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Correspondence

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SYMPTOM CONTROL IN TARDIVE DYSKINESIA

DEAR Sir,

I would like to report the results of a small uncontrolled open ended study conducted over the last 2½ years in which acceptable control of the symptoms of tardive dyskinesia was achieved in eight consecutive cases. This was done by giving sodium valproate (Epilim) in doses above 400 mgms/day concurrently with existing neuroleptic treatments.

The eight cases included seven women and one man aged between 45 and 60 years who had been taking neuroleptics for a minimum period of 10 years and had established tardive dyskinesia. In each case sodium valproate was introduced into the existing neuroleptic treatment programme and the dose increased from 200 mgms/day to a maximum of 1600 mgms/day. Control of symptoms was usually achieved two weeks after attaining a dose in excess of 400 mgms/day and lost again if the dose was reduced below this figure. Once control was achieved it was maintained without alteration of the dose. In all but one case the symptoms of Tardive Dyskinesia were completely relieved. No case has suffered a return of symptoms except temporarily when intensely agitated. In each of these cases control was restored by treatment of the agitation. In no case was control achieved at the expense of increased parkinsonism or deterioration of the mental state. No case experienced side effects.

There have been a considerable number of papers written about the use of sodium valproate to control tardive dyskinesia (Casey *et al*, 1979; Chien *et al*, 1978; Linnoila *et al*, 1976; Nair *et al*, 1980) and some of the results appear to conflict. However, observations made during this study bring together several points which would seem to reduce this conflict and suggest a possible mode of action whereby sodium valproate may effect control.

Firstly, there was a two week minimum gap between achieving a dose of 400 mg/day and the onset of control of symptoms. This occurred in all eight cases and is apparent in previous studies which publish a graph of these results against time, but has not been noted by any of the authors as a recurring pattern (Casey *et al*, 1979; Linnoila *et al*, 1976; Nair *et al*, 1980). It is this very time lapse which contributes to many of the conflicting results in the use of this drug in this way.

Secondly, sodium valproate differs from most other substances known to relieve tardive dyskinesia (Crane, 1973; Kobayashi, 1977; *Lancet* Editorial, 1979) in that (a) it does not cause tardive dyskinesia itself, (b) it does not require increasing doses to maintain control even over prolonged periods of time, and (c) it is not anticholinergic.

Thirdly, sodium valproate is a known neuro-transmitter conserver and its observed mode of action in control of tardive dyskinesia resembles most closely that of other neuro-transmitter conservers in other conditions (MAOI's + tricyclics in depression). This observation is leading to a new and apparently fruitful approach (Casey *et al*, 1980; Nair *et al*, 1979; Tamminga *et al*, 1977; Tamminga *et al*, 1979) based on a broader concept of the aetiology of symptoms and therefore wider possibilities for successful intervention. The successful use of sodium valproate to control the symptoms of tardive dyskinesia in this study would support this concept and suggest that it be further tested in the form of a larger controlled clinical trial.

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CORPUS CALLOSUM DYSFUNCTION IN SCHIZOPHRENIA

DEAR SIR,

May we account for the difference between our original findings, and those of Professor Shagass and his colleagues? As we reported some time ago (*Journal,* November 1982, **141,** 535), our stimulus was not just simple vibration as used by Shagass *et al,* but included a larger amplitude sudden finger extension; and we reported that this latter was the critical component for producing the evoked potentials. We accept, therefore, that our work was not directly comparable to that of Salamy (1978).

The relevance of stimulus parameters is shown by the results, remarkably similar to ours, reported by Gulmann *et al* (1982), who used a standard electrical stimulus to the median nerve, and who did not use a common vertex reference. Their main finding was of a substantially reduced conduction time, though this only achieved significance in one direction. Their median conduction time from left to right of 16 m/secs in schizophrenics could not possibly have been produced by a normal pathway as it would have required conduction velocities of more than 90 metres/second and far thicker myelinated fibres than have been described in the human corpus callosum (Swadlow *et al,* 1979), which supports our hypothesis of an abnormal ipsilateral pathway in schizophrenia. Connolly (*Journal,* April 1982 , **140,** 429–30; May 1983, **142,** 536) has failed repeatedly to understand the concept of a "negative" transmission time, though this convention was also used by Gulmann and his colleagues to denote an ipsilateral response occurring earlier than the corresponding contralateral one.

The crucial work on the corpus callosum was performed in a patient with an angiographically proven tumour in this area (Goya, 1976). When either median nerve was stimulated electrically, only a contralateral response could be recorded, the delayed ipsilateral response expected in normals being abolished completely. Not only does this demonstrate that the ipsilateral response in normals is not just an artefact produced by an active reference electrode, but that it is dependent on the integrity of the corpus callosum, thus validating the contralateral-ipsilateral latency difference as a measure of conduction time. It also gives the lie to Professor Shagass' confident assertion that such a conducting pathway does not exist, a view derived apparently by over-generalisation from the anatomy of monkeys.

Shagass has re-iterated Connolly's clanger (*Journal,* April 1982, **140,** 429–30) in believing that patients with agenesis of the corpus callosum have split-brain symptoms and signs, which they most certainly do not (Sperry, 1968). Furthermore, neuropathological work published subsequent to, and perhaps partially stimulated by our predictions, has shown gliosis of the corpus callosum in late onset schizophrenia (Nasrallah, *Journal,* July 1982, **141,** 99–100), and thickening in early onset disease (Bigelow *et al, Journal,* March 1982, **142,** 284–7).

Further research seems indicated in this controversial field. One of us has been using visual evoked potentials as an independent measure of corpus callosum function, and these results will be submitted shortly.

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