

Figure S1. The role of Sig-1R agonist on ER-mitochondrion contact in the astrocytes of mice with T1DM.

(a) Quantitative analysis of the distance for ER-mitochondria contacts in astrocytes of CON, CON + PRE-084, STZ, and STZ + PRE-084 mice ($n = 3$). (b) Quantitative analysis of astrocytic ER-mitochondria contact percentage ($n = 3$). Each point represents the average value of a mouse for corresponding index. The data were presented as mean \pm SEM and analyzed using one-way ANOVA with Tukey's multiple comparisons test. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. Sig-1R, sigma-1 receptor; ER, endoplasmic reticulum; T1DM, type 1 diabetes mellitus; CON, control mice; STZ, mice with T1DM.

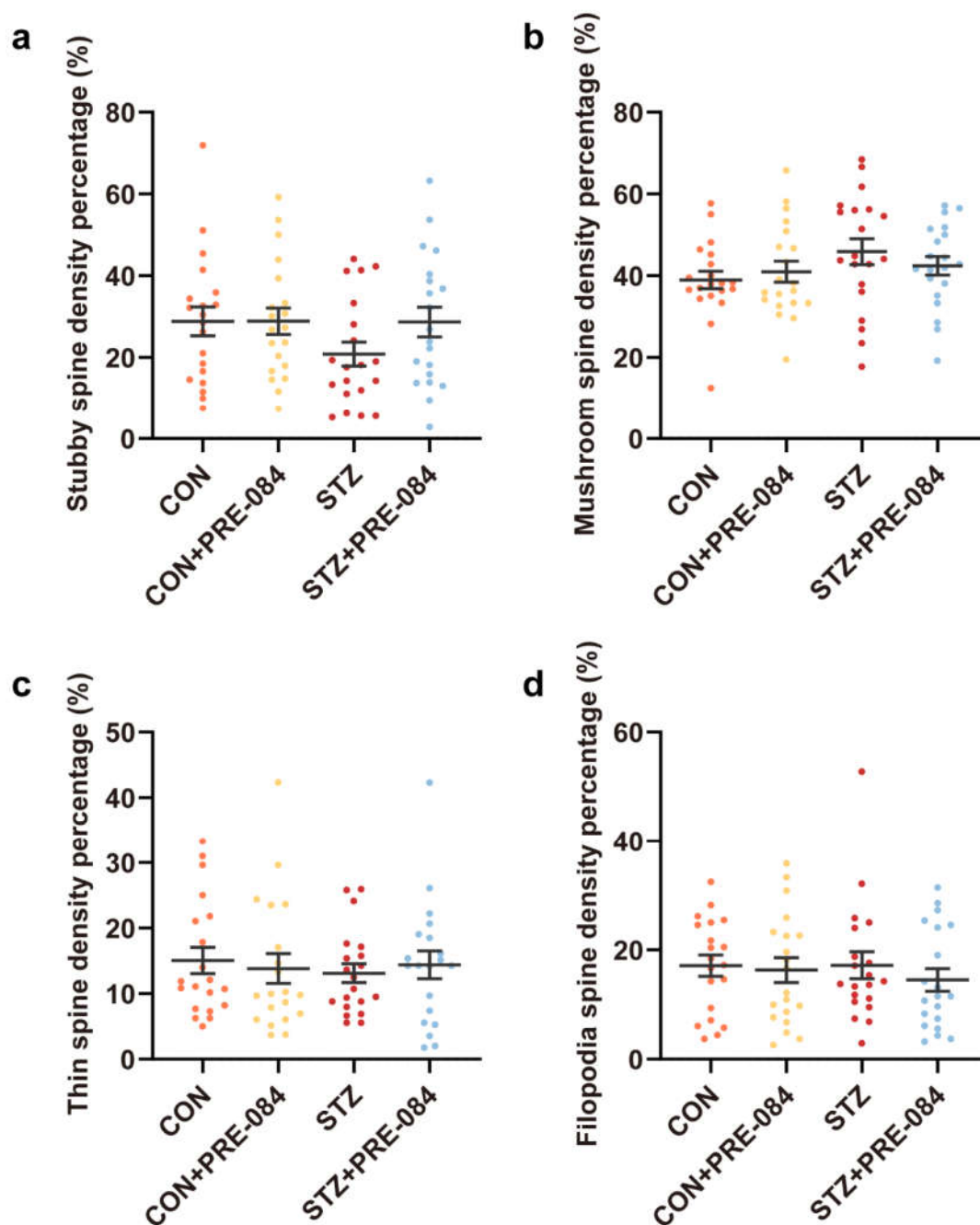


Figure S2. The effect of Sig-1R agonist on different spine density percentage.

(a) Quantitative analysis of stubby spine density percentage in CON, CON + PRE-084, STZ, and STZ + PRE-084 mice ($n = 20$). (b) Quantitative analysis of mushroom spine density percentage in each group ($n = 20$). (c) Quantitative analysis of thin spine density percentage in each group ($n = 20$). (d) Quantitative analysis of filopodia spine density percentage in each group ($n = 20$). The data were presented as mean \pm SEM and analyzed via one-way ANOVA with Tukey's multiple comparison tests, and Kruskal-Wallis test followed by Dunn's multiple comparison tests. Sig-1R, sigma-1 receptor; CON, control mice; STZ, mice with type 1 diabetes mellitus.

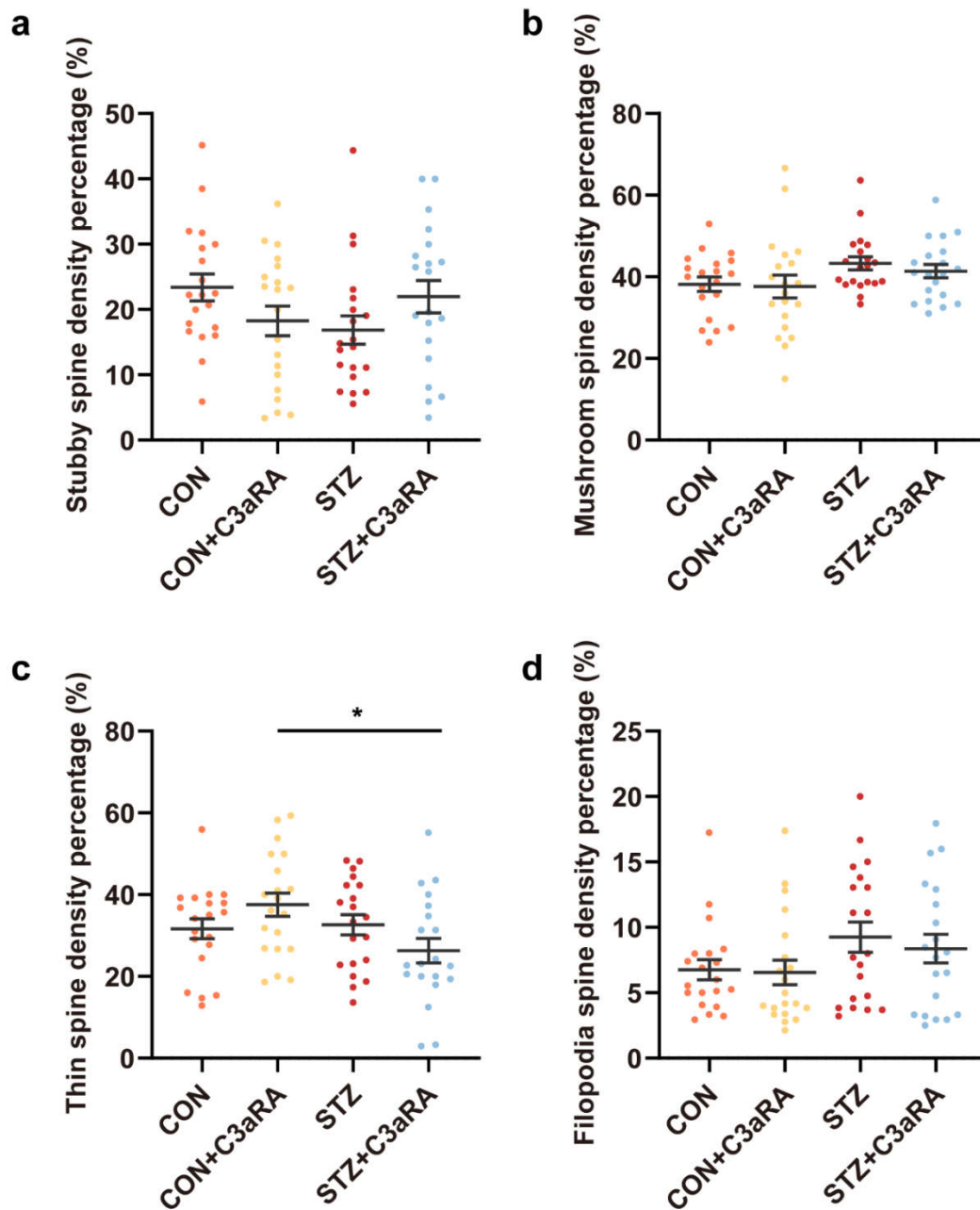


Figure S3. The role of C3aRA on different types of the spine density percentage.

(a) Quantitative analysis of stubby spine density percentage in CON, CON + C3aRA, STZ, and STZ + C3aRA mice ($n = 20$). (b) Quantitative analysis of mushroom spine density percentage in each group ($n = 20$). (c) Quantitative analysis of thin spine density percentage in each group ($n = 20$). (d) Quantitative analysis of filopodia spine density percentage in each group ($n = 20$). The data were presented as mean \pm SEM and analyzed via one-way ANOVA with Tukey's multiple comparison tests, and Kruskal-Wallis test followed by Dunn's multiple comparison tests. * $p < 0.05$. C3aRA, complement component 3a receptor antagonist; CON, control mice; STZ, mice with type 1 diabetes mellitus.