Brainstem hypoperfusion in CFS

Sir,

Costa and his colleagues (Q J Med 1995; 88:767–73) are to be congratulated for providing more information about chronic fatigue syndrome.

Hypocapnia is a powerful and readily available cerebral vasoconstrictor. The 'cerebral vasoconstriction, and reduction in cerebral blood flow, are initiated when the arterial pCO2 has fallen 2 mmHg below normal. When the pCO2 has fallen by 25 mmHg, cerebral blood flow is decreased by about one third ... the maximum possible reduction of blood flow that can be achieved by respiratory alkalaeemia is of the order of 40 per cent'.

Unless proved otherwise, it might be rational and prudent to attribute the findings of Costa's group to dysfunctional breathing, an essential element of effort syndrome.

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References


Sir,

In 1948, Kety and Schmidt were the first to report a generalized reduction of cerebral blood flow (CBF) associated with hyperventilation-induced alkalosis in young men. It is known that hypocapnia and resulting respiratory alkalosis may be either produced by voluntary hyperventilation or a secondary manifestation of a wide range of well defined pathological conditions. Dynamic stress (skeletal muscle exercise), fever, high altitude, hyperthyroidism (thyrotoxicosis), heart failure, pulmonary insufficiency, diabetes (acidotic state) and many pharmacological agents (salicylates, analectics) may all produce hyperventilatory states as a secondary manifestation, sometimes with hypoxia, sometimes with hypocapnia, and frequently with hypocapnia. The literature on metabolic and circulatory effects, particularly regional blood flow (including regional cerebral blood flow—rCBF) changes, is contradictory and confusing. As early as 1912, Krogh and Lindhard, using the nitrous oxide method, found cardiac output to increase with thoracic type breathing and reduce with abdominal type breathing. In general terms, it is not difficult to cause a severe alkalosis with dizziness, blurred vision, mental confusion, numbness of extremities, muscle spasm, and rarely convulsions with loss of consciousness due to forced hyperventilation. So much so that hyperventilation is sometimes used to provoke seizures in patients with epilepsy in order to identify the site of the epileptic focus. Although the magnitude of responses to raised pCO2 differs in different regions of the brain, with increases in rCBF more marked in cerebral grey matter than in white matter, the effects of reduced pCO2 are not so clear. Whilst reduction of pCO2 from 45 to 29 mmHg evokes the expected arterial vasoconstriction in baboons, a further reduction to 21 mmHg produces vasodilation of large cerebral arteries. Further, based on the work of Wollman et al., Heistad and Kontos stated in their chapter on the Handbook of Physiology that 'Pronounced hypocapnic alkalosis seem to have a cerebral vasodilating effect whose mechanism is not understood well. Extreme alkalosis in anaesthetised humans, induced by intravenous administration of NaHCO3 during hyperventilation-induced hypocapnic alkalosis, produced a 17% increase in CBF'. The matter is further complicated taking into consideration the findings of Severinghaus et al., demonstrating that men exposed to high altitude for 3–5 days have higher levels of CBF than those at sea level at the same pCO2. Furthermore, during prolonged arterial hypocapnia in dogs or humans, CBF initially decreases but later tends to rise towards values that, under the experimental conditions described by Raichle et al., correspond to a normal pCO2.

In summary, it appears that reduced CBF under hypocapnia and alkalosis is generalized, not focal. There is so far no experimental evidence to suggest that regional differences exist. Our data, shows regional CBF abnormalities, particularly severe in the brainstem of patients with ME/CFS and not in major depression. Although we did not measure end tidal CO2 in the individuals enrolled in our study, none of them (normals, ME/CFS, depressed, epileptics) was, at clinical observation, obviously hyperventilating immediately before, during and after the intravenous injection of the radiotracer and performance of the single photon emission tomographic acquisition (45 to 60 min in total). Using a Hyperventilation Questionnaire based on the original Nijmegen Questionnaire, we found no difference in the frequency of historical episodes of hyperventilation between our samples of ME/CFS and major depression patients. The incidence of proven hyperventilators amongst patients with ME/CFS has been reported by Saisch et al. as a minority (13%), and