

LETTER TO THE EDITOR

CHANGES IN COGNITIVE FUNCTIONS IN EPILEPTICS ON SODIUM VALPROATE MONOTHERAPY

Sir

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Virtually all anti-epileptic drugs (A.E.D's) can affect mental functions. Greater attention is now being given by epileptologists in assessing cognitive effects of A.E.D's with a view to offer the patients excellent seizure control with least possible negative impact in cognition. Sodium valproate has the advantage of causing minimal dysfunction in cognitive functions as compared to other well known A.E.D's (1). The present study was designed to observe changes in psychomotor and cognitive functions in epileptics taking monotherapy of sodium valproate and correlate these changes if any with serum levels of valproic acid..

Twenty male and female patients of primary generalised tonic-clonic seizure disorder, taking monotherapy of sodium valproate since more than 1 year, were selected from O.P.D. of Neurology in the Gandhi Memorial & Associated Hospitals, Lucknow for this study. Their age range was 15-30 years (Mean  $22.4 \pm 3.2$ ). Care was taken that their intellectual and social capability was adequate for reliability of medication and performance of tests of cognition. Patients with history of head injury, cerebrovascular accidents, diabetes, ICSOL's, alcoholism or any other addiction were not included in the study. Patients of hepato-renal/hemopoietic, or such like disorders contraindicating use of the above drug, were also not considered. Informed consent was obtained from all patients prior to their inclusion. A written format comprising of simple and commonly used questions grouped together as tests of orientation, attention, memory (recent and remote), immediate recall, general knowledge, calculation and compre-

hension were used for assessment of cognitive functions. Patients after a complete interview were awarded different scores (modified WAIS) established especially for Indian population (2).

*Bender Gestalt Test (B.G.T.)* - The B.G.T. cards were used to analyse visuospatial functions. These cards (9 in number) were displayed one after another in a fixed defined sequence to the patients who were instructed to copy them on a single sheet of paper. No time limit was present and eraser was allowed. Scores were awarded according to (Hains methods) as 0-5 = Normal; 6-12 = Border line and 13-24 = critical of visual motor incoordination. Serum valproic acid was estimated simultaneously, using the Fluorescence Polar Immunoassay Analyser (FPIA). All the 20 patients were revalued every 3 months.

There was no significant alteration in any of the parameters of cognition, except immediate recall and BGT score, which showed a tendency to improve between visit I and III i. e. after 9 months of initial evaluation (Table I). There was no correlation between serum levels of valproic acid and cognitive functions.

Studies on changes in cognitive functions on using Sodium Valproate have been difficult to gauge because of its recent advent, as well as non systematic and inconsistent findings (3). Immediate recall and BGT recording showing improvement of sodium valproate has been observed by other authors (3) also who have reported that patients become more active, more alert and cooperative, hence easier to manage.

TABLE I : Cognitive functions during different visits (M±SEM).

Functions	Max score	Visit I	Visit II	Visit III
Orientation	5	5±0	5±0	5±0
Calculation	12	7.45±0.82	7.60±0.94	7.60±0.99
General knowledge	11	7.95±0.6	8.05±0.75	8.10±0.71
Comprehension	6	4.5±0.60	4.7±0.571	4.6±0.598
Attention	34	27.7±2.38	28.05±2.38	28.2±2.56
Immediate Recall	130	119.10±3.25	102.05±3.08	121.25±3.41*
Recent Memory	5	4.75±0.44	4.65±0.48	4.70±0.47
Past Memory	10	8.45±0.51	8.45±0.60	8.45±0.60
B.G.T. Scoring	6	5.25±1.11	4.60±1.09	4.3±0.92*
Valproic acid levels (µg/ml)	-	24.33±21.49	44.54±20.67	40.76±13.75

\*P&lt;.01

Hasan et al (4) reported a better school performance in children using sodium valproate. However, detrimental effect of sodium valproate has also been reported by Thompson (5) who observed slowing down of mental process, especially when demand for task is increased. Sommerback (6) also observed deleterious effect of sodium valproate, by commenting that it "reduced psychomotor tempo functions". In the present study, no correlation was observed between serum valproic acid levels and cognitive functions, concluding that sodium valproate, especially when used in monotherapy causes no impairment of cognitive functions.

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## REFERENCES

1. Gram L. Experimental studies and controlled clinical testing of valproate and vigabatrin, *Acta Neurol Science* 1988; 78:241-270.
2. Srivastava PK, Agarwal AK, Kumar S. Effect of education on some clinical tests used in mental status examination. *I J Psy* 1989; 31 (2) : 134-138.
3. Haigh H, Forsythe WI. The treatment of childhood epilepsy with sodium valproate. *Dev Med Child Neurol* 1975; 17 : 743-748.
4. Hasan MN Lalji HCK, Parsonage MG. Sodium valproate in the treatment of resistant epilepsy. *Acta Neurologica Scandinavica* 1976; 54 : 209-218.
5. Thompson PJ, Trimble MR. Sodium valproate and cognitive functioning in normal volunteers. *Br J Clin Pharmacol* 1981; 12 : 819-824.
6. Sommerback KW, Theilgard A, Rasmussen KE, Lohrera V, Gram L, Wulff K. Valproate sodium: Evaluation of the so called psychotropic effects. A controlled study. *Epilepsia* 1977; 18 : 159-166.

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