Is hypoxia-inducible factor 1 an actor in migraine pathogenesis?

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OBJECTIVES: To determine if partial hypoxia and CoCl2, treatments increasing hypoxia-inducible factor 1 (HIF-1) expression, can activate trigeminovascular nociceptors in rat.

BACKGROUND: Among several particularities, the migrainous brain is characterized by a reduced mitochondrial energy reserve between attacks. Hypoxia can trigger migraine attacks by hitherto unknown mechanisms. Hypoxia up-regulates HIF-1, which increases the transcription of genes coding for proteins that promote blood flow or inflammation. We thus postulate that HIF-1 could be a pivotal link between impaired oxygen metabolism and trigeminovascular activation and play a key role in migraine pathophysiology.

RESULTS: CoCl2 injection (30 mg/kg, s.c.), but not partial hypoxia (8% O2, 1 hour), induces a significant enhancement of c-fos expression (marker of neuronal activity) in the trigeminal nucleus caudalis (TNC). Preliminary results show that CoCl2 also induces an increase of nNOS (marker of central sensitisation) in TNC which is abolished by a pretreatement with 17AAG, an HIF-1 inhibitor.

CONCLUSION: CoCl2 may be a novel experimental model to study metabolic activation of the trigeminovascular system. Whether its effect involves HIF-1 is under investigation.