

VARIATIONS IN PLASMA *a*-AMINO ACID NITROGEN OF SCHIZOPHRENICS*

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The concept enlarged by Gjessing⁴ that alterations in nitrogen metabolism correspond with exacerbations and remissions of schizophrenia gave rise to this investigation of plasma *a*-amino acid nitrogen of schizophrenics. Difficulties in studying nitrogen balance are exaggerated in acutely disturbed schizophrenics because ingestion of a uniform diet and collection of 24-hour specimens of excreta require specialized nursing technique. The measurement of *a*-amino acid nitrogen in plasma affords a method of studying actively metabolized nitrogen compounds. This investigation was begun before the report of Horwitt⁶ that the basal level of unclaked blood *a*-amino acid nitrogen of 8 young "recent" schizophrenics increased markedly 2 weeks after insulin shock therapy.

Experimental methods and subjects

Postabsorptive *a*-amino acid nitrogens of plasma from heparinized venous blood were measured by the ninhydrin carbon dioxide method of Hamilton and Van Slyke,⁵ with modifications recommended by Hamilton and described previously.¹⁰ In 6 patients the serum protein, albumin, and globulin were measured in blood taken at the same time as was the plasma for amino acids. The methods have previously been described.²

The subjects were 38 schizophrenic patients admitted to the Psychiatric wards. Usually blood was not taken until from 3 to 5 days after admission so that variations due to dehydration or irregularities in diet would be eliminated. After admission, fluids and food were always given even if feeding by tube or parenteral administration of fluid was necessary.

Results

Figures 1 through 7 demonstrate the decreases in plasma *a*-amino acids when schizophrenic patients were acutely disturbed and also show the rises as remissions occurred.

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Figure 10A shows the plasma α -amino acid nitrogen values of 38 schizophrenic patients. Only one determination on each patient was included. When the amino acids of a patient were measured more than once the value used was that of the patient's worst clinical day studied.

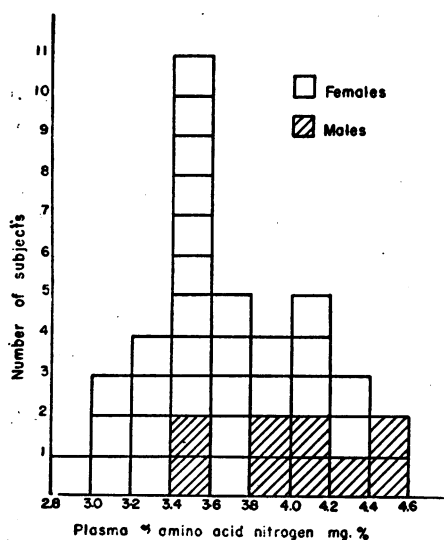


Figure 10A

Fig. 10A: Plasma α -amino acid nitrogens of 38 schizophrenic patients. When amino acids of a patient were measured more than once the value used was that of the patient's worst clinical day studied.

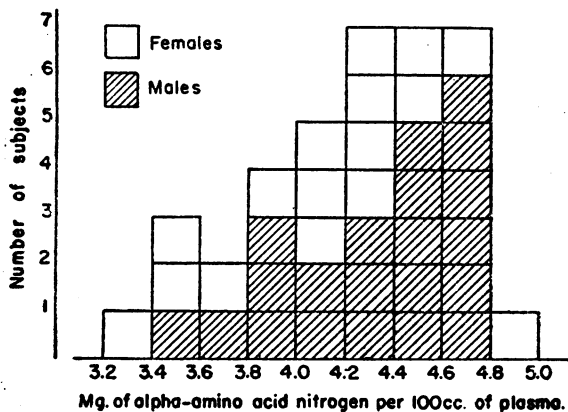


Figure 10B

Fig. 10B: Plasma α -amino acid nitrogen of 37 normal subjects. From Woodruff and Man.¹⁰

The values were distinctly lower than those of the 37 normal subjects studied by Woodruff and Man¹⁰ (Fig. 10B). The latter found after correction for urea nitrogen 4.13 mg. per cent of α -amino acid nitrogen as the average value for 37 normal males and females and 4.03 mg. per cent as the average value for 16 females. Since 29 of the 38 schizophrenics were females the amino acids of the schizophrenics have been compared with the average value for normal females, 4.03 mg. per cent of plasma α -amino acid nitrogen. In the 37 normals, 12 subjects had amino acid nitrogens below 4.03 mg. per cent. Thirty-one of the α -amino acid nitrogens of the 38

schizophrenics were below this average value for females. The range of values for the schizophrenics was from 2.97 to 4.57 mg. per cent. In comparison the normals of Woodruff and Man had α -amino acid nitrogens ranging from 3.27 to 4.87 mg. per cent.

In 6 patients there was no correlation between fluctua-

tions in plasma *a*-amino acid nitrogen and changes in serum protein, albumin, and globulin. Two patients had constant concentrations of serum protein, albumin, and globulin, although the amino acids of one rose, and those of the other fell. The proteins of 2 patients fell as the amino acids of one remained constant and of the other fell. The proteins of the other 2 patients increased and decreased as the amino acids rose.

Discussion

Only 2 of the 7 patients in Figs. 1 through 7 were studied several times before electroshock so that they present the only 2 examples of the behavior of plasma *a*-amino acid nitrogens of untreated schizophrenic patients. In Fig. 1 (patient 3696) plasma *a*-amino acid nitrogens rose from their low levels of 3.30 and 3.45 mg. per cent to 3.98 mg. per cent before electroshock was started. This patient had been in the hospital for 3 days before the initial plasma amino acid. She was eating satisfactorily and was not overactive. During the last few days before admission she had had an exacerbation of symptoms which had been recognized 4 years previously. At admission she was mute and passively cooperative. Between the initial low plasma *a*-amino acid nitrogen and the higher value of 3.98 mg. per cent 2 weeks later, she had improved somewhat without any special treatment except good hospital care. The further rise in her amino acids accompanied marked clinical improvement. This happened to occur during the course of 7 electroshocks. The plasma amino

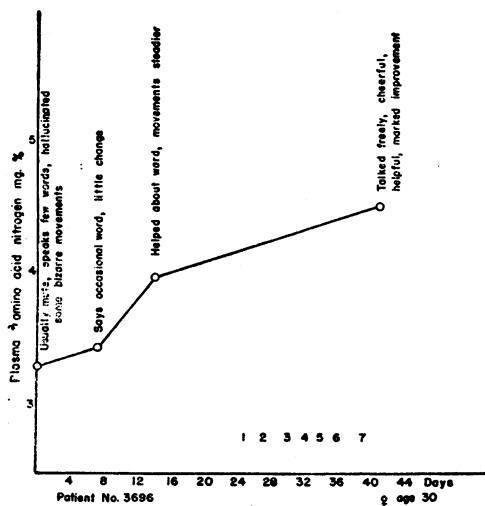


Figure 1
Figs. 1 through 9: Plasma *a*-amino acid nitrogens and notes on condition of schizophrenic patients. At the bottom of the charts days are counted after the initial blood study on each patient. The horizontal numbers above days represent the number of electroshock treatments and are spaced when these treatments were given.

acids shown in Fig. 2 (patient 3825) were measured 3 times before electroshock was started. The plasma *a*-amino acid nitrogens of this patient 4 and 6 days after admission were 3.49 and 3.55 mg. per cent. She had eaten well but had been active and noisy. Two days after the

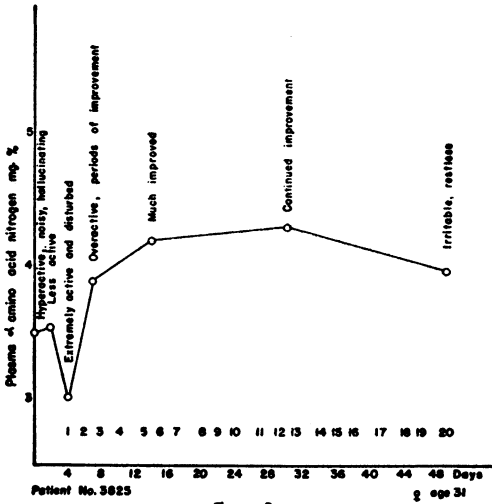


Figure 2

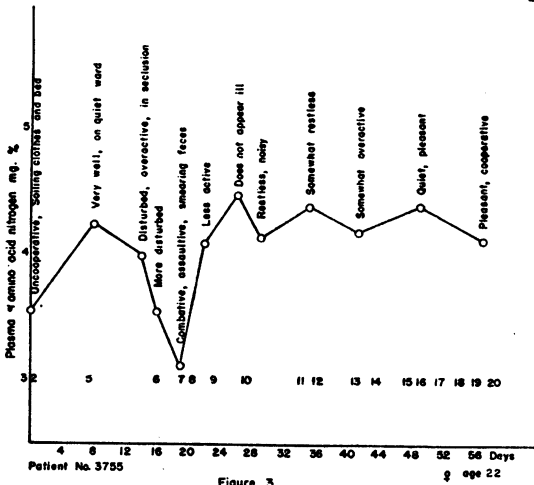


Figure 3

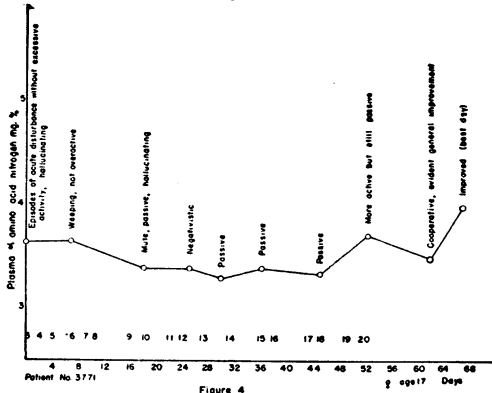


Figure 4

second blood study she became combative, assaultive, and overactive. She ate poorly during the 24 hours preceding the third blood study; and the plasma *α*-amino acid nitrogen dropped to 3.01 mg. per cent. At this time electroshock was started; the patient improved clinically and the plasma amino acids rose markedly.

That the increases in plasma *α*-amino acid nitrogens of the 2 previous patients were related to clinical remissions rather than to specific metabolic effects of electroshock is substantiated by the behavior of the plasma *α*-amino acid nitrogens of other patients treated with electroshock.

Patient 3755, (Fig. 3) had her lowest plasma *α*-amino acid nitrogen of 3.13 mg. per cent at the time when she was combative and assaultive after the administration of 6 electroshocks.

Even after 6 electroshocks the amino acids of patient 3771 (Fig. 4), fell as her negativism and hallucinations progressed. Thereafter the amino acids were as low as 3.40 mg. per cent on 5 different occasions during 27 days, while 12 more electroshocks were administered. The amino acids of patient 3399 (Fig. 5), dropped from

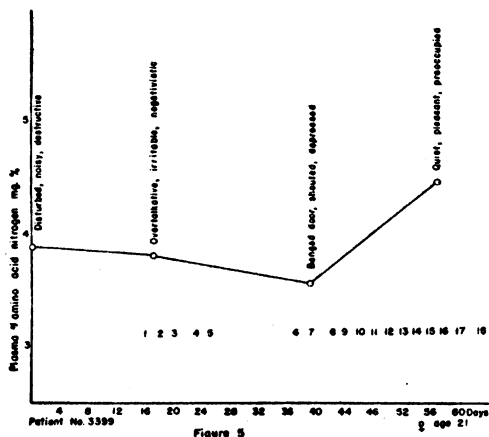


Figure 5

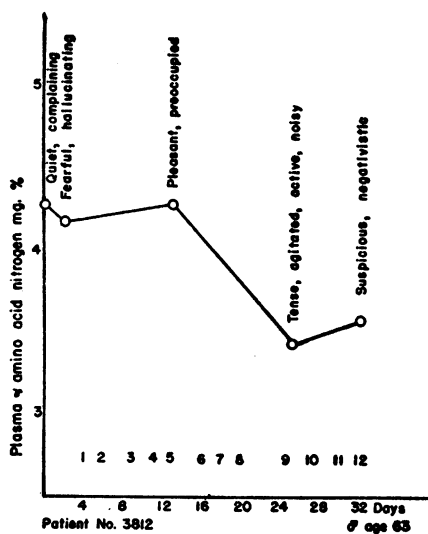


Figure 6

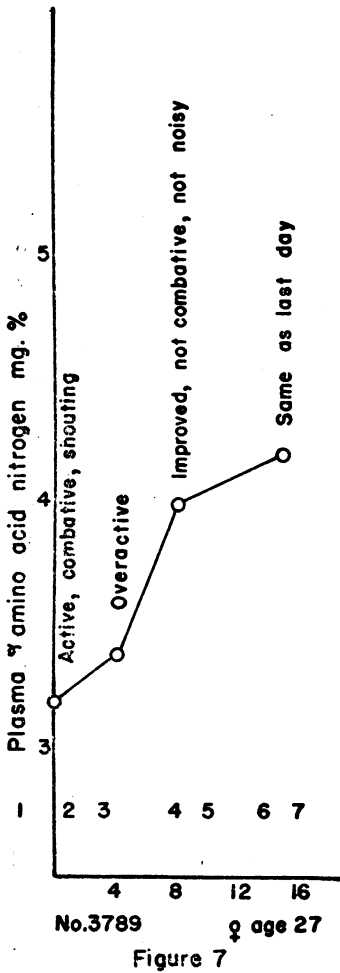
3.82 to 3.50 mg. per cent during 23 days when 6 electroshocks were given. The amino acids of patient 3812 (Fig. 6), dropped markedly with an exacerbation of his illness which occurred in the hospital after 5 electroshocks.

Many factors influence the level of circulating amino acids^{1, 3, 9} and the metabolism of the latter is only partially understood.^{8, 9} The fall in the plasma *a*-amino acid nitrogen of acutely ill schizophrenics

might be a condition specific to the changes in metabolism of the schizophrenic. On the other hand, the decreases in the plasma *a*-amino acid nitrogen at the time of a schizophrenic exacerbation resemble the fall in amino acids accompanying the injury reaction.⁸ After major operations plasma amino acids fall abruptly and remain low until recovery is well advanced.⁸ As has already been reported, unless patients were severely debilitated initially the amino acids fell and remained low in proportion to the severity of the operation. The mere fact that caloric intake was restricted

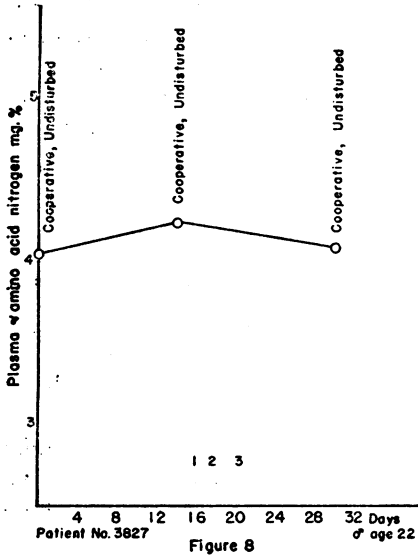
was not as relevant as was the severity of the operation. Similarly in these schizophrenic patients depression of the amino acids correlated with the severity of the exacerbation but not with any reduction in food intake. Special daily caloric and fluid intake records were kept. Patient 3771 (Fig. 4) ate well on the days preceding her 5 lowest plasma *a*-amino acid nitrogens. Patient 3696 (Fig. 1) took a normal diet and was not overactive on the days preceding her first 2 low amino acids.

Patient 3825 (Fig. 2) was disturbed and extremely overactive, but had 750 cc. of a milk egg-nog by mouth, and 1500 cc. of saline intravenously during the 24 hours preceding her lowest *a*-amino acid nitrogen of 3.01 mg. per cent. Patient 3789 (Fig. 7)

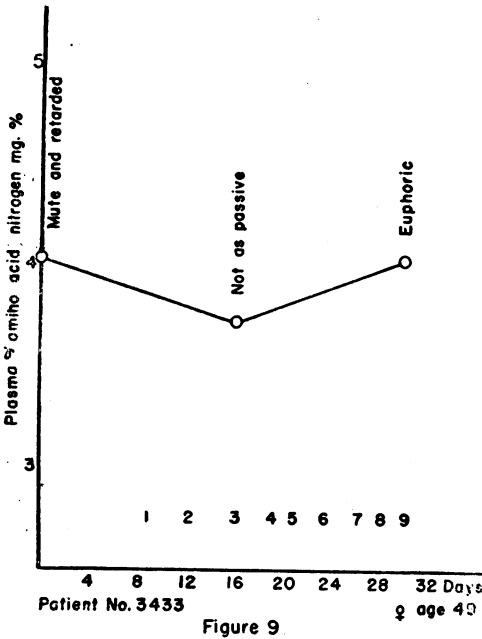


ate exceedingly well on the days preceding her 2 lowest plasma *a*-amino acid nitrogens of 3.20 and 3.40 mg. per cent, but on those days was so ill that she was active, combative, and shouting. Patient 3755 (Fig. 3) ate well of both breakfast and dinner and took milk for supper the day preceding her lowest plasma *a*-amino acid nitrogen, 3.13 mg. per cent.

That it is the severity of the schizophrenic process which produces a fall in plasma *a*-amino acid nitrogen is corroborated by other evidence. Repeated determinations of plasma *a*-amino acid nitrogens of other schizophrenics whose clinical condition did not change acutely have not varied as have the amino acids of the patients with marked exacerbations and remissions (Figs. 1 through 7). These data are too numerous to diagram, but 2 examples are illustrated in Figs. 8 and 9. In another report from this laboratory the rises of plasma *a*-amino acid nitrogens of 7 schizophrenic patients during 27 days of improvement following prefrontal lobotomy are illustrated.⁷ The final increased amino acids were associated with the remission of schizophrenic symptoms in the patients.



The effect upon the plasma *a*-amino acid nitrogen of the overactivity of some of the acutely disturbed schizophrenics cannot be evaluated. That the low levels of amino acid are not the direct result of the activity of the schizophrenic might be assumed from analysis of some of the data in the figures. The schizophrenic 3696 in Fig. 1 was never overactive, although she had plasma *a*-amino acid nitrogens as low as 3.30 and 3.45 mg. per cent when she was acutely ill. Patient 3771 (Fig. 4) had no periods of excessive activity but 5 different amino acids were as low as 3.40 mg. per cent. On the other hand,



examination of the figures does reveal that some of the lowest amino acids occurred when the muscular exercise of the patient had increased beyond his or her normal activity. For example, see the lowest amino acids of 3825 (Fig. 2), of 3755 (Fig. 3), of 3399 (Fig. 5), of 3812 (Fig. 6), and of 3789 (Fig. 7). The plasma amino acids of normal subjects after muscular exercise are being studied, but the results are not conclusive as yet. In 2 normal male and 2 normal female adults, 2 hours of strenuous exercise after a light carbohydrate breakfast did not decrease the plasma *a*-amino

acid nitrogen to low levels; but 1 and 4 hours after exercise the amino

acids were slightly lower, never more than 0.25 mg. per cent, than on control days when the subjects did not exercise and ate the same quantity of carbohydrate.

That plasma amino acids are low in schizophrenics and fall in acute disturbances in that disease suggests that investigations should be conducted to determine the effect upon the disease of increasing chemotherapeutically plasma *a*-amino acid nitrogen levels.

Conclusions

Plasma *a*-amino acid nitrogens were below the normal average for females, 4.03 mg. per cent, in 31 of 38 schizophrenic patients.

In 7 patients studied at intervals the amino acids fell in acute exacerbations and rose when the symptomatic manifestations of the illness improved.

The decreases were correlated neither with diminished caloric intake nor always with overactivity, but rather with acute manifestations of the disease. The fall in plasma amino acids resembles the drop of these nitrogen compounds in acute illness or after injury.

The increases of plasma *a*-amino acid nitrogen in schizophrenics do not result from the metabolic effects of electroshock.

The effect upon schizophrenic disease of chemotherapeutically increasing plasma *a*-amino acid nitrogen should be investigated.

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