obtained by using different techniques. The activity of the mitochondrial enzyme towards tyrosine is negligible when measured at physiological tyrosine concentrations (60 μ M) especially if aspartate, the physiological substrate, is present (Ohisalo & Pispä, 1976; Ohisalo, 1977). Therefore, the nonspecific mitochondrial aspartate aminotransferase is probably of no significance in normal tyrosine metabolism, although it has been suggested to cause the appearance of transaminated tyrosine metabolites in hereditary tyrosinaemia (Fellman *et al.*, 1969). Further, isotopic tracer studies have suggested that oxidation of tyrosine in extrahepatic tissues is quantitatively insignificant (Noda & Ichihara, 1976).

In conclusion, there is no specific tyrosine aminotransferase (EC 2.6.1.5) in rat brain; the low 'tyrosine aminotransferase activity' that can be demonstrated at unphysiological tyrosine concentrations is due to aspartate aminotransferase (EC 2.6.1.1) and is of no significance in normal tyrosine metabolism.

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Brain tyrosine aminotransferase: identity and possible role in the regulation of catecholamine synthesis

In the preceding letter, Ohisalo *et al.* (1982) suggested that brain tyrosine aminotransferase is identical to aspartate aminotransferase and that its activity is normally too small to exert a significant effect on tyrosine metabolism. We should like to make a brief comment on the identity of this enzyme and to present evidence suggesting that its activity can in fact influence the intracerebral availability of tyrosine for catecholamine synthesis.

We have never suggested that transamination of brain tyrosine is achieved by a specific aminotransferase, and the isoelectric-focusing data of Ohisalo *et al.* (1982) leave no doubt that transamination of aspartate and tyrosine is catalysed mainly by the same enzyme. Moreover, such a conclusion has already been reached more than 6 years ago from work on the transfer of the amino groups of kynurenine (Noguchi *et al.*, 1975a) and other aromatic amino acids (Noguchi *et al.*, 1975b). We, however, feel that further work on the cerebral-cytosolic form of this non-specific enzyme may be fruitful in relation to the possible influence of dietary, hormonal and other physiological conditions, because previous work with the two isoenzymes of hepatic aspartate aminotransferase has revealed that only the cytosolic, but not the mitochondrial, form is sensitive to factors such as low- and high-protein diets, cortisol, adrenalectomy and starvation (Nakata *et al.*, 1964). Also, if the reported (Laboritt & Thuret, 1977; Snape & Badawy, 1981) enhancement by cortisol of tyrosine transamination is confined to the cerebral-cytosolic form, which is less than 20% of the total-brain enzyme, then it could represent some 6–7-fold increase in this form and may therefore cause a dramatic effect on intracellular tyrosine compartmentation.

Table 1. *Inhibition of rat brain catecholamine synthesis at 12 h after acute ethanol administration*

Fed male Wistar rats (150–170 g) received, 12 h before being killed between 14:00 h and 14:30 h, an intraperitoneal injection either of ethanol [4 g/kg body wt. in 0.9% (w/v) NaCl (20 ml/kg body wt.)] or of an equal volume of 0.9% (w/v) NaCl alone. Liver, serum and brain tyrosine concentrations were determined by the method of Waalkes & Udenfriend (1957). Brain tyrosine, dopamine, 3,4-dihydroxyphenylacetic acid and noradrenaline were separated by ion-exchange chromatography of an HClO_4 extract, and were quantified fluorimetrically by various procedures (see Bertler *et al.*, 1958; Atack & Magnusson, 1970; Spano & Neff, 1971; Kehr *et al.*, 1972; Atack, 1973). The early elution with aqueous methanol of 3,4-dihydroxyphenylacetic acid was achieved for the first time in the present work. Values are means $\pm$ S.E.M. for each group of six rats. The significance of the differences is indicated as follows: $\dagger P < 0.02$; $*P < 0.01$; $**P < 0.005$; $***P < 0.001$. Abbreviation used: dopac, 3,4-dihydroxyphenylacetic acid.

Treatment	Concentration ($\mu\text{g/ml}$ of serum or per g wet wt. of tissue) of:					
	Liver tyrosine	Serum tyrosine	Brain tyrosine	Brain dopamine	Brain dopac	Brain noradrenaline
0.9%NaCl	20.47 $\pm$ 0.56	18.23 $\pm$ 0.83	23.14 $\pm$ 1.15	0.86 $\pm$ 0.043	0.35 $\pm$ 0.015	0.42 $\pm$ 0.018
Ethanol	19.53 $\pm$ 1.00	13.07 $\pm$ 0.57***	15.52 $\pm$ 1.23**	0.68 $\pm$ 0.028*	0.27 $\pm$ 0.006***	0.36 $\pm$ 0.009†

Our interest in brain 'tyrosine aminotransferase' is primarily related to its possible influence on the intracerebral availability of tyrosine for catecholamine synthesis. Laboritt & Thuret (1977) provided evidence supporting this possibility (see below), and the latter has been further examined in the present work by utilizing the ability of ethanol (4 g/kg body wt.) to cause, at 12 h, a twofold increase in rat brain 'tyrosine aminotransferase' activity (Badawy *et al.*, 1980b). Under these latter conditions, we found (Table 1) that ethanol decreased the concentrations of brain tyrosine, dopamine, 3,4-dihydroxyphenylacetic acid and noradrenaline by 33, 21, 23 and 14% respectively. These changes are consistent with an inhibition of catecholamine synthesis caused by the decrease in brain tyrosine concentration. This latter decrease is unlikely to be caused by a defective cerebral uptake of circulating tyrosine, because of the absence of an increase in the concentration of the latter (Table 1). Similarly, increased hepatic tyrosine degradation caused by enhancement of liver tyrosine aminotransferase activity at 12 h after ethanol administration (see Badawy *et al.*, 1980a) is ruled out, because of the absence of a decrease in the amino acid concentration in this latter organ (Table 1), and in view of evidence (A. A.-B. Badawy, D. L. Williams & M. Evans, unpublished work) that such a hepatic influence on tyrosine availability to the brain, which occurs early after treatment with ethanol, is overcome at 6 h by opposing factors. The 12 h ethanol-induced decrease in brain tyrosine concentration is therefore most likely the result of increased cerebral degradation by the enhanced aminotransferase, and it is equally reasonable to suggest that this enhancement is the cause of the observed (Table 1) decrease in serum tyrosine concentration. Laboritt & Thuret (1977) also found that the decrease in brain tyrosine concentration observed at 2 h after cortisol administration (i.e. at a

time when brain 'tyrosine aminotransferase' activity, but not that of the liver enzyme, was enhanced) was associated with a decrease in the concentration of the circulating amino acid. The findings by these latter authors and those reported here therefore strongly suggest that transamination of brain tyrosine can, under certain conditions, play a quantitatively important role in the regulation of cerebral catecholamine synthesis and the availability of circulating tyrosine.

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