The inhibition of cerebral ABC-type efflux transport by cyclosporine does not alter the intracranial signal of C11-marked morphine in a PET–imaging study in human volunteers.

Several findings indicate a role for ABC-type (ATP-binding cassette) drug efflux transport proteins in influencing the variability of clinical opioid effects. This phenomenon is attributed to variations in expression and activity of efflux transport proteins at the blood-brain-barrier, which are known to transport opioids in humans. Intracranial PET signals of drug-transport substrates such as verapamil have been shown to vary due to cyclosporine (CsA)-mediated transport inhibition in humans.

The present study therefore investigated the influence of CsA, a known efflux transport inhibitor, on morphine disposition 6 healthy human volunteers, who received 0.5 mg/kg/h CsA over two hours, with an injection of 10-20 mCi of of [^{11}C]morphine over 10 seconds after the first hour, followed by a PET scan of the head and arterial blood draws over one hour, in a self-controlled crossover study with and without CsA.

Radioactivity counts in the arterial and venous systems as well as the samples from the arterial line followed an expected sudden increase and subsequent decline in all scans. However, there was very little activity in cerebral capillary regions, which was unchanged after the addition of CsA. Given the quality control as well as metabolite measurements, there was very little cerebral uptake of radioactive drug into the brain, regardless of ABC-transport inhibition.

We conclude that the PET-visible amount of morphine readily bound to intracerebral receptors is very small, even if an intervention known to increase central morphine effects is conducted. This phenomenon cannot be readily explained by morphine serum levels and warrants further investigation.

Summary:

ABC-type (ATP-binding cassette) efflux transporters may influence clinical opioid effects. PET imaging of cerebral [^{11}C]morphine uptake did not show variations due to cyclosporine (CsA)-mediated transport inhibition in humans.

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