

Dietary-induced binge-like eating impairs acoustic startle responses to acute nisoxetine in male mice

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Supplemental Materials

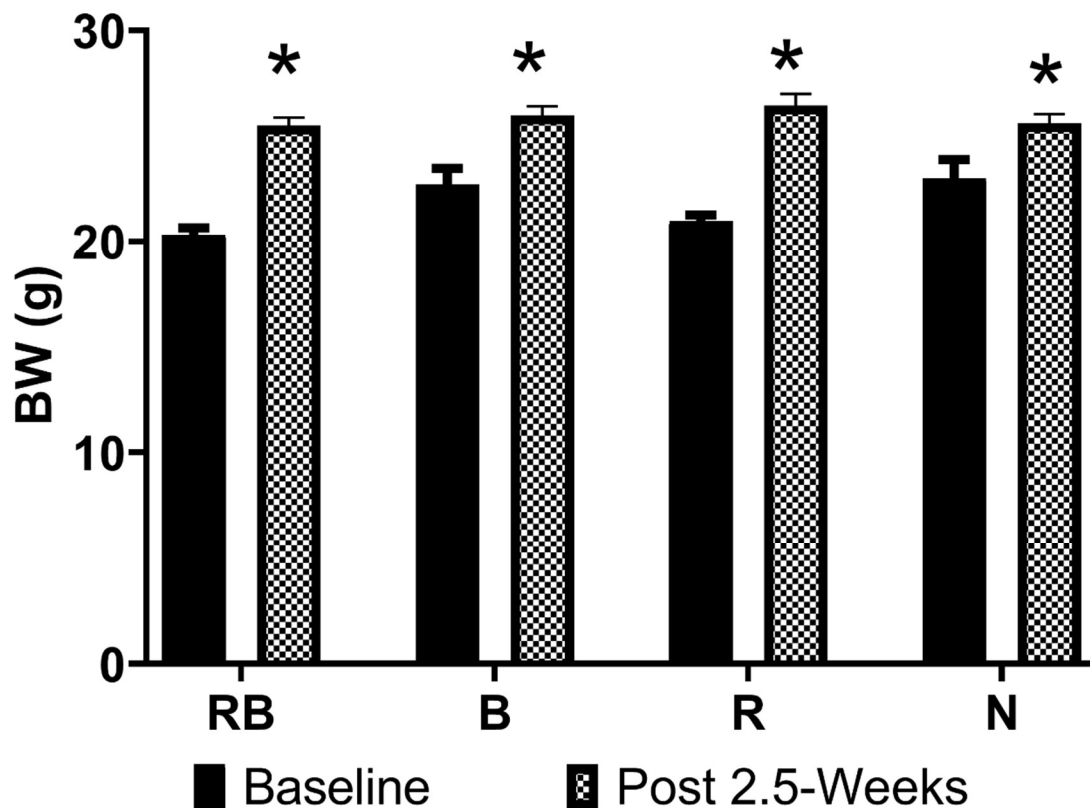


Figure 1S: Body weight over 2.5 on the dietary induced binge eating protocol on standard chow. All groups have a greater BW following 2.5 weeks on standard chow compared to their baseline BW ($p < 0.01$).

Pulse responses before and after dietary-induced binge-like eating and feeding protocol on standard chow.

The MANOVA analysis resulted in a group effect [$F(3, 26) = 4.0, p < 0.05$], treatment effect [$F(1, 26) = 8.7, p < 0.01$], pulse effect [$F(3, 78) = 409.4, p < 0.001$], treatment X group effect [$F(3, 26) = 3.5, p < 0.05$], and a pulse X group effect [$F(9, 78) = 2.1, p < 0.05$].

For the group effect, N animals had an overall greater response to the difference pulses compared to RB ($p < 0.05$).

For the treatment effect, animals had a greater response to the different pulses 2.5 weeks post-feeding protocol compared to baseline ($p < 0.05$).

For the pulse effect, the overall response to each stimulus was significantly different from each other ($p < 0.01$) (i.e., null was less than P74, P90, and startle; P74 was greater than null and less than P90 and startle; P90 was greater than null and P74 but less than startle; startle was greater than null, P74, and P90).

For the treatment X group effect, the overall response of R animals during baseline testing was less than their response 2.5 weeks following the feeding protocol on standard chow ($p < 0.05$).

For the pulse X group effect, animals in all groups responded less to the null stimulus and P74 compared to P90 and the startle stimulus ($p < 0.001$). There were no differences between groups at each stimulus level (e.g., R null is not different from RB null, N null, and B null).

Pulse responses following treatment with saline, NISL, or NISH on standard chow feeding protocol

The MANOVA analysis resulted in a group effect [$F(3, 26) = 4.8, p < 0.01$], a treatment effect [$F(2, 52) = 51.5, p < 0.001$], a pulse effect [F

(3, 78) = 273.3, $p < 0.001$], a pulse X group effect [$F(9, 78) = 3.4$, $p < 0.01$], and a treatment X pulse effect [$F(6, 156) = 25.1$, $p < 0.001$].

For the group effect, N animals had an overall greater response to the different stimuli compared to R ($p < 0.05$) and RB ($p < 0.01$) animals.

The overall treatment effect showed differences across all treatments. Treatment with saline produced an overall lower response than treatment with NISL ($p < 0.001$) or NISH ($p < 0.001$), and NISL produced a greater response than treatment with NISH ($p < 0.001$).

For the pulse effect, the overall response to each stimulus was different from each other ($p < 0.001$) (i.e., null was less than P74, P90 and startle; P74 was greater than null and less than P90 and startle; P90 was greater than null and P74 but less than startle; startle was greater than null, P74, and P90).

For the pulse X group effect, animals in all groups responded less to the null stimulus and P74 stimulus compared to P90 and the startle stimulus ($p < 0.001$). Additionally, N animals had a greater response to the startle stimulus compared to R ($p < 0.001$), RB ($p < 0.001$), and B ($p < 0.05$) animals.

For the treatment X pulse effect, treatment with saline produced a smaller response during the null stimulus and P74 stimulus compared to P90 and the startle stimulus ($p < 0.001$). The same outcome occurred upon treatment with NISH ($p < 0.001$). Treatment with NISL produced different reactions at each stimulus ($p < 0.01$). There were no response differences to the null and P74 stimulus across the three treatments. Conversely, responses to P90 and the startle stimulus were different across the three treatments, with NISL having produced the greatest reaction ($p < 0.001$).

Pulse responses following treatment with 10% DMSO, GBRL, GBRH, or NISH:GBRL in combination on the standard chow feeding protocol

The MANOVA resulted in a group effect [$F(3, 34) = 6.3, p < 0.01$], a treatment effect [$F(3, 102) = 22.8, p < 0.001$], a pulse effect [$F(3, 102) = 226.0, p < 0.001$], a pulse X group effect [$F(9, 102) = 6.8, p < 0.001$], and a treatment X pulse effect [$F(9, 306) = 13.1, p < 0.001$].

For the group effect, N animals produced an overall greater response compared to R ($p < 0.01$) and RB ($p < 0.01$) animals.

For the treatment effect, treatment with GBRL produced an overall greater response compared to treatment with 10% DMSO saline ($p < 0.001$), GBRH ($p < 0.001$) and NISH:GBRL ($p < 0.001$).

The pulse effect revealed no differences in the overall response to the null stimulus compared to P74. However, the overall response to P90 and the startle stimulus was greater compared to null ($p < 0.001$) and P74 ($p < 0.001$), with the highest response having occurred during the startle stimulus ($p < 0.001$).

For the pulse X group effect, the response to P90 and the startle stimulus was greater compared to null and P74 for R ($p < 0.05$), N ($p < 0.001$), and B ($p < 0.001$) groups. R animals had a lower response to P90 compared to N animals ($p < 0.05$), and a lower response to the startle stimulus compared to N ($p < 0.001$) and B ($p < 0.05$) groups. The RB group was the only group to have a significantly different reaction during the startle stimulus compared to all other stimuli ($p < 0.01$). Additionally, the RB group also had a lower response to the startle stimulus compared to N ($p < 0.001$) and B ($p < 0.05$) groups.

For the treatment X pulse effect, all treatments produced a lesser response to the null and P74 stimulus compared to P90 ($p < 0.001$) and the startle stimulus ($p < 0.001$). Treatment with 10% DMSO saline resulted in a lower response to P90 and the startle stimulus compared to treatment with GBRL ($p < 0.001$). Additionally, treatment with GBRL

produced a greater response to P90 and the startle stimulus compared to treatment with GBRH ($p < 0.001$) and NISH:GBRL ($p < 0.001$).

Pulse responses before and after dietary-induced binge-like eating and feeding protocol on standard HFD.

The MANOVA analysis resulted in a group effect [$F(3, 36) = 4.4, p < 0.05$], a treatment effect [$F(1, 36) = 16.7, p < 0.001$], a pulse effect [$F(3, 108) = 233.7, p < 0.001$], a pulse X group effect [$F(9, 108) = 4.1, p < 0.001$], and a treatment X pulse effect [$F(3, 108) = 12.4, p < 0.001$].

For the group effect, RB animals had an overall lower response to the pulses compared to N ($p < 0.05$) and B ($p < 0.05$) animals.

For the treatment effect, the overall response to the pulses were lower after the animals had undergone 2.5 weeks on the HFD feeding protocol compared to baseline ($p < 0.001$).

For the pulse effect, the overall response to the startle pulse was greater compared to all other pulses ($p < 0.001$). The overall response to the P90 pulse was greater than null ($p < 0.001$) and P74 ($p < 0.001$) and lower than the startle pulse ($p < 0.001$).

For the pulse X group effect, both R and RB groups had a lower response to the startle stimulus compared to the response of N ($p < 0.001$) and B ($p < 0.001$) groups to the startle stimulus. The R group had a lower response to the null stimulus compared to the startle stimulus ($p < 0.001$). Similarly, the RB animals had a lower response to the null stimulus compared to the startle stimulus ($p < 0.001$). The N group had a lower response both P90 ($p < 0.01$) and the startle stimulus ($p < 0.001$). A similar response was observed for animals in the B group, with a muted response to the null stimulus compared to P90 ($p < 0.05$) and the startle stimulus ($p < 0.001$).

For the treatment X pulse effect, the response to the startle stimulus was greater during baseline testing compared to testing 2.5 weeks post-feeding protocol on HFD ($p < 0.001$). During baseline testing, the response to the null stimulus was lower compared to P90 ($p < 0.001$) and the startle stimulus ($p < 0.001$). The response to P74 was lower than P90 ($p < 0.001$) and the startle stimulus ($p < 0.001$). The response to P90 was greater than both null ($p < 0.001$) and P74 ($p < 0.001$) and lower than the startle stimulus ($p < 0.001$). Finally, the reaction to the startle stimulus was greater than all other stimuli ($p < 0.001$). The same pattern of significance was observed following 2.5 weeks on the HFD feeding protocol ($p < 0.01$).

Pulse responses following treatment with 10% DMSO saline, NISH, GBRH, or NISH:GBRL on HFD

The MANOVA resulted in a treatment effect [$F(3, 108) = 13.8, p < 0.001$], a pulse effect [$F(3, 108) = 155.9, p < 0.001$], and a treatment X pulse effect [$F(9, 324) = 4.4, p < 0.001$].

For the treatment effect, the overall response when treated with 10% DMSO saline was greater than when treated with NISH ($p < 0.001$) and NISH:GBRL ($p < 0.001$). The response following treatment with NISH was lower than when treated with GBRH ($p < 0.001$) and the response when treated with GBRH was greater than when treated with NISH:GBRL ($p < 0.001$).

For the pulse effect, the overall response to the startle stimulus was greater than the reaction to any other stimulus ($p < 0.001$).

For the treatment X pulse effect, the response to the startle stimulus when treated with 10% DMSO saline was greater than when treated with NISH ($p < 0.001$) and NISH:GBRL ($p < 0.001$). The response to the null stimulus when treated with NISH was lower than when treated with GBRH ($p < 0.001$). The response to the startle stimulus when treated with NISH was lower compared to treatment with GBRH ($p < 0.001$).

The response to the startle stimulus when treated with GBRH was greater compared to treatment with NISH:GBRL ($p < 0.001$). Additionally, the reaction to the startle stimulus was greater than all other pulses for each treatment type (Tukey's $p < 0.001$).