oxide produced by neurons can also increase arteriolar dilatory tone, allowing increased blood flow to areas which have an increased energy requirement.
Here, we show that nitric oxide can also modulate pericyte vasodilatory tone in a manner depending on the oxygen concentration. Capillaries dilated by glutamate constricted in response to a non-specific nitric oxide synthase inhibitor at high (95%) but not low (20%) superfused oxygen concentrations. In addition, tonic nitric oxide levels provide basal dilatory tone to capillaries, as inhibition of nitric oxide synthase, in the absence of added glutamate, constricted capillaries at pericytes (this experiment was performed using 95% oxygen). This basal nitric oxide is derived from neuronal, not endothelial, nitric oxide synthase, as an inhibitor of the neuronal nitric oxide synthase isoform (1 μM 1400W) had the same effect on capillary tone as did the non-specific inhibitor (100 μM L-nitroarginine). These data extend to CNS capillaries the notion that nitric oxide can regulate vessel diameter, as is already established for CNS arterioles.

Peppiatt CM, Howarth C, Mobbs P, Attwell D (2006) Bidirectional control of CNS capillary diameter by pericytes. Nature 443:700-704.

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Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

C10

Evidence of a mechanosensory role for CD31 in cardiovascular disease

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CD31 (PECAM-1) has been shown to form a mechanosensory complex with VE-cadherin and VEGFR which can modulate endothelial cell (EC) responses to shear stress through NF-κB activation.[1] Since CD31 is expressed on leukocytes, EC and platelets and has been shown to play a prominent role in the transmigration of leukocytes into sites of inflammation,[2] we hypothesized that it might contribute to the development of atherogenesis in a shear dependent manner. To test this hypothesis we generated Pecam1$^{-/-}$Apoe$^{-/-}$ mice to determine the role of CD31 in an established model of murine atherosclerosis. At 10 weeks of age, Pecam1$^{-/-}$Apoe$^{-/-}$ mice or control mice (age and sex-matched) were placed on a high fat diet (20% coco butter, 1.25% cholesterol) or retained on normal chow diet, for a further 13 weeks. Aortas were then excised and stained with oil red O (ORO) to determine plaque burden and serum lipid levels and leukocyte counts taken. No differences were found in weight gain, serum cholesterol or tri-glyceride levels between CD31 deficient and control groups on either a chow or high fat diet. White blood cell counts and the percentage of circulating neutrophils, monocytes and peripheral blood lymphocytes also remained similar between mouse groups. Mice kept on a chow diet showed no differences in percentage of plaque burden between CD31 deficient or control mice in the whole aorta. However, a detailed analysis of anatomically distinct areas of the aorta showed a large reduction in plaque burden in the inner curvature of the aortic arch, a well-defined area of disturbed non-laminar flow. Mice kept on high fat diet showed a larger plaque burden compared to those on chow diet, but no differences were seen in percentage plaque burden between CD31 deficient or control mice in the whole aorta. Complete analysis of the aortic regions revealed a reduction in plaque burden in areas of disturbed flow (aortic arch and inner curvature) and an elevation in plaque burden in areas of steady (laminar) flow (thoracic and abdominal aortas) in Apoe$^{-/-}$ mice lacking CD31 compared to the control groups.
Thus, under conditions of laminar flow, CD31 appears to act as a mechanotransducer of anti-atherogenic signals into EC, and therefore removal of CD31 leads to an increase in plaque burden. Conversely, in areas of complex flow, CD31 transduces pro-atherogenic signals, the loss of which moderates the disease process. This indicates that the mechanosensory role of CD31 is essential in the development of atheromas at areas of disturbed flow.

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Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

C11

A novel in vitro model for studying responses of endothelial cells under physiological flow conditions

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Haemodynamic forces occur naturally at branches of medium and large arteries and contribute to the development of atherosclerotic lesions. These forces modulate gene expression in the endothelium through complex mechanosensitive pathways. Low and oscillatory flow patterns promote a pro-atherogenic genotype, while high laminar flow activates athero-protective genes. To simulate pathophysiological, atherogenic blood flow patterns we have developed an *in vitro* perfusion system which allows exposure of endothelial cells grown in micro-slides to low or oscillatory flow patterns. Using this perfusion system we have examined the preconditioning effect of oscillatory flow on endothelial cells.
Preconditioning human umbilical vein endothelial cells (HUVECs) with oscillatory flow enhanced their responses to inflammatory stimulation. Thus, subsequent exposure of HUVECs for 18-22 hours with the inflammatory cytokine TNFα (5 ng/ml) resulted in increased detection of pro-inflammatory and chemoattractant factors such as IL-8 and MCP-1, when compared to non-preconditioned cells (Table 1). When com-