Rats that undergo the Category E 6-hydroxydopamine administration surgery regain body weight lost at surgery faster when provided Bacon Softies™ compared to regular or wet feed

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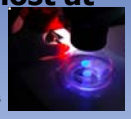
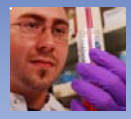
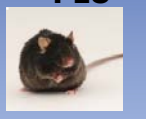

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Abstract

Surgical procedures produce stress in laboratory animals. Proper nutrition post-operatively is critical to their recovery in order to minimize weight and protein loss. This study investigated whether providing nutritional supplementation to rats undergoing a unilateral 6-hydroxydopamine lesion of the nigrostriatal pathway would improve body weight gain after surgery. We hypothesized that animals that received Bacon Softies™, a nutritionally complete, palatable recovery diet, would regain body weight lost at surgery more quickly than animals provided regular feed or feed softened with water. Forty-eight male NTac:SD rats were used and were divided into six weight- and age-matched groups. Groups C-F were modified with the 6-OHDA procedure according to standard Taconic protocols. The animals were anesthetized with isoflurane in oxygen, received 30mL/kg fluid support at the time of surgery and a lidocaine/bupivicaine local block at the incision site. The groups received the following treatments: (A) feed and water (no surgery); (B) feed, water and Bacon Softies (no surgery); (C) feed and water; (D) feed, water and wet feed; (E) feed, water and Bacon Softies, acclimated to the Bacon Softies 2 days prior to surgery; (F) feed, water and Bacon Softies. All animals and feed were weighed daily for 7 days after surgery. Group C-F animals received a rotational evaluation at days 14 and 21. There was a significant decrease in body weight in Group C and D animals compared to controls through day 7 ($p < 0.001$). Animals in Group E regained body weight lost at surgery by day 5 and animals in Group F regained body weight lost at surgery by day 6. There were no differences in body weight in Group E and F animals compared to Group B by days 3 and 5, respectively and to Group A by days 5 and 7, respectively. There were no differences in spin rates or body condition scores between groups. These data suggest that a refinement in clinical post-operative care by providing nutritional support may decrease recovery time in Category E procedures in rats.

Introduction

Bacon Softies™ are a nutritionally complete soft diet that aid in the recovery of post-operative and debilitated rodents. The acute post operative period can be critical to an animal's successful recovery from surgery. Maintaining the animals nutritional and hydration status are pivotal requirements needed to support wound and tissue healing as well as the functional success of the surgical modification. Two well-accepted measures of an animal's recovery post-operatively are 1) regaining body weight lost to surgery and 2) evaluations of body condition scores. Commercially-available products were evaluated to encourage appropriate nutrition, hydration and enrichment in NTac:SD rats. Category E procedures are those during which animals do not receive pain relief for painful procedures; withholding analgesia must be scientifically justified. Since the 6-OHDA lesion surgery is a category E procedure, nutritional support may aid the animals in post-operative recovery in the face of no pain relief.

Table 1. Distribution of animals by group.

Group A	Negative Control, regular feed & water
Group B	Positive Control, regular feed & water & Bacon Softies™
Group C	Regular feed & water, 6-OHDA surgery
Group D	Regular feed & water & wet feed, 6-OHDA surgery
Group E	Regular feed & water, Bacon Softies™ before and after surgery, 6-OHDA surgery
Group F	Regular feed & water, Bacon Softies™ after surgery, 6-OHDA surgery

Table 2. Average total feed consumption (gram). Wet feed consumption was adjusted for added water.

	Day 0-1	Day 1-2	Day 2-3	Day 3-4	Day 4-5	Day 5-6
A	24.4	22.9	25.1	20.6	21.0	21.9
B	26.7	19.6	22.7	25.4	24.0	23.0
C	8.7	11.0	17.5	10.4	17.1	17.0
D	16.7	17.2	22.5	16.8	20.7	20.3
E	19.9	17.8	21.7	20.3	25.0	25.2
F	17.9	17.0	20.7	18.7	24.3	28.3

Group	Day -2	Day -1	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
AVG A	272.1	278.0	283.3	289.9	297.9	300.2	305.4	310.9	315.9	321.7
AVG B	272.0	277.1	280.9	284.1	294.4	298.2	304.4	309.1	313.7	322.2
AVG C	271.8	277.9	278.5	256.7†††, ***	256.4†††, ***	256.6†††, ***	256.0†††, ***	259.7†††, ***	263.8†††, ***	270.5†††, ***
AVG D	272.3	278.1	284.1	259.8†††, ***	263.1†††, ***	261.3†††, ***	261.0†††, ***	262.3†††, ***	264.1†††, ***	267.7†††, ***
AVG E	272.8	276.5	282.6	262.9†††, **	272.8†, *	275.2†	277.7†	285.3	289.6	295.3
AVG F	271.8	278.5	282.9	262.9†††, **	269.6††, *	272.9†, *	275.1†, *	282.3†	283.2†	289.6

Materials and Methods

Surgery & Animals

Forty eight NTac: SD female animals were used at 8 weeks of age and between 230-265 grams body weight. Animals were weighed prior to surgery and placed into 6 weight-matched groups of n=8 animals. Sixteen animals were used as controls (Group A-B). These animals did not receive any surgery but served as control animals. Thirty six animals were grouped to undergo the 6-OHDA procedure according to standard Taconic protocols (Group C-F) to unilaterally lesion the nigrostriatal pathway. The animal's haircoat was removed and skin was prepped aseptically. Animals were anesthetized with isoflurane in oxygen and modified according approved protocols. They received 30mL/kg fluid support at the time of surgery and a lidocaine/bupivicaine local block at incision site.

Husbandry

Animals were maintained in an Murine Pathogen Free barrier in static caging with wire-bar cage lids. They were provided NIH 31M feed and water ad lib. All animals were covered under Taconic IACUC-approved protocols.

Groups

- A: N= 8 regular feed and water, negative control (no surgery)
- B: N= 8 regular feed and water, Bacon Softies™, positive control (no surgery)
- C: N= 8 regular feed and water
- D: N= 8 regular feed and water, wet feed provided cage-level and changed out daily
- E: N= 8 regular feed and water, Bacon Softies™, acclimated for 2 days prior to surgery and post-operatively for 7 days in addition to standard feed and water (Bacon Softies™ provided cage-level and changed out daily)
- F: N = 8 regular feed and water, Bacon Softies™ post-operatively for 7 days in addition to standard feed and water (Bacon Softies™ provided cage level and changed out daily) (**Table 1**).

Study Design

- Day -3: Receipt of animals into surgery barrier
- Day -2: Weigh animals, randomize into weight-matched groups, ear tag; Acclimation time, Begin Group E animals on Bacon Softies
- Day -1: Acclimation to Bacon Softies™, Group E
- Day 0: surgery, body weight (BW), body condition score (BCS)
- Day 0-3: clinical scoring of all animals
- Day 0-7: daily BW, BCS, feed intake measured for Groups A-F
- Day 14: 15 minute short spins with apomorphine administration as described in Taconic approved protocol.
- Day 21: 30 minute long spins with apomorphine as described in Taconic approved protocol.

Statistics

Data are expressed as means +/- SEM. Differences among groups in body weight, body condition score and spin rates were assessed using ANOVA. Differences within groups were compared using the student's t-test. Differences were considered significant at $P<0.05$. All statistical analyses were performed using MiniTab software or MicroSoft Excel.

Figure 1. Body Weight Gain from Day -2. Animals re-gained weight lost at surgery on day 5 in Gp E and day 6 in Gp F. Animals in Gps C and D do not regain BW lost at surgery by day 7. Please see Table 3 for statistical comparisons between groups.

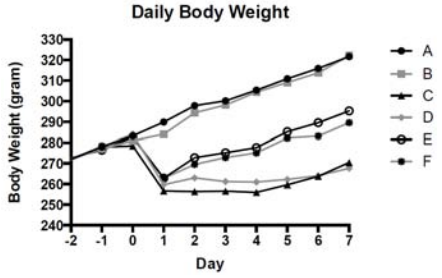


Table 3. Body Weight Day to Day. Groups C-D had significantly ($p<0.05$) lower body weights gain compared to groups A and B (negative and positive controls) through all 7 days after surgery. Groups E and F had significantly ($p<0.05$) lower body weights compared to groups A and B (negative and positive controls) at days 1-4; however there was no significant difference in body weight from the controls by day 5 and 7 for group E (Bacon Softies™ acclimated) respectively and by day 3 and 5 for group F (Bacon Softies™ non-acclimated) respectively. Taken together, this suggests improved recovery in animals in groups receiving Bacon Softies (E and F) compared to groups receiving standard chow and moistened chow (C and D respectively). †Indicates significance with respect to group A; * indicates significance with respect to Group B

Results

Post-operative animals receiving Bacon Softies™ (groups E and F) returned to pre-surgical body weight by day 5 and 6 respectively. Post-operative animals receiving standard chow or moistened chow (groups C and D respectively) had not returned to pre-surgical body weight by day 7 (**Figure 1**).

Groups C-D had significantly ($p<0.05$) lower body weights compared to groups A and B (negative and positive controls) through all 7 days after surgery.

Groups E and F had significantly ($p<0.05$) lower body weights compared to groups A and B (negative and positive controls) at days 1-4. However there was no significant difference in body weight from the controls by day 3 and 5 for group E (Bacon Softies™ acclimated) and by day 5 and 7 for group F (Bacon Softies™ non-acclimated). **Taken together, this suggests improved recovery in animals in groups receiving Bacon Softies (E and F) compared to groups receiving standard chow and moistened chow (C and D respectively) (Table 3).**

There were statistical increases in body weight at Day 7 compared to Day 0 in Groups A and B ($P < 0.001$). Groups C and D had negative changes in body weight, while Groups E and F had positive changes.(**Figure 2**).

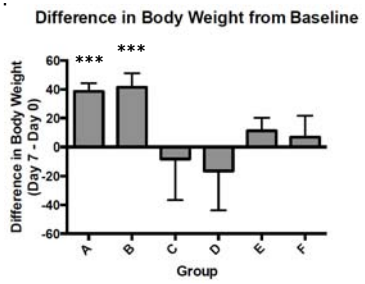
Post-operative animals receiving Bacon Softies™ (Groups E-F) preferentially consumed Bacon Softies™ over the standard chow on all days (data not shown).

There are no differences in spin rates or body condition scores between Groups C-F at any time point (data not shown).

Discussion

The Bacon Softies™ help surgically-modified animals regain weight lost at surgery faster than animals that receive regular or wet feed. This is demonstrated in the results because the surgically modified animals in Groups E and F show no differences in body weight compared to positive and negative controls. Animals in Group F acclimated to the Bacon Softies™ regain body weight lost at surgery faster than animals in Group E that are not acclimated. This may be because rats are neophobic animals, and the acclimation period introduces them to the nutritional supplement during a period of reduced stress compared to the acute post operative period. Providing animals with Bacon Softies™ does not interfere with the model performance. Body condition scores were not statistically different between groups, suggesting that the scoring systems may not identify animals that do not regain weight lost at surgery during the acute post operative period for this procedure. **These findings are important, especially in Category E surgical procedures, and it suggests that providing animals with nutritional support post operatively may encourage recovery when withholding analgesia is scientifically justified.**

Figure 2. Difference in Body Weight from Baseline. There were statistical differences in body weight at Day 7 compared to Day 0 in Groups A and B ($P < 0.001$). Groups C and D had negative changes in body weight, while Groups E and F had positive changes.



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