Intranasal administration of resolvin E1 attenuates lipopolysaccharide-induced depression-like behaviors via BDNF/VEGF release and mTORC1 activation in the medial prefrontal cortex

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We have recently demonstrated that infusion of eicosapentaenoic acid-derived resolvin E1 (RvE1) into the medial prefrontal cortex (mPFC) exerts antidepressant effects via brain-derived neurotrophic factor (BDNF) and vascular endothelial growth factor (VEGF) release and subsequent activation of mechanistic target of rapamycin complex 1 (mTORC1) in a murine lipopolysaccharide (LPS)-induced depression model. In the present study, we examined the roles of BDNF/VEGF release and mTORC1 activation within the mPFC in the antidepressant actions of intranasal (i.n.) administration of RvE1 in LPS-induced depression model mice using the tail suspension and forced swim tests. The results demonstrate that the antidepressant effects of i.n. RvE1 are completely blocked by intraperitoneal injection of an AMPA receptor antagonist NBQX or an L-type voltage-dependent Ca^{2+} channel (L-VDCC) blocker verapamil. We also demonstrate that the antidepressant effects of i.n. RvE1 are blocked by intra-mPFC infusion of a BDNF neutralizing antibody (nAb), a VEGF nAb or an mTORC1 inhibitor rapamycin. Together, the current results suggest that the antidepressant actions of i.n. RvE1 are mediated by BDNF/VEGF release which is probably caused by activation of AMPA receptors and L-VDCCs, and subsequent activation of mTORC1 in the mPFC.