compared with those of the control towns. Our methods produced closer matching between Samaritan and control towns and larger samples than Bagley's study. The results are in line with controlled evaluations of American Suicide Prevention Centres and with Holding's (1975) study of the Samaritans and do not support the hypothesis that the fall in the suicide rate is due to the Samaritans.

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Crisis Intervention after Deliberate Self-Poisoning: A Trial of Task Centred Casework. J. S. GIBBONS, J. BUTLER, P. J. URWIN and J. L. GIBBONS. Department of Sociology and Social Administration, and Faculty of Medicine, University of Southampton.

Four hundred patients, aged at least 17 and coming from a defined geographical area, who attended the Casualty Department of Southampton General Hospital between April 1975 and March 1976 after deliberate self-poisoning, were randomly assigned to an experimental, crisis-oriented social work service (E) or to the routine service (C) (referral to a general practitioner, to a psychiatric out-patient clinic or to some other form of support). A further 139 patients were excluded because they needed immediate psychiatric intervention or were already in intensive treatment, usually with a psychiatrist. The experimental service used a contractual approach, setting a maximum time limit of 3 months service.

After a year there was no difference between E and C groups in the proportion of patients who repeated self-poisoning. The excluded patients repeated over twice as much. E patients were significantly more satisfied with the service they had received and showed more changes in some areas of social functioning.

TRANSMITTERS IN DEMENTIA

Cholinergic Mechanisms in Alzheimer's Disease. PETER DAVIES. MRC Brain Metabolism Unit, Department of Pharmacology, 1 George Square, Edinburgh.

We have attempted to evaluate the status of various neurotransmitter systems in clearly defined cases of this condition measuring key enzymes, receptors, and in some cases the transmitter and/or its metabolites in brains obtained at autopsy. Over a period of two years, seven brains have been collected which satisfied our criteria for acceptance as cases of Alzheimer's disease. Clinically they showed profound progressive dementia, and neuropathologically the presence of great numbers of neuritic plaques and neurofibrillary tangles in sections of frontal, temporal and parietal cortex, without evidence of significant cerebro-vascular disease. A further fourteen brains were collected from cases free of obvious neurological or psychiatric disorder, and in which no gross cerebral abnormalities were detected.

By far the most striking neurochemical abnormalities we have found in the brains from cases of Alzheimer's disease are reductions to less than 25 per cent of normal values in the activities of two enzymes, choline acetyltransferase (the enzyme responsible for the synthesis of acetylcholine) and acetylcholinesterase (responsible for its degradation) in hippocampal, temporal, frontal and parietal cortex (Davies and Maloney, 1976). These same brain regions show the most extensive pathological changes which are characteristic of Alzheimer's disease.

The activities of these two enzymes in hippocampus, temporal cortex and parietal cortex are almost without exception below the lower end of the normal range of activities. In other brain regions, whilst the mean activities of these enzymes are lower than in normals, there is considerable overlapping of the data from normals and Alzheimer's disease cases. The data seem to suggest that central cholinergic neurones generally are vulnerable to whatever agent or process produces Alzheimer's disease. In certain brain regions however, these neurones appear to be particularly badly affected, and it seems possible that the extent of the loss of enzymes of the cholinergic system in hippocampal, temporal and parietal cortex indicates a functional deficit in cholinergic transmission in these areas. Whether this apparent deficiency can explain any or all of the clinical manifestations of this condition, such as memory loss and spatial disorientation, is not clear but there are grounds for thinking that this may be so (Drachman and Leavitt, 1974). Whether the smaller losses of these enzymes from other brain regions are indications of functional deficiencies of acetylcholine or not is likewise unclear. The extent of the normal range of values, and of the overlaps between data from normals and cases of Alzheimer's disease suggests that post-mortem measurements of enzyme activities may not be a sensitive indicator of the previous cognitive function of an individual.

To date, there has been no clear indication that neurotransmitter systems other than the cholinergic are significantly affected in Alzheimer's disease, and

it would therefore seem reasonable to try to find means of making good the apparent deficiency of acetylcholine to alleviate the symptoms of this condition.

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Cholinergic and GABA Systems in Dementia and Normal Old Age. E. K. PERRY and R. H. PERRY. Department of Neuropathology, Regional Neurological Centre, Newcastle General Hospital.

Biochemical evidence is provided to suggest that an abnormality of the hippocampal cholinergic system is involved in the pathology of senile dementia. The activities of cholinergic and GABA system enzymes have been measured in necropsy brain tissue obtained from mentally normal and abnormal elderly subjects, including those with senile dementia of Alzheimer type (SDAT), multi-infarct dementia (MID), depression and schizophrenia. Loss of the GABA system enzyme, glutamate decaroxylase, is not apparently specifically involved in SDAT since substantial reductions were also found in depression and MID. In contrast, significant reductions in the cholinergic enzyme, choline acetyltransferase, were almost entirely confined to SDAT. Within the brain regions examined the cholinergic enzyme in the hippocampal structure was lowest in SDAT. The biochemical abnormality thus parallels in distribution the previously established morphological changes (such as neurofibrillary tangles and senile plaques) found in diseased brains (Tomlinson *et al,* 1970).

A correlation between biochemical (cholinergic system) and morphological (Alzheimer type) abnormalities is further exemplified by the effects of age on the cholinergic enzyme in the brains of mentally normal subjects. Whereas glutamate decarboxylase was unaltered in any of the regions examined, choline acetyltransferase in the hippocampus declined significantly ($P < 0{\cdot}001$) with increasing age (Perry *et al,* 1977). This age-related loss of cholinergic enzyme activity parallels the distribution of Alzheimer type changes which occur in normal aged brains, most extensively as in SDAT, in the hippocampus (Tomlinson *et al,* 1968).

Anatomically the hippocampal structure is well established, and neurochemically the cholinergic system is increasingly implicated, in memory function. Based on the evidence presented it is concluded that the decline in intellectual function commonly associated with ageing and symptomatic of SDAT may be related to progressive malfunction of cortical cholinergic systems. By inference, pharmacological potentiation of cholinergic mechanisms may be a worthwhile approach to the amelioration of both conditions.

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Selective Vulnerability of Neurones in Alzheimer's Disease. DAVID M. BOWEN and ALAN N. DAVISON. Miriam Marks Department of Neurochemistry, Institute of Neurology, Queen Square, London WC1N 3BG.

It is unclear whether or not neuronal loss occurs in Alzheimer's disease for there is no exact way of estimating atrophy under the microscope. Neurones and glia, however, contain characteristic chemical substances which we have used as potential indices of the relative number of neural cells. Homogenates of the whole temporal lobe were analysed. The results (expressed per lobe) indicate that about one half of the nerve cells can be lost from this region in Alzheimer's disease. The markers of glial cells were relatively unaffected (Bowen *et al,* 1977). Information about whether or not a certain type of neurone is selectively vulnerable has been obtained by measuring choline acetyltransferase and glutamate decarboxylase activities as markers of acetylcholine and γ-aminobutyrate-containing neurones respectively; high affinity binding of atropine has been utilized as an index of acetylcholine receptor binding sites. The results (expressed per unit mass) indicate that cholinergic neurones are particularly vulnerable (Spillane *et al,* 1977; White *et al,* 1977).

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