Acta vet. scand. 1976, *17*, 113—130.

From the Department of Physiology, Endocrinology and Blood-grouping, Royal Veterinary and Agricultural University, Copenhagen, Denmark.

TRYPTOPHAN METABOLISM IN PIGS

RELATION TO SYNTHESIS AND FUNCTION OF SEROTONIN*

By

*J. Hyldgaard-Jensen, R. Cmiljanić**, Inger Wegger* and *R. Andrić****

HYLDGAARD-JENSEN, J., R. CMILJANIĆ, I. WEGGER and R. ANDRIĆ: *Tryptophan metabolism in pigs. Relation to synthesis and function of serotonin.* Acta vet. scand. 1976, *17*, 113—130. — Contrary to blood serotonin the level of free and total tryptophan is distinctly influenced by feed intensity and composition. Piglets show a considerably higher plasma free tryptophan and blood serotonin content than adult pigs, just as boars possess a significantly higher blood level of tryptophan and serotonin than sows. A pronounced individual variation of blood serotonin and a much less variable content among littermate pigs provide evidence that blood serotonin is genetically controlled. Tryptophan is readily absorbed and distributed in a characteristic manner among investigated organs and tissues. A genetical control of blood serotonin and its possible relation with type of reaction exhibited by ergometer exercised pigs support the influence of tryptophan and serotonin on the ability of pigs to withstand controlled environmental conditions such as physical exercise.

pigs; tryptophan; serotonin; metabolism; environmental and genetic interactions.

In man and laboratory animals information on special functions of the essential amino acid tryptophan (Trp) and 1 of its metabolic products serotonin (5-HT) has accumulated during

---

* The investigations were supported by the Danish Technical Research Council.

** Institute for the Application of Nuclear Energy in Agriculture, Veterinary Medicine and Forestry, Zemun, Yugoslavia.

*** Clinic for Surgery, Veterinary Faculty, University of Belgrade, Yugoslavia.

recent years. Thus, the transmitter 5-HT being localized to definite areas of the central nervous system has been related to animal and human behaviour (*Sneddon* 1973), vascular and termal regulation (*Page* 1954, *Feldberg & Myers* 1963, *Bligh et al.* 1971, *Biber et al.* 1973) as well as to the adreno-cortical activity (*Vermes et al.* 1972, *Fuxe et al.* 1974). Hereby Trp and 5-HT influence an individual's adaptability to the environment taken in the widest sense. Reduced adaptability in pigs during "stress" conditions quite often results in an abnormal muscle metabolism post mortem (PSE) or in an acute death (PSS) (*Topel et al.* 1973, *Cassens et al.* 1975).

In elucidating the importance of Trp and 5-HT for porcine adaptability investigations have been carried out aiming to show the effect of environmental as well as genetical factors on the Trp — 5-HT metabolism. The transport and turnover of Trp were investigated in order to evaluate the Trp — 5-HT relation in this species. Literature data on the blood Trp and 5-HT content are scarce and often highly discrepant (*Page* 1968, *Heikkinen* 1968). This is likely to be caused by a previous lack of sufficiently accurate and sensitive methods for their determination, but may also be due to lack of information on the normal physiological variations to which blood Trp and 5-HT are subjected. From the present work it appears that factors such as nutrition, age, sex and genetics all should be considered when determining the porcine blood Trp and 5-HT content.

MATERIAL AND METHODS

Danish Landrace pigs were fed twice daily (8 a.m. and 3 p.m.) with a diet composed of 80.5 % barley, 15 % soya cakes, 3 % meat and bone meal, 1.4 % salt mixture and 0.1 % vitamin-trace element mixture. The feed contained 2.0 mg Trp per g. Unless otherwise stated blood sampling was done at the same time of the day and on fasted pigs. Four female pigs (littermates) were used to show the effect of feeding, starvation and carbohydrate feeding on the blood Trp and 5-HT content. Sex influence on blood Trp and 5-HT was investigated on 8 littermate pigs (4 females + 4 males) during the age period 14—30 weeks and on 19 pigs (10 females + 9 males) ranging in age from 19 to 23 weeks. Pigs representing various age levels during the period from shortly before birth until sexual maturity were used to

elucidate age dependent changes in the blood Trp and 5-HT level. Effect of Trp loading was investigated on 4 female pigs previously catheterized to the portal vein. Catheters (Nelaton 10FG) were inserted into the portal vein through an incision of the splenic vein and fixed to the skin surface. Catheters were perfused daily with saline containing 200 i.u. heparin per ml. Portal and peripheral (v. cava cran.) blood samples were drawn simultaneously following the uptake of a normal feed ration or a feed ration supplemented with extra Trp. Six pigs (weight 60—80 kg) were exercised in an ergometer at a speed of 100 m/min. for periods from 5 to 30 min. Blood samples were collected before and at intervals during and after exercise. The variation of blood Trp and 5-HT within litters was compared with the variation between litters using 18 litters each comprising 2 female and 2 castrated male pigs ranging in age from 12 to 15 weeks. The absorption of Trp was investigated in 5 littermate pigs (weight 13.5—15 kg). Labelled Trp (L-(G-^{3}H)Trp) and 250 mg stable Trp were introduced by means of a stomach tube. Blood samples were taken after 30, 60 min. and at killing i.e. 2, 4, 8, 12 and 24 hrs. after the introduction of ^{3}H-Trp. Faeces and urine were collected throughout the experimental period.

Blood

Heparin plasma was used for the Trp determination. Blood used for 5-HT determination was transferred to siliconized tubes containing 0.05 ml K_3EDTA sol., 2 mg potassium sorbate and 30 mg ascorbic acid. "Trombocyte free" plasma for 5-HT determination was obtained by centrifuging the blood at 2000 $\times$ g for 20 min. (4°C). Plasma ultrafiltrate for determination of free Trp was prepared by centrifuging plasma in CF Diaflo membranes (800 $\times$ g for 30 min. at 15°C). Blood and plasma were either analyzed the same day or stored at —20°C up to 1 week.

Analyses

Plasma total and free Trp were determined fluorometrically as described by *Denckla & Dewey* (1967). L-cystein, 7.4 mM, was added to both plasma and standards to obtain a linear relation between the Trp content and the fluorescense intensity. Blood and plasma 5-HT were also determined fluorometrically (*Yuwiler et al.* 1970).

Lymphocytes were isolated by centrifugation of blood in a Ficoll-Isopaque medium (*Böyum* 1968).

Following an alkaline hydrolysis of tissues (16 hrs. at 120°C), the total tissue Trp content was determined by treating the neutralized hydrolysate similarly as plasma tryptophan. Tritium activity in hydrolysates was measured by liquid scintillation counting and results corrected for quenching by means of an internal standard.

RESULTS

Intravascular compartmentalization of 5-HT

Determination of the 5-HT content in formed elements of blood showed that 5-HT is almost completely confined to the platelets. Purified fractions of erythrocytes and leucocytes (lymphocytes) contain less than 2 % of whole blood 5-HT. A comparison of the 5-HT content in whole blood, serum and plasma showed that a considerable part of platelet 5-HT is released during coagulation and that "platelet free" plasma has a low 5-HT content.

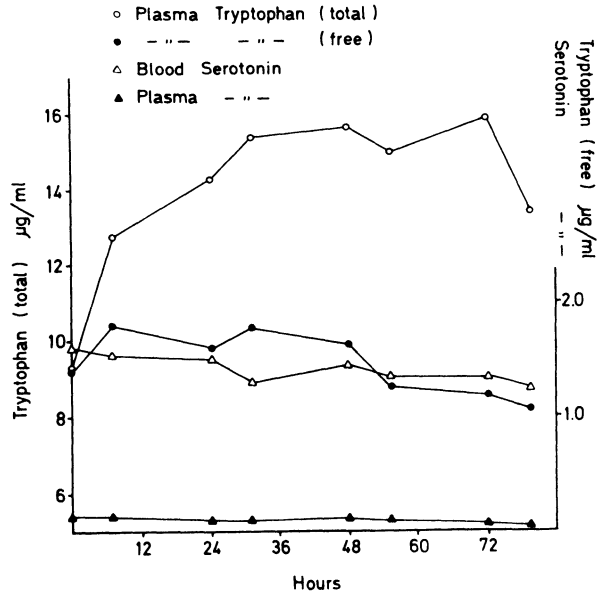

Figure 1. Effect of food deprivation on levels of plasma Trp (total and free), blood 5-HT and plasma 5-HT. Each dot represents the mean value for 4 pigs.

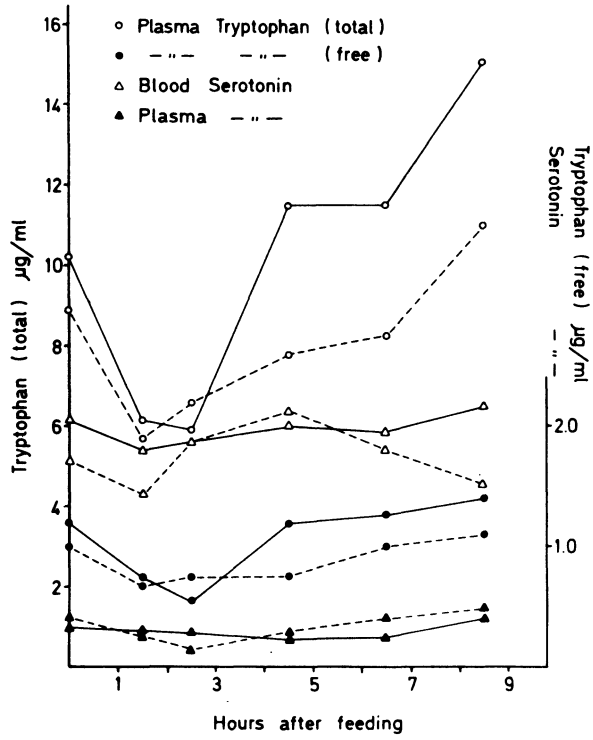

Figure 2. Effect of a carbohydrate meal on levels of plasma Trp (total and free), blood 5-HT and plasma 5-HT. Two different levels of carbohydrate were used: (———) 150 g sucrose + 150 g potato starch, (- - - - -) 300 g sucrose + 300 g potato starch.

Effect of environmental factors

Plasma total and free Trp levels are doubled within 1—2 hrs. after normal feeding. About 6 hrs. later the total Trp level has fallen slightly below the prefeeding value, whereas the free Trp is still weakly elevated. Blood 5-HT is not significantly altered by normal feeding. Similar insignificant changes in blood 5-HT were noted throughout a 24-hr. period. During this period plasma total and free Trp showed a maximum late in the afternoon, however, levels at the start and end were very similar. This corresponds to the finding that levels of Trp and 5-HT in blood samples taken twice weekly from the same pigs only showed minor variations (5—10 %).

In pigs fasted 24 hrs. the plasma total and free Trp levels were elevated by 50 % (Fig. 1). When fasting was prolonged, the Trp level increased a little further, until it after 3 days' star-

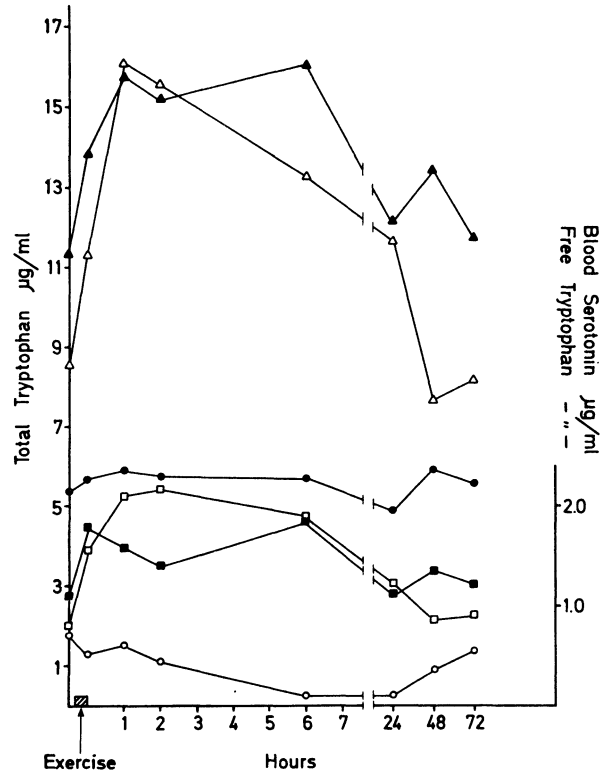

Figure 3. Effect of ergometer exercise (20 min., 100 m/min.) on levels of blood 5-HT (○, ●), plasma total Trp (△, ▲) and free Trp (□, ■). Curves with solid and open dots refer to pigs normally having a high and low blood 5-HT content, respectively.

vation began to decrease. In contrast blood 5-HT decreased throughout most of the fasting period. Carbohydrate feeding induces a short, but distinct fall in plasma total and free Trp (Fig. 2). The decrease was succeeded by an increase, the trend of which depended on the amount of carbohydrate given. Plasma 5-HT showed a slight decrease which coincided with that of plasma free Trp.

Plasma total and free Trp both increase markedly during and after physical exercise (Fig. 3). The changes were, however, only to some extent depending on the degree of exercise. Contrary to that exercise induces a decrease in blood 5-HT, the extent of which seems to depend on both the degree of exercise and on the pig's normal blood 5-HT level.

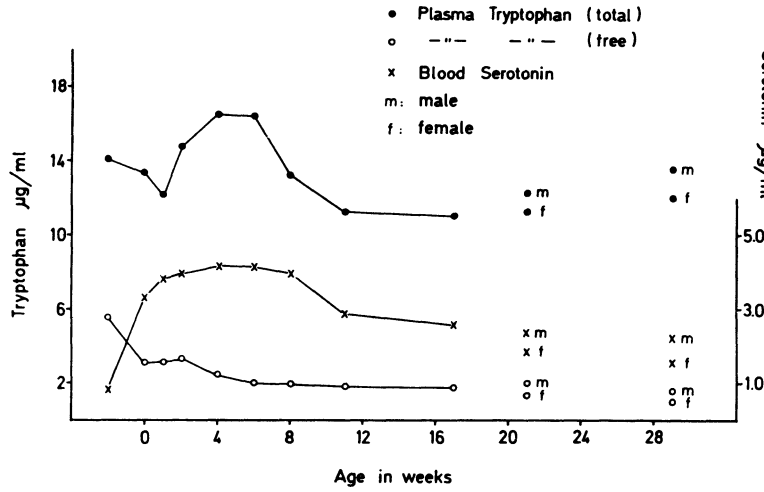

Figure 4. Age-dependent changes in blood 5-HT and plasma Trp (total and free).

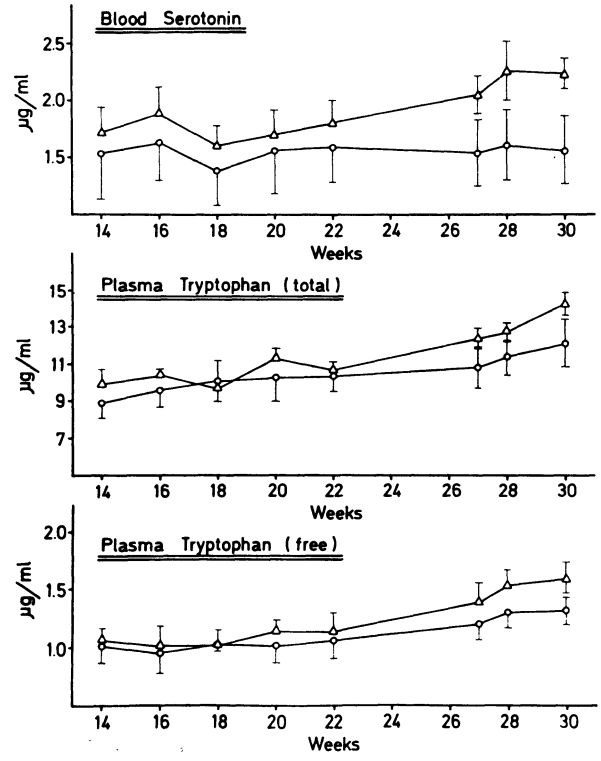

Figure 5. Levels of blood 5-HT and plasma Trp (total and free) in male (△——△) and female (○——○) pigs at various stages of age. Each dot represents the mean ± s for 4 littermates.

Table 1. Mean Trp- and 5-HT-content (μg/ml) in blood from 9 male and 10 female pigs ranging in age from 19 to 23 weeks and originating from 3 different litters.

	Blood 5-HT	Plasma 5-HT	Plasma Trp (total)	Plasma Trp (free)
Sows	1.88 (±0.45)	0.37 (±0.28)	11.3 (±1.6)	1.54 (±0.28)
Boars	2.34 (±0.43)	0.45 (±0.21)	12.5 (±1.8)	1.91 (±0.14)

Age, sex and genetical factors

Blood levels of Trp and 5-HT vary distinctly according to the age of pigs (Fig. 4). A low 5-HT and a high free Trp, thus, are typical for the foetal stage. Shortly before birth the blood 5-HT rises abruptly and stays for the first 1—2 months at a level 2—3 times higher than that of sexually mature pigs. The free Trp level decreases sharply with age, thus, in foetuses it amounts to 40 % of total Trp, in piglets 26 %, in weaned pigs 15 % and at sexual maturity about 10 %.

The influence of sex appears from Fig. 5. At sexual maturity boars have a significantly higher blood 5-HT and plasma Trp

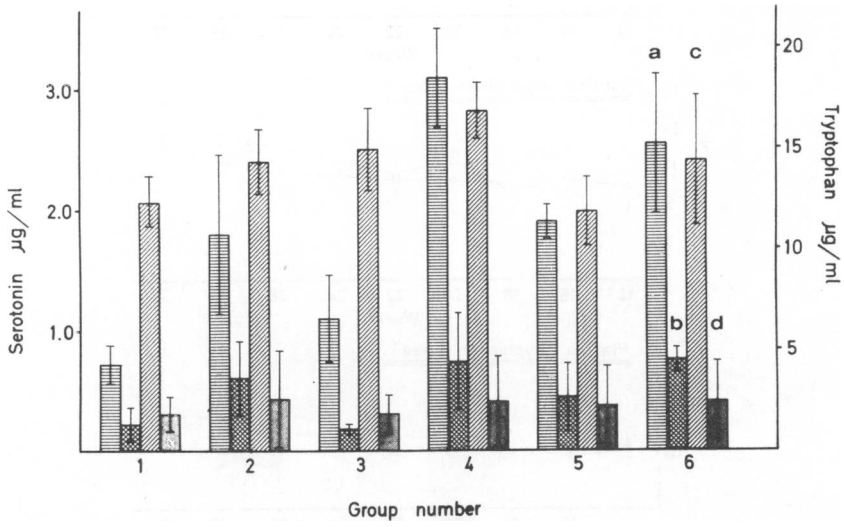

Figure 6. Mean levels of blood 5-HT (a), plasma 5-HT (b), total Trp (c) and free Trp (d) in 6 litters, each with 4 pigs (2 female and 2 castrated males).

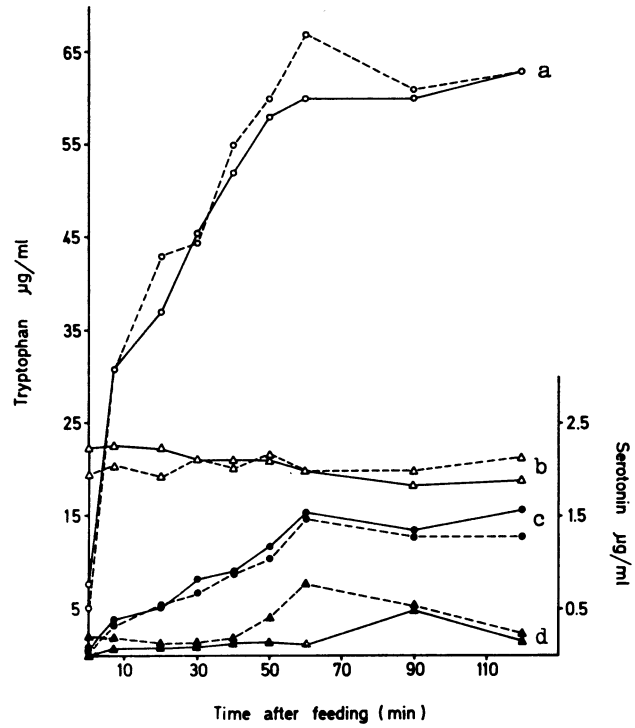

Figure 7. Changes in portal (- - - - -) and peripheral (———) blood content of total plasma Trp (a), free Trp (c), blood 5-HT (b) and plasma 5-HT (d) following the uptake of a normal feed ration supplemented with 3 g L-tryptophan.

content than that of sows. A similar finding was done in a material comprising 9 boars and 10 sows originating from 3 litters (Table 1).

Mean levels of plasma Trp and blood 5-HT in a group of litters varied distinctly (Fig. 6). Besides, the variation within litters was considerably less than between litters: blood 5-HT, $v^2 = 16.61$, $P < 0.001$; plasma 5-HT, $v^2 = 3.81$, $0.01 < P < 0.05$; total Trp, $v^2 = 5.23$, $P < 0.01$; free Trp, $v^2 = 4.37$, $P \leq 0.01$. The following correlations reflect the reproducibility of the blood 5-HT and Trp content: blood 5-HT, $r = 0.78$, $P < 0.001$; total Trp, $r = 0.46$, $P < 0.01$; free Trp, $r = 0.40$, $P < 0.05$.

Table 2. Tritium activity in intestinal content, faeces and urine and calculated retention of ^{3}H-Trp, percentage of dose.

Hours after administration	2	4	8	12	24
Intestinal content	13.7	9.1	6.4	9.3	6.4
Faeces	0.05	0.11	0.004	0.29	0.39
Urine	—	—	—	8.72	12.86
Retention	86.3	90.8	93.8	81.7	80.4

The tryptophan-serotonin relation

The addition of extra Trp (3 g L-tryptophan) to a normal feed ration is reflected by a clear difference in the portal and peripheral blood Trp and 5-HT content (Fig. 7). Thus the portal plasma Trp and 5-HT level showed an earlier and more pro-

Table 3. Tritium activity (ncpm·10^{-3}/g wet weight) in different organs and tissues. Total Trp concentration (mg/g of wet weight) is shown in brackets.

Hours after administration	2	4	8	12	24
Liver	72.55 (3.42)	68.98 (2.70)	63.69 (2.78)	75.27 (2.61)	53.20 (2.45)
Spleen	49.76 (2.14)	46.81 (2.05)	53.35 (2.05)	40.24 (1.96)	40.50 (2.10)
Kidney	39.90 (2.55)	41.94 (2.06)	34.76 (1.94)	46.78 (2.36)	40.32 (1.94)
Brain	7.66 (1.40)	9.00 (1.31)	10.56 (1.39)	11.33 (1.44)	11.11 (1.29)
Thymus	28.24 (1.29)	32.23 (1.40)	32.75 (1.30)	30.83 (1.30)	31.77 (1.43)
Lung	25.95 (1.75)	26.41 (1.61)	31.27 (1.81)	23.41 (1.59)	23.51 (1.58)
Heart	14.68 (1.94)	17.80 (2.03)	17.27 (2.14)	17.77 (1.54)	21.11 (1.98)
M. psoas m.	9.27 (2.04)	10.65 (2.00)	10.05 (2.14)	10.14 (1.95)	11.00 (1.88)
Fundus ventric.	40.29 (1.50)	45.91 (1.40)	36.00 (1.40)	41.16 (1.44)	32.08 (1.53)
Duodenum	84.37 (1.69)	96.86 (1.65)	72.05 (1.54)	70.08 (1.55)	54.92 (1.73)
Jejunum	87.17 (1.80)	74.33 (1.83)	99.26 (1.84)	62.22 (1.68)	59.28 (1.73)

nounced increase than that of the peripheral blood. Under these conditions a close correlation can be demonstrated between the total and free Trp ($r = 0.94$, $P < 0.001$) as well as between free Trp and plasma 5-HT ($r = 0.84$, $P < 0.001$).

Rate of ^{3}H-Trp absorption is high and rapid judged by the fact that almost maximal retention was achieved after 2 hrs. (Table 2). The highest activity in plasma was found after 30 min. During the next 2—3 hrs. the activity fell to a constant level less than 50 % of the initial level. Duodenum, the front part of jejunum and liver possessed the highest tritium activity (Table 3). Within the single organ or tissue the total Trp content varied only little among investigated animals (Table 3). Liver, spleen and kidney possess a significantly higher content than that of organs like brain, thymus and stomach.

DISCUSSION

Amino acids are commonly regarded as more or less essential nutrients, which serve nutritionally in maintenance and growth of cell structures and other proteins. However, as exemplified by methionin's importance as methyl-donator, tyrosine as precursor in the catecholamine synthesis and with particular relevance to the present study tryptophan as precursor of serotonin, it has become clear that amino acids serve other and more specific functions. Through such functions several amino acids among those Trp influence an animal's adaptability to the environment (*Topel et al.* 1973, *Cassens et al.* 1975).

The 5-HT synthesis seems within certain limits to be dependent on the Trp supply. This view is amply supported by several investigations (*Wurtman & Fernstrom* 1972) as well as by the present results (Fig. 7). Blood (platelet) 5-HT is generally considered to reflect both the synthesis and metabolism of 5-HT (*Heikkinen* 1968), however, to what extent the blood participates in the transfer of 5-HT from one tissue to the other is still unclear. As 5-HT is lipid-insoluble and hardly penetrates f. ex. the blood-brain barrier, it seems more likely that 5-HT is synthetized within the single tissue on the basis of free Trp supplied from the circulating blood. Studies of the normal Trp content in blood, the Trp metabolism as well as those conditions controlling the relative presence of bound and free Trp are thus important steps in the elucidation of the normal 5-HT metabolism and changes herein.

Data on normal blood Trp and 5-HT are highly divergent not only among the various species (*Page* 1968) but also within the same species (*Heikkinen*). The choice of sufficiently accurate and optimized methods seems very important, hence for the determination of 5-HT, the presence of EDTA and ascorbic acid is required both to achieve maximal blood 5-HT and stability of 5-HT during the analyses and storage of blood. This may explain why earlier reported levels (0.2—0.3 μg/ml) on porcine blood 5-HT (*Erspamer* 1954, *Topel et al.* 1973) are considerably lower than those found in the present work. Besides, such discrepancy may also as shown here be related to differences in age, feeding, sex or breed of animals. As the conventional amino acid methods do not permit Trp to be analyzed very few data appear on blood and tissue Trp content. However, using similar fluorometric technique as in the present work, *Curzon et al.* (1973) have recently reported data on the Trp content in plasma and brain from fasting pigs, which correspond with those presently obtained.

During the coagulation process platelet 5-HT is released, evidently as a result of the formed trombin (*Holmsen & Day* 1970). This explains why serum 5-HT is almost as high as whole blood 5-HT. In spite of the low plasma 5-HT and a possible risk of an in vitro release of platelet-bound 5-HT, the in vivo existence of free plasma 5-HT is supported by the results of the Trp loading experiments (Fig. 7). Numerous in vitro studies have shown that platelets actively take up 5-HT (*Crawford* 1967). If this applies to in vivo conditions, this could explain why free, active 5-HT normally is kept at a low level.

Contrary to blood 5-HT the plasma Trp level is markedly influenced by feeding, and standardization of blood sampling and other environmental factors is therefore necessary. Rhythmic diurnal changes in plasma Trp have been reported in poultry *Meyer et al.* 1973) and rats (*Wurtman et al.* 1968). Whether a similar phenomenon exists in pigs cannot be answered unless they are fed ad libitum. The increase in free Trp during starvation, which corresponds to similar findings in rats (*Tagliamonte et al.* 1973), is likely to be caused by a simultaneous increase in plasma free fatty acids (NEFA), which compete with free Trp in their common binding to the plasma proteins (*Curzon et al.*). A similar mechanism could explain the fall in plasma Trp following carbohydrate feeding. Thus, an increased output

of insulin decreases the NEFA concentration thereby inducing a decrease in plasma free Trp.

Physical exercise is accompanied by an increased adrenalin output, which is known to cause an elevation of the plasma NEFA concentration. On this basis the rise in free Trp in physically exercised pigs is understandable. In spite of this blood 5-HT is decreased which therefore hardly can be explained by a decreased synthesis, but rather by a faster turnover rate. Increased turnover of 5-HT is previously demonstrated in other species exposed to various "stress" conditions (*Thierry et al.* 1968). The fact that a lowered blood 5-HT was particularly pronounced in pigs, which normally possess a low blood 5-HT level and react most severely towards physical exercise seems to emphasize the importance of 5-HT for pigs' adaptability under such conditions.

The results from the Trp loading experiments reveal a close relation between the Trp and 5-HT metabolism in pigs. A lower Trp content in peripheral blood than that of portal blood is thus indicating that the liver is capable of metabolizing this amino acid. The rapid progressing increase in portal plasma 5-HT further suggests that blood 5-HT originates from an intestinal synthesis and that the liver in accordance with earlier findings in rats (*Heikkinen*) has a considerable capacity to remove 5-HT from the blood stream.

Quantitative investigations regarding the Trp absorption in pigs as well as in other domestic animals are very scarce. *Candlish et al.* (1970) found in sheep that activity was demonstrable in urine already 10 min. after introduction of D,L-^{14}C-Trp in the rumen. In this respect there is good agreement with the observed rapid uptake of ^{3}H-Trp from the porcine intestinal tract. The accumulation of the absorbed ^{3}H-Trp indicates a tissue variance in respect of the amount taken up as well as the rate at which Trp is metabolized. However, these preliminary investigations are unable to show to what extent the measured activity is attached to Trp or to metabolic products such as 5-HT. Use of Trp labelled with ^{15}N in the heterocyclic ring will be needed to elaborate these findings further.

The physiological significance of a high free plasma Trp and blood 5-HT just after birth is not known. The trend of changes in plasma free Trp may, however, be related to a coinciding change in the plasma proteins (*Brummerstedt-Hansen* 1967).

The age dependent variation noted for both plasma Trp and blood 5-HT as well as a relative specific tissue distribution of 5-HT could be valuable aids for the evaluation of the physiological role of this amino acid and amine in the body.

Hormonal influence on blood 5-HT is previously shown by the addition of thyroxine (*Rastogi & Singhal* 1974) and glucocorticoids (*Went & Csaba* 1973, *Neckers & Sze* 1975) to rats and rabbits. That sex hormones also have a regulatory function on plasma Trp and blood 5-HT is supported by an observed sex difference in pigs as well as in poultry (*Meyer et al.*). As for pigs the sex difference in poultry was first significant at sexual maturity. Sexually mature boars are known to have a significantly higher growth rate than that of sows and hence it was attempted to show whether a correlation exists between growth of pigs and the blood Trp and 5-HT content. Results obtained indicate that there might be a correlation between blood 5-HT and growth ($r = 0.68$, $P < 0.05$). Indirect evidence for a possible positive correlation is derived from the decrease in blood 5-HT during fasting and a high blood 5-HT content during the period in which pigs possess the highest growth coefficient e. g. the postnatal period. Whether such correlation could be explained on the basis of an observed stimulatory effect of 5-HT on growth hormone secretion in man and rats (*Collu et al.* 1972, *Imura et al.* 1973) or rather be due to an effect of sex hormones, which may act both on the growth processes and the 5-HT synthesis, remains to be solved.

Porcine blood 5-HT is subjected to a pronounced individual variation. As the pigs were kept under the same environmental conditions and blood 5-HT is much less variable among closely related (littermates) pigs, evidence has been provided that blood 5-HT is genetically controlled. A genetical control of mice blood 5-HT has recently been reported (*Eleftheriou & Bailey* 1972). Whether a genetically based low or high blood 5-HT content reflects distinct physiological differences in pigs is too early to predict. Normally blood 5-HT is kept constant due to a well balanced mechanism including synthesis, storage, release and break down of 5-HT. Apart from an optimal supply of Trp, the tissue content of those enzyme systems controlling the Trp — 5-HT metabolism is equally important (*Ciaranello et al.* 1974). The fact that a major part of an organism's 5-HT is located in platelets makes studies of platelet 5-HT particular useful in providing

information on the transport and metabolism of 5-HT at the extra- and intracellular level. Platelet defects as found in both man (*Bouillon & O'Brien* 1971, *Murphy et al.* 1973) and rats (*Tschopp & Zucker* 1972) are characterized by an abnormal low or high blood 5-HT level as well as by an unusual reaction type of rats towards various environmental stress factors (*Weiss et al.* 1974). Thus it is possible that a low or high blood 5-HT level in pigs may be related to an abnormal reaction type towards f. ex. physical exercise. This opinion is supported by results from the ergometer exercised pigs, which showed that pigs with a low blood 5-HT level also exhibited the poorest ability to withstand physical exercise.

ACKNOWLEDGEMENT

The authors wish to address their gratitude to Professor, dr. med. vet. Johs. Moustgaard on whose initiative the present work was undertaken. For valuable assistance during the work we wish to thank dr. Birthe Palludan.

REFERENCES

Biber, B., J. Fara & O. Lundgren: Intestinal vascular responses to 5-hydroxytryptamine. Acta physiol. scand. 1973, *87*, 526—534.

Bligh, J., W. H. Cottle & M. Maskrey: Influence of ambient temperature on the thermoregulatory responses to 5-hydroxytryptamine, noradrenaline and acetylcholine injected into the lateral cerebral ventricles of sheep, goats and rabbits. J. Physiol. (Lond.) 1971, *212*, 377—392.

Bouillon, D. J. & R. A. O'Brien: Abnormalities of 5-hydroxytryptamine uptake and binding by blood platelets from children with Down's syndrome. J. Physiol. (Lond.) 1971, *212*, 287—297.

Brummerstedt-Hansen, E.: The Serum Proteins in the Pig. An Immunoelectrophoretic Study. Thesis, Munksgaard, Copenhagen 1967.

Böyum, A.: Separation of leucocytes from blood and bone marrow. Scand. J. clin. Lab. Invest. 1968, *21*, suppl. 97.

Candlish, E., N. E. Stanger, T. J. Devlin & L. J. La Croix: Tryptophan absorption and metabolism in sheep. Canad. J. Anim. Sci. 1970, *50*, 337—344.

Cassens, R. G., D. N. Marple & G. Eikelenboom: Animal physiology and meat quality. *In* Advances in Food Research. C. O. Chichester et al., eds. Vol. 21, p. 71, Acad. Press, N. Y. 1975.

Ciaranello, R. D., A. Lipsky & J. Axelrod: Association between fighting behaviour and catecholamine biosynthetic enzyme activity in two inbred mouse sublines. Proc. nat. Acad. Sci. (Wash.) 1974, *71*, 3006—3008.

Collu, R., F. Fraschini, P. Visconti & L. Martini: Adrenergic and serotonergic control of growth hormone secretion in adult male rats. Endocrinology 1972, *90*, 1231—1237.

Crawford, N.: Serotonin absorption by normal and "carcinoid" platelets. Clin. chim. Acta 1967, *18*, 297—307.

Curzon, G., B. D. Kantamaneni, J. Winch, A. Rojas-Bueno, I. M. Murray-Lyon & R. Williams: Plasma and brain tryptophan changes in experimental acute hepatic failure. J. Neurochem. 1973, *21*, 137—145.

Denckla, W. D. & H. K. Dewey: The determination of tryptophan in plasma, liver and urine. J. Lab. clin. Med. 1967, *69*, 160—169.

Eleftheriou, B. E. & D. W. Bailey: A gene controlling plasma serotonin levels in mice. J. Endocr. 1972, *55*, 225—226.

Erspamer, V.: Pharmacology of indolealkylamines. Pharmacol. Rev. 1954, *6*, 425—444.

Feldberg, W. & R. D. Myers: A new concept of temperature regulation of amines in the hypothalamus. Nature (Lond.) 1963, *200*, 1325.

Fuxe, K., J. Schubert, T. Hökfelt & G. Jonsson: Some aspects of the interrelationship between central 5-hydroxytryptamine neurons and hormones. Adv. biochem. Psychopharmacol. 1974, *11*, 67—74.

Heikkinen, E. S.: Inactivation of 5-hydroxytryptamine in rats. Acta physiol. scand. 1968. Suppl. 311, p. 7—82.

Holmsen, H. & H. J. Day: The selectivity of the trombin-induced platelet release reaction. J. Lab. clin. Med. 1970, *75*, 840—844.

Imura, H., Y. Nakai & T. Yoshimi: Effect of 5-hydroxytryptophan (5-HTP) on growth hormone and ACTH release in man. J. clin. Endocr. 1973, *36*, 204—206.

Meyer, D. C., P. D. Sturkie & K. Gross: Diurnal rhythm in serotonin of blood and pineals of chickens. Comp. Biochem. Physiol. 1973, *46A*, 619—623.

Murphy, D. L., J. R. Mendell & W. K. Engel: Serotonin and platelet function in Duchenne Muscular Dystrophy. Arch. Neurol. (Chic.) 1973, *28*, 239—243.

Neckers, L. & P. Y. Sze: Regulation of 5-hydroxytryptamine metabolism in mouse brain by adrenal glucocorticoids. Brain Res. 1975, *93*, 123—132.

Page, I. H.: Serotonin (5-hydroxytryptamine). Physiol. Rev. 1954, *34*, 563—587.

Page, I. H.: Serotonin. Year Book Medical Publ., Chicago 1968.

Rastogi, R. B. & R. L. Singhal: Thyroid hormone control of 5-hydroxytryptamine metabolism in developing rat brain. J. Pharmacol. exp. Ther. 1974, *191*, 72—81.

Sneddon, J. M.: Platelet Serotonin. *In* Progress in Neurobiology. Kerkut, G. A. & J. W. Phillis, eds. Vol. 1, pp. 151—198, Pergamon Press, Oxford 1973.

Tagliamonte, A., G. Biggio, L. Vargiu & G. L. Gessa: Free tryptophan in serum controls brain tryptophan level and serotonin synthesis. Life Sci. 1973, *12*, 277—287.

Thierry, Anne-Marie, M. Fekete & J. Glowinski: Effects of stress on the metabolism of noradrenaline, dopamine and serotonin (5-HT) in the central nervous system of the rat. II. Modifications of serotonin metabolism. Europ. J. Pharmacol. 1968, *4*, 384—389.

Topel, D. G., D. G. Wilson, G. M. Weiss & L. L. Christian: Influence of phenoxybenzamine and propanolol on blood serotonin and pH, plasma cortisol and M. longissimus pH and color in swine. J. Animal Sci. 1973, *36*, 1077—1080.

Tschopp, T. B. & M. B. Zucker: Hereditary defect in platelet function in rats. Blood 1972, *40*, 217—226.

Vermes, I., G. Dull, G. Telegdy & K. Lissák: Possible role of serotonin in the monosamine induced inhibition of the stress mechanism in the rat. Acta physiol. Acad. Sci. hung. 1972, *42*, 219—223.

Weiss, H. J., T. B. Tschopp, J. Rogers & H. Brand: Studies of platelet 5-hydroxytryptamine (serotonin) in storage pool disease and albinism. J. clin. Invest. 1974, *54*, 421—432.

Went, M. & B. Csaba: Effect of cortisone treatment and adrenalectomy on 5-hydroxytryptophan decarboxylase and monoamino oxidase activity in mouse tissues. Acta physiol. Acad. Sci. hung. 1973, *43*, 233—237.

Wurtman, R. J. & J. D. Fernstrom: L-tryptophan, L-tyrosine, and the control of brain monoamine biosynthesis. *In* Perspectives in Neuropharmacology. S. H. Snyder, ed. Oxford Univ. Press 1972, p. 143.

Wurtman, R. J., C. M. Rose, C. Chou & F. Larin: Daily rhythms in the concentrations of various amino acids in human plasma. New. Engl. J. Med. 1968, *279*, 171—175.

Yuwiler, A., S. Plotkin, E. Geller & E. R. Rrrvo: A rapid accurate procedure for the determination of serotonin in whole human blood. Biochem. Med. 1970, *3*, 426—436.

SAMMENDRAG

Tryptofanomsætningen hos svin.
Relation til syntese og funktion af serotonin.

Effekten af såvel ydre som genetiske faktorer på blodets Trp- og 5-HT-indhold er undersøgt hos Dansk Landrace svin.

Ved tilførsel af mærket (^{3}H-Trp) og ikke mærket Trp er endvidere undersøgt tryptofans resorption, transport, fordeling samt relation til serotoninsyntesen.

Plasmaets indhold af fri og total Trp er i modsætning til blodets 5-HT markant påvirkelig af næringstilførselens omfang og sammensætning. Unge grise viste et væsentligt højere plasma fri Trp og blod

5-HT indhold end voksne grise, ligesom kønsmodne orner besidder et signifikant højere Trp- og 5-HT-indhold i blodet end sogrise. En betydelig mindre variation af blod 5-HT indenfor kuld end mellem disse tyder på en genetisk kontrol af blodets 5-HT-indhold.

Trp optages hurtigt fra svinets tarmkanal og fordeles på en karakteristisk måde mellem de undersøgte væv og organer. Resultaterne af Trp-belastningen tyder på en nær relation mellem tryptofan- og serotoninomsætningen hos svin.

Den genetiske kontrol af blodets 5-HT-indhold samt dettes sammenhæng med grises reaktion på ergometerbelastning synes at understrege tryptofans og serotonins betydning for grises adaptationsevne under disse betingelser.

(Received January 19, 1976).

Reprints may be requested from: J. Hyldgaard-Jensen, Department of Physiology, Endocrinology and Bloodgrouping, Royal Veterinary and Agricultural University, Bülowsvej 13, DK-1870 Copenhagen V, Denmark.