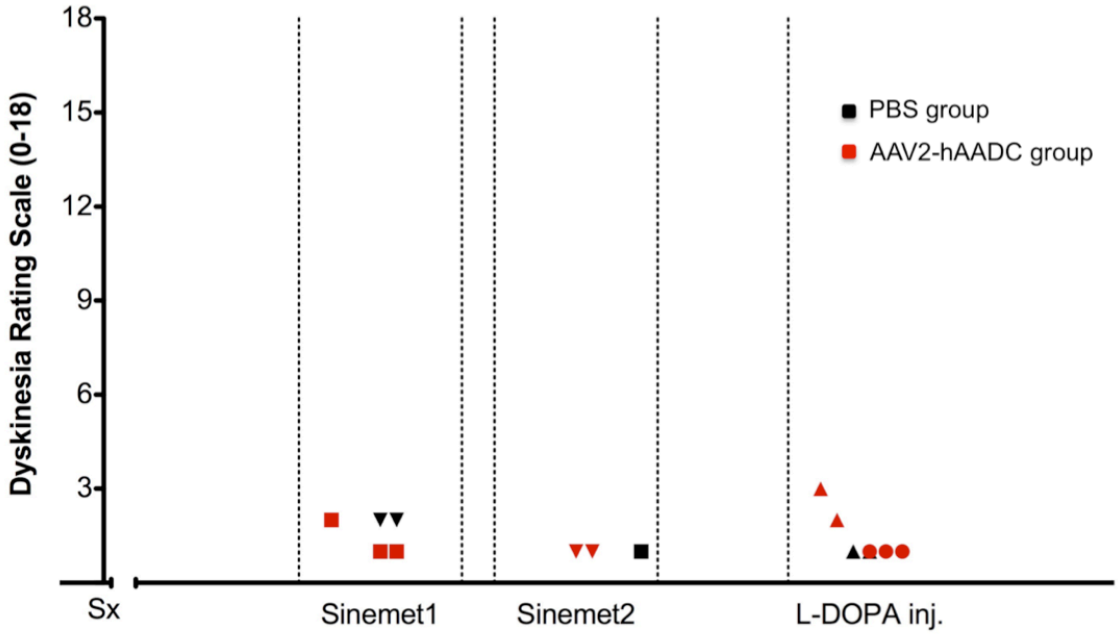
No induction of L-DOPA-induced dyskinesia

We used a clinical rating scale (CRS) to assess the severity of parkinsonism. CRS scores before surgery showed that animals were mildly parkinsonian (average CRS: 10 ± 3). Parkinsonism showed some signs of being slightly improved up to 8 months after AAV2-hAADC infusion, although it was not statistically significant (average CRS: 8 ± 4; $p<0.05$). In order to test whether administration of anti-parkinsonian medication was safe after receiving a higher AAV2-hAADC dose, we challenged the animals with L-DOPA. All animals received oral L-DOPA (Sinemet® 250 mg) on a daily basis and split in two half-doses (125 mg in the morning and 125 mg in the afternoon), for a one-month period before AAV2-hAADC delivery, and for 2 one-month periods after treatment with a 2-month washout interval between them. The severity of dyskinesia was scored for different segments of the animal's body including face, trunk, arms and legs on a scale from 0 to 3, with 0 = absent, 1 = mild, 2 = moderate, 3 = severe. The severity of the rating is based on the frequency and amplitude of the abnormal movement. The dyskinetic score was obtained by adding the scores of all body segments for a maximal score of 18. CRS scores were reduced after L-DOPA administration in all cases either AAV2-hAADC or PBS treated animals. However, none of the animals exhibited consistent L-DOPA-induced dyskinesia with only minor transient dyskinesia observed in some animals in both AAV2-hAADC and PBS groups (**Suppl. Fig. 1**). To confirm these observations with oral L-DOPA, animals were given intramuscular L-DOPA injections (single daily dose for 7 days, 10 mg/kg) at the end of the study. Identical results were obtained. Our data show an almost complete absence of significant behavioral adverse effects (i.e., L-DOPA-induced dyskinesia) after real-time CED of a high dose of AAV2-hAADC and until the end of the study (~8 months after surgery).



Supplementary Figure 1. Lack of L-DOPA-induced dyskinesia after chronic and acute L-DOPA administration

Graph shows dyskinetic events recorded after challenging the animals with L-DOPA. Symbols represent data from individual animals. Sinemet 1 and 2 refer to the 2 non-consecutive months of oral L-DOPA given to the animals after surgery. The washout between them was approximately 2 months. Sx: surgery; inj.: injection.