NEWS AND VIEWS

Plasma Tryptophan and Brain Function

THE indoleamine 5-hydroxytryptamine (5-HT) (serotonin) is thought to act as a neurotransmitter in the mammalian central nervous system. Although the precise role of this amine in brain function is not known, it has been shown to play an important part in regulating patterns of sleep in cats and other experimental animals. There is at present a great deal of interest in the possibility that some forms of depressive illness in man may be related to a deficiency of cerebral 5-HT (see Ashcroft *et al.*, *Lancet*, ii, 573 ; 1972), and it has been plausibly suggested that antidepressant drugs may act by enhancing the availability of 5-HT at synapses in the brain.

An understanding of the biochemical mechanisms involved in the regulation of 5-HT synthesis in the brain is thus of considerable importance. The article by Knott and Curzon on page 453 of this issue of *Nature* helps to add another missing link to the understanding of this regulatory process. There is now ample evidence that the rate of synthesis of 5-HT in the brain is regulated principally by the availability of the precursor amino-acid L-tryptophan, the normal concentration of which in the tissue is considerably below the K_m for the first enzyme in the 5-HT biosynthetic pathway, tryptophan hydroxylase (Eccleston *et al.*, *J. Neurochem.*, **12**, 493; 1965). Furthermore, Tagliamonte and his colleagues reported last year (*Nature New Biology*, **229**, 125; 1971) that various treatments and drugs which caused increased synthesis of brain 5-HT all led to significant increases in the concentration of tryptophan in the brain.

On the other hand, it has hitherto not been clear how the tryptophan pool in brain is controlled. Tagliamonte and his colleagues and Knott and Curzon had previously failed to establish any consistent correlation between brain and plasma tryptophan concentrations. For example, food deprivation or immobilization stress led to significant increases in brain tryptophan and 5-HT synthesis without any corresponding changes in plasma tryptophan. Nevertheless, brain tryptophan must presumably be derived from the plasma, for mammalian tissues are incapable of synthesizing this essential amino-acid. This paradox has now been resolved virtually simultaneously by Knott and Curzon and by the Italian group (Gessa, Biggio and Tagliamonte, *Fed. Proc.*, **31**, 2168; 1972). The solution lies in the fact that tryptophan is alone among circulating amino-acids in being highly bound to plasma proteins. Knott and Curzon have now repeated their experiments on food deprivation and immobilization stress in rats, and measured not only the total tryptophan content of plasma but also the much smaller ultrafiltrable fraction of free plasma amino-acid. They find that in rat plasma about 95 per cent of the total tryptophan is tightly bound to plasma macromolecules. The small free tryptophan fraction in plasma, however, showed changes which correlated well with changes in brain tryptophan.

After 24 h of food deprivation, for example, there was no significant change in total plasma tryptophan but very large increases in the free plasma amino-acid and in brain. Knott and Curzon also observed that there was an increase in the plasma concentration of non-esterified fatty acids under conditions in which free plasma tryptophan was increased. Heparin, which is known to lead to an increase in plasma free fatty acid content, also caused an increase in the concentration of free tryptophan, suggesting that a casual relationship may exist between these parameters.

The findings of Knott and Curzon thus explain several hitherto paradoxical observations. As the authors point out, their findings suggest that it might be very interesting to measure the concentration of free tryptophan in plasma samples from depressed patients. These findings may also be relevant to improving the mode of administration of L-tryptophan, which is claimed to have useful antidepressant properties (Coppen *et al.*, *Lancet*, i, 1393 ; 1972).—From our Pharmacology Correspondent.

Outburst of Cyg X-3

THE radio outburst of Cyg X-3 early in September this year is described by one of the discoverers of the event, P. C. Gregory, as "the most impressive outburst ever witnessed by radio astronomers" (see page 439 of this issue of *Nature*). Certainly, radio astronomers and other observers have been so excited by this event that as the news spread everyone who had any chance of detecting the object, at any wavelength, seems to have directed instruments towards the constellation Cygnus. As a result of this unique focusing of astronomical attention on one object, more than a score of contributions probing the nature of Cyg X-3 have been gathered into a special issue of *Nature Physical Science* (next Monday, October 23) produced to coincide with the "discovery" articles of Gregory *et al.* (this issue, page 440) and Hjellming and Balick (this issue, page 443). But why are the astronomers so excited?

Perhaps the most important aspect of this event is that it demonstrates, for the first time, the existence of violently variable radio sources within our Galaxy. Cyg X-3 was being monitored because it is an X-ray source, and thus of particular interest in any case. But the outburst had no counterpart at X-ray frequencies and there is no reason to suppose that such radio outbursts should only occur in objects which are strong X-ray emitters ; indeed, flares of this kind could have occurred many times in sources throughout the Galaxy and been completely missed by conventional surveys.

Basically, then, the excitement is the result of the discovery of what may be the archetype for a new category of highly energetic objects located within the Galaxy. The most violent events in which anything like

Additional copies of next Monday's *Nature Physical Science*, which contains reports of observations of Cyg X-3 at radio, infrared and X-ray frequencies, will be available (see page X).