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Comment

Brain Taurine Content as a Function of Cerebral Metabolic Rate: Osmotic Regulation of Glucose Derived Water Production

N. M. van Gelder[1]

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Brain contains normally very low levels of free glucose since it is practically all oxidized on entering cells; little of this glucose thus exerts any osmotic pressure intracellularly. Moreover, when glucose is in excess, it is rapidly incorporated into glycogen. This mechanism prevents the potential damaging osmotic effects of non-metabolized, free glucose. However, the human brain (1.2 kg) basal glucose consumption averages at around 15-20 mmol/kg/hr (10), indicating that each hour slightly over 2 ml of water is added to the intracellular content (see Table I). Strong evidence indicates that neural tissue resists volume changes (see 13) by continuous adjustment of the intracellular free solute content (1, 5, 12, 20). Hence, in order to counter continuously threatening hypo-osmolarity, and to balance the intracellular osmolarity (0.3-0.5 mM), the solute needs of the cells to maintain a constant volume can be calculated at about 500 μmol/kg under basal metabolic conditions. (300 mOsmol retain/release 1000 ml water). Since glucose consumption can easily double during hyperexcitable periods, at least double this amount of solute is also required. Finally, glucose consumption in different brain regions can vary by as much as 100% (4), suggesting that in total a minimum of 1.5-2.0 mOsmol of solute/kg brain must be available intracellularly to maintain constant neural volume (Table I).

Thus, by way of a rough approximation any substance which acts as an osmotic regulator in human brain must be present in an amount at least equivalent to 10% of the CNS glucose consumption. It also follows that in species with a higher endogenous cerebral metabolic rate (CMR), the content of such a solute should be higher, to offset the increased hourly intracellular water production.

For reasons already discussed previously—metabolic inertness, charge neutrality, solubility, sequestration—taurine has been suggested to act as such an osmoregulatory solute (7, 13, 20). If this is the case, a rough correlation between the CMR and neural tissue taurine content should be apparent (Table II). A quick survey of available data seems to indicate that such a relationship may indeed exist (Figure 1). The fact that linearity falls off at the lower end of the curve seems to suggest that the amount of taurine in brain must remain at a minimum value to sustain brain function in most species. Note however that the guinea pig demonstrates a taurine/CMR ratio of only 0.01, because of the exceptionally low cerebral taurine content (0.3 mmol/kg) in this species (11). Either the animal represents an oddity or, indeed, Figure 1 demonstrates merely a fortuitous coincidence.

Also, because of insufficient data, it is not possible at this time to determine whether this relationship extends to more circumscribed regions of the CNS. However, this need not necessarily be the case. Within the brain the CRM does not vary much more than two fold (4), and this has already been taken into account in estimating the amount of taurine (solute) needed to compensate for glucose derived water production in different regions and during different conditions of excitability (Table I). It does imply, however, that in regions demonstrating a high endogenous glucose consumption, the reserve fraction of the taurine pool which serves to compensate for enhanced excitability, may in fact be very

[1] Centre de Recherche en Sciences Neurologiques, Dept. Physiology, Université de Montréal, Case postale 6128, Succursale A, Montréal, Québec H3C 3J7, Canada.

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Table I. Intracellular Osmolarity Regulation and Solute Content

Glucose consumption (human)	: 18–24 mmol/1.2 kg/hr
20 mmol glucose oxidized yields	: 120 mmol H_2O/1.2 kg/hr
Volume of intracellular water	: 120 × 18 = 2.16 ml H_2O/hr
To maintain intracellular osmolarity (0.3–0.5 mM), the 2 ml produced/hr requires	: 600 μmol/1.2 kg
Minimum osmotic solute content required/kg	: 0.5 mmol
Maximum required (i.e. seizures)	: (+) 0.5 mmol
Assume 50% reserve solute availability	: (+) 0.5 mmol
Predicted osmotic solute in human brain to balance H_2O production from glucose	: 1.5 mmol
Suggested osmotic solute content	: 0.1 × CMR (mmol/kg/*hr*)

Table II. Suggested Relation between Neural Glucose Consumption and Taurine Content

	CMR glucose mmol/kg/hr	Taurine Content mmol/kg fresh wt.
Human	15	1.5
Rat	60	6.0
Mouse	80–100	8–10
Monkey	30	1.7–2.4[a]
Dog	15–25	1.4–2.3[a]

Ref: 3, 4, 10, 11, 18, 19.
[a] Species or breed dependent.

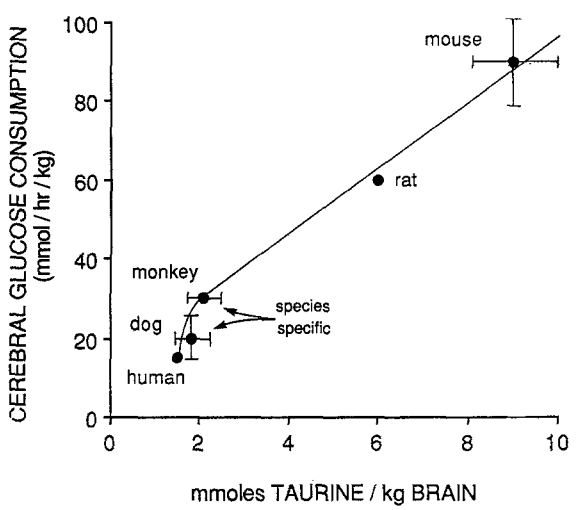

Fig. 1. A plot of brain taurine content against the cerebral metabolic rate (CRM) of several species. The neural tissue taurine content in a species may be determined by the amount of solute which is needed to osmotically balance the excess water produced during glucose consumption. Release of taurine from cells causes water efflux which can then be processed as CSF, while (re)uptake of taurine and intracellular sequestration renders the amino acid osmotically inert (14, 15). Values for CMR and taurine (3, 4, 10, 11, 18, 19).

small. It would make these brain areas exceptionally vulnerable to ischemia, or damage caused by unusually sustained and exaggerated excitation and synchronized discharge (2, 5, 6, 8).

The proposed relationship between cerebral taurine content and glucose consumption will explain the observed interconnection between taurine and glutamic acid in brain, even though these two amino acids are not directly related metabolically (16, 17). Glutamic acid content, transformation to glutamine and release-retention mechanisms of glutamic acid or taurine are closely dependent on glucose metabolism (9, 13, 17).

One can envisage the participation of taurine in the regulation of intracellular water content as follows: Taurine + water is released from neurons and taken up by glia (water gain). These cells synthetise and release glutamine + water (which can be transported to the blood). Glial taurine, now hyperosmotic to the extracellular fluid, is released (20) and sequestered by the neuron (no osmotic effect). With taurine serving to maintain cell osmolarity and the influx of glucose and the export of glutamine serving to maintain intracranial water balance, glutamic acid release on stimulation and uptake into glia (to glutamine) would serve as the transducing signal between excitation, glucose consumption, and brain water homeostasis (in preparation). Finally, because according to this scheme taurine is continuously redistributed between closely apposing structural elements, little net loss of taurine from the brain is to be expected. Neither is it metabolised and one would predict, as is observed, that the cerebral turnover of taurine is slow, even in those species having a high brain taurine content.

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