energies penetrate to different distances, so that the colour of the developed image is an indication of ion energy. (This technique was originally developed to help in studying the injection of dopant ions into semiconductor crystals.)

The new study has shown particularly clearly that channelling is always accompanied by its converse, blockage. A proportion of incident protons, instead of being channelled, is scattered through large angles, giving a diffuse transmission background. This background pattern is marked by a series of absorption lines, rather like Kikuchi lines in electron diffraction, which represent directions in which the once-scattered ions might have been expected to be channelled. These paradoxical protons are not channelled because they were all scattered by lattice ions, and so, while they were moving in the right directions, their motion started in a lattice plane and not between a pair of adjacent lattice planes, as is needed for proper channelling. A proton moving in a lattice plane is especially likely to be scattered a second time, and so the absorption patterns result. Dearnaley and his colleagues have studied the intriguing transitions from anomalous transmission to anomalous absorption as the direction of incidence of the protons is gradually altered from an exact crystallographic vector, and from this have deduced information about the existence of a potential barrier between axial and planar channelling. The phenomena have all been interpreted in terms of a simple physical model for proton-ion collisions.

DRUGS

Action of Hallucinogenic Drugs

from a Correspondent

THE Neurosciences Research Program of the Massachusetts Institute of Technology held a work session on the mechanism of action of hallucinogenic drugs from November 17 to 19. Some tentative conclusions were reached. There is some evidence that LSD interacts in a complex fashion with serotonin receptors in the brain. Freedman reported that many psychotomimetic drugs increase concentrations of serotonin in the brain and decrease those of its metabolites, indicating a decreased turnover. LSD strongly inhibits the uptake of serotonin and inhibits its central effects, for example in the cortex and superior colliculus (whereas brom-LSD does not). Serotonin depleters, such as PCPA, potentiate the central effects of LSD and MAOIs diminish them. Bradley indicated that microiontophoretic injections of LSD inhibit about 30 per cent of neurones in the reticular formation and can depress serotonin as well as glutamate-induced excitation; thus the absence of a non-specific component in the inhibition induced by LSD could not yet be assumed.

Aghajanian reviewed his work on the inhibitory effects of intravenous LSD on the serotonin-containing cells of the raphe nuclei in the brain stem. LSD, as well as other psychotomimetic drugs, induced marked inhibition of these cells whereas brom-LSD was twenty times less active. Thus LSD in general inhibits central serotonin mechanisms, although there is evidence that in very small doses it potentiates them.

Shulgin and Smythies presented data on the relationship between the structure and activity of the psychoto-

mimetic phenylethylamines and related compounds. Two conclusions are (i) that the 4-methoxy group is sufficient but not necessary for psychotomimetic action in man and (ii) that, for the rest, the data support the hypothesis presented by Snyder that the potency of these molecules depends on their capacity to form equivalents of the B or C rings of LSD by hydrogen bonding. The tryptamine hallucinogens, which are in general more active than the mescaline analogues, could form part of the D ring of LSD. Kopin reported that LSD increases the release of both noradrenaline and serotonin from stimulated brain slices and pointed out that an agent like LSD which could affect several different transmitters in the brain would have an exceedingly complex mechanism of action, for with three possible modes of interaction (potentiate, diminish, no change) and n possible transmitters, there might be 3^n modes of interreaction.

Several people suggested that the structural relationship between the molecules of LSD and serotonin should not lead us to overlook other possible important clues. Alivisatos suggested that the charge transfer complexes which serotonin appears to form with nicotinic acid dinucleotide might approximate to the LSD molecule. The "upper" half of the LSD molecule is similar to nicotinamide. It is also similar to nikethamide and arecoline, and Smythies suggested that the complex LSD molecule might straddle a serotonin receptor together with an allosteric or cooperative site similar to a cholinergic or adrenergic receptor, and that this might account for its great potency which appeared to be more than could be explained by a simple addition of separate actions on ordinary serotonin and noradrenaline receptors. Snyder showed that the LSD molecule can be considered as an analogue of putrescine, linking it to the diamines, the important role of which in brain function is only just beginning to be appreciated.

Axelrod reviewed the list of psychotomimetic compounds that could be formed in the body by known mechanisms. This includes dimethyltryptamine, 5-methoxydimethyltryptamine, *p*-methoxy tyramine and some of their relatives as well as derivatives of melatonin.

Kety and Elkes suggested the following synthesis of the available information. (i) The psychotomimetic drugs, particularly LSD, may produce their complex psychic effects by the inhibition of a basic brain stem mechanism (which might include the raphe nuclei, the afferent inflow into the reticular formation and possibly the locus coeruleus), the function of which is to integrate the sensory inflow and the emotional and ideational state of the organism, and in particular to suppress irrelevant information. This system may depend on a complex interaction of serotonin and noradrenaline mechanisms. The basic requirements of a hallucinogen seem to be that it should (in specific doses) inhibit serotonin systems and potentiate noradrenaline systems. If these systems are normally mutually inhibitory, normal homeostasis might survive interruption of one of these mechanisms but would not survive simultaneous interruption of both in opposite senses. (ii) LSD may also affect serotonin and noradrenaline mechanisms in the retina and other visual systems (Zarcone, V., Gulevich, G., Pink, T., and Dement, W., *Arch. Gen. Psychiat.*, **18**, 194; 1968).