Journal of Cerebral Blood Flow & Metabolism (2011) 31, 1502–1503

www.jcbfm.com

Feature Article Commentary

Cerebral metabolic rate in hypercapnia: controversy continues

Dmitriy A Yablonskiy

Mallinckrodt Institute of Radiology, Biomedical Magnetic Resonance Laboratory, Washington University School of Medicine, St Louis, Missouri, USA

Journal of Cerebral Blood Flow & Metabolism (2011) **31,** 1502–1503; doi:10.1038/jcbfm.2011.32; published online 23 March 2011

Thirty years ago, a publication by Seisjo, entitled 'Cerebral metabolic rate in hypercarbia—a controversy' summarized the current state of knowledge related to the influence of hypercapnia (increased pCO_2) on cerebral metabolic rate of oxygen consumption ($CMRO_2$) (Siesjo, 1980). Seisjo quoted a number of papers that provided controversial results ranging from reduced, to unchanged, to increased $CMRO_2$ and concluded his paper with the following comment: 'Since hypercarbia is a common pathophysiologic condition, its effects on cerebral metabolism and blood flow are of obvious concern to many scientists and clinicians, anesthesiologists included. It is disconcerting that 30 years after the first quantitative report (Kety and Schmidt, 1948), we still do not know how hypercarbia affects cerebral metabolic rate.'

Today, 30 years later, scientists still debate this matter. In the current issue of this journal, Jain *et al* (2011) report on the measurement of global $CMRO_2$ in human brain during rest and hypercapnia. The authors developed a magnetic resonance imaging (MRI)-based technique that allows simultaneous measurements of cerebral blood flow (*CBF*) and venous blood oxygenation level (S_vO_2) with a temporal resolution of 30 seconds. Using the widely accepted principle that $CMRO_2$ is proportional to the product of *CBF* and arterial–venous difference in blood oxygenation level, Jain *et al* found decreases in $CMRO_2$ during mild hypercapnia (5% inspired CO_2) that were small and not significant. At the same time, they found significant increases in *CBF* and S_vO_2—a result that is in agreement with practically all previous studies. A similar result was recently reported by Chen and Pike (2010), whose findings also suggested no significant change in global $CMRO_2$ with mild hypercapnia. However, in another recently published study, Xu *et al* (2011) reported that mild hypercapnia resulted in a 13% suppression of $CMRO_2$. This result is similar to (for example) previously published data in rhesus monkey (Kliefoth *et al*, 1979), but is opposite to reported increases in $CMRO_2$ in rats (Horvath *et al*, 1994). Some of this inconsistency in results between human and animal studies can be attributed to the different physiological conditions under which the experiments were performed. However, the data in Jain *et al* (2011), Chen and Pike (2010) and Xu *et al* (2011) were obtained in normal awake humans, and one can only speculate that differences should be attributed to differences in experimental techniques.

Substantial progress has been made in developing *in vivo* methods to study brain metabolism and hemodynamics since the initial publication (Kety and Schmidt, 1948), and the paper by Jain *et al* contributes significantly to this development. Yet, the accuracy of this and other methods must be further scrutinized before we can put narrow-enough error bars on the results to provide an accurate answer to the old question: How does hypercapnia influence brain metabolism? One more compelling reason to seek a definitive answer to this question lies in current attempts to use hypercapnia to tease out the effects of changes in blood flow and brain metabolism during functional brain activation (so-called calibrated functional MRI (Davis *et al*, 1998; Kim *et al*, 1999)). We hope that the paper by Jain *et al* will help in resolving this controversy as well.

Disclosure/conflict of interest

The author declares no conflict of interest.

References

Chen JJ, Pike GB (2010) Global cerebral oxidative metabolism during hypercapnia and hypocapnia in humans:

Correspondence: Professor DA Yablonskiy, Mallinckrodt Institute of Radiology, Biomedical Magnetic Resonance Laboratory, Washington University School of Medicine, Campus Box 8227, 660 South Euclid Avenue, St Louis, MO 63110, USA.
E-mail: YablonskiyD@wustl.edu;
Website: http://bmr.wustl.edu/~dmitriy
Received 2 March 2011; accepted 4 March 2011; published online 23 March 2011

implications for BOLD fMRI. *J Cereb Blood Flow Metab* 30:1094–9
Davis TL, Kwong KK, Weisskoff RM, Rosen BR (1998) Calibrated functional MRI: mapping the dynamics of oxidative metabolism. *Proc Natl Acad Sci USA* 95:1834–9
Horvath I, Sandor NT, Ruttner Z, McLaughlin AC (1994) Role of nitric oxide in regulating cerebrocortical oxygen consumption and blood flow during hypercapnia. *J Cereb Blood Flow Metab* 14:503–9
Jain V, Langham MC, Floyd TT, Jain G, Magland JF, Wehrli FW (2011) Rapid magnetic resonance measurement of global cerebral metabolic rate of oxygen consumption in humans during rest and hypercapnia. *J Cereb Blood Flow Metab* 31:1504–12
Kety SS, Schmidt CF (1948) The effects of altered arterial tensions of carbon dioxide and oxygen on cerebral blood flow and cerebral oxygen consumption of normal young men. *J Clin Invest* 27:484–92
Kim SG, Rostrup E, Larsson HB, Ogawa S, Paulson OB (1999) Determination of relative CMRO2 from CBF and BOLD changes: significant increase of oxygen consumption rate during visual stimulation. *Magn Reson Med* 41:1152–61
Kliefoth AB, Grubb Jr RL, Raichle ME (1979) Depression of cerebral oxygen utilization by hypercapnia in the rhesus monkey. *J Neurochem* 32:661–3
Siesjo BK (1980) Cerebral metabolic rate in hypercarbia–a controversy. *Anesthesiology* 52:461–5
Xu F, Uh J, Brier MR, Hart Jr J, Yezhuvath US, Gu H, Yang Y, Lu H (2011) The influence of carbon dioxide on brain activity and metabolism in conscious humans. *J Cereb Blood Flow Metab* 31:58–67