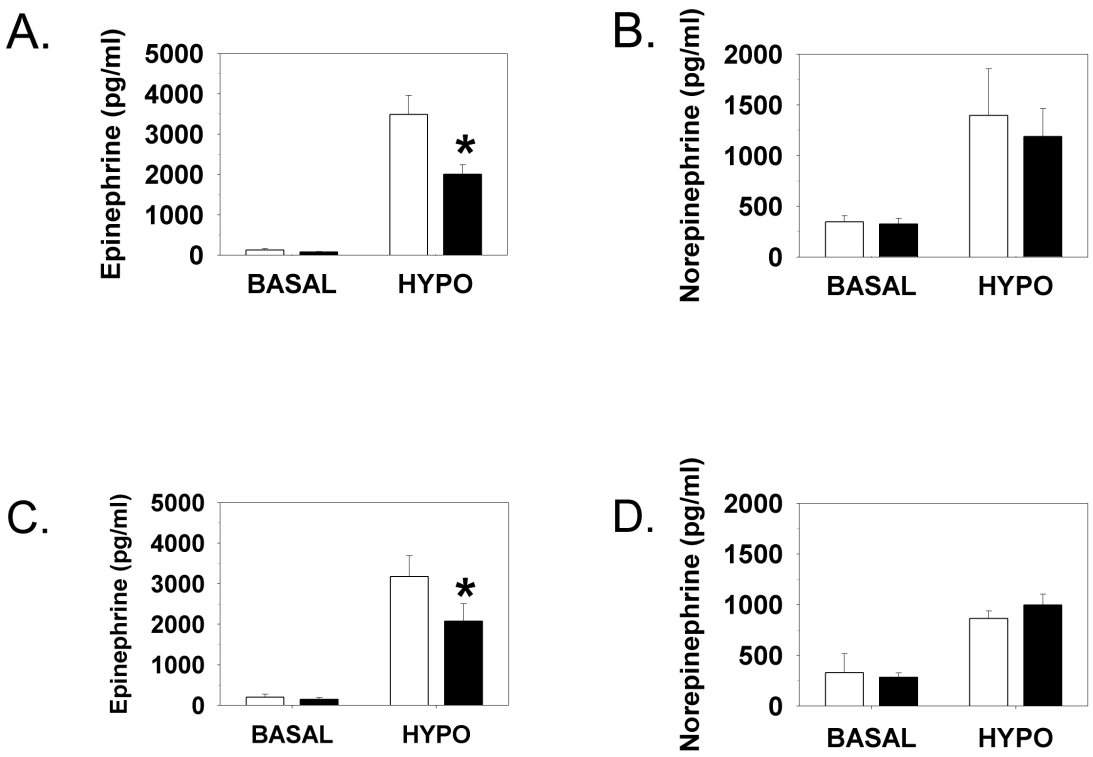
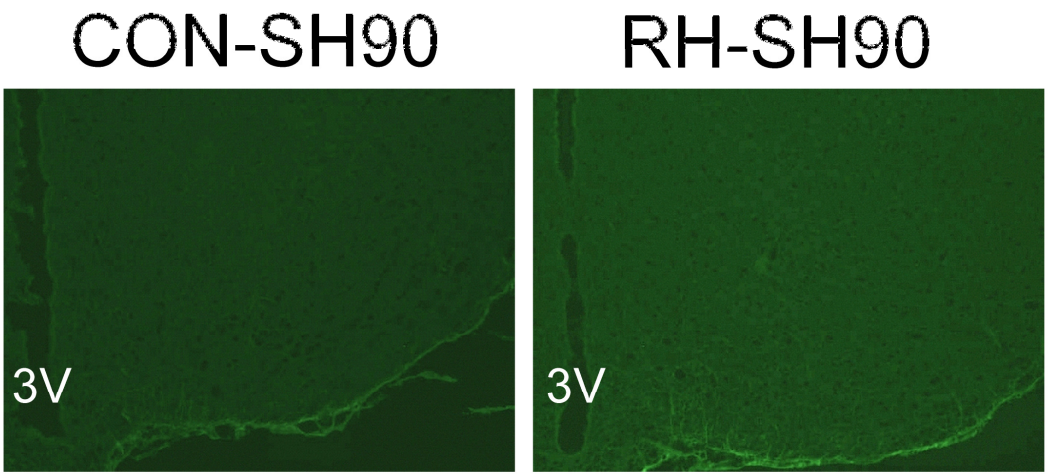
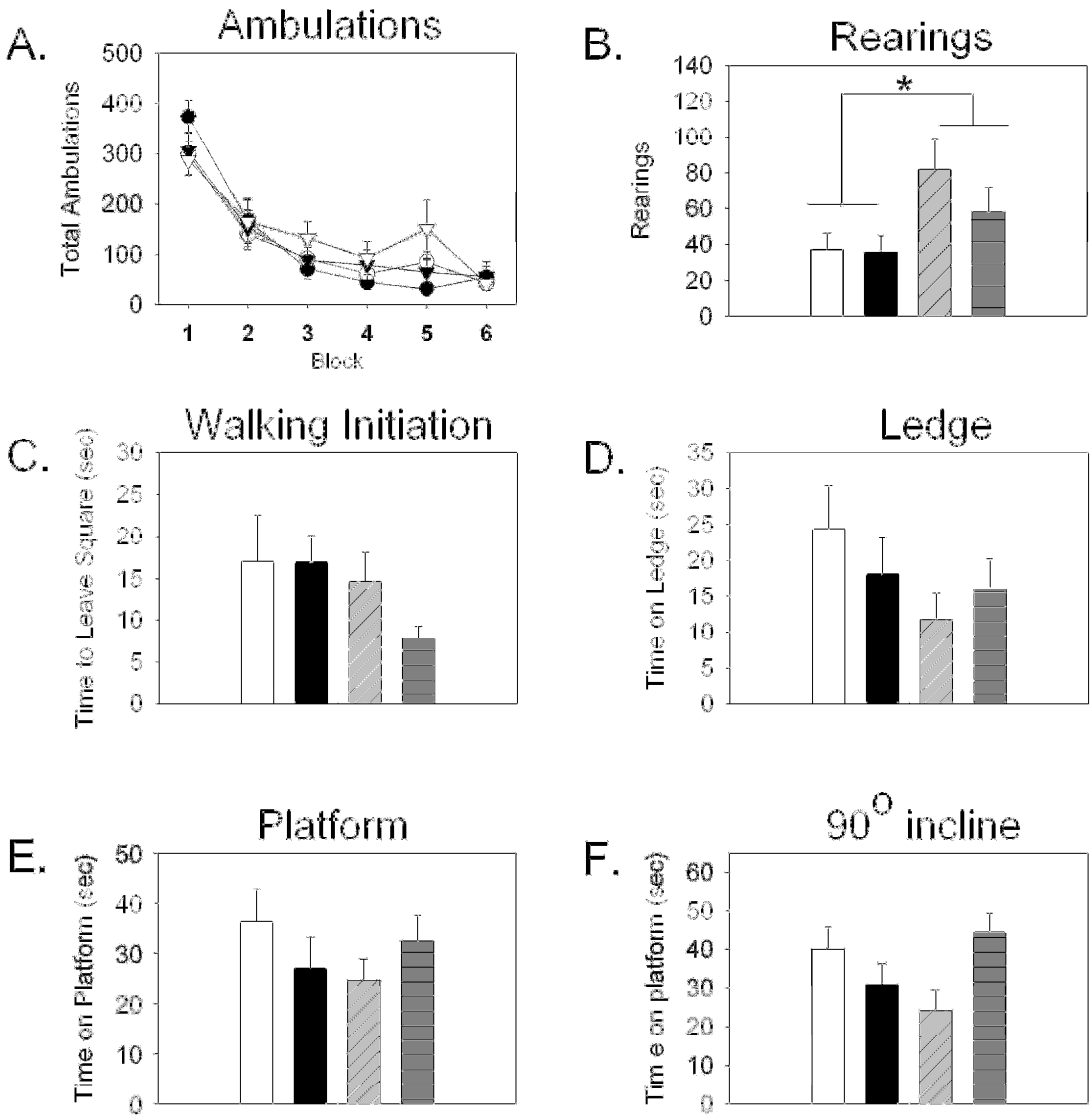


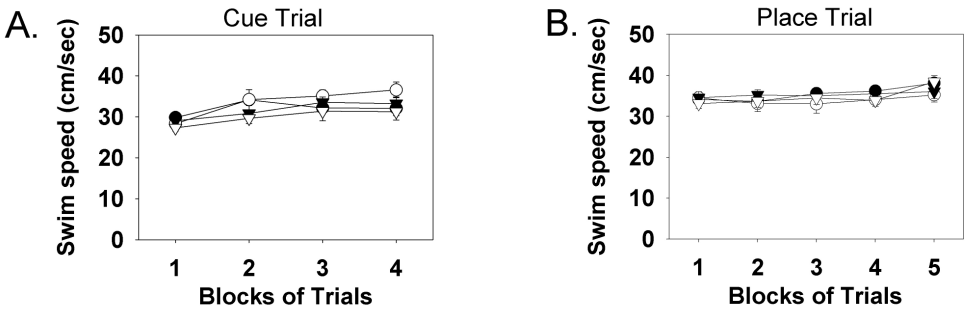
Supplementary Figure 1. Attenuated epinephrine response to hypoglycemia in rats exposed to recurrent moderate hypoglycemia. (A) Epinephrine levels were measured before the onset (basal) and during severe hypoglycemia. Although not different during the basal period, as expected the RH-SH60 rats (black bar) had an attenuated epinephrine response to hypoglycemia compared to CON-SH60 rats (white bar) (* $p < 0.05$, by Student t-test). (B) Norepinephrine levels were not different during either the basal period and rose to a similar levels during severe hypoglycemia for RH-SH60 and CON-SH60 rats. (C) RH-SH90 rats (black bar) had a significantly attenuated epinephrine response to hypoglycemia compared to CON-SH90 (white bar) rats (* $p < 0.05$, by Student t-test). (D) Norepinephrine levels were similar between RH-SH90 and CON-SH90 during the basal period and rose to a similar extent in response to severe hypoglycemia during the hyperinsulinemic clamp.



Supplementary Figure 2. Fluoro-Jade B staining of the hypothalamus. One week after a 90 min episode of severe hypoglycemia, no Fluoro-Jade B staining was observed in the hypothalamus of either CON-SH90 and RH-SH90 groups. The third ventricle (3V) is denoted in the figures. (40X magnification).



Supplementary Figure 3. Locomotor activity and sensorimotor function 6-8 weeks following severe hypoglycemia or euglycemic clamp. (A) No significant differences were observed between groups in terms of ambulations (CON-EUG, open triangle, n=7; RH-EUG, closed triangle, n=9; CON-SH90, open circle, n=11; RH-SH90, closed circle, n=9). (B) The SH90 groups (CON-SH90, diagonal hatch, and RH-SH90, grey horizontal hatch) exhibited significantly ($p = 0.017$) more rearing than the EUG groups (CON-EUG, white bar, and RH-EUG, black bar). Sensorimotor function was also assessed by walking initiation task (C), ability to balance on a ledge (D), remain on a platform (E), or stay on a 90° inclined screen (F). Analyses conducted on the data from these tests indicate no sensorimotor deficits in rats exposed to severe hypoglycemia.



Supplementary Figure 4. Swim speeds during the Morris water maze test. Morris water maze testing was performed 6-8 weeks following severe hypoglycemic or euglycemic clamps. During the cue trial (A) and the place trial (B), no significant difference in swim speeds were observed between CON-EUG (open triangle, n=7), RH-EUG (closed triangle, n=9), CON-SH90 (open circles , n=11), and RH-SH90 (closed circles, n=9).