COMPARATIVE NEUROCOGNITIVE EFFECTS OF FIVE PSYCHOTROPIC ANTICONVULSANTS AND LITHIUM

ABSTRACT

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CONTEXT: Many of the new antiepileptic drugs have psychiatric indications, and most are prescribed by psychiatrists for patients with mood disorders, even absent a specific indication. Epileptic drugs in general, even the newer ones, are known to effect cognition, sometimes in untoward ways. Research on the neurocognitive effects of anti-epileptic drugs, however, has been done exclusively in normal volunteers and in patients with seizure disorders.

METHOD: A naturalistic, cross-sectional study of patients on one of 5 different psychotropic anticonvulsants or lithium. Cognition measured by a computerized neurocognitive screening battery, CNS Vital Signs.

SUBJECTS: 159 patients with bipolar disorder, age 18-70, treated with carbamazepine (N=16), lamotrigine (38), oxcarbazepine (19), topiramate (19) and valproic acid (37); 30 bipolar patients on lithium, for purposes of comparison.

RESULTS: Significant group differences were detected in tests of memory, psychomotor speed, processing speed, reaction time, cognitive flexibility and attention. Rank order analysis indicated superiority for lamotrigine (1.8) followed by oxcarbazepine (2.1), lithium (3.3), topiramate (4.3), valproic acid (4.5) and carbalzepine (5.0).

CONCLUSIONS: The relative neurocognitive effects of the various psychotropic antiepileptic drugs in patients with bipolar disorder are concordant with those described in the seminal literature in normal volunteers and patients with epilepsy. Lamotrigine and oxcarbamazepine have the least neurotoxicity, and topiramate, valproate and carbamazepine have the most. Lithium effects on neurocognition are intermediate. Choosing a mood-stabilizing drug with minimal neurocognitive effects may enhance patient compliance over the long-term.

Figure 1. Relative Effects on Cognition (Highest Score = most favorable profile)

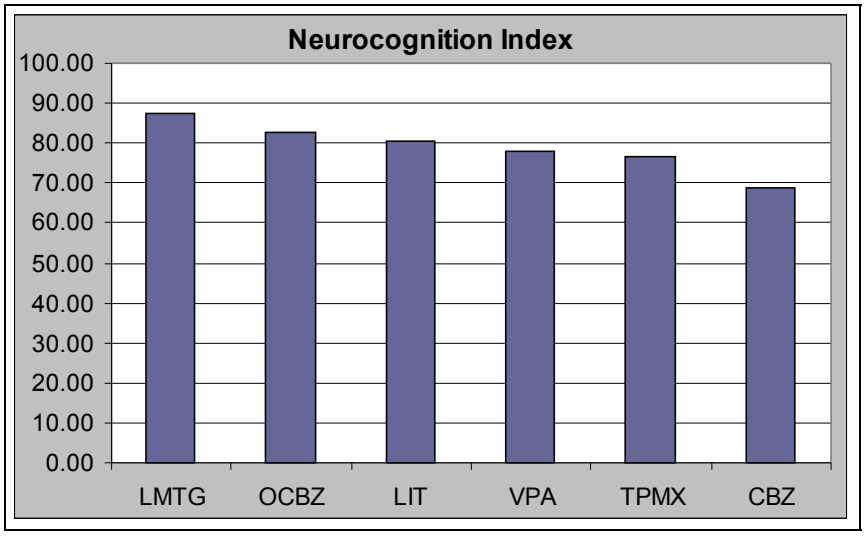

TABLE 1. 159 PATIENTS ON MOOD-STABILIZERS & MEAN TEST SCORES

	CBZ	LMTG	LIT	OCBZ	TPM	VPA		
N	16	38	30	19	19	37	159	
AGE	43.19	42.05	30.60	36.47	41.11	41.24	**F**	**P<**
NCI	**70.15**	**86.73**	**77.75**	**83.91**	**74.16**	**76.48**	2.27	0.05
MEMORY	**66.95**	**88.02**	**79.62**	**87.75**	**84.79**	**83.67**	1.76	0.12
PSYCHOMOTOR	**68.78**	**85.70**	**83.29**	**85.84**	**80.05**	**74.13**	2.41	0.04
REACTION TIME	**78.62**	**84.22**	**79.30**	**80.56**	**73.56**	**65.95**	1.91	0.10
COGN FLEX	**60.28**	**87.03**	**71.79**	**77.74**	**55.24**	**68.71**	3.13	0.01
COMPLEX ATTENTION	**65.75**	**84.53**	**67.11**	**73.28**	**53.48**	**75.12**	2.29	0.05
VIGILANCE	**83.86**	**90.07**	**77.57**	**80.55**	**67.57**	**79.95**	1.26	0.28
VBM	44.87	47.85	46.58	48.47	48.16	47.99	0.59	0.71
VIM	37.69	44.95	42.59	44.58	42.63	41.81	3.21	0.01
FTT	85.59	100.18	101.53	98.12	99.08	90.62	1.44	0.21
SDC	34.81	47.32	47.53	49.84	40.53	37.03	3.91	0.00
STsrt*	425.69	368.39	347.57	357.89	379.66	452.64	1.76	0.12
STcrt*	750.94	660.03	686.50	706.42	775.89	778.46	2.15	0.06
STstrt*	773.73	808.21	798.98	791.42	810.00	945.35	3.19	0.01
Sterr*	7.66	3.11	3.40	5.84	3.84	3.08	2.38	0.04
SATcorr	33.52	46.11	40.10	45.84	36.25	35.70	3.59	0.00
SATerr*	17.05	9.32	13.71	11.53	22.26	14.19	3.16	0.01
SATrt*	1175.09	1114.44	1124.88	1032.47	1016.14	1212.49	2.22	0.06
SATq*	2.45	1.55	2.41	1.40	1.93	2.03	1.67	0.14
CPTcorr	36.97	39.13	38.13	39.18	36.57	38.05	1.45	0.21
CPTerrs*	8.67	1.68	3.91	3.58	18.30	3.89	3.28	0.01
CPTrt*	526.66	450.29	511.88	433.22	487.26	541.74	2.07	0.07

NOTES, Table 1: CBZ carbamazepine, LMTG lamotrigine, LIT lithium, OCBZ oxcarbazine, TPMX topiramate, VPA valproate. NCI Neurocognition Index, PMS Psychomotor speed, RT Reaction Time, COGN FLEX cognitive flexibility, VBM Verbal Memory, VIM Visual Memory, FTT finger tapping test total right and left taps, SDC Symbol Digit Coding, ST Stroop Test, SAT Shifting Attention Test, Q Efficiency ((SAT RT/per cent correct)/1000), CPT Continuous Performance Test. An asterisk indicates that a lower score is better. In the right columns is the F statistic from the multivariate analysis and its P value.

Table 2. Rank Order

	CBZ	LMTG	LIT	OCBZ	TPM	VPA
NCI	6	1	3	2	5	4
MEMORY	6	1	5	2	3	4
PSYCHOMOTOR	6	2	3	1	4	5
REACTION TIME	4	1	3	2	5	6
COGN FLEX	5	1	3	2	6	4
COMPLEX ATTENTION	5	1	4	3	6	2
VIGILANCE	2	1	5	3	6	4
VBM	6	4	5	1	2	3
VIM	6	1	4	2	3	5
FTT	6	2	1	4	3	5
SDC	6	3	2	1	4	5
STsrt*	5	3	1	2	4	6
STcrt*	4	1	2	3	5	6
STstrt*	1	4	3	2	5	6
Sterr*	6	2	3	5	4	1
SATcorr	6	1	3	2	4	5
SATerr*	5	1	3	2	6	4
SATrt*	5	3	4	2	1	6
SATq*	6	2	5	1	3	4
CPTcorr	5	2	3	1	6	4
CPTerrs*	5	1	4	2	6	3
CPTrt*	5	2	4	1	3	6
RANK	**5.0**	**1.8**	**3.3**	**2.1**	**4.3**	**4.5**

Table3. Multivariate Analysis of Drugs with High, Medium and Low Neurotoxicity

	HIGH	MED	LOW		
N	72	31	57		
NCI	74.47	78.32	85.79	5.32	0.006
MEMORY	80.39	79.53	87.93	1.74	0.179
PSYCHOMOTOR	74.50	83.08	85.75	5.70	0.004
REACTION TIME	70.78	78.32	83.00	3.87	0.023
COGN FLEX	63.28	73.25	83.93	6.45	0.002
COMPLEX ATTENTION	67.32	68.36	80.78	2.73	0.068
VIGILANCE	77.55	77.43	86.90	1.49	0.228
VBM	47.36	46.56	48.06	0.51	0.603
VIM	41.10	42.60	44.83	5.18	0.007
FTT	91.74	101.03	99.50	2.67	0.073
SDC	37.46	47.68	48.16	7.22	0.001
STsrt*	427.39	353.74	364.89	2.12	0.123
STcrt*	771.67	691.48	675.49	4.70	0.010
STstrt*	871.50	802.66	802.61	1.86	0.159
Sterr*	4.30	3.29	4.02	0.33	0.716
SATcorr	35.36	40.60	46.02	8.69	0.000
SATerr*	16.95	13.39	10.06	4.89	0.009
SATrt*	1152.36	1121.41	1087.12	0.85	0.430
SATq*	2.09	2.36	1.50	4.94	0.008
CPTcorr	37.42	38.09	39.15	2.92	0.057
CPTerrs*	8.75	3.93	2.32	2.60	0.077
CPTrt*	524.01	507.40	444.60	4.28	0.015

Figure 1. Reaction Times in Low and High Toxicity Groups.