

Table 1 ASM drug load score system

Medication load score	CBZ	ESL	LCM	LEV	LTG	OXC	VPA
1	200mg	400mg	100mg	500mg	50mg	300mg	400mg
2	400mg	500mg	150mg	750mg	100mg	450mg	600mg
3	600mg	600mg	200mg	1000mg	150mg	600mg	800mg
4	800mg	7000mg	250mg	1250mg	200mg	750mg	1000mg
5	1000mg	800mg	300mg	1500mg	250mg	900mg	1200mg
6	1200mg	900mg	350mg	1750mg	300mg	1200mg	1400mg
7	1400mg	1000mg	400mg	2000mg	350mg	1500mg	1600mg
8	1600mg	1200mg	450mg	2250mg	400mg	1800mg	1800mg
9	1800mg	1400mg	500mg	2500mg	450mg	2100mg	2000mg
10	2000mg	1600mg	600mg	3000mg	500mg	2400mg	2500mg
11	2600mg	1800mg	700mg	3500mg	650mg	2700mg	3000mg
12	3200mg	2000mg	800mg	4000mg	800mg	3000mg	3500mg

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medication load is normalized for each ASM according to British National Formulary (BNF) guidelines (<https://bnf.nice.org.uk/drug/>). CBZ: carbamazepine; ESL: eslicarbazepine; LCM: lacosamide; LEV: levetiracetam, LTG: lamotrigine TPM: topiramate; OXC; oxcarbazepine VPA: valproic acid; ZNS: zonisamide

Table 2. Demographic and clinical features of patients taking ASMs with moderate cognitive effects in mono/dual/triple therapy

	Monotherapy (n= 60)	Dual therapy (n= 60)	Triple therapy (n= 60)	P value
Sex, F/M	28/32	26/34	23/37	0.622
Age at the scan (SD), y	34.0 (9.3)	32.5 (9.5)	33.3 (10.4)	0.686
Epilepsy duration at the scan (SD), y	14.5 (11.1)	13.8 (10.8)	14.6 (9.7)	0.910
Handedness, Right/Left/Ambidextrous	54/6	56/4	54/6	0.760
Localization of epilepsy, n, (%)				0.774
Temporal	43 (71.7)	41 (68.3)	43 (71.7)	
Frontal	11 (18.3)	15 (25.0)	14 (23.3)	
Parietal	6 (10)	4 (6.7)	3 (5.0)	
Lateralization of epilepsy, n, (%)				0.672
Left	31 (51.7)	33 (55.0)	30 (50.0)	
Right	26 (43.3)	19 (31.6)	23 (38.3)	
Bilateral	2 (3.3)	7 (11.7)	6 (10.0)	
Undetermined	1 (1.7)	1 (1.7)	1 (1.7)	
History of febrile seizures, n, (%)	6 (10.0)	7 (11.7)	5 (8.3)	0.831
Hippocampal sclerosis, n,	13 (21.7)	22 (31.9)	15 (25.0)	0.156
Seizure frequency				0.843
Less than once a month, n,	7 (11.7)	6 (10.0)	4 (6.7)	
Monthly to weekly	19 (31.7)	19 (31.7)	15 (25.0)	
Weekly to daily	20 (33.3)	19 (31.7)	25 (41.7)	
Daily seizures	14 (23.3)	16 (26.6)	16 (26.6)	
History of GTCS, n,	39 (65.0)	45 (75.0)	39 (65.0)	0.397
Scanner, original/upgrade, n	21/39	17/43	16/44	0.577
Drug load score, median, range	6.5 (1.00-12.00)	13.00(2.50-24.00)	18.5(7.00-35.00)	0.000

Abbreviations: ASM: anti-seizure medication; GTCS; generalized tonic clonic seizures; SD:standard deviation

Figure Legend:

Cortical changes are demonstrated on a surface-rendered brain template and subcortical changes are demonstrated superimposed on MNI 152 template with a bar chart indicating z score. (A) One-sample *t* tests of functional magnetic resonance imaging activation and deactivation maps for the 3 different patient groups are demonstrated on a surface-rendered brain template. Task-relevant regions (red) include bilateral inferior and middle frontal gyrus (left > right), bilateral supplementary motor area, the left dorsolateral parietal region, and bilateral inferior occipital lobes. Areas of task-related deactivations (blue) include the bilateral precuneus, posterior cingulate, angular gyrus, and medial prefrontal and lateral temporal cortex. $P < 0.05$, FWE-corrected. (B) patients on monotherapy show greater activation in frontal cognitive networks and deactivation in task-negative networks than patients with 2 ASMs. Patients on monotherapy or on two ASMs show greater frontal and parietal activations than patients on 3 ASMs. $P < 0.005$, uncorrected at the threshold of 20 voxels. (C) Among those on moderate ASMs, the drug load score is negatively correlated with functional activation in right piriform cortex, (20 voxels, $P < 0.005$) and left inferior frontal gyrus, left inferior parietal lobule and left hippocampus with less stringent threshold (10 voxels, $P < 0.005$).