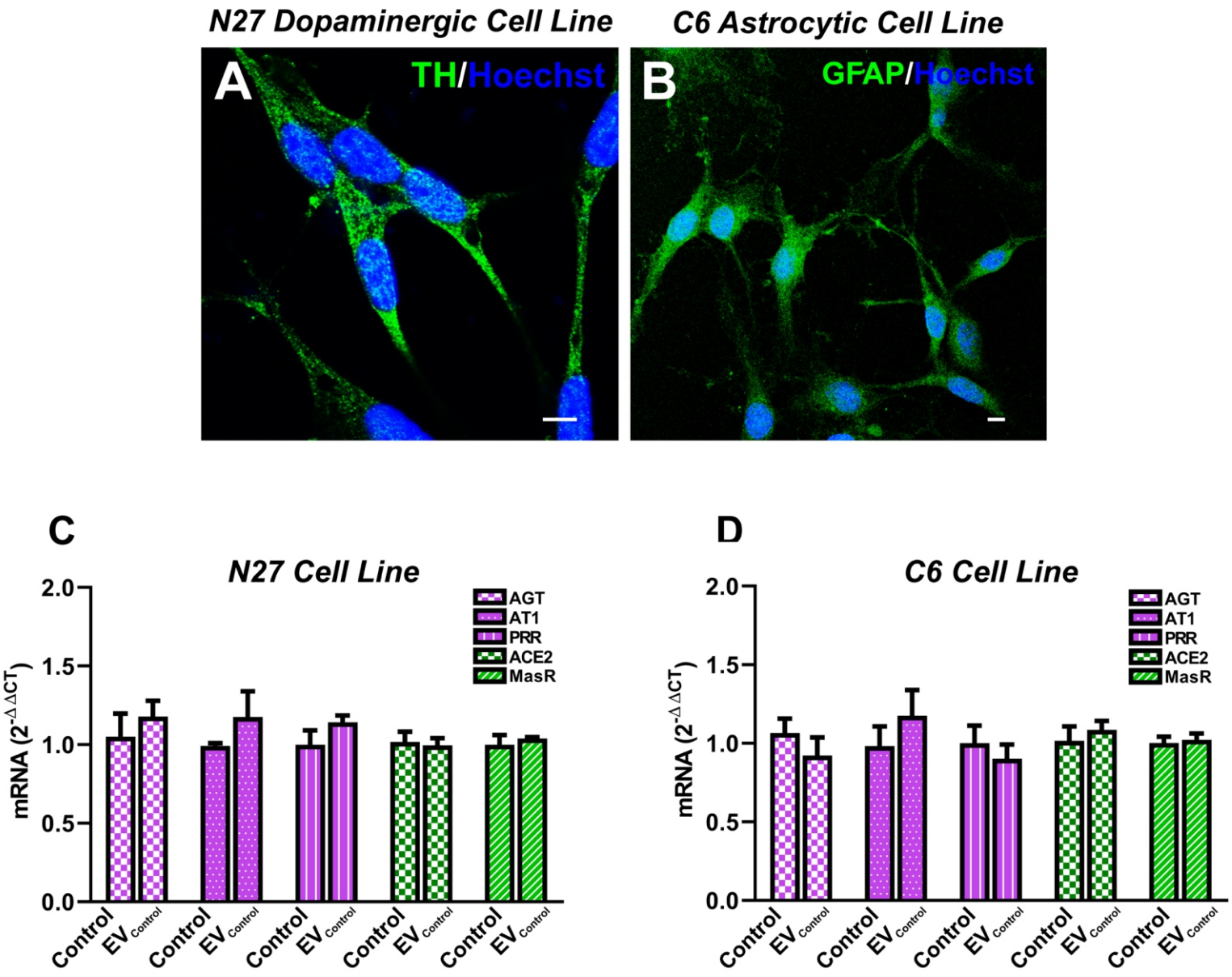

Figure S1. Additional control experiments. Photomicrographs of representative dopaminergic cell line N27 (**A**; TH-positive, green) and C6 astrocytic cell line (**B**; GFAP-positive, green) show that the cell lines express the phenotype of dopaminergic neurons and astrocytes. Nuclei are labeled in blue with Hoechst. Labelling was carried out as previously described [20]. Scale bar: 5 µm. Effects of treatment with $EV_{Control}$ in N27 dopaminergic cell line (**C**) and C6 astrocytic cell line (**D**). No changes were observed after treatment with $EV_{Control}$ relative to Control (i.e. cultures treated with EV vehicle, PBS). Data are given as mean ± SEM. All comparisons were carried out using the Student t-test, except for AT1 in the N27 cell line, where the Mann-Whitney Rank Sum Test was used (n=3-4/group). ACE2: angiotensin-converting enzyme 2; AGT: angiotensinogen; AT1: angiotensin type 1 receptor; $EV_{Control}$: EVs isolated from the serum of control animals; MasR: Mas-related receptor; PRR: (pro)-renin receptor.

Table S1. Results of Statistical Analysis

Figure	Groups	Statistical test	Statistics	p value
1C	Control *vs* MetS *vs* MetS+CAND	Kruskal-Wallis One Way Analysis of Variance on Ranks	H(2)= 11.942	0.003
1D	Control *vs* MetS *vs* MetS+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 18.955	<0.001
2A	Control *vs* MetS *vs* MetS+CAND	Kruskal-Wallis One Way Analysis of Variance on Ranks	H(2)= 12,784	0,002
2B	Control *vs* MetS *vs* MetS+CAND	One Way Analysis of Variance	$F_{(2,14)}$= 28,116	<0,001
2C	Control *vs* MetS *vs* MetS+CAND	One Way Analysis of Variance	$F_{(2,14)}$= 11,980	<0.001
2D	Control *vs* MetS *vs* MetS+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 0,924	0.418
2E	Control *vs* MetS *vs* MetS+CAND	One Way Analysis of Variance	$F_{(2,13)}$= 4,721	0,029
3A	Control *vs* MetS *vs* MetS+CAND	Kruskal-Wallis One Way Analysis of Variance on Ranks	H(2)= 11.789	0.003
3B	Control *vs* MetS *vs* MetS+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 2.369	0.128
3C	Control *vs* MetS *vs* MetS+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 24,197	<0,001
3D	Control *vs* MetS *vs* MetS+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 9,608	0.002
3E	Control *vs* MetS *vs* MetS+CAND	Kruskal-Wallis One Way Analysis of Variance on Ranks	H(2)= 12.538	0.002
3F	Control *vs* MetS *vs* MetS+CAND	Kruskal-Wallis One Way Analysis of Variance on Ranks	H(2)= 13,053	0.001
3G	Control *vs* MetS *vs* MetS+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 24,197	<0,001
3H	Control *vs* MetS *vs* MetS+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 52,772	<0,001
4A	Control *vs* MetS *vs* MetS+CAND	Kruskal-Wallis One Way Analysis of Variance on Ranks	H(2)= 8,180	0.017
4B	Control *vs* MetS *vs* MetS+CAND	One Way Analysis of Variance	$F_{(2,12)}$= 62,291	<0.001
4C	Control *vs* MetS *vs* MetS+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 15.048	<0.001
4D	Control *vs* MetS *vs* MetS+CAND	Kruskal-Wallis One Way Analysis of Variance on Ranks	H(2)= 11.380	0.003
5I	$EV_{Control}$ *vs* EV_{MetS} *vs* 6-0HDA *vs* 60HDA+ EV_{MetS} *vs* 60HDA+ EV_{MetS}+CAND	One Way Analysis of Variance	$F_{(4,25)}$= 32.781	<0.001
5J	Control *vs* $EV_{Control}$ *vs* CAND	Kruskal-Wallis One Way Analysis of Variance on Ranks	H(2)= 0.363	0.834
6A	Control *vs* EV_{MetS} *vs* EV_{MetS}+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 12.651	<0.001
6B	Control *vs* EV_{MetS} *vs* EV_{MetS}+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 90.922	<0.001
6C	Control *vs* $EV_{Control}$ *vs* EV_{MetS} *vs* EV_{MetS}+CAND	One Way Analysis of Variance	F(3,20)= 59.941	<0.001
6D	Control *vs* $EV_{Control}$ *vs* EV_{MetS} *vs* EV_{MetS}+CAND	Kruskal-Wallis One Way Analysis of Variance on Ranks	H(3)= 15.754	0.001
6E	Control *vs* $EV_{Control}$ *vs* EV_{MetS} *vs* EV_{MetS}+CAND	Kruskal-Wallis One Way Analysis of Variance on Ranks	H(3)= 9.025	0.029
7A	Control *vs* EV_{MetS} *vs* EV_{MetS}+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 6.470	0.009
7B	Control *vs* EV_{MetS} *vs* EV_{MetS}+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 5.584	0.015
7C	Control *vs* $EV_{Control}$ *vs* EV_{MetS} *vs* EV_{MetS}+CAND	Kruskal-Wallis One Way Analysis of Variance on Ranks	H(3)= 14.820	0.002
7D	Control *vs* EV_{MetS} *vs* EV_{MetS}+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 18.527	<0.001

Table S1. Results of Statistical Analysis

7E	Control *vs* EV_{MetS} *vs* EV_{MetS}+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 8.013	0.004
7F	Control *vs* $EV_{Control}$ *vs* EV_{MetS} *vs* EV_{MetS}+CAND	One Way Analysis of Variance	$F_{(3,20)}$= 3.999	0.022
8A	Control *vs* EV_{MetS} *vs* EV_{MetS}+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 10.692	0.001
8B	Control *vs* EV_{MetS} *vs* EV_{MetS}+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 5.323	0.018
8C	Control *vs* EV_{MetS} *vs* EV_{MetS}+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 27.324	0.001
8D	Control *vs* EV_{MetS} *vs* EV_{MetS}+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 3.982	0.041
8E	Control *vs* EV_{MetS} *vs* EV_{MetS}+CAND	Kruskal-Wallis One Way Analysis of Variance on Ranks	H(2)= 8.082	0.018
8F	Control *vs* EV_{MetS} *vs* EV_{MetS}+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 9.911	0.002
8G	Control *vs* EV_{MetS} *vs* EV_{MetS}+CAND	Kruskal-Wallis One Way Analysis of Variance on Ranks	H(2)= 9.739	0.008
8H	Control *vs* EV_{MetS} *vs* EV_{MetS}+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 5.180	0.019
8I	Control *vs* EV_{MetS} *vs* EV_{MetS}+CAND	One Way Analysis of Variance	$F_{(2,16)}$= 36.022	<0.001
8J	Control *vs* EV_{MetS} *vs* EV_{MetS}+CAND	One Way Analysis of Variance	$F_{(2,15)}$= 13.221	<0.001