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Transcultural psychopharmacotherapy

The following are extracts from the *Transcultural Psychopharmacotherapy Newsletter*, No. 2. (sponsored by the WHO Division of Mental Health)*

Ethnic difference in the sensitivity to alcohol

It has been empirically known for years that there is a difference in the sensitivity to alcohol beverages between Asian and European peoples. Many Japanese adults, but practically no Europeans, suffer flushing, palpitation, nausea, headache, etc., (flushing syndrome) whenever they drink a small quantity of alcohol.

Although there are multiple forms of aldehyde dehydrogenase (ALDH) in the liver, the mitochondrial ALDH (here referred to as ALDH2) with a very low Km for acetaldehyde, is believed to be responsible for the oxidation of most of the acetaldehyde generated during alcohol metabolism.

It was reported by Goedde *et al* in 1980 that ALDH2 in the liver is deficient in nearly half of the liver specimens of Japanese, while it was never absent in Germans. Mizoi *et al* confirmed in 1983 that, after ingesting the same amount of alcohol, ALDH2-deficient individuals showed a marked accumulation of blood acetaldehyde associated with manifest flushing syndrome, while ALDH2-positive persons showed scarcely any changes in the blood acetaldehyde level and physical conditions. There was a non-significant difference in the blood alcohol concentration between the two groups.

Ohmoro *et al*, Hokkaido University School of Medicine, investigated the ratio of ALDH2 deficiency in healthy and schizophrenic subjects and alcoholic addicts in Sapporo, using hair root samples, during 1982–84. The ALDH2 deficiency was found in 43% (50/117 cases) of normal volunteers and 33% (27/82) of schizophrenic patients, but in only 4% (5/113) of alcohol addicts. The ratio of drinking habit (drink everyday or almost every day for enjoyment or relaxation) was also significantly different between healthy ALDH2 positive and deficient individuals, i.e., 46% (31/67) in the former while only 18% (9/50) in the latter. It is apparently due to the flushing syndrome which ALDH2-deficient persons suffer ($p<0.001$), since it was shown that they enjoy the same happy or relaxed feeling by taking alcohol as that ALDH2 positive individuals usually experience.

We performed a multi-center study of ALDH2 deficiency in different populations during 1984–86 by cooperation of centers in Basel, Casablanca, Lucknow, Moscow, Mexico City, Nedlands and Zagreb, and the WHO Headquarter. Our colleagues in Taipei and Manila also joined the project. Hair root specimens were obtained by informed consent from normal volunteers and schizophrenic subjects and sent in the frozen container to the Sapporo centre.

The ALDH2 deficiency was found in 35% (14/40) of Taipei and 12% (4/34) of Manila subjects, but in none of 146 samples collected in any areas other than Asia, i.e., in Europe (Basel 7 cases, Moscow 26, Zagreb 24), Australia (Nedlands 12; European descents), India (Lucknow 26), Morocco (Casablanca 31) and Mexico (Mexico City 20).

Whilst alcoholism is regarded as a socio-psycho-biological disorder, we believe that inherited ALDH2 deficiency in Asian people is one of the important factors for the relatively low rate of alcoholism in that continent.

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Video news

Videotape reviews

PET: images of brain function in schizophrenia

Those familiar with television programmes like *Horizon* will recognise the production style of this professional video. Talking heads and images of modern technology are combined with a familiar voice-over to illustrate the use of positron emission tomography or PET in the investigation of the pathophysiology of schizophrenia.

Based on the work of the MRC Cyclotron Unit of the Hammersmith Hospital, the video concentrates on the ability of PET to measure regional cerebral blood flow as an indicator of the underlying neuronal function. As a consequence PET, unlike other imaging techniques such as CT or MRI, can provide information about cerebral function rather than structure.

Early PET studies frequently reported the presence of "hypofrontality" in patients with schizophrenia. This was not a consistent finding, perhaps reflecting diagnostic heterogeneity. Tim Crow proposed, after the finding of structural abnormalities on CT in the early '70s, an influential two dimensional model of schizophrenia. Positive symptoms such as delusions and hallucinations were attributed to a functional dopaminergic hyperactivity and negative features such as poverty of speech and flattening of affect were attributed to structural change. More recently Peter Liddle, in a series of studies, found that the symptoms and signs of schizophrenia segregate to three syndromes, and this finding has been replicated by other workers. The syndromes are psychomotor poverty including poverty of speech, flattening of affect and reduced spontaneous movements; reality distortion including delusions and hallucinations; and an additional category of disorganisation which includes formal thought disorder and incongruity of affect. These syndromes bear a striking similarity to the three sub-types of schizophrenia that Kraepelin originally described: catatonic, paranoid and hebephrenic.

Although the three syndromes can coexist within the same individual, each separate syndrome should reflect a characteristic cerebral pathophysiology. The relevant question is whether the current level of sophistication of PET technology and data analysis is capable of demonstrating these differences in cerebral function. The findings of the Hammersmith team are striking. In a group of chronic schizophrenic patients with stable phenomenology they found that ratings for the syndrome of psychomotor poverty correlated with reduced blood flow in the left dorsolateral prefrontal cortex and the left parietal association cortex; reality distortion with increased blood flow in the left parahippocampal gyrups and prefrontal cortex; and disorganisation with increased flow to the right anterior cingulate and thalamus. But what do these correlations mean?

The Hammersmith team have not only demonstrated a correlation between cerebral function and specific syndromes in schizophrenia, but have started to demonstrate how these particular patterns of altered cerebral function may be linked with specific psychological processes. Chris Frith, a neuropsychologist, proposed that delusions and hallucinations occur as a consequence of the inability of individuals to monitor their own mental activity so that, for example, their thoughts or movements are experienced as having an alien quality. By performing PET studies in normal volunteers undergoing appropriate cognitive tasks, he found that blood flow increased in the left parahippocampal gyrus during self-monitoring, a change which mirrored the finding for the reality distortion syndrome of schizophrenia. The task of verbal fluency which involves spontaneous generation of mental activity produced an increase in blood flow in the left dorsolateral prefrontal cortex in control subjects. This corresponded