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Soft neurological dysfunction and gender in schizophrenia

SIR: Evidence from the literature suggests that male and female schizophrenics differ in terms of: age at onset, clinical picture, response to neuroleptics (DeLisi *et al*, 1989), frequency of early brain injury, family history of psychosis, preponderance of positive as opposed to negative symptoms (Nasrallah & Wilcox, 1989) and neuromorphological abnormalities (e.g. Flaum *et al*, 1990). The most plausible explanation for these differences, according to Castle & Murray (1991), is that more male than female schizophrenics have a form of disease due to neurodevelopmental anomaly.

Nasrallah & Wilcox (1989) suggest that neurological factors may play an important aetiological (causative and/or additive) role in the development of schizophrenia in males, while hereditary factors may be more important for schizophrenia in females.

A group of 64 patients with schizophrenic disorder (43 males, 21 females) diagnosed according to DSM–III–R critera were included in the present study. All the patients were consecutively admitted to our university ward from the catchment area served by the hospital.

Inclusion critera were: age between 18 and 50; informed consent; no history of neurological disorder, drug abuse or alcoholism. Male and female schizophrenics had been ill for a mean of 7.75 years (s.d. 5.17) and 9.20 years (s.d. 7.54) respectively. Their ages ranged from 20 to 50 years (mean (s.d.) 30.04 (7.48)) for males and from 21 to 50 years (mean (s.d.) 34.28 (8.22)) for females. All the patients were on neuroleptic medication (dose range 200–3000 mgEq/chlorpromazine; mean (s.d.) 354 (289) for males and 357 (277) for females).

Patients were assessed by a standardised neurological examination focused on neurological soft signs (NSS) which was developed by our own research group and used in a previous study on schizophrenic patients, their first-degree relatives and healthy controls (Rossi *et al*, 1990). A revised form developed from its longer parent instrument (Rossi *et al*, 1990) was used in the present study. Twelve items of the original 19 formed the present NSS scale. No informative items were excluded from the instrument after the first study.

A two-tailed *t*-test for independent samples was performed. The alpha level was *a priori* fixed at 0.05.

Comparing the groups, a significant difference was found in age ($t = -2.24$, 69 d.f., $P = 0.028$). No significant differences were found in duration of illness ($t = -0.95$, 68 d.f., $P = 0.343$ NS) or current drug dosage ($t = -0.04$, 66 d.f., $P = 0.96$ NS) between the two groups. No between-group difference was found for NSS total score ($t = -0.30$, 69 d.f., $P = 0.76$ NS).

Female schizophrenics were found to have the same NSS total score compared with males, after age and mgEq/CPZ were taken into account using these two variables as covariates in the ANCOVA (main effects: $F = 0.941$, 3, 64 d.f., $P = 0.42$ NS). However age and mgEq/chlorpromazine were not significantly related to NSS total score (multiple regression analysis: no variable entered at 0.05 limit in the total sample and in male and female groups separately).

Our results failed to support the hypothesis of gender differences at neurological examination in schizophrenia, contrasting with Nasrallah & Wilcox's (1989) hypothesis of a pre-eminent role of neurological factors in the aetiology of schizophrenia in males, based on a retrospective evaluation of childhood brain injury. Since we found an excess of NSS in schizophrenics and their first-degree relatives in our previous study (Rossi *et al*, 1990), minimal brain damage can be considered as a potential marker of a gender-independent vulnerability.

Other factors (perhaps genetic) may play a differential role in eliciting schizophrenia in both sexes, or in modulating schizophrenia in males and females with a spread of neuromorphological and outcome differences.

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Lethal catatonia and NMS

SIR: We would like to make some remarks in connection with the two letters by Tan & Ong (*Journal*, June 1991, **158,** 858 and November 1991, **159,** 729–730).

They suggested that the mother and the younger daughter in our paper on the familial occurrence of neuroleptic malignant syndrome (NMS) (*Journal*, June 1991, **158,** 850–853) could be diagnosed as lethal catatonia (probably they meant that of psychogenic origin) rather than NMS, since they had past histories of catatonia. However, we believe that the episodes presented were neuroleptic-induced, e.g. the first episode of the mother, which was not preceded by catatonia, developed within eight days of the initiation of neuroleptic treatment.

More importantly, Tan & Ong appear to consider NMS and lethal catatonia (LC) as separate entities, despite the following discussions suggesting that NMS is a subtype of LC; Gelenberg (1976), and Barnes *et al* (1986) emphasised that catatonia was a syndrome with various causes, and neuroleptics could cause catatonic state. Mann *et al* (1986) emphasised that LC was also a syndrome rather than a specific disease based on a comprehensive review, and suggested that NMS was a neuroleptic-induced iatrogenic form of LC. More recently, White & Robins (*Journal*, March 1991, **158,** 419–421) described five cases of NMS in which catatonia preceded the syndrome. This paper and our paper indicate that a patient with a past history of catatonia is at high risk of developing NMS, suggesting that NMS and LC have a common pathogenesis, probably hypodopaminergic function.

Tan & Ong suggested that NMS and LC should be differentiated, since the treatment of LC would be the continuation of neuroleptics and ECT. However, as reviewed by Mann *et al* (1986), neuroleptics are generally inadequate in treating LC and, in fact, may aggravate or complicate the disorder. The two case reports by Kish *et al* (1990) illustrate this view; these two cases, in which clinical pictures were indistinguishable from NMS, were diagnosed as LC, and neuroleptics were continued, which ended in death despite electroconvulsive therapy (ECT). This finding suggests that neuroleptics should be discontinued in the conditions now labelled as NMS or LC, regardless of which diagnosis is given. Incidentally, Tan & Ong misquoted Mann *et al* (1986) who suggested the discontinuation of neuroleptics whenever LC was suspected, for the reasons mentioned above. The report by Mahmood (*Journal*, March 1991, **158,** 437–438) on the effectiveness of bromocriptine for catatonic stupor, and the review by Davis *et al* (1991) on the effectiveness of ECT for NMS also suggest that the two disorders respond to common measures.

Our paper on the familial occurrence of NMS suggests that the predisposition to this syndrome may be genetically transmitted. This further suggests the close linkage between NMS and LC, since the familial tendency to catatonia (including LC) has also been reported (Barnes *et al*, 1986).

Thus, it is far more practical to consider NMS as a subtype of LC than to consider them as separate entities for the understanding and management of these disorders.

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Pisa syndrome–a confusing term

SIR: I read with interest the article by Turk & Lask ("Pisa syndrome in an adolescent on neuroleptic medication", *Journal*, March 1991, **158,** 422–423). The case report, concerning a 15-year-old girl, and the discussion are important because they describe an impressive acute dystonic reaction which could have been mistaken for malingering or naughtiness. I want to make two remarks.