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DOES BDNF DERIVED FROM THE CEREBRAL MICROVASCULATURE CONTROL COGNITION?

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While neuronal brain-derived neurotrophic factor (BDNF) is largely involved in cognition through the phosphorylation of neuronal TrkB receptors at Tyrosine 816, the role of BDNF derived from endothelium of the cerebral microvasculature remains enigmatic. The growing literature on the link between endothelial function (EF) and cognition combined with evidence that changes in EF coincide with changes in the same way in endothelial BDNF expression led us to suspect a control of cognition by BDNF derived from cerebral capillaries. To test this hypothesis, the cerebral BDNF/TrkB pathway was investigated in arthritis, which combines endothelial dysfunction, cognitive deficit and decreased brain BDNF levels. Lewis rats were subjected to adjuvant-induced arthritis (AIA, n=23). Their brains were collected at day 31±2 post-immunization, a time at which EF is impaired and clinical inflammation maximal. BDNF and/or p-TrkB Y816 levels (Western blot analysis) and localization (immunohistochemical analysis) were evaluated on microvessels-enriched fractions (MEF) isolated from the forebrain and brain slices passing throughout the hippocampus. Endothelial nitric oxide synthase (eNOS) levels were used as an indicator of EF. Non-AIA rats were used as controls (n=17). As compared to controls, AIA rats exhibited low BDNF and eNOS levels in MEF with a positive association between these two parameters, in parallel with low BDNF and p-TrkB Y816 staining in endothelial cells. These effects coexisted with decreased BDNF and p-TrkB Y816 expression by both endothelial cells (arterioles) and neurons of the hippocampus. Endothelial BDNF staining was positively correlated not only with endothelial but also neuronal p-TrkB Y816 staining. By contrast, no association was found between these two parameters for the neurons. Importantly, changes in the endothelial/neuronal BDNF/TrkB pathway were disconnected from the severity of inflammatory symptoms. The present study supports decreased BDNF synthesis by the cerebral endothelium as an attractive causal event in impaired cognition associated to endothelial dysfunction.

Biography

Martin Pedard is Resident in Pharmacy at the University Hospital Center of Dijon (France), and PhD Student in U1093 (Université de Bourgogne Franche-Comté, Dijon, France). As part of his thesis, he is working on the role of endothelial BDNF on the link between endothelial function and brain health. These works have allowed him to publish its results in journals specialised in neurology, vascular function or physiology. He is also working clinically to identify a new biomarker of stroke outcome.

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