Sensitization of the carotid body chemoreceptors by sustained hypoxia under permanent blockade of adenosine receptors

Sensitization of the carotid body (CB) function to sustained hypoxia consists in an exaggerated function of this chemoreceptor leading to a hyperventilation greater than expected from the prevailing PO₂. Sensitization seems to be critical in the adaptation to high altitude physiological hypoxia and in the compensation of pathological hypoxia occurring in lung diseases. Yet, CB mechanisms responsible for this sensitization remain largely unknown. On the other hand, being caffeine very commonly ingested, and an antagonist of adenosine a key excitatory CB transmitter, we wanted to define if chronic caffeine might alter this sensitization process.

We used four groups of rats: N, control normoxic; CafN, normoxic ingesting caffeine (1mg/ml in drinking water); CH, exposed to 12% O₂ (≈4000 m above sea level, 15 days), and; CafH, exposed to hypoxia and ingesting caffeine. We studied sensitization at chemoreceptor cell level (measuring their release of dopamine and adenosine), at the carotid sinus nerve (CSN) level by measuring neural activity and at intact animal level measuring ventilation.

CH produced profound changes in chemoreceptor cell dopamine increasing its content, rate of synthesis, basal and acute hypoxia elicited release; all changes being exaggerated by caffeine ingestion. CH reduced basal and augmented acute hypoxia-induced adenosine release, changes being unaffected by caffeine. CH elicited CB sensitization measured as CSN activity and as ventilation; chronic caffeine abrogated sensitization at CSN level but respected the ventilatory response to CH. Data indicate that adenosine plays critical and opposed roles at CB (excitatory) and central (inhibitory) levels to set ventilation to CH. Caffeine by inhibiting adenosine receptors at both levels maintains ventilatory responses to CH causing no harm in adaptation to or compensation of sustained hypoxia.
