

## References

- Attwell, D., & Laughlin, S. B. (2001). An energy budget for signaling in the grey matter of the brain. *Journal of Cerebral Blood Flow and Metabolism*, *21*, 1133–1145.
- Auestad, N., Korsak, R. A., Morrow, J. W., & Edmond, J. (1991). Fatty acid oxidation and ketogenesis by astrocytes in primary culture. *Journal of Neurochemistry*, *56*, 1376–1386.
- Bachelard, H., & Badar-Goffer, R. (1993). NMR spectroscopy in neurochemistry. *Journal of Neurochemistry*, *61*, 412–429.
- Bell, J. D., Brown, J. C., Sadler, P. J., Macleod, A. F., Sonksen, P. H., Hughes, R. D., et al. (1987). High resolution proton nuclear magnetic resonance studies of human cerebrospinal fluid. *Clinical Science (London)*, *72*, 563–570.
- Ben-Yoseph, O., Camp, D. M., Robinson, T. E., & Ross, B. D. (1995). Dynamic measurements of cerebral pentose phosphate pathway activity in vivo using [1,6-<sup>13</sup>C<sub>2</sub>,6,6-<sup>2</sup>H<sub>2</sub>]glucose and microdialysis. *Journal of Neurochemistry*, *64*, 1336–1342.
- Berkich, D. A., Ola, M. S., Cole, J., Sweatt, A. J., Hutson, S. M., & LaNoue, K. F. (2007). Mitochondrial transport proteins of the brain. *Journal of Neuroscience Research*, *85*, 3367–3377.
- Berl, S., Clarke, D. D., & Schneider, D. (1975). *Metabolic compartmentation and neurotransmission: Relation to brain structure and function*. New York: Plenum Press.
- Berl, S., Nicklas, W. J., & Clarke, D. D. (1970). Compartmentation of citric acid cycle metabolism in brain: Labelling of glutamate, glutamine, aspartate and gaba by several radioactive tracer metabolites. *Journal of Neurochemistry*, *17*, 1009–1015.
- Blumberg, R. M., Cady, E. B., Wigglesworth, J. S., McKenzie, J. E., & Edwards, A. D. (1997). Relation between delayed impairment of cerebral energy metabolism and infarction

- following transient focal hypoxia-ischaemia in the developing brain. *Experimental Brain Research*, *113*, 130–137.
- Bolaños, J. P., Heales, S. J., Land, J. M., & Clark, J. B. (1995). Effect of peroxynitrite on the mitochondrial respiratory chain: differential susceptibility of neurones and astrocytes in primary culture. *Journal of Neurochemistry*, *64*, 1965–1972.
- Brown, A. M. (2004). Brain glycogen re-awakened. *Journal of Neurochemistry*, *89*, 537–552.
- Cahill, G. F., Jr. (2006). Fuel metabolism in starvation. *Annual Review of Nutrition*, *26*, 1–22.
- Cerdan, S., Kunnecke, B., & Seelig, J. (1990). Cerebral metabolism of [1,2-<sup>13</sup>C<sub>2</sub>]acetate as detected by in vivo and in vitro <sup>13</sup>C NMR. *Journal of Biological Chemistry*, *265*, 12916–12926.
- Chih, C. P., & Roberts, E. L., Jr (2003). Energy substrates for neurons during neural activity: A critical review of the astrocyte-neuron lactate shuttle hypothesis. *Journal of Cerebral Blood Flow and Metabolism*, *23*, 1263–1281.
- Choi, I. Y., Lee, S. P., Kim, S. G., & Gruetter, R. (2001). In vivo measurements of brain glucose transport using the reversible Michaelis–Menten model and simultaneous measurements of cerebral blood flow changes during hypoglycemia. *Journal of Cerebral Blood Flow and Metabolism*, *21*, 653–663.
- Clarke, D. D., & Sokoloff, L. (1999). Circulation and energy metabolism. In G. J. Siegel, B. W. Agranoff, D. S. Albers, S. K. Fisher & M. D. Uhler (Eds.), *Basic Neurochemistry* (6th ed.). Philadelphia: Lippincott Williams and Wilkins.
- Cooper, A. J., & Plum, F. (1987). Biochemistry and physiology of brain ammonia. *Physiological Reviews*, *67*, 440–519.
- Cremer, J. E. (1982). Substrate utilization and brain development. *Journal of Cerebral Blood*

- Flow and Metabolism*, 2, 394–407.
- Cruz, N. F., & Dienel, G. A. (2002). High glycogen levels in brains of rats with minimal environmental stimuli: Implications for metabolic contributions of working astrocytes. *Journal of Cerebral Blood Flow and Metabolism*, 22, 1476–1489.
- Danbolt, N. C. (2001). Glutamate uptake. *Progress in Neurobiology*, 65, 1–105.
- Davis, J. N., Carlsson, A., MacMillan, V., & Siesjö, B. K. (1973). Brain tryptophan hydroxylation: Dependence on arterial oxygen tension. *Science*, 182, 72–74.
- Dienel, G. A., Ball, K. K., & Cruz, N. F. (2007). A glycogen phosphorylase inhibitor selectively enhances local rates of glucose utilization in brain during sensory stimulation of conscious rats: implications for glycogen turnover. *Journal of Neurochemistry*, 102, 466–478.
- Dienel, G. A., & Cruz, N. F. (2003). Neighborly interactions of metabolically-activated astrocytes in vivo. *Neurochemistry International*, 43, 339–354.
- Dienel, G. A., & Cruz, N. F. (2008). Imaging brain activation: Simple pictures of complex biology. *Annals of the New York Academy of Sciences*, 1147, 139–170.
- Dienel, G. A., & Cruz, N. F. (2009). Exchange-mediated dilution of brain lactate specific activity: implications for the origin of glutamate dilution and the contributions of glutamine dilution and other pathways. *Journal of Neurochemistry*, 109(Suppl. 1), 30–37.
- Dienel, G. A., & Hertz, L. (2001). Glucose and lactate metabolism during brain activation. *Journal of Neuroscience Research*, 66, 824–838.
- Dienel, G. A., Nelson, T., Cruz, N. F., Jay, T., Crane, A. M., & Sokoloff, L. (1988). Over-estimation of glucose-6-phosphatase activity in brain in vivo.

- Apparent difference in rates of [2-<sup>3</sup>H]glucose and [U-<sup>14</sup>C]glucose utilization is due to contamination of precursor pool with <sup>14</sup>C-labeled products and incomplete recovery of <sup>14</sup>C-labeled metabolites. *Journal of Biological Chemistry*, 263, 19697–19708.
- DiMauro, S., Bonilla, E., Zeviani, M., Nakagawa, M., & DeVivo, D. C. (1985). Mitochondrial myopathies. *Annals of Neurology*, 17, 521–538.
- DiNuzzo, M., Mangia, S., Maraviglia, B., & Giove, F. (2010). Changes in glucose uptake rather than lactate shuttle take center stage in subserving neuroenergetics: evidence from mathematical modeling. *Journal of Cerebral Blood Flow and Metabolism*, 30, 586–602.
- Dringen, R., Gebhardt, R., & Hamprecht, B. (1993). Glycogen in astrocytes: possible function as lactate supply for neighboring cells. *Brain Research*, 623, 208–214.
- Dringen, R., Hoepken, H. H., Minich, T., & Ruedig, C. (2007). Pentose phosphate pathway and NADPH metabolism. In G. E. Gibson & G. A. Dienel (Eds.), *Brain energetics. Integration of molecular and cellular processes* (pp. 41–62). Berlin: Springer-Verlag.
- Edmond, J., Robbins, R. A., Bergstrom, J. D., Cole, R. A., & de Vellis, J. (1987). Capacity for substrate utilization in oxidative metabolism by neurons, astrocytes, and oligodendrocytes from developing brain in primary culture. *Journal of Neuroscience Research*, 18, 551–561.
- Erecin'ska, M., Zaleska, M. M., Nissim, I., Nelson, D., Dagani, F., & Yudkoff, M. (1988). Glucose and synaptosomal glutamate metabolism: Studies with [<sup>15</sup>N]glutamate. *Journal of Neurochemistry*, 51, 892–902.
- Fiermonte, G., Palmieri, L., Todisco, S., Agrimi, G., Palmieri, F., & Walker, J. E. (2002). Identification of the mitochondrial glutamate transporter. Bacterial expression,

- reconstitution, functional characterization, and tissue distribution of two human isoforms. *Journal of Biological Chemistry*, *277*, 19289–19294.
- Fitzpatrick, S. M., Hetherington, H. P., Behar, K. L., & Shulman, R. G. (1990). The flux from glucose to glutamate in the rat brain in vivo as determined by  $^1\text{H}$ -observed,  $^{13}\text{C}$ -edited NMR spectroscopy. *Journal of Cerebral Blood Flow and Metabolism*, *10*, 170–179.
- Fox, P. T., & Raichle, M. E. (1986). Focal physiological uncoupling of cerebral blood flow and oxidative metabolism during somatosensory stimulation in human subjects. *Proceedings of the National Academy of Sciences of the United States of America*, *83*, 1140–1144.
- Fox, P. T., Raichle, M. E., Mintun, M. A., & Dence, C. (1988). Nonoxidative glucose consumption during focal physiologic neural activity. *Science*, *241*, 462–464.
- Gandhi, G. K., Cruz, N. F., Ball, K. K., & Dienel, G. A. (2009). Astrocytes are poised for lactate trafficking and release from activated brain and for supply of glucose to neurons. *Journal of Neurochemistry*, *111*, 522–536.
- Gibson, G. E., & Duffy, T. E. (1981). Impaired synthesis of acetylcholine by mild hypoxic hypoxia or nitrous oxide. *Journal of Neurochemistry*, *36*, 28–33.
- Gordon, G. R., Choi, H. B., Rungta, R. L., Ellis-Davies, G. C., & MacVicar, B. A. (2008). Brain metabolism dictates the polarity of astrocyte control over arterioles. *Nature*, *456*, 745–749.
- Gotoh, J., Itoh, Y., Kuang, T. Y., Cook, M., Law, M. J., & Sokoloff, L. (2000). Negligible glucose-6-phosphatase activity in cultured astroglia. *Journal of Neurochemistry*, *74*, 1400–1408.
- Gruetter, R., Novotny, E. J., Boulware, S. D., Rothman, D. L., Mason, G. F., Shulman, G. I., et al. (1993). Non-invasive measurements of the cerebral steady-state glucose concentration

- and transport in humans by  $^{13}\text{C}$  nuclear magnetic resonance. *Advances in Experimental Medicine and Biology*, 331, 35–40.
- Gruetter, R., Seaquist, E. R., & Ugurbil, K. (2001). A mathematical model of compartmentalized neurotransmitter metabolism in the human brain. *American Journal of Physiology Endocrinology Metabolism*, 281, E100–E112.
- Henry, P. G., Öz, G., Provencher, S., & Gruetter, R. (2003). Toward dynamic isotopomer analysis in the rat brain in vivo: Automatic quantitation of  $^{13}\text{C}$  NMR spectra using LCModel. *NMR in Biomedicine*, 16, 400–412.
- Herrero-Mendez, A., Almeida, A., Fernandez, E., Maestre, C., Moncada, S., & Bolaños, J. P. (2009). The bioenergetic and antioxidant status of neurons is controlled by continuous degradation of a key glycolytic enzyme by APC/C-Cdh1. *Nature Cell Biology*, 11, 747–752.
- Hertz, L., Dringen, R., Schousboe, A., & Robinson, S. R. (1999). Astrocytes: Glutamate producers for neurons. *Journal of Neuroscience Research*, 57, 417–428.
- Hertz, L., & Hertz, E. (2003). Cataplerotic TCA cycle flux determined as glutamate-sustained oxygen consumption in primary cultures of astrocytes. *Neurochemistry International*, 43, 355–361.
- Hertz, L., Peng, L., & Dienel, G. A. (2007). Energy metabolism in astrocytes: high rate of oxidative metabolism and spatiotemporal dependence on glycolysis/glycogenolysis. *Journal of Cerebral Blood Flow and Metabolism*, 27, 219–249.
- Holden, J. E., Mori, K., Dienel, G. A., Cruz, N. F., Nelson, T., & Sokoloff, L. (1991). Modeling the dependence of hexose distribution volumes in brain on plasma glucose concentration: implications for estimation of the local 2-deoxyglucose lumped constant. *Journal of*

*Cerebral Blood Flow and Metabolism*, 11, 171–182.

Horinaka, N., Kuang, T. Y., Pak, H., Wang, R., Jehle, J., Kennedy, C., et al. (1997). Blockade of cerebral blood flow response to insulin-induced hypoglycemia by caffeine and glibenclamide in conscious rats. *Journal of Cerebral Blood Flow and Metabolism*, 17, 1309–1318.

Hur, E. M., & Zhou, F. Q. (2010). GSK3 signalling in neural development. *Nature Reviews Neuroscience*, 11, 539–551.

Hyder, F., Patel, A. B., Gjedde, A., Rothman, D. L., Behar, K. L., & Shulman, R. G. (2006). Neuronal–glial glucose oxidation and glutamatergic-GABAergic function. *Journal of Cerebral Blood Flow and Metabolism*, 26, 865–877.

Iadecola, C., & Nedergaard, M. (2007). Glial regulation of the cerebral microvasculature. *Nature Neuroscience*, 10, 1369–1376.

Itoh, Y., Esaki, T., Shimoji, K., Cook, M., Law, M. J., Kaufman, E., et al. (2003). Dichloroacetate effects on glucose and lactate oxidation by neurons and astroglia in vitro and on glucose utilization by brain in vivo. *Proceedings of the National Academy of Sciences of the United States of America*, 100, 4879–4884.

Jalil, M. A., Begum, L., Contreras, L., Pardo, B., Iijima, M., Li, M. X., et al. (2005). Reduced N-acetylaspartate levels in mice lacking aralar, a brain- and muscle-type mitochondrial aspartate-glutamate carrier. *Journal of Biological Chemistry*, 280, 31333–31339.

Jankowska-Kulawy, A., Bielarczyk, H., Pawelczyk, T., Wroblewska, M., & Szutowicz, A. (2010). Acetyl-CoA and acetylcholine metabolism in nerve terminal compartment of thiamine deficient rat brain. *Journal of Neurochemistry*, 115, 333–342.

- Jansen, J. F., Backes, W. H., Nicolay, K., & Kooi, M. E. (2006).  $^1\text{H}$  MR spectroscopy of the brain: absolute quantification of metabolites. *Radiology*, *240*, 318–332.
- Jost, C. R., Van Der Zee, C. E., In 't Zandt, H. J., Oerlemans, F., Verheij, M., Streijger, F., et al. (2002). Creatine kinase B-driven energy transfer in the brain is important for habituation and spatial learning behaviour, mossy fibre field size and determination of seizure susceptibility. *European Journal of Neuroscience*, *15*, 1692–1706.
- Kennedy, C., & Sokoloff, L. (1957). An adaptation of the nitrous oxide method to the study of the cerebral circulation in children; normal values for cerebral blood flow and cerebral metabolic rate in childhood. *Journal Clinical Investigation*, *36*, 1130–1137.
- Kinnala, A., Suhonen-Polvi, H., Aarimaa, T., Kero, P., Korvenranta, H., Ruotsalainen, U., et al. (1996). Cerebral metabolic rate for glucose during the first six months of life: an FDG positron emission tomography study. *Archives of Diseases in Childhood Fetal and Neonatal Edition*, *74*, F153–F157.
- Kumagai, A. K., Kang, Y. S., Boado, R. J., & Pardridge, W. M. (1995). Upregulation of blood–brain barrier GLUT1 glucose transporter protein and mRNA in experimental chronic hypoglycemia. *Diabetes*, *44*, 1399–1404.
- Künnecke, B., Cerdan, S., & Seelig, J. (1993). Cerebral metabolism of  $[1,2-^{13}\text{C}_2]$ glucose and  $[\text{U}-^{13}\text{C}_4]$ 3-hydroxybutyrate in rat brain as detected by  $^{13}\text{C}$  NMR spectroscopy. *NMR in Biomedicine*, *6*, 264–277.
- Kvamme, E., Torgner, I. A., & Roberg, B. (2001). Kinetics and localization of brain phosphate activated glutaminase. *Journal of Neuroscience Research*, *66*, 951–958.
- Lai, J. C., Walsh, J. M., Dennis, S. C., & Clark, J. B. (1977). Synaptic and non-synaptic mitochondria from rat brain: isolation and characterization. *Journal of Neurochemistry*,



28, 625–631.

- LaManna, J. C., Piciule, P., & Chavez, J. C. (2007). Genetics and gene expression of glycolysis. In G. E. Gibson & G. A. Dienel (Eds.), *Brain energetics, integration of molecular and cellular processes* (pp. 771–788). Berlin: Springer-Verlag.
- LaNoue, K. F., & Tischler, M. E. (1974). Electrogenic characteristics of the mitochondrial glutamate-aspartate antiporter. *Journal of Biological Chemistry*, *249*, 7522–7528.
- Leino, R. L., Gerhart, D. Z., Duelli, R., Enerson, B. E., & Drewes, L. R. (2001). Diet-induced ketosis increases monocarboxylate transporter (MCT1) levels in rat brain. *Neurochemistry International*, *38*, 519–527.
- Linde, R., Schmalbruch, I. K., Paulson, O. B., & Madsen, P. L. (1999). The Kety-Schmidt technique for repeated measurements of global cerebral blood flow and metabolism in the conscious rat. *Acta Physiologica Scandinavica*, *165*, 395–401.
- Lovatt, D., Sonnewald, U., Waagepetersen, H. S., Schousboe, A., He, W., Lin, J. H., et al. (2007). The transcriptome and metabolic gene signature of protoplasmic astrocytes in the adult murine cortex. *Journal of Neuroscience*, *27*, 12255–12266.
- Lowry, O. H., & Passonneau, J. V. (1964). The relationships between substrates and enzymes of glycolysis in brain. *Journal of Biological Chemistry*, *239*, 31–42.
- Lowry, O. H., & Passonneau, J. V. (1966). Kinetic evidence for multiple binding sites on phosphofructokinase. *Journal of Biological Chemistry*, *241*, 2268–2279.
- Mac, M., & Nalecz, K. A. (2003). Expression of monocarboxylic acid transporters (MCT) in brain cells. Implication for branched chain alpha-ketoacids transport in neurons. *Neurochemistry International*, *43*, 305–309.

- Madsen, P. L., Hasselbalch, S. G., Hagemann, L. P., Olsen, K. S., Bulow, J., Holm, S., et al. (1995). Persistent resetting of the cerebral oxygen/glucose uptake ratio by brain activation: evidence obtained with the Kety-Schmidt technique. *Journal of Cerebral Blood Flow and Metabolism*, *15*, 485–491.
- Malik, P., McKenna, M. C., & Tildon, J. T. (1993). Regulation of malate dehydrogenases from neonatal, adolescent, and mature rat brain. *Neurochemical Research*, *18*, 247–257.
- Mangia, S., Giove, F., Tkac, I., Logothetis, N. K., Henry, P. G., Olman, C. A., et al. (2009b). Metabolic and hemodynamic events after changes in neuronal activity: current hypotheses, theoretical predictions and in vivo NMR experimental findings. *Journal of Cerebral Blood Flow and Metabolism*, *29*, 441–463.
- Mangia, S., Simpson, I. A., Vannucci, S. J., & Carruthers, A. (2009a). The in vivo neuron-to-astrocyte lactate shuttle in human brain: evidence from modeling of measured lactate levels during visual stimulation. *Journal of Neurochemistry*, *109*(Suppl. 1), 55–62.
- Mangia, S., Tkac, I., Logothetis, N. K., Gruetter, R., Van de Moortele, P. F., & Ugurbil, K. (2007). Dynamics of lactate concentration and blood oxygen level-dependent effect in the human visual cortex during repeated identical stimuli. *Journal of Neuroscience Research*, *85*, 3340–3346.
- Martinez-Hernandez, A., Bell, K. P., & Norenberg, M. D. (1977). Glutamine synthetase: glial localization in brain. *Science*, *195*, 1356–1358.
- Mason, G. F., & Rothman, D. L. (2004). Basic principles of metabolic modeling of NMR (13)C isotopic turnover to determine rates of brain metabolism in vivo. *Metabolic Engineering*, *6*, 75–84.
- Matthews, C. K., & van Holde, K. E. (1996). *Biochemistry* (ed.). Redwood City, CA: Benjamin

- Cummings. (pp. 474–477)
- McKenna, M. C. (2007). The glutamate–glutamine cycle is not stoichiometric: fates of glutamate in brain. *Journal of Neuroscience Research*, *85*, 3347–3358.
- McKenna, M. C., Gruetter, R., Sonnewald, U., Waagepetersen, H. S., Schousboe, A., (2006c). Energy metabolism of the brain. In A., Siegel, G. J., Albers, R. W., Brady, S. T., Price, D. L., (Eds), *Basic neurochemistry*, 7th edition. Burlington, MA: Elsevier Academic Press. (pp. 531–557)
- McKenna, M. C., Hopkins, I. B., Lindauer, S. L., & Bamford, P. (2006a). Aspartate aminotransferase in synaptic and nonsynaptic mitochondria: differential effect of compounds that influence transient hetero-enzyme complex (metabolon) formation. *Neurochemistry International*, *48*, 629–636.
- McKenna, M. C., Sonnewald, U., Huang, X., Stevenson, J., & Zielke, H. R. (1996). Exogenous glutamate concentration regulates the metabolic fate of glutamate in astrocytes. *Journal of Neurochemistry*, *66*, 386–393.
- McKenna, M. C., Stevenson, J. H., Huang, X., & Hopkins, I. B. (2000). Differential distribution of the enzymes glutamate dehydrogenase and aspartate aminotransferase in cortical synaptic mitochondria contributes to metabolic compartmentation in cortical synaptic terminals. *Neurochemistry International*, *37*, 229–241.
- McKenna, M. C., Tildon, J. T., Couto, R., Stevenson, J. H., & Caprio, F. J. (1990). The metabolism of malate by cultured rat brain astrocytes. *Neurochemical Research*, *15*, 1211–1220.
- McKenna, M. C., Tildon, J. T., Stevenson, J. H., Boatright, R., & Huang, S. (1993). Regulation of energy metabolism in synaptic terminals and cultured rat brain astrocytes: differences

- revealed using aminooxyacetate. *Developmental Neuroscience*, *15*, 320–329.
- McKenna, M. C., Tildon, J. T., Stevenson, J. H., & Hopkins, I. B. (1994). Energy metabolism in cortical synaptic terminals from weanling and mature rat brain: evidence for multiple compartments of tricarboxylic acid cycle activity. *Developmental Neuroscience*, *16*, 291–300.
- McKenna, M. C., Tildon, J. T., Stevenson, J. H., Hopkins, I. B., Huang, X., & Couto, R. (1998). Lactate transport by cortical synaptosomes from adult rat brain: Characterization of kinetics and inhibitor specificity. *Developmental Neuroscience*, *20*, 300–309.
- McKenna, M. C., Tildon, J. T., Stevenson, J. H., Huang, X., & Kingwell, K. G. (1995). Regulation of mitochondrial and cytosolic malic enzymes from cultured rat brain astrocytes. *Neurochemical Research*, *20*, 1491–1501.
- McKenna, M. C., Waagepetersen, H. S., Schousboe, A., & Sonnewald, U. (2006b). Neuronal and astrocytic shuttle mechanisms for cytosolic–mitochondrial transfer of reducing equivalents: current evidence and pharmacological tools. *Biochemical Pharmacology*, *71*, 399–407.
- Meyer, R. A., Sweeney, H. L., & Kushmerick, M. J. (1984). A simple analysis of the “phosphocreatine shuttle”. *American Journal of Physiology*, *246*, C365–C377.
- Molinari, F., Kaminska, A., Fiermonte, G., Boddaert, N., Raas-Rothschild, A., Plouin, P., et al. (2009). Mutations in the mitochondrial glutamate carrier SLC25A22 in neonatal epileptic encephalopathy with suppression bursts. *Clinical Genetics*, *76*, 188–194.
- Morfini, G., Szebenyi, G., Brown, H., Pant, H. C., Pigino, G., DeBoer, S., et al. (2004). A novel CDK5–dependent pathway for regulating GSK3

- activity and kinesin-driven motility in neurons. *EMBO Journal*, 23, 2235–2245.
- Nakao, Y., Itoh, Y., Kuang, T. Y., Cook, M., Jehle, J., & Sokoloff, L. (2001). Effects of anesthesia on functional activation of cerebral blood flow and metabolism. *Proceedings of the National Academy of Sciences of the United States of America*, 98, 7593–7598.
- Nehlig, A. (2004). Brain uptake and metabolism of ketone bodies in animal models. *Prostaglandins Leukot Essent Fatty Acids*, 70, 265–275.
- Nehlig, A., Wittendorp-Rechenmann, E., & Lam, C. D. (2004). Selective uptake of [<sup>14</sup>C]2-deoxyglucose by neurons and astrocytes: high-resolution microautoradiographic imaging by cellular <sup>14</sup>C-trajectory combined with immunohistochemistry. *Journal of Cerebral Blood Flow and Metabolism*, 24, 1004–1014.
- Ogawa, S., Lee, T. M., Kay, A. R., & Tank, D. W. (1990). Brain magnetic resonance imaging with contrast dependent on blood oxygenation. *Proceedings of the National Academy of Sciences of the United States of America*, 87, 9868–9872.
- Olstad, E., Olsen, G. M., Qu, H., & Sonnewald, U. (2007). Pyruvate recycling in cultured neurons from cerebellum. *Journal of Neuroscience Research*, 85, 3318–3325.
- Öz, G., Berkich, D. A., Henry, P. G., Xu, Y., LaNoue, K., Hutson, S. M., et al. (2004). Neuroglial metabolism in the awake rat brain: CO<sub>2</sub> fixation increases with brain activity. *Journal of Neuroscience*, 24, 11273–11279.
- Öz, G., Henry, P. G., Seaquist, E. R., & Gruetter, R. (2003). Direct, noninvasive measurement of brain glycogen metabolism in humans. *Neurochemistry International*, 43, 323–329.
- Öz, G., Seaquist, E. R., Kumar, A., Criego, A. B., Benedict, L. E., Rao, J. P., et al. (2007). Human brain glycogen content and metabolism: implications on its role in brain energy metabolism. *American Journal of Physiology Endocrinology Metabolism*, 292, E946–951.

- O'Brien, J., Kla, K. M., Hopkins, I. B., Malecki, E. A., & McKenna, M. C. (2007). Kinetic parameters and lactate dehydrogenase isozyme activities support possible lactate utilization by neurons. *Neurochemical Research*, *32*, 597–607.
- Pan, J. W., de Graaf, R. A., Petersen, K. F., Shulman, G. I., Hetherington, H. P., & Rothman, D. L. (2002). [2,4-<sup>13</sup>C<sub>2</sub>]-beta-Hydroxybutyrate metabolism in human brain. *Journal of Cerebral Blood Flow and Metabolism*, *22*, 890–898.
- Pardo, B., Rodrigues, T. B., Contreras, L., Garzon, M., Llorente-Folch, I., Kobayashi, K., et al. (2011). Brain glutamine synthesis requires neuronal-born aspartate as amino donor for glial glutamate formation. *Journal of Cerebral Blood Flow and Metabolism*, *31*, 90–101.
- Patel, A. B., Chowdhury, G. M., de Graaf, R. A., Rothman, D. L., Shulman, R. G., & Behar, K. L. (2005). Cerebral pyruvate carboxylase flux is unaltered during bicuculline-seizures. *Journal of Neuroscience Research*, *79*, 128–138.
- Patel, M. S. (1974). The relative significance of CO<sub>2</sub>-fixing enzymes in the metabolism of rat brain. *Journal of Neurochemistry*, *22*, 717–724.
- Patel, M. S., Johnson, C. A., Rajan, R., & Owen, O. E. (1975). The metabolism of ketone bodies in developing human brain: development of ketone-body-utilizing enzymes and ketone bodies as precursors for lipid synthesis. *Journal of Neurochemistry*, *25*, 905–908.
- Paulson, O. B. (2002). Blood–brain barrier, brain metabolism and cerebral blood flow. *European Neuropsychopharmacology*, *12*, 495–501.
- Pellerin, L., Bouzier-Sore, A. K., Aubert, A., Serres, S., Merle, M., Costalat, R., et al. (2007). Activity-dependent regulation of energy metabolism by astrocytes: an update. *Glia*, *55*, 1251–1262.
- Pelligrino, D. A., LaManna, J. C., Duckrow, R. B., Bryan, R. M., Jr., & Harik, S. I. (1992).

- Hyperglycemia and blood–brain barrier glucose transport. *Journal of Cerebral Blood Flow and Metabolism*, *12*, 887–899.
- Phukan, S., Babu, V. S., Kannoji, A., Hariharan, R., & Balaji, V. N. (2010). GSK3beta: role in therapeutic landscape and development of modulators. *British Journal of Pharmacology*, *160*, 1–19.
- Prichard, J., Rothman, D., Novotny, E., Petroff, O., Kuwabara, T., Avison, M., et al. (1991). Lactate rise detected by  $^1\text{H}$  NMR in human visual cortex during physiologic stimulation. *Proceedings of the National Academy of Sciences of the United States of America*, *88*, 5829–5831.
- Qu, H., Haberg, A., Haraldseth, O., Unsgard, G., & Sonnewald, U. (2000).  $(^{13}\text{C})$  MR spectroscopy study of lactate as substrate for rat brain. *Developmental Neuroscience*, *22*, 429–436.
- Qu, H., Konradsen, J. R., van Hengel, M., Wolt, S., & Sonnewald, U. (2001). Effect of glutamine and GABA on  $[U-(^{13}\text{C})]$ glutamate metabolism in cerebellar astrocytes and granule neurons. *Journal of Neuroscience Research*, *66*, 885–890.
- Quistorff, B., Secher, N. H., & Van Lieshout, J. J. (2008). Lactate fuels the human brain during exercise. *FASEB Journal*, *22*, 3443–3449.
- Ramos, M., del Arco, A., Pardo, B., Martinez-Serrano, A., Martinez-Morales, J. R., Kobayashi, K., et al. (2003). Developmental changes in the  $\text{Ca}^{2+}$ -regulated mitochondrial aspartate–glutamate carrier aralar1 in brain and prominent expression in the spinal cord. *Brain Research. Developmental Brain Research*, *143*, 33–46.
- Reivich, M., Kuhl, D., Wolf, A., Greenberg, J., Phelps, M., Ido, T., et al. (1979). The  $[^{18}\text{F}]$ fluorodeoxyglucose method for the measurement of local cerebral

- glucose utilization in man. *Circulation Research*, *44*, 127–137.
- Ronnett, G. V., Ramamurthy, S., Kleman, A. M., Landree, L. E., & Aja, S. (2009). AMPK in the brain: its roles in energy balance and neuroprotection. *Journal of Neurochemistry*, *109*(Suppl. 1), 17–23.
- Sanchez-Abarca, L. I., Taberero, A., & Medina, J. M. (2001). Oligodendrocytes use lactate as a source of energy and as a precursor of lipids. *Glia*, *36*, 321–329.
- Satrustegui, J., Contreras, L., Ramos, M., Marmol, P., del Arco, A., Saheki, T., et al. (2007). Role of aralar, the mitochondrial transporter of aspartate-glutamate, in brain N-acetylaspartate formation and Ca<sup>2+</sup> signaling in neuronal mitochondria. *Journal of Neuroscience Research*, *85*, 3359–3366.
- Scafidi, S., Fiskum, G., Lindauer, S. L., Bamford, P., Shi, D., Hopkins, I., et al. (2010). Metabolism of acetyl-L-carnitine for energy and neurotransmitter synthesis in the immature rat brain. *Journal of Neurochemistry*, *114*, 820–831.
- Schousboe, A., Sonnewald, U., & Waagepetersen, H. S. (2003). Differential roles of alanine in GABAergic and glutamatergic neurons. *Neurochemistry International*, *43*, 311–315.
- Settergren, G., Lindblad, B. S., & Persson, B. (1976). Cerebral blood flow and exchange of oxygen, glucose, ketone bodies, lactate, pyruvate and amino acids in infants. *Acta Paediatrica Scandinavica*, *65*, 343–353.
- Sickmann, H. M., Walls, A. B., Schousboe, A., Bouman, S. D., & Waagepetersen, H. S. (2009). Functional significance of brain glycogen in sustaining glutamatergic neurotransmission. *Journal of Neurochemistry*, *109*(Suppl. 1), 80–86.
- Siesjö, B. K. (1978). *Brain energy metabolism*. New York: John Wiley & Sons.



- Simpson, I. A., Appel, N. M., Hokari, M., Oki, J., Holman, G. D., Maher, F., et al. (1999). Blood–brain barrier glucose transporter: effects of hypo- and hyperglycemia revisited. *Journal of Neurochemistry*, *72*, 238–247.
- Simpson, I. A., Carruthers, A., & Vannucci, S. J. (2007). Supply and demand in cerebral energy metabolism: the role of nutrient transporters. *Journal of Cerebral Blood Flow and Metabolism*, *27*, 1766–1791.
- Simpson, I. A., Dwyer, D., Malide, D., Moley, K. H., Travis, A., & Vannucci, S. J. (2008). The facilitative glucose transporter GLUT3: 20 years of distinction. *American Journal of Physiology Endocrinology Metabolism*, *295*, E242–253.
- Sokoloff, L. (1960). The metabolism of the central nervous system in vivo. In J. Field, H. Magoun & V. Hall (Eds.), *Handbook of physiology neurophysiology* (pp. 1843–1864) (ed.). Washington, DC: American Physiological Society.
- Sokoloff, L., Reivich, M., Kennedy, C., Des Rosiers, M. H., Patlak, C. S., Pettigrew, K. D., et al. (1977). The [ $^{14}\text{C}$ ]deoxyglucose method for the measurement of local cerebral glucose utilization: theory, procedure, and normal values in the conscious and anesthetized albino rat. *Journal of Neurochemistry*, *28*, 897–916.
- Sonnewald, U., & McKenna, M. (2002). Metabolic compartmentation in cortical synaptosomes: influence of glucose and preferential incorporation of endogenous glutamate into GABA. *Neurochemical Research*, *27*, 43–50.
- Sonnewald, U., & Rae, C. (2010). Pyruvate carboxylation in different model systems studied by ( $^{13}\text{C}$ )MRS. *Neurochemical Research*, *35*, 1916–1921.
- Sonnewald, U., Westergaard, N., Petersen, S. B., Unsgard, G., & Schousboe, A. (1993). Metabolism of [ $\text{U-}^{13}\text{C}$ ]glutamate in astrocytes studied by  $^{13}\text{C}$  NMR spectroscopy:

- incorporation of more label into lactate than into glutamine demonstrates the importance of the tricarboxylic acid cycle. *Journal of Neurochemistry*, *61*, 1179–1182.
- Sonnewald, U., Westergaard, N., Schousboe, A., Svendsen, J. S., Unsgard, G., & Petersen, S. B. (1993). Direct demonstration by [<sup>13</sup>C]NMR spectroscopy that glutamine from astrocytes is a precursor for GABA synthesis in neurons. *Neurochemistry International*, *22*, 19–29.
- Takahashi, T., Shirane, R., Sato, S., & Yoshimoto, T. (1999). Developmental changes of cerebral blood flow and oxygen metabolism in children. *American Journal of Neuroradiology*, *20*, 917–922.
- Tildon, J. T., & Cornblath, M. (1972). Succinyl-CoA: 3-ketoacid CoA-transferase deficiency. A cause for ketoacidosis in infancy. *Journal of Clinical Investigation*, *51*, 493–498.
- Tildon, J. T., McKenna, M. C., Stevenson, J., & Couto, R. (1993). Transport of L-lactate by cultured rat brain astrocytes. *Neurochemical Research*, *18*, 177–184.
- Tomaszewicz, M., Rossner, S., Schliebs, R., Cwikowska, J., & Szutowicz, A. (2003). Changes in cortical acetyl-CoA metabolism after selective basal forebrain cholinergic degeneration by 192IgG-saporin. *Journal of Neurochemistry*, *87*, 318–324.
- Ueki, M., Mies, G., & Hossmann, K. A. (1992). Effect of alpha-chloralose, halothane, pentobarbital and nitrous oxide anesthesia on metabolic coupling in somatosensory cortex of rat. *Acta Anaesthesiologica Scandinavica*, *36*, 318–322.
- van den Berg, C. J., & Garfinkel, D. (1971). A stimulation study of brain compartments. Metabolism of glutamate and related substances in mouse brain. *Biochemical Journal*, *123*, 211–218.
- Vannucci, S. J., & Simpson, I. A. (2003). Developmental switch in brain nutrient transporter expression in the rat. *American Journal of Physiology Endocrinology Metabolism*, *285*,

E1127–E1134.

- Vereczki, V., Martin, E., Rosenthal, R. E., Hof, P. R., Hoffman, G. E., & Fiskum, G. (2006). Normoxic resuscitation after cardiac arrest protects against hippocampal oxidative stress, metabolic dysfunction, and neuronal death. *Journal of Cerebral Blood Flow and Metabolism*, *26*, 821–835.
- Waagepetersen, H. S., Bakken, I. J., Larsson, O. M., Sonnewald, U., & Schousboe, A. (1998b). Comparison of lactate and glucose metabolism in cultured neocortical neurons and astrocytes using <sup>13</sup>C-NMR spectroscopy. *Developmental Neuroscience*, *20*, 310–320.
- Waagepetersen, H. S., Bakken, I. J., Larsson, O. M., Sonnewald, U., & Schousboe, A. (1998a). Metabolism of lactate in cultured GABAergic neurons studied by <sup>13</sup>C nuclear magnetic resonance spectroscopy. *Journal of Cerebral Blood Flow and Metabolism*, *18*, 109–117.
- Waagepetersen, H. S., Hansen, G. H., Fenger, K., Lindsay, J. G., Gibson, G., & Schousboe, A. (2006). Cellular mitochondrial heterogeneity in cultured astrocytes as demonstrated by immunogold labeling of alpha-ketoglutarate dehydrogenase. *Glia*, *53*, 225–231.
- Waagepetersen, H. S., Qu, H., Hertz, L., Sonnewald, U., & Schousboe, A. (2002). Demonstration of pyruvate recycling in primary cultures of neocortical astrocytes but not in neurons. *Neurochemical Research*, *27*, 1431–1437.
- Waagepetersen, H. S., Sonnewald, U., Larsson, O. M., & Schousboe, A. (2000). A possible role of alanine for ammonia transfer between astrocytes and glutamatergic neurons. *Journal of Neurochemistry*, *75*, 471–479.
- Waagepetersen, H. S., Sonnewald, U., Larsson, O. M., & Schousboe, A. (2001). Multiple compartments with different metabolic characteristics are involved in biosynthesis of intracellular and released glutamine and citrate in astrocytes. *Glia*, *35*, 246–252.

- Walls, A. B., Heimbürger, C. M., Bouman, S. D., Schousboe, A., & Waagepetersen, H. S. (2009). Robust glycogen shunt activity in astrocytes: Effects of glutamatergic and adrenergic agents. *Neuroscience*, *158*, 284–292.
- Waniewski, R. A., & Martin, D. L. (1998). Preferential utilization of acetate by astrocytes is attributable to transport. *Journal of Neuroscience*, *18*, 5225–5233.
- Westergaard, N., Drejer, J., Schousboe, A., & Sonnewald, U. (1996). Evaluation of the importance of transamination versus deamination in astrocytic metabolism of [<sup>13</sup>C]glutamate. *Glia*, *17*, 160–168.
- Westergaard, N., Sonnewald, U., Unsgard, G., Peng, L., Hertz, L., & Schousboe, A. (1994). Uptake, release, and metabolism of citrate in neurons and astrocytes in primary cultures. *Journal of Neurochemistry*, *62*, 1727–1733.
- Wheatley, D. N. (1998). Diffusion theory, the cell and the synapse. *Biosystems*, *45*, 151–163.
- Wibom, R., Lasorsa, F. M., Tohonen, V., Barbaro, M., Sterky, F. H., Kucinski, T., et al. (2009). AGC1 deficiency associated with global cerebral hypomyelination. *New England Journal of Medicine*, *361*, 489–495.
- Williamson, D. H., Bates, M. W., Page, M. A., & Krebs, H. A. (1971). Activities of enzymes involved in acetoacetate utilization in adult mammalian tissues. *Biochemical Journal*, *121*, 41–47.
- Yu, A. C., Drejer, J., Hertz, L., & Schousboe, A. (1983). Pyruvate carboxylase activity in primary cultures of astrocytes and neurons. *Journal of Neurochemistry*, *41*, 1484–1487.
- Yudkoff, M. (1997). Brain metabolism of branched-chain amino acids. *Glia*, *21*, 92–98.
- Yudkoff, M., Nelson, D., Daikhin, Y., & Erecin'ska, M. (1994). Tricarboxylic acid cycle in rat brain synaptosomes. Fluxes and interactions with aspartate aminotransferase and

- malate/aspartate shuttle. *Journal of Biological Chemistry*, 269, 27414–27420.
- Yudkoff, M., Nissim, I., Daikhin, Y., Lin, Z. P., Nelson, D., Pleasure, D., et al. (1993). Brain glutamate metabolism: neuronal-astroglial relationships. *Developmental Neuroscience*, 15, 343–350.
- Yudkoff, M., Nissim, I., & Pleasure, D. (1988). Astrocyte metabolism of [<sup>15</sup>N]glutamine: implications for the glutamine-glutamate cycle. *Journal of Neurochemistry*, 51, 843–850.
- Zielke, H. R., Zielke, C. L., & Baab, P. J. (2009). Direct measurement of oxidative metabolism in the living brain by microdialysis: a review. *Journal of Neurochemistry*, 109(Suppl. 1), 24–29.