in anxiety and stress vulnerability, we view LoS rats as more similar to people who are depressed or are prone to developing depression and would have more to gain from the social housing. Therefore, we hypothesized that social housing would differentially impact the two lines, with a robust increase in running in the LoS line and relatively little impact on HiS rats.

### Method

#### Rats

Adult experimentally naïve female rats (60-90 days old) from Generations 46 and 47 from the Occidental colony were used (HiS, n = 30; LoS, n = 30). Immediately prior to the experiment, they were individually housed in stainless steel cages on a 12:12 light/dark cycle (0700-1900 light) with an ambient temperature of 72 ± 4°F. Purina 5001 Rodent Chow and water were freely available. All
procedures complied with a protocol approved by the Occidental College Institutional Animal Care and Use Committee.

Apparatus

Sessions occurred in stainless steel running wheels equipped with a side cage, 350 mm in diameter (Model 86041; Lafayette Instruments, Lafayette IN). One running wheel was a different Lafayette Instruments version of the model with the same diameter as the other wheels.

Procedure

The experimental procedure was eight days long (see Table 1). On four of those days, each rat was placed in an assigned running wheel for one hour. Rats were run in squads of six, always between 12:00 pm and 5:00 pm. After a squad of six rats was placed in the running wheel, the experimenter left the room and closed the door; automated counters monitored wheel running.

Running sessions were conducted on Days 1 and 2 of the experimental procedure. These sessions (Baseline 1 and Baseline 2) provided a baseline measure of running during individual housing. After data collection on Day 2, all rats were re-housed. Thirty-two of the rats remained singly-housed (Single condition) and the other rats were reunited with a littermate (Pair condition). Litters were balanced across experimental conditions. Rats were left undisturbed for two days (Days 3 and 4) and then had a 1-hr running session on Day 5 (Test 1). They were again left undisturbed for two days and had their final 1-hr running session on Day 8 (Test 2). Rats were weighed on Days 5 and 8 before the running session.

Rats were feed freely in their home cages. Food was unavailable only during running sessions (one hour on each of the four days). They were not food deprived.

Results

Baseline Bodyweight and Running

Initial bodyweights did not differ significantly between lines (M ± SEM, 278.8 ± 4.0 g for the LoS line, 265.5 ± 4.2 g for the HiS line).

Running increased from Day 1 to Day 2. A 2x2 mixed design ANOVA with line and day as variables yielded a significant main effect of day, F(1,48) = 23.41, p < .001. No line effects were significant. (See Figure 1.)

Running and Bodyweight after Housing Assignment

Increases from baseline running after rats were pair-housed (Pair) or were kept singly-housed (Single) are shown in Figure 2. Running continued to increase relative to baseline. As predicted, the running increases were larger in the pair-housed rats. A 2x2x2 mixed design ANOVA with line, housing condition, and day as variables revealed a significant housing condition x day interaction, F(1,44) = 9.27, p = .004. Bonferroni-adjusted contrasts revealed a significant difference between days only in the Pair condition (p < .001). No effects involving line were significant. Thus, contrary to our expectations, the effects of housing were the same in HiS an LoS rats.

The older running wheel yielded lower and more variable running and was excluded in the ANOVA above. Whether including it would have affected our conclusion was examined by repeating the ANOVA with data from that wheel included. The housing condition x day interaction remained significant, F(1,56) = 6.83, p = .011, as was the Day 3-Day 4 contrast in the Pair condition, p < .001.

Bodyweights on the final running day did not differ significantly between lines (281.7 ± 4.0 g for the LoS line, 267.5 ± 4.2 g for the HiS line).

Discussion

As predicted, pair housing increased voluntary exercise. We expected that the LoS rats would be more sensitive to housing condition because they are more prone to anxiety and negative affect, mirroring people who have depression. However, LoS and HiS rats were equally sensitive to housing condition. To the extent that these findings generalize to people, we can infer that socializing with loved ones might ameliorate depression due both to its direct, positive effects and indirectly due by increasing motivation to exercise. Studies on the effect of
social activity on exercise in people would yield potentially beneficial results.

A limitation of this study with respect to human depression is the use of rats prone to depressive symptoms but in whom a depression-like syndrome (e.g. helplessness) had not been induced. Such a manipulation may reveal social housing effects and differences between LoS and HiS rats that were not detected here. Nonetheless, the present study lays a foundation for future research with rat depression models by providing a time- and cost-effective procedure for generating a reliable social housing effect.

A further limitation is that the effect of pair-housing was not distinguished from the effect of being reunited with a sibling. An assumption was that reunion with a sibling – a familiar rat – would make a rat less stressed than when paired with a rat who is a non-sibling – a stranger. This assumption was based partially on what would presumably happen with humans; that is, being reunited with a close family member or loved one would be considered a stress reliever for people with depression, more so than socializing with a stranger. However, family relationships can be emotionally complicated. To be sure that these reunions are indeed stress-relieving, a follow-up study could directly assess the behavioral or physiological effects of being reunited with the close kin.

Finally, this study was conducted once, with a particular set of parameters. We chose to measure acute rather than long-term effects of social housing on exercise. Being pair-housed increased exercise over the course of a week, but it might or might not continue to have an effect over the course of weeks or months. Determining longer-term effects would be valuable, especially given that exercise as a method of regulating depression is more useful both mentally and physically when sustained. Also, wheel running was the measure of voluntary exercise, and it was measured for one hour on four days over an 8-day course. Whether a different measure or duration of exercise would yield the same results remains to be determined.

An important future direction for research concerns the mechanisms of the effect of pair-housing reported here. One fruitful direction is examination of effects of pair-housing on well-established neurohormonal mediators of stress and mood, including dopamine, serotonin, and glucocorticoids (Hammels et al., 2015; McEwen et al., 2015). At a higher level of organization, pair-housing might have increased exercise due specifically to social interactions (play, contact, etc.) or more generally by providing an enriched environment (Crofton, Zhang, & Green, 2015). In their study of stress attenuation, Nyhuis et al. (2010) examined whether non-specific enrichment or in intervention-specific effect (in their case, exercise) was responsible, and they concluded that their effect was intervention specific. Nonetheless, in the present study, pair-housed rats may have exercised more because pair housing provided an enriched environment, and enrichment – and not social interaction specifically – increased running. A control study comparing pair-housed rats to singly-housed rats provided with an enriched environment, such as larger cages that have compartments and tubes that a rat can use for stimulation, would be informative as to the mechanism of the group difference and thus its potentially useful practical applications.

References


Author Note

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Appendix

Table 1
Procedural Schedule

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<th>Day</th>
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</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>Baseline</td>
<td>Day 3</td>
<td>Day 4</td>
<td>Test 1</td>
<td>Test 2</td>
<td>Day 8</td>
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<tr>
<td>One hour in wheel</td>
<td>One hour in wheel</td>
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Note. The above table describes the procedural schedule for each squad of rats.

MODERN PSYCHOLOGICAL STUDIES

92
Figure 1. Mean wheel revolutions (± SEM) in LoS and the HiS rats on baseline running days.

Figure 2. Mean running increases from baseline (± SEM) for each group on Test 1 and Test 2.