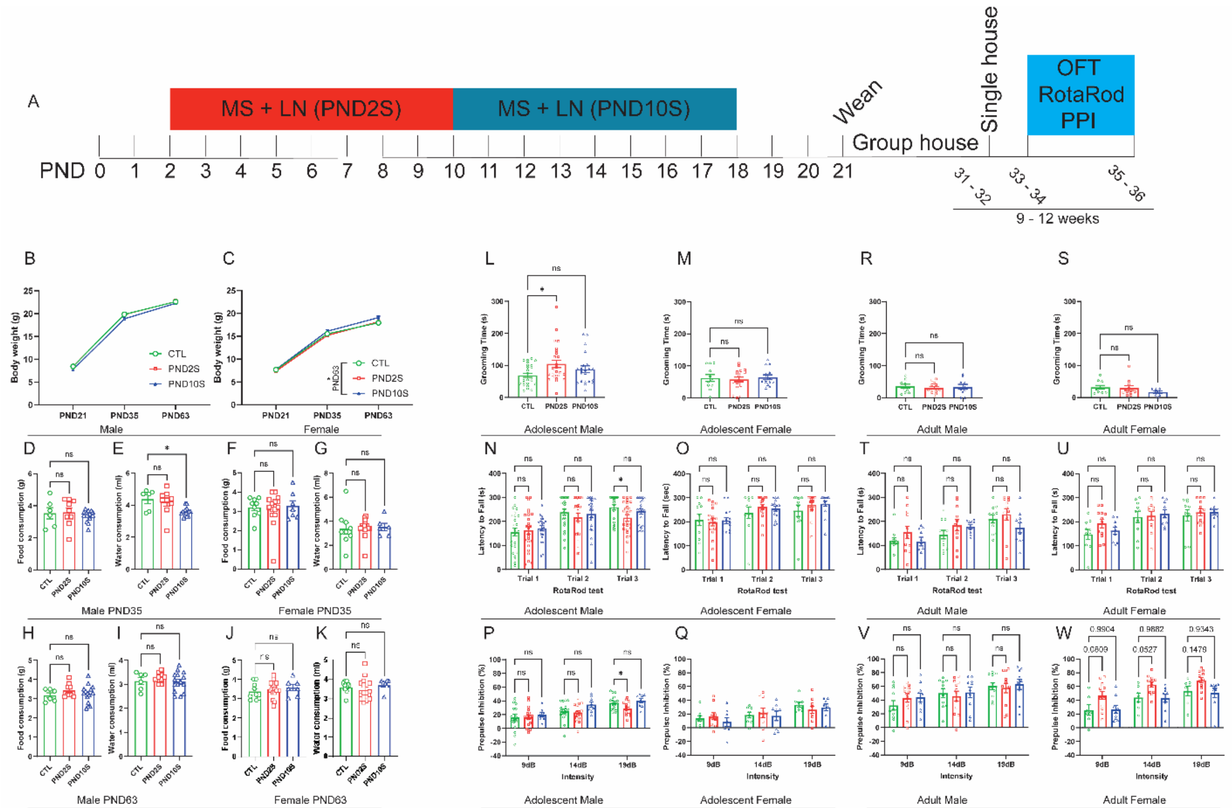

Figure S1. PND2S produces sexually dimorphic behavioral phenotypes. (A) Schematic timeline of ELS and behavioral testing. **(B, C)** Influence of ELS on body weight of male and female mice across development. **(D-G)** Influence of ELS on food and water consumptions of male and female mice in adolescence. **(H-K)** Influence of ELS on food and water consumptions of male and female mice in adulthood. PND2S, but not PND10S, elevated grooming time in **(L)** adolescent males (W[2.000, 42.26] = 3.741, p=0.0319) but not **(M)** females (F[2,41]=0.1995, p=0.8199). PND2S, but not PND10S, reduced latency to fall during rotarod test in **(N)** adolescent males (Trial × ELS: F[4,138]=1.572, p=0.1852) but not **(O)** females (F[4,82]=0.4743, p=0.7545). PND2S, but not PND10S impaired prepulse inhibition in **(P)** adolescent males (ELS: F[2,39]=2.059, p=0.1412) but not **(Q)** females (ELS: F[2,23]=0.1518, p=0.8600). ELS did not influence **(R, S)** grooming behaviors, **(T, U)** motor learning skill, and **(V, W)** prepulse inhibition in adult mice of either sex. One-way ANOVA, Welch's ANOVA, or two-way ANOVA followed by Dunnett's multiple comparisons test: *p<0.05.

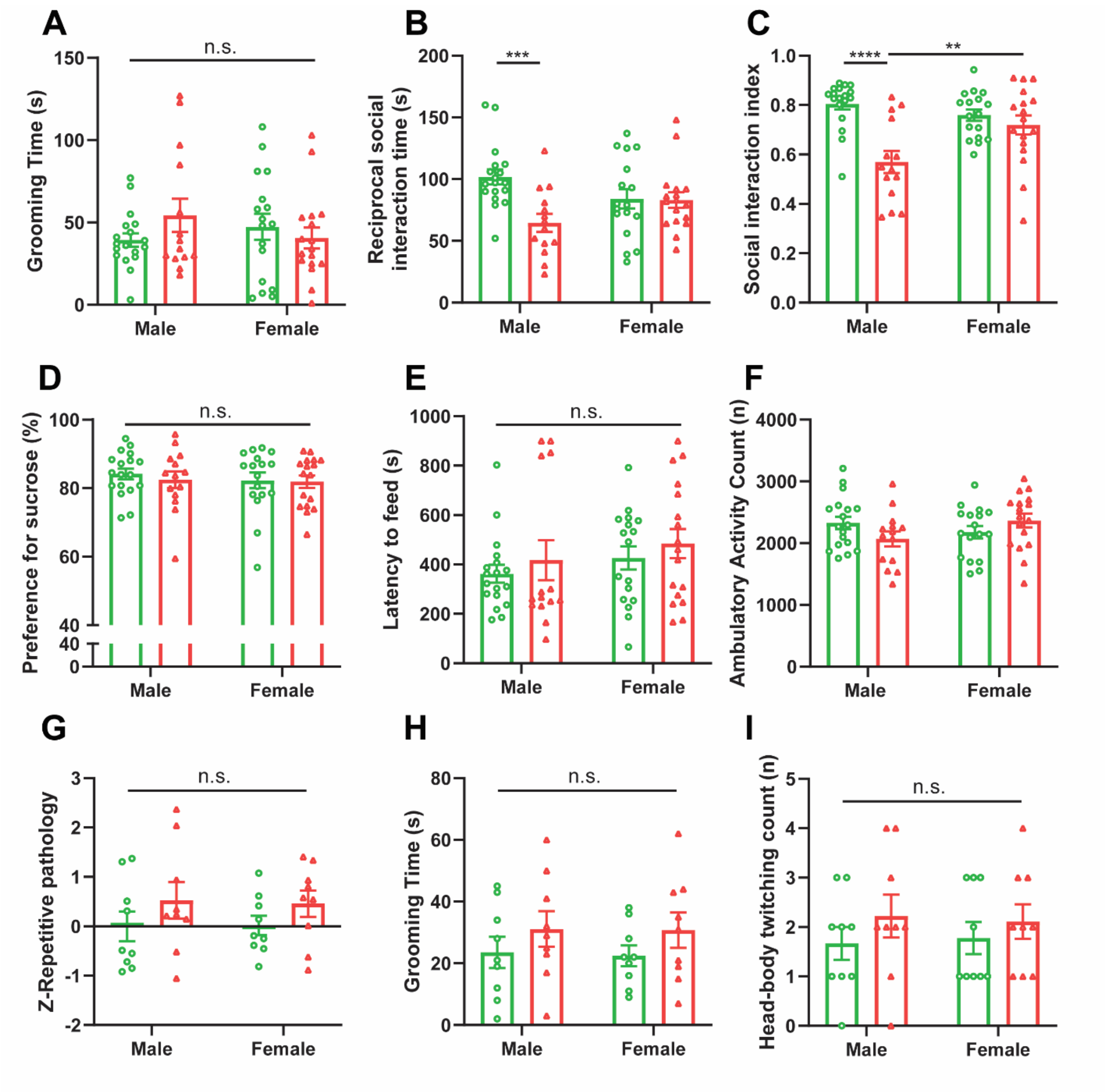

Figure S2. Behavioral effects of ELS on adult mice. (A) No effects of sex or of ELS were seen on grooming behaviors in adult mice. **(B)** Reciprocal social interaction was reduced by ELS in adult males but not females (Sex × ELS: $F[1, 62]=6.778$, $p=0.0115$; ELS: $F[1, 62]=7.549$, $p=0.0079$). **(C)** In the three-chamber sociability test, ELS reduced social preference in adult males but not females (Sex × ELS: $F[1, 62]=9.053$, $p=0.0038$; ELS: $F[1, 62]=18.10$, $p<0.0001$). **(D)** No effects of sex or of ELS were seen on sucrose preference in adult mice (Sex × ELS: $F[1, 62]=0.1105$, $p=0.7407$). **(E)** No effects of sex or of ELS were seen on latency to feed in the novelty-suppressed feeding test in adult mice (Sex × ELS: $F[1, 62]=0.0004$, $p=0.9838$). **(F)** A significant interaction between ELS and sex was observed in the locomotor activity (Sex × ELS: $F[1, 62]=4.256$, $p=0.0433$). In an independent cohort, ELS did not influence **(G)** repetitive pathology Z scores (Sex × ELS: $F[1, 32]=0.0215$, $p=0.8842$), **(H)** grooming behavior in adult mice (Sex × ELS: $F[1, 32]=0.006$, $p=0.9393$), and **(I)** head-body twitching (Sex × ELS: $F[1, 32]=0.0936$, $p=0.7617$). Two-way ANOVA followed by Sidak's multiple comparison test: $^{**}p<0.01$, $^{***}p<0.001$, $^{****}p<0.0001$.

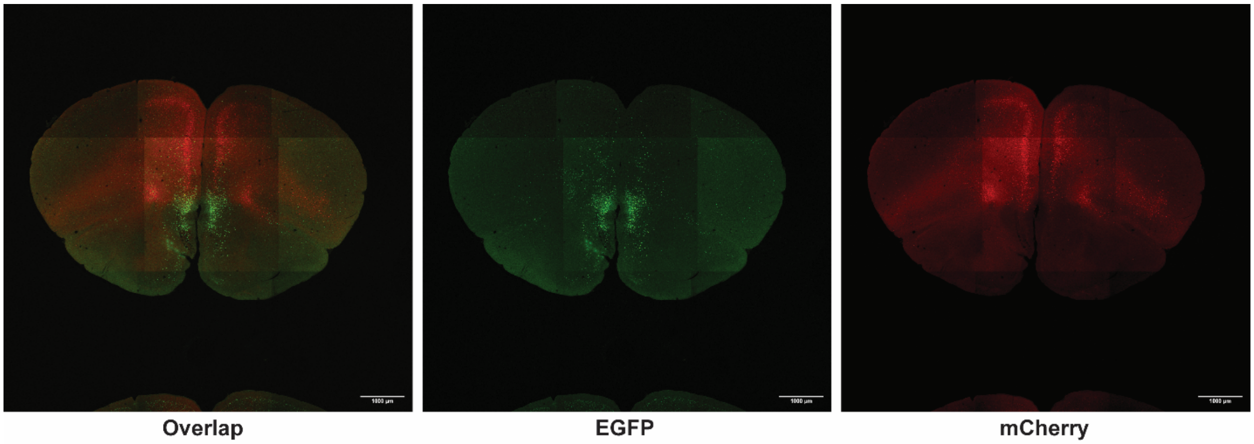

Figure S3. Representative images of cortico-striatal and cortico-septal projection neurons. Scale bars, 1000 μm.

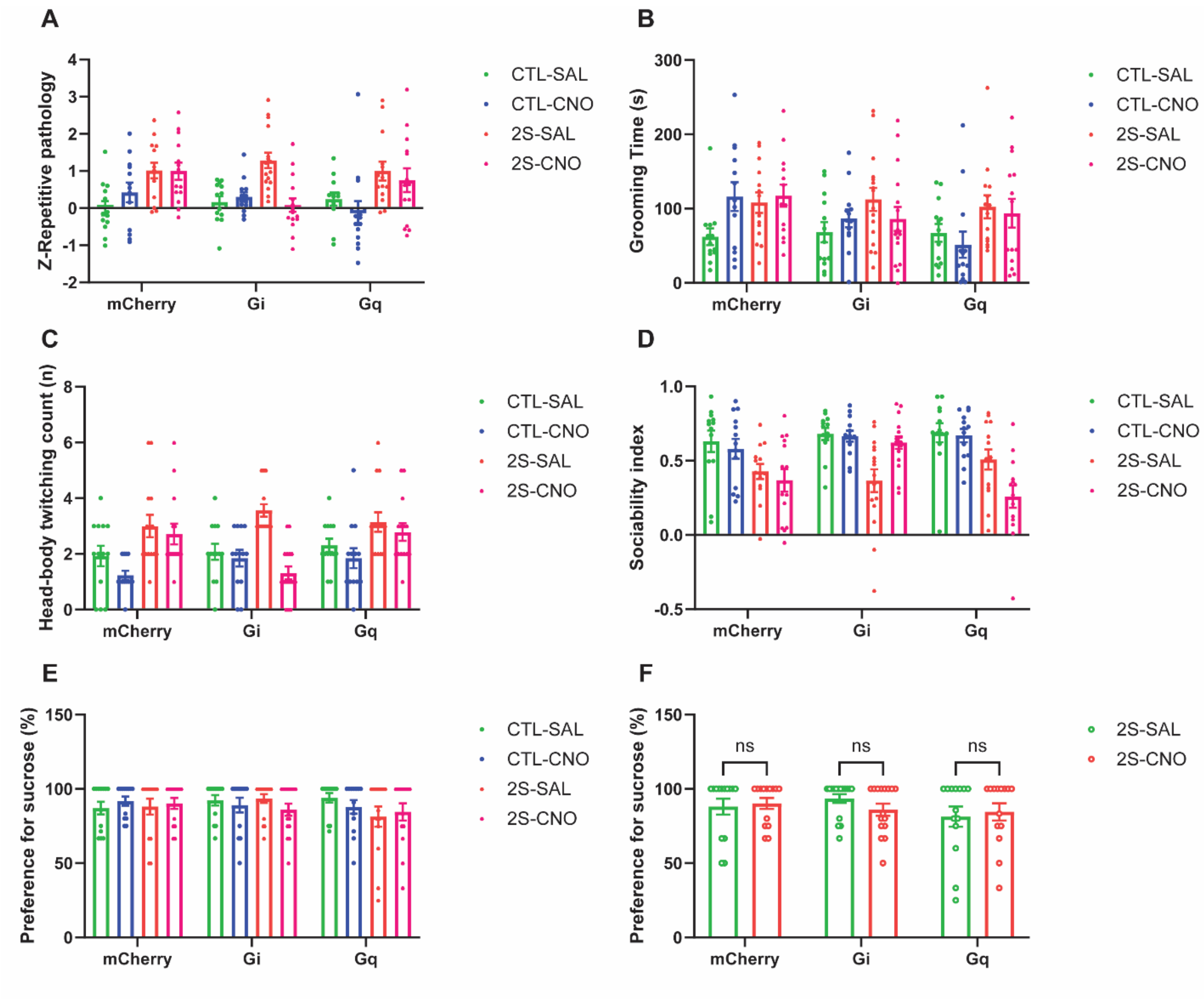

Figure S4. Effects of chemogenetic manipulation of cortico-striatal projection neurons on repetitive behavioral pathology, sociability, and anhedonia in adolescent male mice. ELS influenced **(A)** repetitive pathology Z scores (ELS: F[1,77]=29.79, p<0.0001; ELS x CNO: F[1,77]=4.063, p=0.0473), **(B)** grooming (ELS: F[1,77]=9.470, p=0.0029), and **(C)** head-body twitching (ELS: F[1,77]=22.45, p<0.0001; CNO: F[1,77]=17.81, p<0.0001; DREADD x ELS x CNO: F[2,77]=5.207, p=0.0076) in adolescent male mice that received DREADD infusions. **(D)** Chemogenetic manipulation of cortico-striatal projection neurons bidirectionally regulated sociability (ELS: F[1,77]=36.58, p<0.0001; DREADD x CNO: F[2,77]=4.946, p=0.0095; DREADD x ELS x CNO: F[2,77]=4.605, p=0.0129). **(E)** ELS did not influence anhedonia in adolescent male mice (ELS: F[1,77]=1.017, p=0.3164). **(F)** Chemogenetic manipulations of cortico-striatal projection neurons did not influence anhedonia in stressed adolescent male mice (DREADD x CNO: F[2,41]=1.480, p=0.2395). Three-way ANOVA for **A – E**, two-way repeated measures ANOVA followed by Sidak's multiple comparison test for **F**. ns = non-significant.

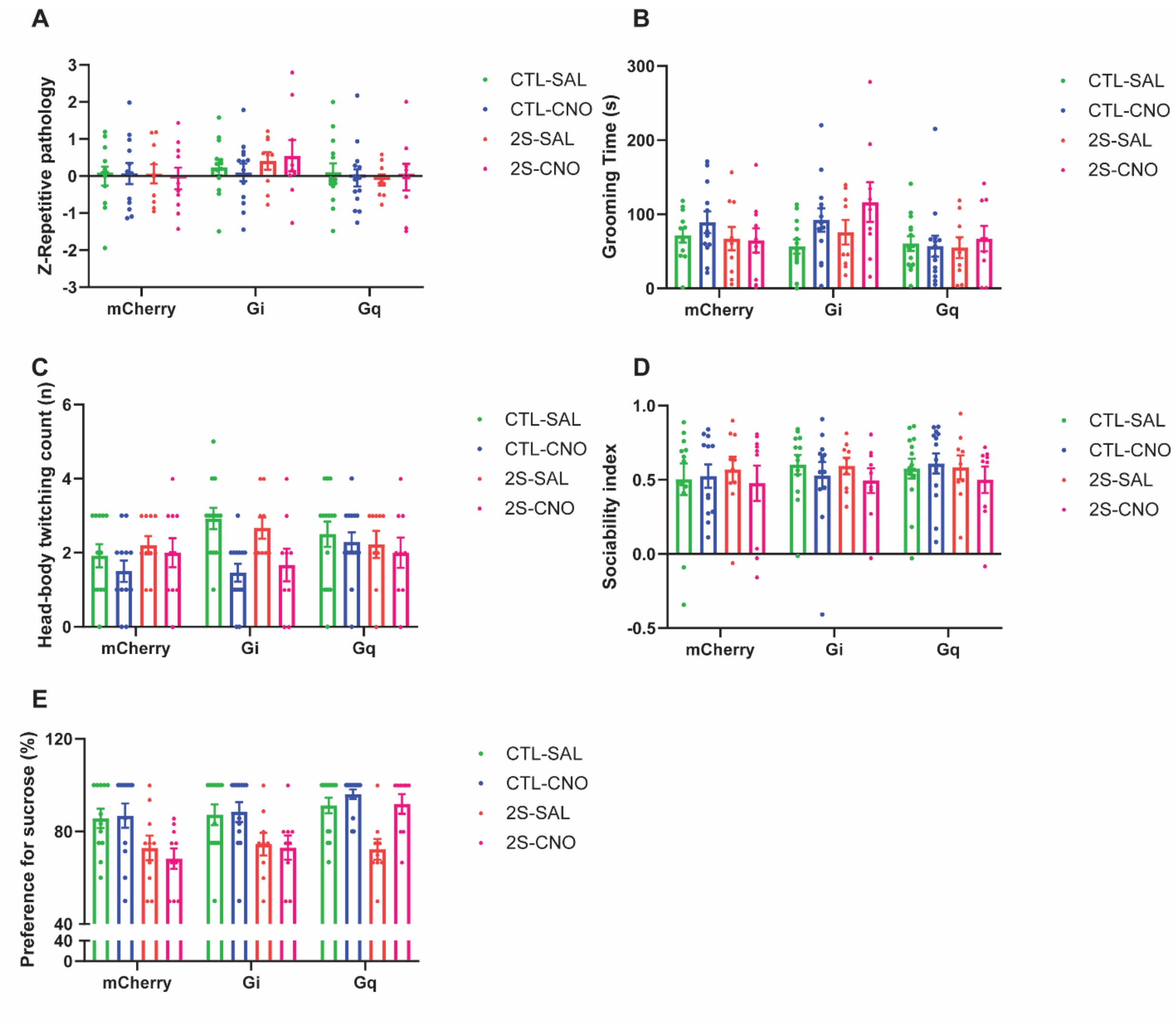

Figure S5. Effects of chemogenetic manipulation of cortico-striatal projection neurons on repetitive behavioral pathology, sociability, and anhedonia in adolescent female mice. ELS did not significantly influence **(A)** repetitive pathology Z scores (ELS: F[1,61]=0.1272, p=0.7225), **(B)** grooming (ELS: F[1,61]=0.1069, p=0.7448), **(C)** head-body twitching (ELS: F[1,61]=0.01914, p=0.8904; DREADD x CNO: F[2,61]=3.438, p=0.0385), and **(D)** sociability (ELS: F[1,61]=0.2594, p=0.6124) in adolescent female mice. **(E)** Anhedonia induced by ELS in adolescent female mice was rescued by chemogenetic activation of cortico-striatal projection neurons (ELS: F[1,61]=26.29, p<00001; DREADD x CNO: F[2,61]=3.448, p=0.0381). All panels use three-way ANOVA.

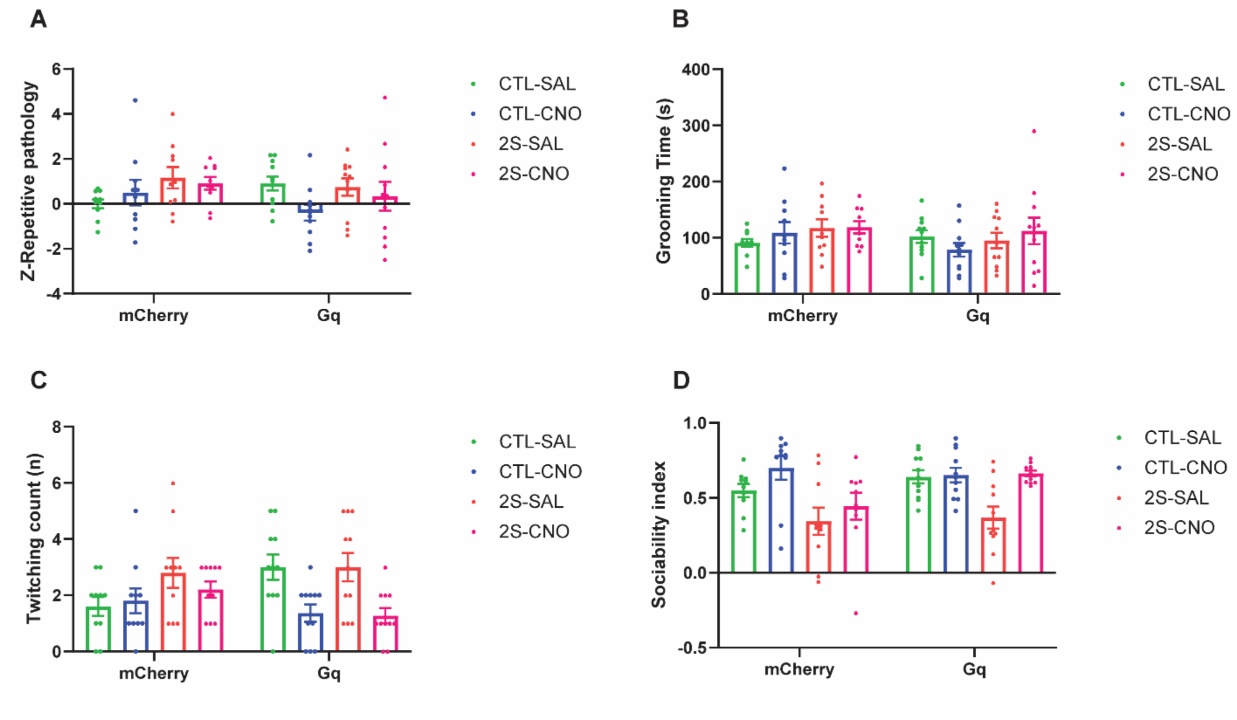

Figure S6. Chemogenetic manipulation of cortico-septal projection neurons modulate sociability. Chemogenetic activation of cortico-septal projection neurons in adolescent ELS males did not influence **(A)** repetitive pathology Z scores, **(B)** grooming time, and **(C)** head-body twitching. Chemogenetic activation of cortico-septal projection neurons in adolescent ELS males **(D)** rescued deficits in sociability (ELS: $F[1,38]=12.75$, $p=0.0010$; DREADD x ELS x CNO: $F[1,38]=4.266$, $p=0.0457$). Three-way ANOVA for **A – D**.

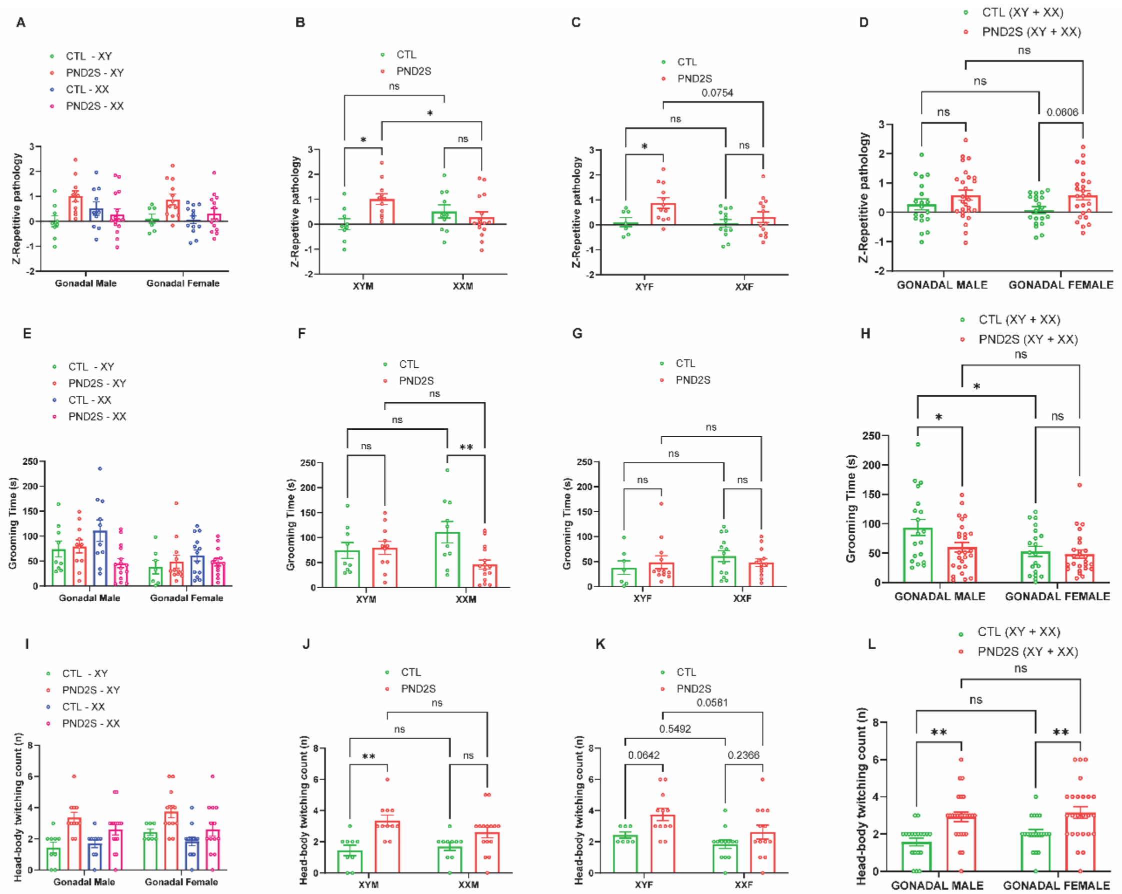

Figure S7. Effects of ELS on repetitive behavioral pathology in the FCG mouse model. (A) Chromosomal sex mediated ELS-induced elevation in repetitive pathology z-scores (Chromosomal sex × ELS: F[1,82]=7.892, p=0.0062). **(B)** XYM but not XXM mice showed increased repetitive pathology z-scores following ELS (Chromosomal sex × ELS: F[1,41]=6.806, p=0.0126). **(C)** ELS increased repetitive pathology z-scores in XYF but not XXF mice (ELS: F[1,41]=6.119, p=0.0176). **(D)** Combining the mice by their gonadal sex, ELS increased repetitive pathology z-scores at trend level in both sexes (ELS: F[1,86]=6.360, p=0.0135). **(E)** Gonadal males spent more time grooming than gonadal females (Gonadal sex: F[1,82]=9.441, p=0.0029). **(F)** ELS reduced grooming time in XXM but not XYM mice (Chromosomal sex × ELS: F[1,41]=5.759, p=0.0210). **(G)** ELS did not influence grooming time in gonadal female mice (Chromosomal sex × ELS: F[1,41]=1.084, p=0.3038). **(H)** Combining the mice by their gonadal sex, males spent more time grooming than females (Gonadal sex: F[1,86]=7.692, p=0.0068). **(I)** ELS increased twitching in the FCG mouse model (ELS: F[1,82]=22.53, p<0.0001). **(J)** ELS increased twitching in XYM mice (ELS: F[1,41]=16.85, p=0.0002). (**K**) ELS increased twitching in gonadal females (ELS: F[1,41]=7,284, p=0.0101). **(L)** Combining the mice by their gonadal sex, both males and females showed increased twitching following ELS (ELS: F[1,86]=21.87, p=0<0.0001). Three-way ANOVA for **A, E, I**. Two-way ANOVA followed by Sidak's multiple comparison test for **B, C, D, F, G, H, J, K, L**. *p<0.05, **p<0.01.

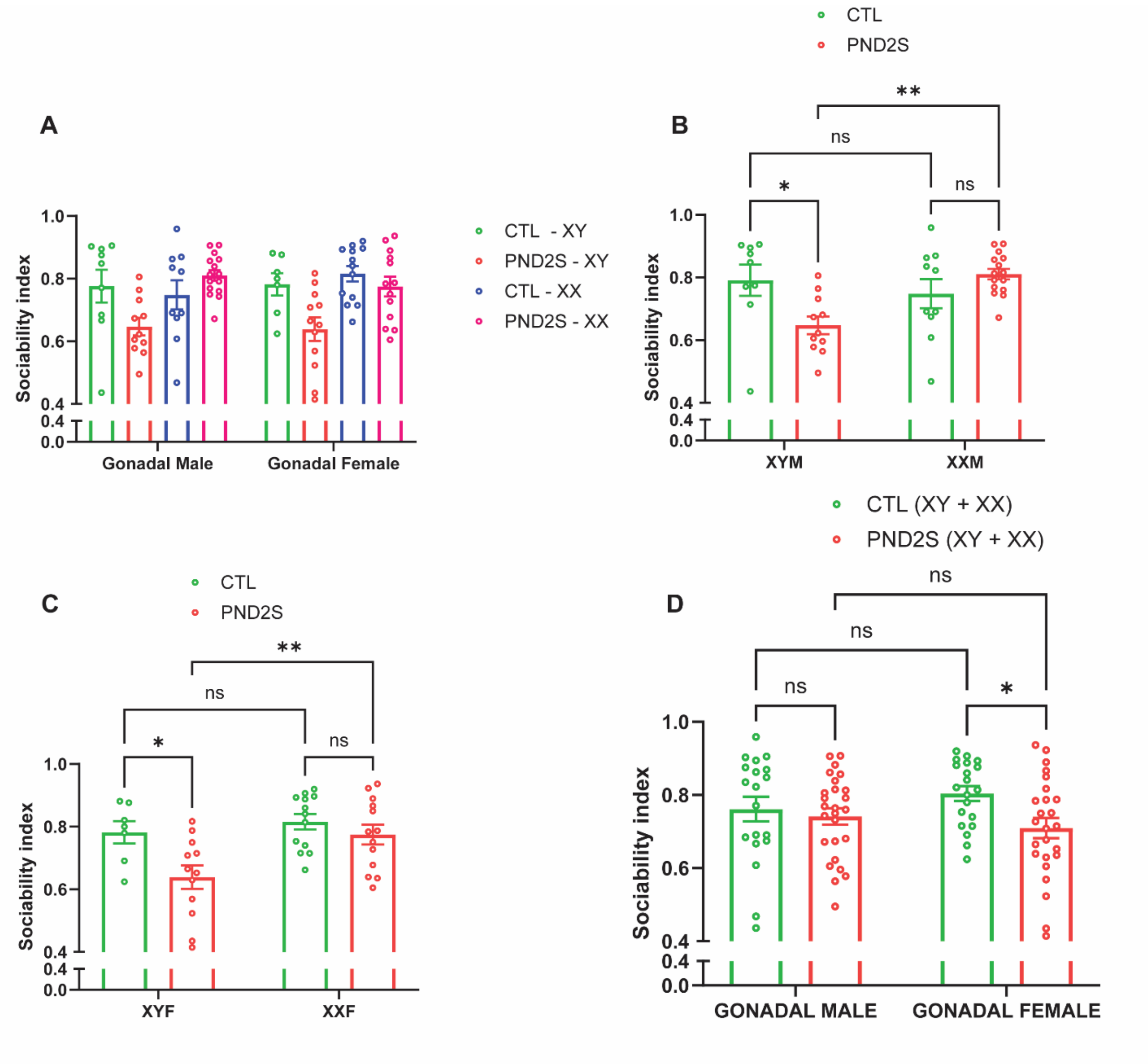

Figure S8. Effects of ELS on sociability in the FCG mouse model. (A) Chromosomal sex mediated ELS-induced social deficits (Chromosomal sex × ELS: F[1,82]=9.165, p=0.0033). **(B)** ELS reduced sociability in XYM but not XXM mice (Chromosomal sex × ELS: F[1,41]=9.086, p=0.0044). **(C)** ELS reduced sociability in XYF but not XXF mice (Chromosomal sex: F[1,41]=6.350, p=0.0157; ELS: F[1,41]=7.478, p=0.0092). **(D)** ELS-induced social deficits in gonadal males and females (ELS: F[1,86]=4.694, p=0.0330). Three-way ANOVA for **A**. Two-way ANOVA followed by Sidak's multiple comparison test for **B – D**. *p<0.05, **p<0.01.

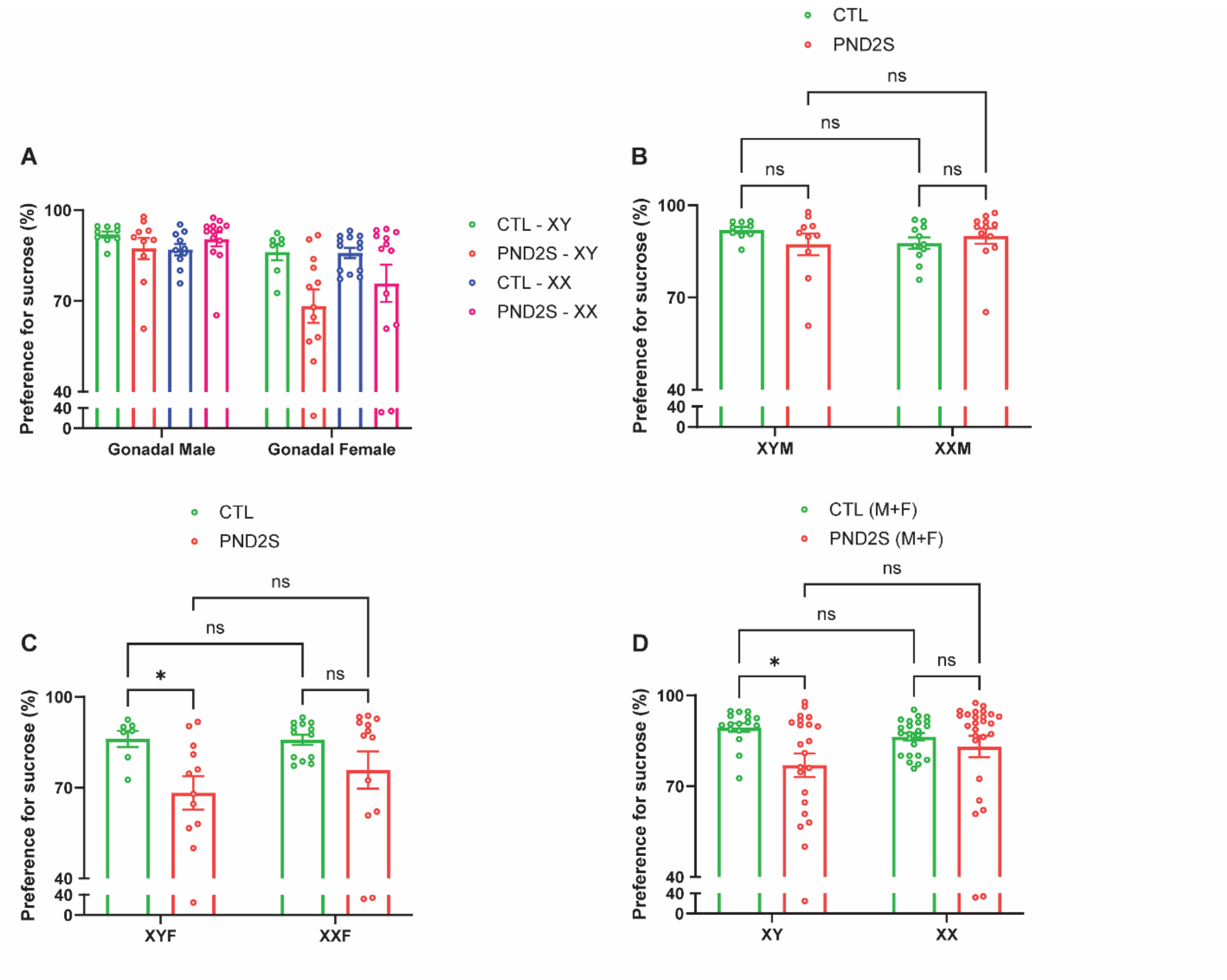

Figure S9. Effects of ELS on sucrose preference in the FCG mouse model. (A) Gonadal sex mediated ELS-induced anhedonia (Gonadal sex × ELS: F[1,79]=5.597, p=0.0204). **(B)** ELS did not influence sucrose preference in gonadal male mice (ELS: F[1,38]=0.2143, p=0.6461). **(C)** ELS reduced sucrose preference in gonadal female mice (ELS: F[1,41]=7.817, p=0.0078). **(D)** ELS-induced anhedonia in XY and XX mice (ELS: F[1,83]=6.487, p=0.0127). Three-way ANOVA for **A**. Two-way ANOVA followed by Sidak's multiple comparison test for **B – D**. *p<0.05.