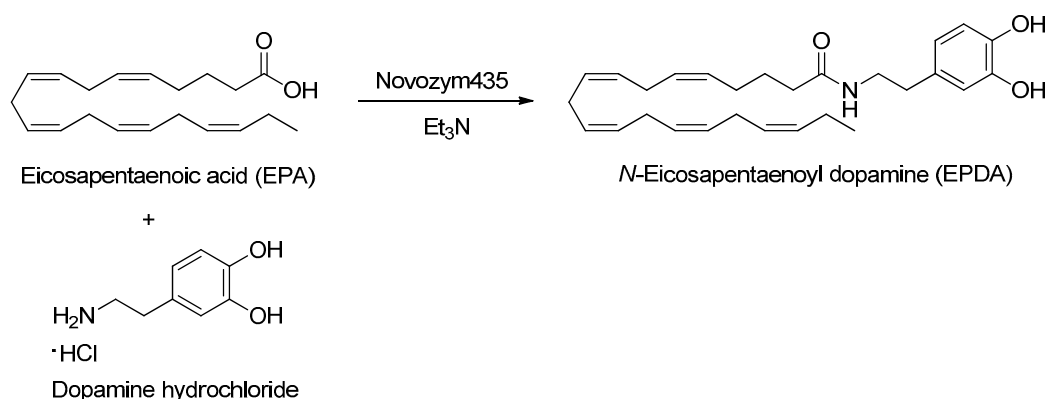


Figure S1. The enzymatic synthesis reaction scheme and characterization data of *N*-eicosapentaenoyl dopamine (EPDA). EPDA was synthesized from EPA and dopamine hydrochloride as described in the main manuscript.



Complete data for characterization of *N*-eicosapentaenoyl dopamine (EPDA):

{(Z,Z,Z,Z,Z)-Eicosa-5,8,11,14,17-pentaenoic acid [2-(3,4-dihydroxyphenyl)ethyl]amide}, colorless oil. IR (film) 3315 (s, br), 3011 (s), 2966 (m), 2930 (w), 1647 (s), 1520 (m) cm^{-1} ; ^1H NMR δ 6.83-6.50 (m, 3 H, aromatic), 5.82-5.75 (m, 1 H, NH), 5.45-5.25 (m, 10 H, 5 HC=CH), 3.51-3.39 (m, 2 H, CH_2NH), 2.90-2.72 (m, 8 H, 4 CH=CH $\text{CH}_2\text{CH=CH}$), 2.67 (t, $J = 7.1$ Hz, 2 H, $\text{CH}_2\text{CH}_2\text{NH}$), 2.21-1.99 (m, 6 H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{C=O} + \text{CH}_2\text{CH}_3$), 1.74-1.61 (m, 2 H, $\text{CH}_2\text{CH}_2\text{C=O}$), 0.97 (t, $J = 7.5$ Hz, 3 H, CH_3). (Note: the OH signals were too broad to be detected); ^{13}C NMR δ 174.2, 144.5, 143.3, 132.1, 130.5, 129.0, 128.9, 128.7, 128.4, 128.3, 128.2, 128.1, 127.9, 127.1, 120.5, 115.5, 115.3, 41.1, 36.2, 35.0, 26.6, 25.7, 25.6, 20.6, 14.3; MS m/z 436.2 $[\text{M}-\text{H}]^-$. MS/MS $[\text{M}-\text{H}]^-$ (ESI $^-$, 30 eV) m/z 436.2 (56), 134.0 (38), 123.0 (100).

Table S1. Effect of EPDA on LPS-stimulated RAW 264.7 macrophages by XTT / LDH assays

Treatment	Concentration (μM)	Viability (%) RAW264.7	Cytotoxicity (%) RAW264.7
Vehicle	-	100	100
EPDA	0.01	100 $\pm$ 4	116 $\pm$ 3
	0.1	105 $\pm$ 4	118 $\pm$ 12
	1.0	100 $\pm$ 5	99 $\pm$ 7
	2.5	112 $\pm$ 9	109 $\pm$ 12
Triton X-100	-	27 $\pm$ 2	212 $\pm$ 6

Table S2. Effects of EPDA on viability of LPS-stimulated human THP-1 macrophages

Treatment	Concentration (μ M)	Viability (%)		
		THP-1		
		24h	48h	72h
Vehicle	-	100	100	100
EPDA	0.1	92 $\pm$ 1	104 $\pm$ 2	91 $\pm$ 8
	1.0	89 $\pm$ 6	90 $\pm$ 15	88 $\pm$ 1