- Further fall in intracellular PO2 – AMP → adenosine via endo-nucleotidase (activated by hypoxia)
- Adenosine is mainly responsible for matching O2 delivery to VO2
- ATP release from RBCs has also been implicated via P2Y recs

What about neural influences on coronary circulation?

- Coronary vessels have symp NAd nerve supply – fibres also supply SAN, AVN and ventricles
    - Experimentally, activation of coronary sympathetic nerves → coronary vasoconstriction
    - Physiologically, sympathetic activation → increased HR, contractility + coronary vasodilation → increased functional hyperaemia
- On the other hand
    - Experimentally, activation of coronary parasympathetic (vagus) nerves → coronary vasodilation
    - Physiologically, parasympathetic activation, decreased HR and coronary vasoconstriction – due to decreased cardiac work (decreased functional hyperaemia)

Cerebral circulation – v sensitive to CO2 conc

- 12% of CO goes to brain
- Whole brain extracts ~40% of O2 from each ml of blood
- Has relatively high VO2 under 'resting' conditions
- Need O2 and glucose for metabolism and generates CO2
- Neuronal activity requires more O2 and glucose
    - Neurones can increase their O2 extraction but large increases in activity requires increase in O2. Glucose delivery i.e. vasodilation
    - Cerebral arterioles are very sensitive to changes in local O_2 and CO_2 as well as to locally released metabolites
    - Any increase in gross cerebral blood flow is restricted by skull
    - Vasodilation occurs regionally: "compensated by reduction in blood flow elsewhere in brain
- Extra cerebral arterial vessels run over surface of brain and then branch into brain tissue to form capillaries

Responses of cerebral circulation to changes in CO_2 and O_2

- Vasoconstrictor/Dilator responses to changes in local CO_2 are thought to occur by
    - Changes in stimulation of synthesis of dilator prostaglandins - After CO_2 crosses blood brain barrier (capillary endothelium)
    - Dilator responses to changes in local PO_2 occur via
        - Adenosine, prostaglandins and NO via endothelium – which cross blood brain barrier to act on VSM
    - Brain arterioles also response to substances released by glial cells
    - Arterioles are more responsive to CO_2 partial pressure
- CO2 is a result of oxidative metabolism

Cerebral Flow-metabolism coupling

- Glial cells form a network with end-feet on arterioles and neurones
- During changes in neuronal activity:
    - Neurones release K^+
    - Glial cells siphon up K^+ and release K^+ at other end of cell close to supplying arterioles
    - K^+ causes hyperpolarisation of VSM
    - Glial cells also synthesis and release other vasodilators:
        - Prostaglandins + Adenosine
    - Allows very tight coupling between neuronal activity and supplying arterioles