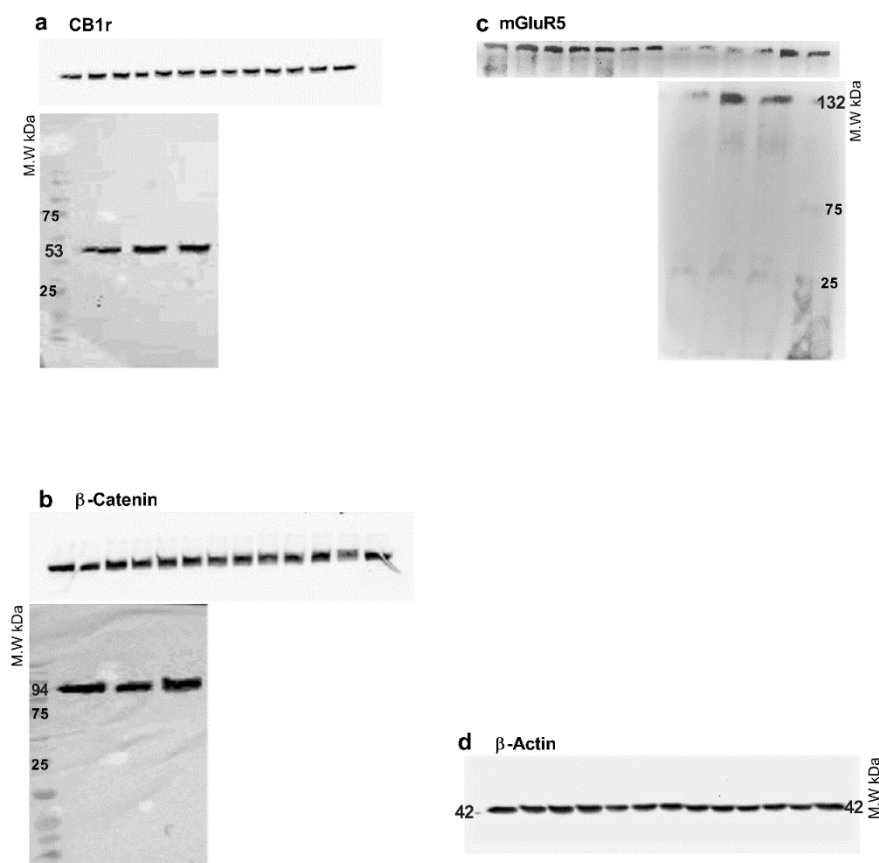


# Supplementary Materials

## Figure S1. Antibody specificity

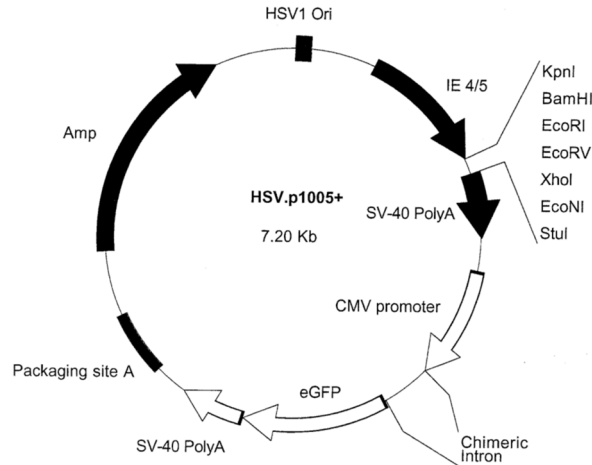
Demonstration of antibodies and their specificity: (a) Anti CB1r {predicted molecular weight (PMW): 53 kDa, abcam, UK; ab25932 [ERP23934-20]}; (b) anti  $\beta$ -Catenin (PMW: 94 kDa; abcam, UK; ab32572 [E247]); (c) anti mGluR5 (PMW: 132 kDa; abcam, UK; ab76316 [ERP2425Y]); (d)  $\beta$ -actin (PMW: 45 kDa; Cell Signaling, USA; #5125 [13E5]).



\*\*SuperMarker2700 ; Cat# 9597580SM2700 ; Bio-Lab Israel

## Figure S2. An illustration of a modified HSV amplicon plasmid

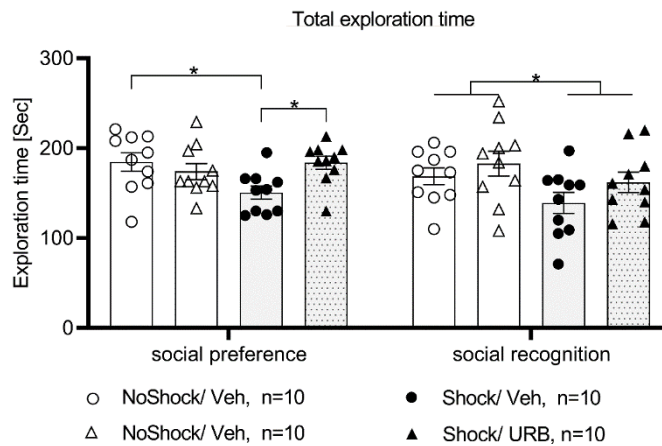
An illustration of a modified HSV amplicon plasmid with an added transcription cassette expressing GFP, producing a separate transcript [i.e., promoter and poly(A)] for GFP (provided by Nestler's lab). The target gene is still driven by the IE 4/5 promoter, while the GFP is driven by a CMV promoter. The two transcription cassettes are in a nose-to-tail orientation. Co-expression is generally above 90%. In the short-term experimental design, HSV has advantages over many other viral vectors, since the viral expression in vivo lasts only about 8 days (see, e.g., Neve et al., 2005).



**Figure S3. The effects of URB597 on exploration time during the social preference and the social recognition tests**

A two-way ANOVA (shock×drug; 2×2) on total exploration time revealed a significant main effect of shock in social recognition ( $F(1,36)= 4.606$ ,  $p<0.05$ ) as well as a drug×shock interaction for social preference ( $F(1,36)= 6.56$ ,  $p<0.05$ ).

Post hoc analysis revealed that during the social preference test, the Shock/Veh group demonstrated decreased exploration time compared with the NoShock/Veh and Shock/URB597 groups (both  $p<0.05$ ). During the social recognition test, the Shock groups showed a significant decrease in exploration time compared with the NoShock groups (all  $p<0.05$ ). Hence, URB597 restored the shock- and reminders-induced decrease in total exploration time in the social preference task but not in the social recognition task. (\*,  $p<0.05$ )



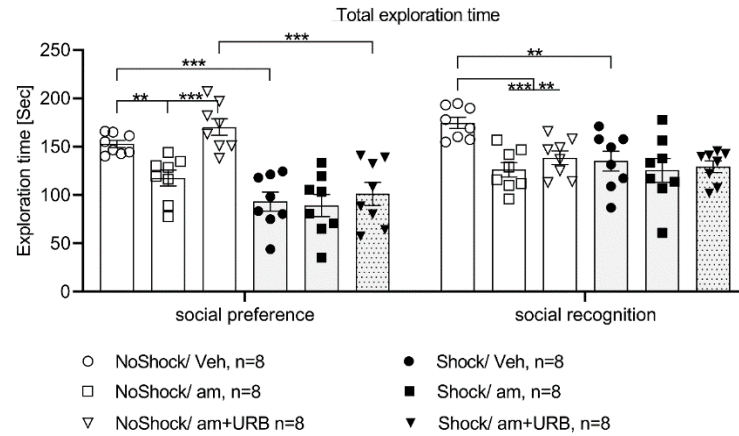
**Table S1.** Pearson bivariate correlation between the expression of  $\beta$ -catenin and behavior

Task	NAc	mPFC
ASR	-.461** <sup>1</sup>	-.300
Social preference	.291	.117
Social recognition	.367*	.255
T- maze acquisition	.291	.117
T- maze reversal	.367*	.255
FST immobility	-.302	-.100
FST climbing	.439**	.419**
FST swimming	-.084	-.021

<sup>1</sup> Significant correlations were found between NAc  $\beta$ -catenin levels and the following behaviors: ASR: ( $r = -0.461$ ,  $p < 0.01$ ), social recognition: ( $r = 0.367$ ,  $p < 0.05$ ), WTM acquisition: ( $r = -0.513$ ,  $p < 0.01$ ), WTM reversal: ( $r = -0.434$ ,  $p < 0.01$ ) and FST climbing: ( $r = 0.439$ ,  $p < 0.01$ ). This suggests that decreased  $\beta$ -catenin levels in the NAc were associated with enhanced startle response, impaired social recognition, impaired performance in the WTM, and decreased climbing in the FST. A significant correlation also was found between mPFC  $\beta$ -catenin levels and climbing in the FST: ( $r = 0.419$ ,  $p < 0.01$ ), suggesting that lower  $\beta$ -catenin levels in the mPFC were associated with decreased climbing (i.e., decreased coping behavior) (\*,  $p < 0.05$ ; \*\*,  $p < 0.01$ ).

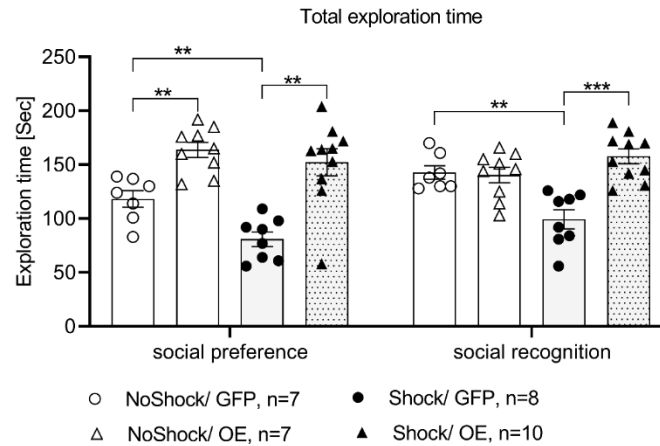
**Figure S4. The effects of URB597 and AM251 on exploration time during the social preference and the social recognition tests**

A two-way ANOVA (shock $\times$ drug; 2 $\times$ 2) on total exploration time revealed significant main effects of shock [preference:  $F(5,42) = 47.4$ ,  $p < 0.001$ ; recognition:  $F(5,42) = 5.641$ ,  $p < 0.05$ ] and drug [preference:  $F(5,42) = 6.134$ ,  $p < 0.01$ ; recognition:  $F(5,42) = 6.248$ ,  $p < 0.01$ ], with no significant drug $\times$ shock interactions. Post hoc analysis revealed that during the social preference test, the Shock/Veh and the Shock/am+URB groups showed decreased exploration time compared with their NoShock groups (NoShock/Veh and No Shock/am+URB groups, respectively: both  $p < 0.001$ ). Also, the NoShock/am group demonstrated decreased exploration time compared with the NoShock/Veh group ( $p < 0.01$ ) and the NoShock/am+URB group ( $p < 0.001$ ). For social recognition, the NoShock/Veh group demonstrated increased exploration time compared with the NoShock/am group ( $p < 0.001$ ), the NoShock/am+URB group ( $p < 0.01$ ), and the Shock/am group ( $p < 0.01$ ). Hence, the exploration time of the shocked rats co-administrated with URB597 and AM251 was similar to shocked rats treated with vehicle, suggesting that the effects of URB597 on exploration time were blocked by AM251 treatment (\*\*,  $p < 0.01$ ; \*\*\*,  $p < 0.001$ ).



**Figure S5. The effects of NAc  $\beta$ -catenin overexpression on exploration time during the social preference and the social recognition tests**

A two-way ANOVA (shock $\times$ virus; 2 $\times$ 2) on exploration time revealed significant main effects of shock [preference:  $F(3,30)=6.567$ ,  $p<0.05$ ] and drug [preference:  $F(3,30)=37.558$ ,  $p<0.001$ ; recognition:  $F(3,30)=14.218$ ,  $p<0.01$ ], with a significant drug $\times$ shock interaction [recognition:  $F(3,30)=16.610$ ,  $p<0.001$ ]. Post hoc analysis revealed that during the social preference test, the GFP groups (NoShock/GFP and Shock/GFP) demonstrated decreased exploration time compared with the OE groups (NoShock/OE and Shock/OE, respectively; both  $p<0.01$ ). Also, the Shock/GFP group demonstrated decreased exploration compared with the NoShock/GFP group ( $p<0.01$ ). During the social recognition test, the Shock/GFP group showed decreased exploration compared with both the NoShock/GFP group ( $p<0.01$ ) and the Shock/OE group ( $p<0.001$ ). This suggests that NAc  $\beta$ -catenin overexpression prevented the shock- and reminders-induced decrease in exploration (\*\*,  $p<0.01$ ; \*\*\*,  $p<0.001$ ).



**Figure S6. The effects of NAc  $\beta$ -catenin downregulation on exploration time during the social preference and the social recognition tests**

A three-way ANOVA (shock $\times$ virus $\times$ drug; 2 $\times$ 2 $\times$ 2) on exploration time revealed a significant main effect of shock [preference:  $F(7,76) = 46.203$ ,  $p < 0.001$ ; recognition:  $F(7,76) = 21.836$ ,  $p < 0.001$ ] and a significant shock $\times$ virus interaction [preference:  $F(7,76) = 6.734$ ,  $p < 0.05$ ]. Post hoc analysis revealed that during the social preference test, the Shock/GFP+Veh, Shock/DR+Veh and Shock/DR+URB groups demonstrated decreased exploration compared to their respective non-shocked controls (NoShock/GFP+Veh,  $p < 0.01$ ; NoShock/DR+URB,  $p < 0.001$ ; and NoShock/DR+Veh,  $p < 0.05$ ). Also, the Shock/DR+URB group showed decreased exploration compared with the Shock/GFP+URB group ( $p < 0.05$ ). During the social recognition test, the Shock/DR+Veh group showed decreased exploration compared to NoShock/DR+Veh group ( $p < 0.01$ ) (\*\*,  $p < 0.01$ ; \*\*\*,  $p < 0.001$ ).

