CHAPTER IV

RESULTS

1. Subject characteristics.

During November 2004 to February 2006, 30 epileptic patients and 15 normal volunteers were enrolled in the present study. Subjects consisted of 27 males and 18 females with age ranging from 15 – 52 years. The average age of the subjects was 31.13 ± 10.52, 28.13 ± 10.64, and 31.60 ± 8.17 years for normal volunteer, epileptic patients receiving sodium valproate (VPA group), and epileptic patients receiving phenytoin (PHT group), respectively. As shown in Table 21 no statistically significant was noted among the three groups with regards to average age, TMSE, and AUDIT score. However, 11 out of 15 in normal volunteers group have had education that equal to or higher than the bachelor degree where as the corresponding number in VPA and PHT groups were 5 and 4 patients, respectively. Localized-related epilepsy was a major type of epilepsy in epileptic group (28.89%) and 90% of epileptic patients were seizure free during an enrollment. The average dose per day of PHT and VPA groups were 296.67 ± 44.19 mg/day (median 300 mg/day, range 250 – 300 mg/day) and 1,020 ± 501.36 mg/day (median 1,000 mg/day, range 250 – 2,000 mg/day), respectively. The average blood levels of PHT (13.44 ± 9.31) and VPA (76.39 ± 33.67) (Table 21) were within the therapeutic range. However, fluctuation of these values in individual patients did exist and the details of deviation exhibited by them were shown in Appendix C.

2. Laboratory investigation

There were no abnormal findings of laboratory parameters of all subjects. (Appendix D)

3. Neuropsychological examinations

3.1 Stroop Color Word Test

3.1.1 Reliability

Verifying of Stroop test reliability was done by Test-Retest reliability technique. The correlation coefficient of Pearson's Product Moment exhibits high correlation coefficient values as shown below

Word test; correlation coefficient for a comparison between baseline versus visit 1, visit 1 versus visit 2, and baseline versus visit 2 were 0.920, 0.935, and 0.936, respectively. ($p < 0.0001$).

Color test; correlation coefficient for a comparison between baseline versus visit 1, visit 1 versus visit 2, and baseline versus visit 2 were 0.884, 0.867, and 0.890, respectively. ($p < 0.0001$).

Color-Word test; correlation coefficient for a comparison between baseline versus visit 1, visit 1 versus visit 2, and baseline versus visit 2 were 0.770, 0.716, and 0.835, respectively. ($p < 0.0001$).

3.1.2 SCWT score

In each subtests of Stroop Color Word Test (SCWT), word score (Table 22), color score (Table 23), and color-word score (Table 24) were obtained. Standard score of word score, color score, and color-word score was used to determine ability of reading. For word score, subject who got word score less than 75 was classified as 'failed' category. Similarly, subjects who got score less than 58 for color score and 25 for color-word score were also classified as 'failed'. (Table 25 – 28)

As shown in Table 22 the word score of normal volunteer group, VPA-group, and PHT group were found to be no statistically significant differences among the 3 groups of subjects (94.73 $\pm$ 9.46, 92.87 $\pm$ 9.69, and 90.04 $\pm$ 15.51). Rather similar profile was found in color score (72.91 $\pm$ 13.02, 70.42 $\pm$ 11.94, and 66.76 $\pm$ 14.71) and color-word score (39.16 $\pm$ 8.67, 42.67 $\pm$ 8.38, 38.40 $\pm$ 9.21) of respective groups.

Interference score was calculated by equation in page 44. The more positive the score obtained in interference score, the better the performance of attention. The scores were found to be -1.64 $\pm$ 6.04 for normal volunteers. Whereas, they were 2.86 $\pm$ 4.64 and 0.36 $\pm$ 5.60 for VPA and PHT groups, respectively. There was statistically a significance difference between VPA group versus normal volunteer group.

3.2 WASI®

3.2.1 Reliability

Verifying of reliability of WASI® test was done by Test-Retest reliability technique. The correlation coefficient of Pearson's Product Moment exhibits high correlation coefficient values.

Vocabulary subtest; correlation coefficient for a comparison between baseline versus visit 1, visit 1 versus visit 2, and baseline versus visit 2 were 0.988, 0.985, and 0.994, respectively. ($p < 0.0001$).

Block design subtest; correlation coefficient for a comparison between baseline versus visit 1, visit 1 versus visit 2, and baseline versus visit 2 were 0.865, 0.935, and 0.861, respectively. ($p < 0.0001$).

Similarities subtest; correlation coefficient for a comparison between baseline versus visit 1, visit 1 versus visit 2, and baseline versus visit 2 were 0.892, 0.946, and 0.876, respectively. ($p < 0.0001$).

Matrix reasoning subtest; correlation coefficient for a comparison between baseline versus visit 1, visit 1 versus visit 2, and baseline versus visit 2 were 0.769, 0.833, and 0.757, respectively. ($p < 0.0001$).

3.2.2 WASI® score, *T* score of subtests

From WASI® test, four *T* scores of subtests; Vocabulary *T* score (Table 30), Block design *T* score (Table 31), Similarities *T* score (Table 32), and Matrix reasoning *T* score (Table 33) were obtained; VIQ score, PIQ score, FSIQ-4 score, and FSIQ-2 score were derived follow WASI® manual. The higher score obtained in WASI®, the better the performance.

No statistical difference was detected in vocabulary and block design subtests (Table 30 – 31). However, VPA and PHT groups demonstrated statistically significant lower ability in similarities subtest than those of normal volunteers (48.91 $\pm$ 9.59, 42.20 $\pm$ 11.74, and 42.13 $\pm$ 10.59, for normal volunteers, VPA, and PHT group respectively). Moreover, for PHT group poorer performance in matrix reasoning was also observed with respect to normal volunteers or VPA group (49.51 $\pm$ 9.93, 44.33 $\pm$ 12.04, and 37.91 $\pm$ 12.63, for normal volunteers, VPA and PHT group respectively).

3.2.3 WASI® score, VIQ, PIQ, FSIQ-4, and FSIQ-2 score

From four *T* score of WASI® subtests VIQ, PIQ, FSIQ-4, and FSIQ-2 score were obtained. VIQ score was a summation of *T* score of vocabulary and similarities. (Table 34) Whereas, PIQ score was a summation of *T* score of block design and matrix reasoning. (Table 35). In addition, FSIQ-4 score was obtained by a summation of VIQ and PIQ score but, FSIQ-2 score was obtained by a summation of *T* score of vocabulary and matrix reasoning. (Table 36 – 37)

Significant differences between PHT group and normal volunteers were further observed in PIQ, FSIQ-4, and FSIQ-2 score. Whereas, their VIQ score were not statistically different. Furthermore, the PIQ score of PHT group was even statistically lower than that of VPA group (88.31 $\pm$ 14.81 versus 95.69 $\pm$ 12.92). Unlike PHT group, VPA group did not demonstrated any significant differences to normal volunteers with regard to VIQ, PIQ, FSIQ-4, and FSIQ-2.

3.3 POMS®

3.3.1 Reliability

Verifying of reliability of POMS® test was done by internal consistency technique. Cronbach's alpha exhibits high reliability value. Alpha exhibits 0.9511, 0.9545, 0.9541, and 0.9535 for baseline, visit 1, visit 2, and overall testing consecutively. In addition, standardized item alpha exhibits 0.9465, 0.9499, 0.9505, and 0.9491 for baseline, visit 1, visit 2, and overall testing consecutively.

3.3.2 POMS® score; tension, depression, anxiety, confusion, fatigue, vigor, and TMD score

From self-administered questionnaires, POMS® test, six dimensions of mood; tension (Table 37), depression (Table 38), anxiety (Table 39), confusion (Table 40), fatigue (Table 41), and vigor score (Table 42) were obtained. The higher score obtained in dimensions of tension, depression, anxiety, confusion, and TMD, the poorer the mood status. Whereas, the higher the score obtained in dimension of vigor, the better the mood status. After completion of the test, raw score of questionnaire was filled in POMS® standard scoring grid to evaluate mood profile. (Fig. 14) In addition, TMD, showing degree of mood disturbance, was calculated from the obtained six dimensions of mood using the following equation.

TMD score = (Tension score + Depression score + Anxiety score + Confusion score + Fatigue score) – Vigor score

Among the 3 groups, no significant difference in all dimensions of mood tested were found except the dimension of vigor in which the score obtained by VPA and PHT group were statistically significant lower than of normal volunteers. Accordingly, TMD score which is the net effect of all mood dimensions was rather similar across the 3 groups tested. (Table 43)

4. Adverse events evaluation; AEP score

4.1 Reliability

Verify reliability of AEP was done by internal consistency technique. Cronbach's alpha exhibits high reliability value. Alpha exhibits 0.8718, 0.8336, 0.8474, and 0.8595 for baseline, visit 1, visit 2, and overall testing consecutively. In addition, Standardized item alpha exhibits 0.8712, 0.8304, 0.8580, and 0.8620 for baseline, visit 1, visit 2, and overall testing consecutively.

4.2 AEP score

Modified form of Adverse event profile (AEP) was the tool to evaluate adverse event of subjects during research conducting. The higher the score obtained in AEP score, the poorer the adverse events.

There was no statistically significant difference among 3 groups. (Table 44) However, there were statistically significant differences in four sub-items among 3 groups in sub-items analysis. (Table 45)

Table 21 Subject characteristics

	Normal Volunteers (N = 15)	Sodium Valproate (N = 15)	Phenytoin (N = 15)
Sex:			
Male/Female	9/6	10/5	8/7
Age[1]:			
15-24	4	9	3
25-34	5	1	7
35-44	4	5	4
> 45	2	0	1
Education:			
< Bachelor degree	4	10	11
Bachelor degree	10	3	3
> Bachelor degree	1	2	1
Type of Epilepsy:			
Generalized-related	-	3	5
Localized-related	-	6	8
Unspecified or N/A	-	6	2
TMSE score[2]			
Mean $\pm$ S.D.	28.80 $\pm$ 1.26	29.07 $\pm$ 1.03	28.13 $\pm$ 1.96
AUDIT score[3]			
Mean $\pm$ S.D.	0.47 $\pm$ 1.81	0.47 $\pm$ 1.81	0 $\pm$ 0

Table 21 Subject characteristics (continued)

	Normal Volunteers (N = 15)	Sodium Valproate (N = 15)	Phenytoin (N = 15)
Sodium valproate blood levels[4] (mcg/mL) (Mean ± S.D.)			
Baseline	-	75.99 ± 36.37	-
Visit 1	-	75.50 ± 33.06	-
Visit 2	-	77.68 ± 33.85	-
Average	-	**76.39 ± 33.67**	-
Phenytoin blood levels[5] (mcg/mL) (Mean ± S.D.)			
Baseline	-	-	13.25 ± 9.03
Visit 1	-	-	14.11 ± 10.10
Visit 2	-	-	12.95 ± 9.37
Average	-	-	**13.44 ± 9.31**

[1]no statistically difference (H = 2.005, p = 0.367)

[2]no statistically difference (H = 1.527, p = 0.466)

[3]no statistically difference (H = 1.023, p = 0.600)

[4]therapeutic range 50 – 100 mcg/mL

[5]therapeutic range 10 – 20 mcg/mL

Table 22 Stroop Color Word Test: Word score of subject in 3 different groups.

	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)
Baseline (mean ± S.D.)	94.47 ± 9.30	91.93 ± 9.91	89.53 ± 16.41
Visit 1 (mean ± S.D.)	94.60 ± 10.08	92.87 ± 9.78	89.87 ± 15.17
Visit 2 (mean ± S.D.)	95.13 ± 9.38	93.80 ± 10.23	90.73 ± 16.18
Average[1] (mean ± S.D.)	**94.73 ± 9.46**	**92.87 ± 9.69**	**90.04 ± 15.51**
Median	**100**	**100**	**100**

[1]Kruskal-Wallis H test (H = 1.946; p = 0.378)

Table 23 Number of subjects who failed in word reading of Stroop Color Word Test[#]

(N = 15 in each group)

	Number of subjects		
	Normal Volunteers	Sodium valproate	Phenytoin
Baseline	1	1	3
Visit 1	1	1	3
Visit 2	1	1	3

[#] using 75 as standard score of Word score

Table 24 Stoop Color Word Test: Color score of subject in 3 different groups.

	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)
Baseline (mean ± S.D.)	70.27 ± 11.89	66.53 ± 12.39	63.73 ± 16.02
Visit 1 (mean ± S.D.)	73.80 ±15.52	70.47 ± 11.81	68.07 ± 14.90
Visit 2 (mean ± S.D.)	74.67 ± 13.60	74.27 ±13.08	68.47 ± 14.62
Average[1] (mean ± S.D.)	**72.91 ± 13.02**	**70.42 ± 11.94**	**66.76 ± 14.71**
Median	**75**	**69**	**69**

[1]One Way Analysis of Variance (F = 2.283; p = 0.106)

Table 25 Number of subjects failed in color reading of Stroop Color Word Test[#] (N = 15 in each group)

	Number of subjects		
	Normal Volunteers	Sodium valproate	Phenytoin
Baseline	2	4	6
Visit 1	2	2	6
Visit 2	1	2	5

[#] using 58 as standard score of Color score

Table 26 Stroop Color Word Test: Color Word score of subject in 3 different groups.

	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)
Baseline (mean ± S.D.)	36.13 ± 9.78	40.40 ± 7.16	36.40 ± 9.95
Visit 1 (mean ± S.D.)	38.47 ± 9.29	41.60 ± 10.53	38.53 ± 9.58
Visit 2 (mean ± S.D.)	42.87 ± 9.61	46 ± 9.73	40.27 ± 9.66
Average[1] (mean ± S.D.)	**39.16 ± 8.67**	**42.67 ± 8.38**	**38.40 ± 9.21**
Median	**38**	**44**	**40**

[1]One Way Analysis of Variance (F = 2.537; p = 0.083)

Table 27 Number of subjects failed in color-word reading of Stroop Color Word Test[#]

(N = 15 in each group)

	Number of subjects		
	Normal Volunteers	Sodium valproate	Phenytoin
Baseline	1	1	2
Visit 1	1	1	0
Visit 2	0	0	0

[#] using 25 as standard score of Color-Word score

Table 28 Stroop Color Word Test: Interference score of subject in 3 different groups.

	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)
Baseline (mean ± S.D.)	-3.91 ± 7.48	2.01 ± 4.41	-0.46 ± 5.54
Visit 1 (mean ± S.D.)	-2.60 ± 7.50	1.83 ± 7.91	0.08 ± 7.42
Visit 2 (mean ± S.D.)	1.59 ± 7.11	4.74 ± 5.93	1.44 ± 6.42
Average[1] (mean ± S.D.)	**-1.64 ± 6.04**	**2.86 ± 4.64***	**0.36 ± 5.60**
Median	**-2.810**	**3.140**	**0.180**

[1]One Way Analysis of Variance (F = 4.983; p = 0.008)

*Bonferroni t-test (t = 3.150, p < 0.05; compared with normal volunteer group)

Table 29 WASI® test: *T* score of Vocabulary test in 3 different groups.

	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)
Baseline (mean ± S.D.)	51.40 ± 13.26	48.20 ± 16.62	48.33 ± 16.35
Visit 1 (mean ± S.D.)	51.27 ± 13.07	47.80 ± 16.98	48.33 ± 16.35
Visit 2 (mean ± S.D.)	51.00 ± 13.16	47.13 ± 16.15	48.33 ± 16.35
Average[1] (mean ± S.D.)	**51.22 ± 12.86**	**47.71 ± 16.21**	**48.33 ± 15.98**
Median	**49**	**50**	**48**

[1]Kruskal-Wallis H test (H = 0.387; p = 0.824)

Table 30 WASI® test: *T* score of Block design test in 3 different groups.

	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)
Baseline (mean ± S.D.)	47.93 ± 10.33	48.07 ± 9.11	45.53 ± 10.49
Visit 1 (mean ± S.D.)	50.47 ± 9.83	52.73 ± 8.54	47.60 ± 9.95
Visit 2 (mean ± S.D.)	50.40 ± 10.32	51.80 ± 9.78	47.00 ± 10.35
Average[1] (mean ± S.D.)	**49.60 ± 10.00**	**50.87 ± 9.18**	**46.71 ± 10.07**
Median	**51**	**54**	**48**

[1]Kruskal-Wallis H test (H = 4.750; p = 0.093)

Table 31 WASI®test: *T* score of Similarities test in 3 different groups.

	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)
Baseline (mean ± S.D.)	49.07 ± 9.79	40.53 ± 11.87	41.80 ± 11.43
Visit 1 (mean ± S.D.)	48.80 ± 9.56	42.80 ± 12.60	41.40 ± 10.71
Visit 2 (mean ± S.D.)	48.87 ± 10.09	43.27 ± 11.36	43.20 ± 10.27
Average[1] (mean ± S.D.)	**48.91 ± 9.59**	**42.20 ± 11.74***	**42.13 ± 10.59****
Median	**49**	**46**	**44**

[1]Kruskal-Wallis H test (H = 8.690; p = 0.013)

*Dunn's method (Q = 2.523, p < 0.05; compared with normal volunteers)

**Dunn's method (Q = 2.581, p < 0.05; compared with normal volunteers)

Table 32 WASI® test: *T* score of Matrix reasoning test in 3 different groups.

	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)
Baseline (mean ± S.D.)	48.20 ± 9.16	44.33 ± 13.28	38.87 ± 12.88
Visit 1 (mean ± S.D.)	50.13 ± 10.75	42.93 ± 11.10	38.13 ± 12.69
Visit 2 (mean ± S.D.)	50.20 ± 10.8	45.73 ± 12.32	36.73 ± 13.10
Average[1] (mean ± S.D.)	**49.51 ± 9.93**	**44.33 ± 12.04**	**37.91 ± 12.63**[*#]
Median	**49**	**47**	**38**

[1]One Way Analysis of Variance ($F = 11.313$; $p < 0.001$)

[*]Bonferroni t-test ($t = 4.748$, $p < 0.05$; compared with normal volunteer group)

[#]Bonferroni t-test ($t = 2.628$, $p < 0.05$; compared with sodium valproate group)

Table 33 WASI® test: VIQ score of subject in 3 different groups.

	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)
Baseline (mean ± S.D.)	101.00 ± 17.70	90.53 ± 20.17	93.60 ± 19.40
Visit 1 (mean ± S.D.)	99.87 ± 17.41	94.00 ± 20.49	93.07 ± 18.75
Visit 2 (mean ± S.D.)	99.67 ± 17.56	93.47 ± 19.34	94.47 ± 18.60
Average[1] (mean ± S.D.)	**100.18 ± 17.27**	**92.67 ± 19.64**	**93.71 ± 18.82**
Median	**100**	**92**	**96**

[1]Kruskal –Wallis H test ($H = 3.187$; $p = 0.203$)

Table 34 WASI® test: PIQ score of subject in 3 different groups.

	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)
Baseline (mean ± S.D.)	96.93 ± 11.20	92.13 ± 14.71	88.20 ± 14.59
Visit 1 (mean ± S.D.)	100.40 ± 12.74	96.53 ± 12.16	89.20 ± 15.26
Visit 2 (mean ± S.D.)	100.20 ± 12.58	98.40 ± 15.57	87.53 ± 16.38
Average[1] (mean ± S.D.)	**99.18 ± 11.43**	**95.69 ± 12.92**	**88.31 ± 14.81*#**
Median	**99**	**96**	**87**

[1]One Way Analysis of Variance (F = 7.262; p = 0.001)

*Bonferroni t-test (t = 3.732, p < 0.05; compared with normal volunteer group)

#Bonferroni t-test (t = 2.534, p < 0.05: compared with sodium valproate group)

Table 35 WASI® test: FSIQ-4 score of subject in 3 different groups.

	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)
Baseline (mean ± S.D.)	98.73 ± 13.88	93.40 ± 16.11	89.73 ± 16.94
Visit 1 (mean ± S.D.)	100.13 ± 14.14	94.73 ± 16.59	90.00 ± 16.75
Visit 2 (mean ± S.D.)	100.00 ± 14.46	95.67 ± 17.22	90.07 ± 16.96
Average[1] (mean ± S.D.)	**99.62 ± 13.83**	**94.60 ± 16.20**	**89.93 ± 16.67***
Median	**97**	**94**	**91**

[1]One Way Analysis of Variance (F = 5.701, p = 0.004)

*Bonferroni t-test (t = 3.363, p < 0.05; compared with normal volunteer group)

Table 36 WASI® test: FSIQ-2 score of subject

	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)
Baseline (mean ± S.D.)	100.33 ± 16.02	95.53 ± 18.87	91.00 ± 20.55
Visit 1 (mean ± S.D.)	101.93 ± 15.57	92.07 ± 17.76	89.93 ± 19.03
Visit 2 (mean ± S.D.)	101.60 ± 17.14	95.27 ± 19.54	89.00 ± 19.23
Average[1] (mean ± S.D.)	**101.29 ± 15.91**	**94.29 ± 18.24**	**89.98 ± 19.11***
Median	**98**	**94**	**94**

[1]One Way Analysis of Variance ($F = 4.591$, $p = 0.012$)

*Bonferroni t-test ($t = 3.002$, $p < 0.05$; compared with normal volunteer group)

Table 37 POMS® test: Tension score of subject in 3 different groups.

	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)
Baseline (mean ± S.D.)	15.93 ± 5.96	14.73 ± 5.04	14.13 ± 6.51
Visit 1 (mean ± S.D.)	14.07 ± 6.01	12.73 ± 4.89	13.20 ± 6.29
Visit 2 (mean ± S.D.)	14.27 ± 6.12	12.73 ± 3.61	13.67 ± 5.74
Average[1] (mean ± S.D.)	**14.76 ± 5.60**	**13.40 ± 0.78**	**13.67 ± 5.72**
Median	**13**	**13**	**13**

[1]Kruskal-Wallis H test ($H = 0.923$; $p = 0.630$)

Table 38 POMS® test: Depression score of subject in 3 different groups.

	Normal Voluntcers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)
Baseline (mean ± S.D.)	18.53 ± 15.87	17.67 ±12.16	19.33 ± 11.29
Visit 1 (mean ± S.D.)	17.27 ± 15.50	11.73 ± 9.79	18.93 ± 13.23
Visit 2 (mean ± S.D.)	14.80 ± 13.19	10.87 ± 5.67	19.87 ± 14.10
Average[1] (mean ± S.D.)	**16.87 ± 13.77**	**13.42 ± 8.16**	**19.38 ± 12.12**
Median	**13**	**11**	**16**

[1]Kruskal-Wallis H test (H = 4.949; p = 0.084)

Table 39 POMS® test: Anxiety score of subject in 3 different groups.

	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)
Baseline (mean ± S.D.)	15.33 ± 11.46	15.67 ± 8.94	15.33 ± 8.85
Visit 1 (mean ± S.D.)	14.87 ± 11.71	10.07 ± 6.47	14.33 ± 8.45
Visit 2 (mean ± S.D.)	14.13 ± 10.41	11.20 ± 6.33	15.67 ± 9.51
Average[1] (mean ± S.D.)	**14.78 ± 10.39**	**14.13 ± 10.41**	**15.11 ± 8.45**
Median	**13**	**11**	**14**

[1]Kruskal-Wallis H test (H = 1.944; p = 0.378)

Table 40 POMS® test: Confusion score of subject in 3 different groups.

	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)
Baseline (mean ± S.D.)	12.07 ± 6.39	12.07 ± 4.65	12.67 ± 5.19
Visit 1 (mean ± S.D.)	12.87 ± 6.73	10.33 ± 3.62	12.33 ± 6.66
Visit 2 (mean ± S.D.)	12.13 ± 6.16	10.20 ± 3.84	12.60 ± 5.70
Average[1] (mean ± S.D.)	**12.36 ± 6.15**	**10.87 ± 3.76**	**12.53 ± 5.58**
Median	**11**	**10**	**13**

[1]Kruskal-Wallis H test (H = 1.512; p = 0.470)

Table 41 POMS® test: Fatigue score of subject in 3 different groups.

	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)
Baseline (mean ± S.D.)	9.53 ± 7.61	11.13 ± 6.82	11.20 ± 6.85
Visit 1 (mean ± S.D.)	9.60 ± 7.29	8.40 ± 6.61	11.47 ± 7.18
Visit 2 (mean ± S.D.)	8.60 ± 7.39	8.60 ± 6.46	11.53 ± 6.82
Average[1] (mean ± S.D.)	**9.24 ± 7.02**	**9.38 ± 6.36**	**11.40 ± 6.46**
Median	**7**	**7**	**11**

[1]Kruskal-Wallis H test (H = 4.000; p = 0.135)

Table 42 POMS® test: Vigor score of subject in 3 different groups.

	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)
Baseline (mean ± S.D.)	21.67 ± 5.75	16.73 ± 4.37	15.80 ± 6.17
Visit 1 (mean ± S.D.)	20.07 ± 4.89	17.00 ± 4.55	16.13 ± 5.11
Visit 2 (mean ± S.D.)	19.80 ± 5.60	18.73 ± 5.18	14.93 ± 3.84
Average[1] (mean ± S.D.) Median	**20.51 ± 4.46 21**	**17.49 ± 4.29** 16**	**15.62 ± 4.69* 16**

[1]Kruskal-Wallis H test (F = 10.789; p < 0.001)

*Bonferroni t-test (t = 4.603,p < 0.05; compared with normal volunteers)

**Bonferroni t-test (t = 2.845, p < 0.05; compared with normal volunteers)

Table 43 POMS® test: TMD score of subject in 3 different groups.

	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)
Baseline (mean ± S.D.)	49.73 ± 46.46	56.00 ± 37.16	56.73 ± 33.80
Visit 1 (mean ± S.D.)	48.60 ± 46.00	37.47 ± 28.77	54.13 ± 38.65
Visit 2 (mean ± S.D.)	44.13 ± 42.15	34.87 ± 22.66	58.20 ± 39.04
Average (mean ± S.D.) Median	**47.49 ± 42.68 33**	**42.78 ± 28.49 41**	**56.36 ± 35.25 56**

[1]Kruskal-Wallis H test (H = 0.923; p = 0.630)

Table 44 AEP: AEP results of subject in 3 different groups.

	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)
Baseline (mean ± S.D.)	38.20 ± 11.69	39.27 ± 10.61	36.40 ± 10.22
Visit 1 (mean ± S.D.)	35.33 ± 11.13	36.00 ± 6.60	32.87 ± 7.52
Visit 2 (mean ± S.D.)	33.73 ± 10.97	33.67 ± 7.68	32.93 ± 8.17
Average (mean ± S.D.)	**35.76 ± 11.16**	**36.31 ± 8.59**	**34.07 ± 8.68**
Median	**35**	**36**	**33**

Table 45 AEP: Results of AEP sub-items of subject in 3 different groups.

Average score of Sub items (mean ± S.D.)	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)	Kruskal-Wallis H test (p-value)
Unsteadiness	1.78 ± 1.06	1.87 ± 0.97	1.73 ± 0.99	0.656 (p = 0.720)
Tiredness	2.33 ± 0.98	2.40 ± 1.07	2.27 ± 1.12	0.387 (p = 0.824)
Restlessness	2.47 ± 1.14[1]	2.09 ± 0.92	1.64 ± 0.96	14.257 (p < 0.001)
Feeling of aggression	1.78 ± 0.97	1.67 ± 0.90	1.89 ± 0.96	1.534 (p = 0.464)
Nervousness and/or agitation	1.58 ± 0.78	1.29 ± 0.55	1.47 ± 0.66	3.503 (p = 0.174)
Headache	1.91 ± 0.97	1.76 ± 0.93	1.80 ± 0.89	0.660 (p = 0.719)
Hair loss	1.56 ± 0.92	1.29 ± 0.59	1.27 ± 0.65	6.244 (p = 0.044)
Skin problems e.g. rash, acne	1.91 ± 1.20	1.36 ± 0.71	1.44 ± 0.81	6.244 (p = 0.044)
Double or blurred vision	1.62 ± 0.94	1.33 ± 0.77	1.22 ± 0.42	5.880 (p = 0.053)
Upset stomach	1.62 ± 0.68	1.78 ± 0.88	1.44 ± 0.66	3.831 (p = 0.147)
Difficulty in concentrating	2.11 ± 0.80	2.49 ± 1.14	2.27 ± 1.18	2.212 (p = 0.331)
Trouble with mouth or gums	1.84 ± 1.04	1.44 ± 0.72	1.44 ± 0.66	4.697 (p = 0.096)
Shaky hands	1.31 ± 0.63	2.47 ± 1.29[2,3]	1.82 ± 1.11	21.346 (p<0.001)

Table 45 AEP: Results of AEP sub-items of subject in 3 different groups.

Average score of Sub items (mean ± S.D.)	Normal Volunteers (N = 15)	Sodium valproate (N = 15)	Phenytoin (N = 15)	Kruskal-Wallis H test (p-value)
Weight gain	1.58 ± 0.92	1.27 ± 0.62	1.18 ± 0.49[4]	7.135 (p = 0.028)
Dizziness	1.56 ± 0.81	1.56 ± 0.81	1.33 ± 0.56	1.753 (p = 0.416)
Sleepiness	2.16 ± 1.00	2.58 ± 1.14	2.38 ± 1.07	3.187 (p = 0.203)
Depression	1.53 ± 0.73	1.71 ± 0.97	1.69 ± 0.87	0.611 (p = 0.737)
Memory problems	2.09 ± 0.79	2.40 ± 1.03	2.69 ± 1.04[5]	7.989 (p = 0.018)
Disturbed sleep	1.84 ± 1.11	1.96 ± 1.17	1.84 ± 0.95	0.214 (p = 0.899)
Paresthesia	1.18 ± 0.39	1.33 ± 0.74	1.29 ± 0.69	0.469 (p = 0.791)

[1]Dunn's method (Q = 3.734, p < 0.05; compared with phenytoin)

[2]Dunn's method (Q = 4.618, p < 0.05; compared with normal volunteers)

[3]Dunn's method (Q = 2.428, p < 0.05; compared with phenytoin)

[4]Dunn's method (Q = 2.583, p< 0.05; compared with normal volunteers)

[5]Dunn's method (Q = 2.822, p < 0.05; compared with normal volunteers)