ORIGINAL ARTICLE

Simple Reaction Time: Simple Measure To Quantify Quality of Life of Epileptics

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Abstract

The most activities of CNS are initiated by sensory experience emanating from receptions from eyes and ears and causes immediate reaction from brain. In epileptic patient, neuronal metabolic disturbances produces prolonged depolarization and require antiepileptic drugs to stabilized seizure which decreases responsiveness of neurons to excitation and doesn't necessarily correct the specific etiology of seizure. Considering all these factors, there is need to measure quality of life in patients in order to optimize the outcome by more appropriate intervention, hence simple reaction time (RT) studies for Red, Green, Indigo colors and high and low frequency auditory stimuli was carried out on 40 epileptic subjects (F-20& M -20) and compare with age and sex matched controlled. RTs were found to be delayed in female but failed to reach significance. (Red=173.85±27.63, Green = 175±26.22, Indigo=174.25±24.58, High=171.20±23.63, Low= 177.60±26.13). In males RT for red color was highly significant and rest of parameters was insignificant. (Red=196.40±41.72 {p-0.06}, green=193.45±52.72 Indigo=192.40±40.19, high=187.90±22.45, low= 201.00 ±50.64). The RTs were insignificantly shortened in female epileptic when compared with male epileptics. Also we found significant rise in male epileptics taking polytherepy. The reaction time shows insignificant effect on prolonged use of drugs but that has to be verified with further studies. In concluding, unpleasant effects of drugs can be reduced with meticulous selection and proper dose of AED. This study also suggests reaction analyzer as a better non invasive alternative tool for regular evaluation of hypo reflexes in epileptic patients.

Key Words

Reaction time, Antiepileptic Drugs, Epilepsy, Polytherepy

Introduction

Constant interaction with dynamic environment from riding vehicle to segmenting speech, listening music to drawing painting makes one sensitive to sequential structure of the world, a crucial dimension of cognitive system. These volitional movements are rarely generated by apparent sensory stimulus and can typically executed over longer time period due to esoteric factors viz. attention, motivation and therefore may be under the influence of many neuronal structures scattered throughout the CNS (1). In epilepsy neuronal structure itself are affected and requires several years and decades administration of antiepileptic drugs (AEDs) to control the seizures. Most of the drugs are neuronal depressant and act on normal neuron with certain variation in actions. Reports of prevalence of epilepsy of stands at around 5 per1000 in India (2). Many patients manage to achieve good control, still 1/3 of people live with persistent seizures and left to cope up with consequences of both seizures and drugs.Patients experience significant adverse side effects particularly cognitive effects (3, 4). Thus epilepsy per se has considerable negative impact on quality of life of patients and to which extends, remains unanswerable.

The most dependent variable to study the motor skills of these subjects is reaction time (RT), which is domain of cognition. Reaction time is the time interval between the application of stimulus &appearance of appropriate voluntary response in the subjects (5). The reaction time provides a tool for measuring time required for mental operation and hence provide a window on cognitive process that takes place between presentation of information and thereby measuring their quality of life. Thus the present work is an attempt to find out the reaction time of the patient taking anti epileptic drugs in normal, delayed or shortened?

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Study Design

It is cross sectional study carried out at department of physiology after obtaining permission from institutational ethical committee, Indira Gandhi Medical Collage, Nagpur. The consent followed by detailed history and examination was carried out on 80 subjects, grouped as 20 epileptic female(FE) and 20 male epileptics(ME) in age group of 15-30yrs; and age and sex matched 40 control, 20 female(FC) and male(MC) in each group, according to predesigned proforma .

Selection of patients

All epileptics Patients were registered patients of epileptic clinic, IGGMC Nagpur and were either on single drug or combination of four drug regimen {Phenobarbital(PHB)-60-80mg/day, Phenytoin(PHT)-100-300mg/day, Carbamazepine(CBZ)-200-600mg/day and Sodium Valproate(VPA)-500-1000mg/day) and Tab. Folic acid and Multivitamin capsule. The patients were free from seizure at least for one month. The detailed clinical examination including neurological, ophthalmic and audiometric examination carried out and patients having mental retardation, cerebral palsy and conductive deafness were excluded from studies (5)(6)(7). According to the regimen (Monotherapy and Polytherapy) and duration of drug treatment (<3 and > 3) we further grouped the patients and compared. The respect was given to CBZ monotherpy and PHT+ CBZ polytherapy in males as rest of sample size was inadequate. (*Fig1)*

Selection of control

The age sex matched control group obtained from common population and mayo hospital campus. Subjects were tested for visual acuity, Ischara colour test and Audiometry and subjects with colour, visual and acoustic handicapped were excluded (7)(8). All the controls had sound physical and mental health and neither on any medication, therapy or any kind of placebo.

Method

Visual reaction time for Red, Green, Indigo colour and Auditory reaction time using high and low frequency mode were measured by device "Response Analyzer" by Yantrashilpa ,Pune. Before measuring parameters each subjects has been made familiar with machine and procedure to alleviate any fear or apprehension. Subjects had provided sufficient time to accommodate with instrument. All subjects were right handed and RT was measured using right hand in quite room with good visible condition. All the connection and procedure was done according to the manual of machine. The required stimulus applied by pressing side button and the subject responded by pressing the response key by right index finger. The auto display on the analyzer indicates reaction time. The RTs were recorded for Red, Green Indigo colour and High, Low frequency sounds. The lowest minimum reading was considered (5).The foreperiod for stimulus was changed consistently and throughout procedure to reduced expectancy and warning signals were given prior to each procedure (9).

Statistical Analysis

Data obtained was grouped, mean (x), Standard deviation (SD) calculated and values of patients and control were compared using students t - Test wherever possible. The association of reaction time and duration of treatment was evaluated by using Pearson's correlation and significance was asses by scheming p value.

Results

(1) Our study shows lowest RTs in male control (MC) and Highest RTs in male epileptic (ME), followed by female epileptics (FE) and Female control (FC) group. Male epileptic group on polytherepy shows highest RTs in subgroups (*Table.I & Fig.2).*

(2)Visual and auditory reaction times were insignificantly delayed in FE group when compared with FC group. In ME group, reaction time for red colour was highly significant (p=0.06) when compared with MC and rest of parameters was insignificant (*Table.II*)

(3) The reaction times were more insignificantly delayed in Male epileptics as compared to female epileptics (*Table.II*)

(4) Our study shows significant rise in RTs in male epileptics taking polytherepy {Red(P=0.09),Green

Table. 1 Showing Mean + Standard Deviation of Different Group of Subjects

Subjects	Red	Green	Indigo	High	Low
FE (n=20)	173.85 ± 26.63	175.0 ± 26.22	174.25 ± 24.58	171.20 ± 23.63	177.60 ± 6.13
FC (n=20)	151.63 ± 9.03	152.35 ± 6.56	151.20 ± 7.41	148.30 ± 8.49	151.30 ± 7.71
ME (n=20)	196.4 ± 41.72	193.45 ± 52.72	192.40 ± 40.19	187. 0 ± 22.45	201.00 ± 50.64
MC (n=20)	140.45 ± 6.26	139.55 ± 5.83	139.85 ± 6.42	137.85 ± 5.42	140.20 ± 5.6
FE on CBZ (n=15)	167.47± 19.52	167.33 ± 21.43	168.53 ± 19.73	165.60 ± 15.69	171.13 ± 19.11
ME on CBZ (n=8)	192.75 ± 63.63	190.00 ± 84.76	191.50 ± 59.59	182.38 ± 28.31	194.25 ± 56.56
ME on PHT + CBZ (n=7)	201.14 ± 7.13	192.71 ± 9.12	189.57 ± 21.14	188.42 ± 16.66	198.85 ± 12.59

FE -female epileptic, ME-Male epileptic, FC-female control, MC-male control CBZ-carbamazepine, PHT-phenytoin

Fig.2 Bar Diagram Showings Mean Reaction Times of Different Groups and Subgroup

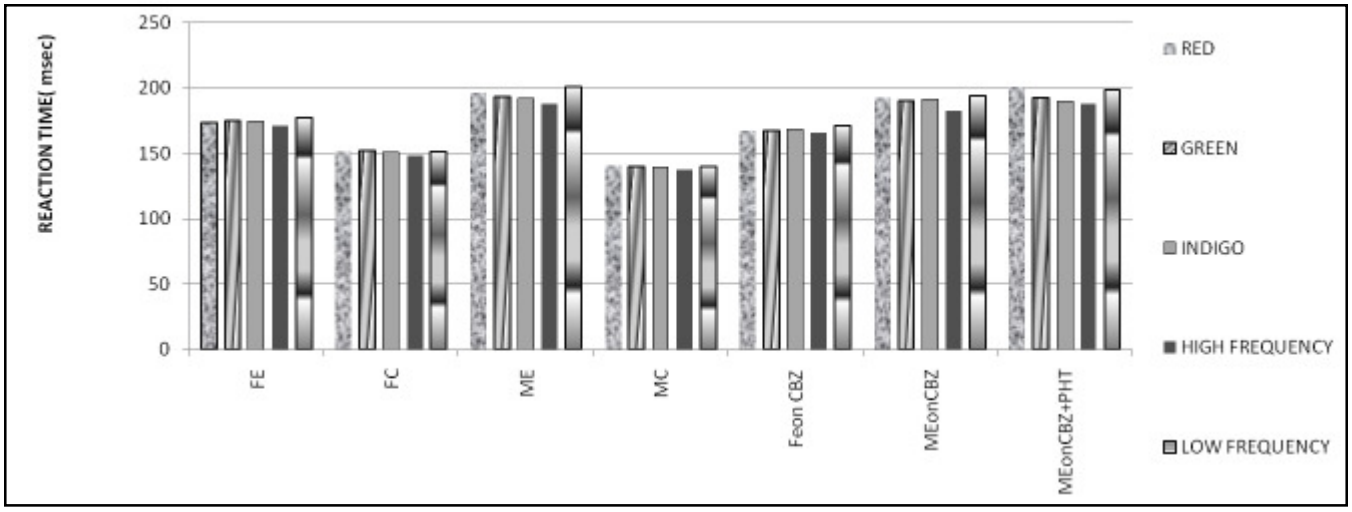

Fig.2 Piechart Showing Distribution of Drugs in Percentage in Epileptic Patients

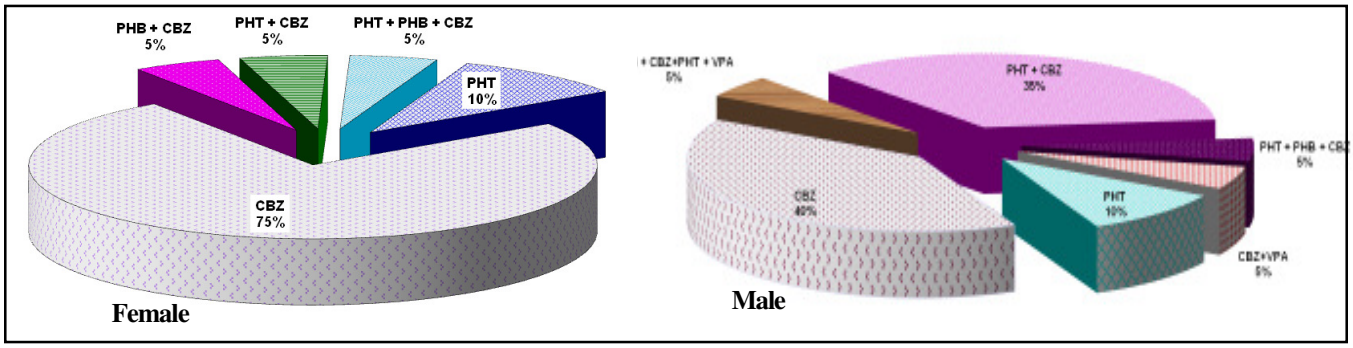

Fig.3 Scattered Diagram Showing Relationship Between Reaction Time and Duration of Drug Treatment

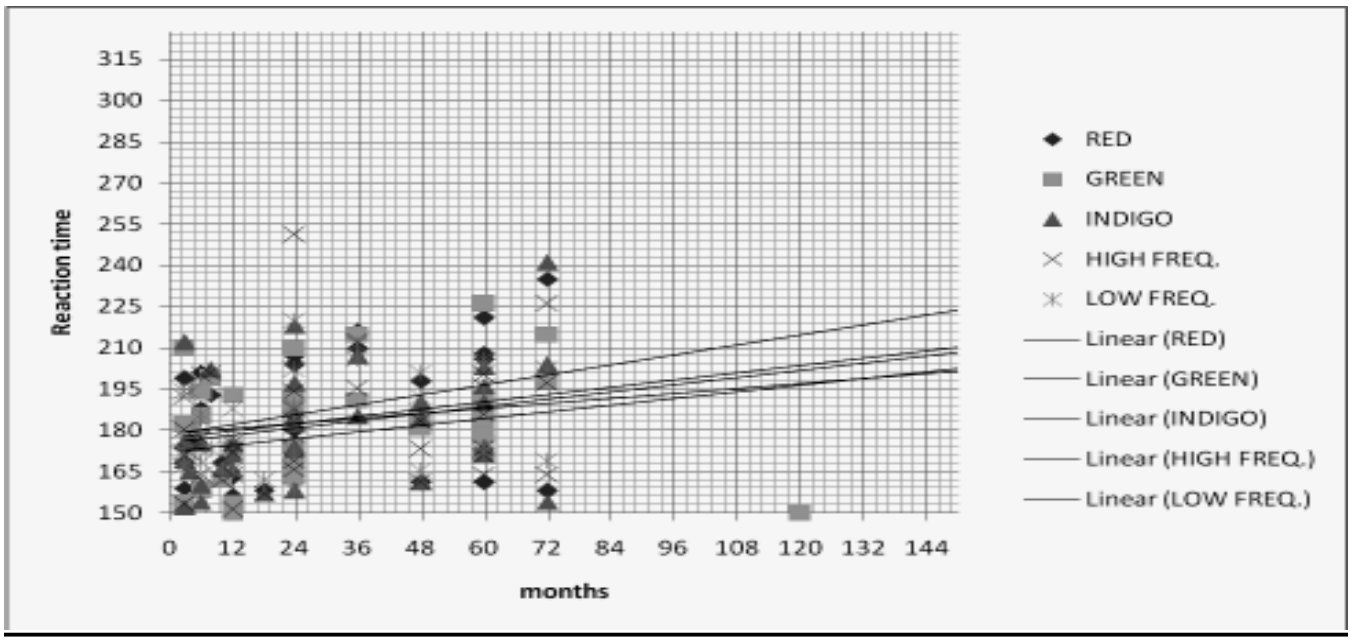

Table 2. 't' Value for Comparisons of Different Groups

Comparisons	Red	Green	Indigo	High	Low	Remark
FE Vs FC	0.001103	0.00058	0.00028	0.00022	0.00014	FE - Insig. .delayed
ME Vs MC	4.346 (P=0.06)	0.0861	0.0473	0.0138	0.0383	ME - Sig. delayed
FE Vs ME	0.0259	0.0861	0.0473	0.0138	0.03839	ME - Insig. delayed
FC Vs FE on CBZ	0.00403	0.00935	0.00282	0.00048	0.00069	FE on CBZ - Insig. delayed
MC Vs ME on CBZ	0.02655	0.06815	0.02204	0.00144	0.01526	ME on CBZ - Insig. delayed
FE on CBZ Vs ME on CBZ	0.2140	0.3955	0.2143	0.0496	0.2617	ME on CBZ - Insig. delayed
ME Vs ME on PHT+CBZ	2.3312 (P=0.09)	3.3454 (P=0.09)	0.00034	7.6422 (P=0.05)	3.9258 (P=0.06)	ME on PHT+CBZ – H Sig. delayed
ME on CBZ Vs ME on PHT+CBZ	0.36086	0.46537	0.46684	0.30920	0.19323	ME on PHT+CBZ – Insig. delayed

(P=0.09, High(P=0.05),Low (P=0.06)} when compared with MC group except for Indigo colour (*Table II)* .

(5). The reaction time shows insignificant effect on prolonged use of drugs with verified range of 3 months to 16 years in male and female. Our study shows moderate to weak association of RTs with duration of drug treatment. Females taking drugs < 3yrs found to have weak negative correlation and male taking drugs > 3yrs group found to have weak negative correlation, but that has to be verified with further studies.(*Table III and Fig 3*).

Discussion

A number of studies claim drugs induced side effects have much greater impact on daily life functioning (10, 11).In epileptic patients there exist slowing of cognitive process between evaluation of stimulus and motor response and this can be improved when reduced but efficient therapy is given. All this consequences now represents a major issue in clinical assessments, hence

Table 3.'r' Value for Correlations of Reaction Time with Duration of Drug T/t in Different Groups & Ssubgroups

Subjects	Red	Green	Indigo	High	Low
FE (n=20)	0.4643 (P = 0.02)	0.3914	0.4834 (P = 0.03)	0.5197 (P= 0.01)	0.4854 (P= 0.03)
ME (n=20)	0.0815	0.0027	0.11108	0.0772	0.025519
FE <3 yrs (n=12)	- 0.5856 (P = 0.05)	- 0.2751	- 0.2333	- 0.3747	- 0.5033
FE≥3yrs (n=8)	0.2520	0.3863	0.4991	0.4765	0.3586
ME <3yrs (n=12)	0.3812	0.2981	0.4221	0.1504	0.3819
ME≥3yrs (n=8)	- 0. 1233	- 0.0515	- 0.0253	- 0.0594	0.2653

the present study was carried out to find out the outcome of use of AED in epileptics by using simple visual and auditory reaction time paradigm, thereby measuring their daily quality of life.In present study we segregated the control, and Epileptic also, in Female and Male groups as previous studies denotes difference in RTs in normal male and females (12,13).and we also got similar difference that reaction times delayed in female in normal subjects .But in epileptic group RTs were delayed in Males as compared to female which was not been assessed in most of the previous studies on epileptics. (*Table.I, Fig.2*). Consistently we found reaction time increased, but failed to reach significance in epileptic group both in male and female as compared to their normal counterparts(*Table2*); similar with the findings by Nesek-Madric *et al* (14) & Alpherts WCJ *et.al* (15) studies except for red colour in male epileptics where it was highly significant with p value 0.006 (*Table.II*) , possibly the AEDs affect the colour vision(16)and had more impact on red colour. Contradictory to the previous reports where reaction time prolongation was more marked in newer healthy control (17), our study shows insignificant delayed RT in epileptic patients who consumed AED for varied duration starting from 3months to 16 years. Many studies suggest AED induced cognitive side effects, increased by rapid initiation, higher doses and polytherapy(18), (19).Considerable evidence also suggest antiepileptic drugs may slow conduction in the central (20) and peripheral nervous system and have depressant effects on neuronal function independent of clinical antiepileptic effect or sedation (21) , and also CBZ was found to have slow nerve conduction in seizure patient (22) and several reports had linked Phenytoin intoxication to nerve conduction slowing (23) but few shows good prognosis of CBZ as compared to other drugs (24, 25).We also got

similar findings that, only polytherapy patients tends to show longer reaction time than monotherapy or controls as maximum number of monotherapy patients received CBZ (*Table 1,II,Fig.1*) and this reaction time prolongation in polytherapy maybe ascribable to synergistic combination of drug or underlying individual brain functioning(26). Moreover frequently repeated seizures typically associated with more severe effect on cognitive functioning, particularly if epilepsy is symptomatic i.e. Secondary to demonstrable brain lesion.(27)& generally required polytherapy for its refractoriness so as to in refractory epileptic subjects. Thus refractoriness plus combination of polytherapy drugs can be substantial reason for significant rise in reaction time in patient receiving polytherapy. Also in our study antiepileptic medicine increase was steady. The patients were not as numerous as in earlier studies, although they were ambulatory epileptic patient population taking single or multiple antiepileptic drug regimes with adequate seizure control. A relatively greater population of patient was taking CBZ or an adjunctive PHT while fewer were on PHB or VPA.

There is also evidence of derangement of central higher cortical processing system by PHT and the patient on PHT suffer from cognitive side effects even when the medication is sufficiently control and the drugs are given within the assume therapeutical interval as compared to CBZ(24). And this could be the possible reason for rising reaction time in the patient on polytherapy than monotherapy patient. The present study also made an attempt to find out the effect of antiepileptic drug exposure for certain longitivity on reaction time and found insignificant correlation of RT with duration of drug treatment in males and moderate correlation in female . Also females taking drugs less than 3year and male taking drugs more than 3years duration shows negative correlations(*Table 3 , Fig3*), similar findings are there for few nerve conduction studies(28), but still this findings has to be verified with further research.

The differences in male and female reaction time possibly due to different processing strategies(12)and stress handling(13) or the difference in reaction time could be due to the effect of hormonal variance(29)or could be physiological gender difference arising from biologically based differences in hemispheric asymmetry(30).Thus all this contributed in showing the differences in female and male counterparts.

The present study shows good findings that drug suppresses the epileptic epicenter but doesn't significantly increase the reaction time. If hypothetically the reaction would have increased, it might have been precipitated hypoactive state i.e. Slowing of sensory perception, slow central processing and slow motor output, and hence would results in slow outcome. Thus the whole system would have gone in hyporeflexia. This slowing would have deteriorated the quality of life and drugs would have been useless. This is helpful for the patients as the patient getting relief from epilepsy without interferable neuronal depression and improves the quality of life of patient.

Conclusion

Thus in conclusion the present study shows that drug suppresses epicenter, but no significant effect on sensory motor and central processing output and neuronal and neural signals transmission links so that the drugs mainly Carbamazepine can be considered as useful drugs to give relief from epileptic attacks with minimum neurological deficit with controlled monitoring. Still, males are affected more than Females and required longer duration of treatment to improve reaction time, but that has to be verified. Although antiepileptic drugs can impair neurophysiological functioning, meticulous selection of patients and controlled drug treatment can minimize the untoward effect of drugs and their positive effect on seizure might improves functioning .As polytherapy patients tends to show increase reaction time, hence should be assessed regularly. Thus Reaction analyszer provides a simple non invasive measure to asses neurological deficit in epileptic patients if coupled with visual and acoustic checkups.

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