Supplemental Table 2: Clinical reports of lithium-associated movement disorder

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
				MCL				
Coats DA	Coats DA, Trautner EM, Gershon S. The treatment of lithium poisoning. Australas Ann Med 1957;6:11-5.	Australia	1957	MCL - Muscular jerks	1 (6)	29	Male	Chronic maniacal excitement
				MCL - Muscular twitches, fasciculation	1 (6)	65	Female	Persistent gross maniacal excitement
				MCL - Twitching of the small muscles of the hands and face and occasional gross limb jerks	1 (6)	73	Female	Agitated senile confusion
				MCL - Ataxia, muscular twitching	1 (6)	45	Female	Maniacal excitement
				MCL - fibrillation	1 (6)	37	Male	Schizophrenia, aggressivity
				MCL - Ataxia, fasciculation	1 (6)	65	Female	Recurrent mania
Verbov JL	Verbov JL, Phillips JD, Fife DG. A case of lithium intoxication. Postgrad Med J 1965;41:190-2.	England	1965	MCL - Spasticity, hyperreflexia, dysarthria, ataxic gait, intention tremor	1	51	Female	Schizophrenia, recurrent attacks of mania
Shopsin B	Shopsin B, Johnson G, Gershon S. Neurotoxicity with lithium: Differential drug responsiveness. Int Pharmacopsychiatry 1970;5:170-82.	US	1970	MCL - Tremor, mask-like facies, grimacing, hypotonia, hyperreflexia, choreoathetosis	1 (4) - of 8 patients, 4 with MD	34	Female	Schizophrenic reaction, chronic undifferentiated type
				MCL - Ataxia, dysarthria		55	Female	Schizophrenic reaction, schizoaffective type with extreme elation
Castaing R	Castaing R, Bony D, Favarel-Garrigues JC, Cardinaud JP. Acute intoxication by lithium carbonate. Eur J Toxicol 1971;4:412-5.	France	1971	MCL	1	...	...	...
Itil TM	Itil TM, Akpinar S. Lithium effect on human electroencephalogram. Clin Electroencephalogr 1971;2:89-102.	US	1971	MCL	1	...	...	...
Favarel-Garrigues B	Favarel-Garrigues B, Favarel-Garrigues JC, Bourgeois M. 2 cases of severe poisoning by lithium carbonate. Ann Med Psychol (Paris) 1972;1:253-7.	France	1972	MCL	2	...	...	...
Setiey A	Setiey A, Moene Y, Chazot G, Trillet M, Courjon J. Unusual clinical and electroencephalographic aspects induced by lithium-dopa association. J Med Lyon 1972;53:1401-3.	France	1972	MCL	1	...	...	...

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Von Hartitzsch B	Von Hartitzsch B, Hoenich NA, Leigh RJ, Wilkinson R, Frost TH, Weddel A, *et al*. Permanent neurological sequelae despite haemodialysis for lithium intoxication. Br Med J 1972;4:757-9.	England	1972	MCL - Ataxia, hyperreflexia, flapping tremor, fluttering of eyelids	1 (2) - 3 cases	50	Female	Manic depressive and recurrent depressive?
				MCL - Ataxia, coarse tremor, muscular twitches, choreiform movements	1 (2) - 3 cases	53	Female	Manic depressive and recurrent depressive?
Juul-Jensen P	Juul-Jensen P, Schou M. Letter: Permanent brain damage after lithium intoxication. Br Med J 1973;4:673.	England	1973	MCL - Spasticity, hyperactive deep reflexes, myoclonic jerks	1 (2)	38	Female	Suicidal intent
				MCL - Ataxia, hyperactive deep reflexes, tremor, rigidity	1 (2)	55	Female	…
Cohen WJ	Cohen WJ, Cohen NH. Lithium carbonate, haloperidol, and irreversible brain damage. JAMA 1974;230:1283-7.	US	1974	MCL - Tremor, rigidity, muscular twitch, ataxia	1 (4)	40	Female	Mania
				MCL - Ataxia, intention tremor, rigidity, tremulousness, DKN	1 (4)	63	Female	Manic-depressive psychosis
				MCL - Coarse tremor, rigidity, dysarthria, postural and parkinsonian tremor, cogwheel movements, lead-pipe rigidity	1 (4)	63	Female	Manic-depressive psychosis
Dyksen MW	Dysken MW, Halaris AE. Post-ECT asterixis associated with primary hyperparathyroidism. Am J Psychiatry 1978;135:1237-8.	US	1978	MCL - Asterixis	1	48	Female	Manic-depressive, manic type
Dyksen MW	Dysken MW, Comaty JE, Pandey GN, Davis JM. Asterixis associated with a high RBC lithium concentration. Am J Psychiatry 1979;136:1610.	US	1979	MCL - Asterixis	1	22	Female	Manic-depressive psychosis
Uchigata M	Uchigata M, Tanabe H, Hasue I, Kurihara M. Peripheral neuropathy due to lithium intoxication. Ann Neurol 1981;9:414.	Japan	1981	MCL - Tremor, rigidity, twitch, dysarthria, unsteady gait	1	56	Male	Manic psychosis
Apte SN	Apte SN, Langston JW. Permanent neurological deficits due to lithium toxicity. Ann Neurol 1983;13:453-5.	US	1983	MCL - Asterixis, tremor, decerebrate posturing, ataxia, choreiform and athetoid movements	1 (2)	38	Male	DPS, suicide attempt

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Rosen PB	Rosen PB, Stevens R. Action myoclonus in lithium toxicity. Ann Neurol 1983;13:221-2.	US	1983	MCL - Repetitive action MCL	1	47	Female	Schizoaffective illness
Sandyk R	Sandyk R, Hurwitz MD. Toxic irreversible encephalopathy induced by lithium carbonate and haloperidol. A report of 2 cases. S Afr Med J 1983;64:875-6.	US	1983	MCL - Tremulousness, extrapyramidal and cerebellar dysfunction	2	...	...	...
Julius SC	Julius SC, Brenner RP. Myoclonic seizures with lithium. Biol Psychiatry 1987;22:1184-90.	US	1987	MCL - Generalized tonic-clonic seizures followed by myoclonic seizures. dysarthria	1 (2)	35	Female	Aggressive outbursts and paranoid delusions
				MCL - Generalized tonic-clonic seizures followed by myoclonic seizures and tremor	1 (2)	48	Female	Manic behavior
Devanand DP	Devanand DP, Sackeim HA, Brown RP. Myoclonus during combined tricyclic antidepressant and lithium treatment. J Clin Psychopharmacol 1988;8:446-7.	US	1988	MCL - Jerks, gait	1	43	Female	Psychotic DPS
				MCL - Jerks, gait	1	70	Female	BD
Lemus CZ	Lemus CZ, Lieberman JA, Johns CA. Myoclonus during treatment with clozapine and lithium: The role of serotonin. Hillside J Clin Psychiatry 1989;11:127-30.	US	1989	MCL	1	22	Male	Schizophrenia
Simon LT	Simon LT, Hsu B, Adornato BT. Carbamazepine-induced aseptic meningitis. Ann Intern Med 1990;112:627-8.	US	1990	MCL	1	50	Male	BD
Vanhooren G	Vanhooren G, Dehaene I, Van Zandycke M, Piessens F, Vandenbergh V, Van Hees J, *et al*. Polyneuropathy in lithium intoxication. Muscle Nerve 1990;13:204-8.	Belgium	1990	MCL	1 (2)	54	Male	Manic-depressive
				MCL	1 (2)	37	Female	Schizophrenia

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Kojima H	Kojima H, Terao T, Yoshimura R. Serotonin syndrome during clomipramine and lithium treatment. Am J Psychiatry 1993;150:1897.	Japan	1993	MCL	1	59	Male	DPS
Prettyman R	Prettyman R. Lithium neurotoxicity at subtherapeutic serum levels. Br J Psychiatry 1994;164:123.	US	1994	MCL - Ataxia	1	38	Male	Chronic psychotic disorder
Rittmannsberger H	Rittmannsberger H, Leblhuber F. Drug-induced asterixis. Dtsch Med Wochenschr 1994;119:585-8.	Austria	1994	MCL - Akinesia, rigor	1	54	Female	Acute schizoaffective psychosis
Loza B	Loza B. A case of serotonin syndrome. Psychiatr Pol 1995;29:529-38.	Poland	1995	MCL	1	61	Female	…
Nisijima K	Nisijima K, Shimizu M, Abe T, Ishiguro T. A case of serotonin syndrome induced by concomitant treatment with low-dose trazodone and amitriptyline and lithium. Int Clin Psychopharmacol 1996;11:289-90.	Japan	1996	MCL - Tremor, hyperreflexia, rigidity	1	59	Male	BD
Rittmannsberger H	Rittmannsberger H. Asterixis induced by psychotropic drug treatment. Clin Neuropharmacol 1996;19:349-55.	Austria	1996	MCL - Asterixis	1 (7)	59	Female	BD
				MCL - Asterixis	1 (7)	21	Female	Mania
				MCL - Asterixis	1 (7)	51	Male	Schizoaffective disorder
				MCL - Asterixis	1 (7)	33	Female	BD
				MCL - Asterixis	1 (7)	54	Female	Schizoaffective disorder
				MCL - Asterixis	1 (7)	48	Female	Schizoaffective disorder
				MCL - Asterixis	1 (7)	21	Female	Schizoaffective disorder
Evidente VG	Evidente VG, Caviness JN. Focal cortical transient preceding myoclonus during lithium and tricyclic antidepressant therapy. Neurology 1999;52:211-3.	US	1999	MCL - Shaking and jerking of the hands during activity	1	65	Male	BD
Lee SH	Lee SH, Yang YY. Reversible neurotoxicity induced by a combination of clozapine and lithium: A case report. Zhonghua Yi Xue Za Zhi (Taipei) 1999;62:184-7.	Taiwan	1999	MCL - Ataxia, tremor, facial spasm	1	…	…	Refractory BD

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Stewart JT	Stewart JT, Williams LS. A case of lithium-induced asterixis. J Am Geriatr Soc 2000;48:457.	US	2000	MCL - Asterixis, tremor	1	86	Male	Irritability and possible BD
Roccatagliata L	Roccatagliata L, Audenino D, Primavera A, Cocito L. Nonconvulsive status epilepticus from accidental lithium ingestion. Am J Emerg Med 2002;20:570-2.	Italy	2002	MCL - NSCE	1	84	Female	…
Caviness JN	Caviness JN, Evidente VG. Cortical myoclonus during lithium exposure. Arch Neurol 2003;60:401-4.	US	2003	MCL	1 (5)	42-72	…	Depression
				MCL	1 (5)	42-72	…	Depression
				MCL	1 (5)	42-72	…	BD
				MCL	1 (5)	42-72	…	BD
				MCL	1 (5)	42-72	…	BD
Smith D	Smith D, Keane P, Donovan J, Malone K, McKenna TJ. Lithium encephalopathy. J R Soc Med 2003;96:590-1.	Ireland	2003	MCL - Multifocal myoclonic jerks	1	67	Male	BD
Bender S	Bender S, Linka T, Wolstein J, Gehendges S, Paulus HJ, Schall U, *et al*. Safety and efficacy of combined clozapine-lithium pharmacotherapy. Int J Neuropsychopharmacol 2004;7:59-63.	Germany	2004	MCL	2	39.5	...	...
Reif A	Reif A, Leonhard C, Mössner R, Lesch KP, Fallgatter AJ. Encephalopathy and myoclonus triggered by valproic acid. Prog Neuropsychopharmacol Biol Psychiatry 2004;28:1061-3.	Germany	2004	MCL - Tremor	1	42	Male	Psychotic depression
Kaplan PW	Kaplan PW, Birbeck G. Lithium-induced confusional states: Nonconvulsive status epilepticus or triphasic encephalopathy? Epilepsia 2006;47:2071-4.	US	2006	MCL	1 (5)	71	Female	BD
				MCL	1 (5)	49	Female	Psychiatric disorder
				MCL	1 (5)	51	Female	BD, mental retardation
				MCL	1 (5)	51	Male	BD, schizophrenia
				MCL	1 (5)	55	Female	BD, acute mania

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Grueneberger EC	Grueneberger EC, Maria Rountree E, Baron Short E, Kahn DA. Neurotoxicity with therapeutic lithium levels: A case report. J Psychiatr Pract 2009;15:60-3.	US	2009	MCL - Fasciculation, myoclonic jerks	1	20	Male	BD type I
Mahasuar R	Mahasuar R, Kuruvilla A, Jacob K. Palatal tremor after lithium and carbamazepine use: A case report. J Med Case Rep 2010;4:176.	India	2010	MCL - Palatal MCL	1	27	Male	Episode suggestive of mania with psychotic symptoms
Almeida AG	Almeida AG, Cerqueira T, Bento L. A case of chronic lithium intoxication. Eur J Intern Med 2011;22:3.	Portugal	2011	MCL - Myoclonic jerks, muscular rigidity, EP tremors	1	…	Female	BD
Bakelants E	Bakelants E, Peter V. A 61-year-old patient with acute neurologic deterioration. Tijdschr Geneeskund 2013;69:37-9.	Belgium	2013	MCL	1	61	Female	BD
Chen WY	Chen WY, Chen AC, Tsai SJ, Lin JJ. Reversible oro-lingual dyskinesia related to lithium intoxication. Acta Neurol Taiwan 2013;22:32-5.	Taiwan	2013	MCL - Orolingual DKN	1	68	Male	BD
Mignarri A.	Mignarri A, Chini E, Rufa A, Rocchi R, Federico A, Dotti MT. Lithium neurotoxicity mimicking rapidly progressive dementia. J Neurol 2013;260:1152-4.	Italy	2013	MCL - Ideomotor apraxia, gait ATX, dysmetria	1	60	Female	BD
Kitami M	Kitami M, Oizumi H, Kish SJ, Furukawa Y. Takotsubo cardiomyopathy associated with lithium intoxication in bipolar disorder: A case report. J Clin Psychopharmacol 2014;34:410-1.	Japan	2014	MCL - ATX, tremor	1	78	Female	BD

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Fitzgerald RT	Fitzgerald RT, Fitzgerald CT, Samant RS, Kumar M, Ramakrishniah R, Van Hemert R, *et al*.. Lithium toxicity and PRES: A novel association. J Neuroimaging 2015;25:147-9.	US	2014	MCL	1 (2)	50	Female	BD
				MCL	1 (2)	61	Male	BD
Loens S	Loens S, Conzen J, Welte GS, Scharn N, Schrader C, Weissenborn K. Reversible posterior leukoencephalopathy syndrome after withdrawal of antipsychotic medication in the context of lithium intoxication. Gen Hosp Psychiatry 2015;37:274. e3-5.	Germany	2015	MCL - Generalized MCL, dysarthria	1	60	Female	Schizoaffective disorder
Vandewalle W	Vandewalle W, Boon E, Sienaert P. Movement disorders due to modern antidepressants and mood stabilizers. Tijdschr Psychiatr 2015;57:132-7.	Belgium	2015	MCL	2	...	...	...
Hayashi Y	Hayashi Y, Nishida S, Takekoshi A, Murakami M, Yamada M, Kimura A, *et al*.. A case of lithium intoxication induced by an antihypertensive angiotensin 1 subtype-specific angiotensin II receptor blocker in an elderly patient with bipolar disorder and hypertension. Nihon Ronen Igakkai Zasshi 2016;53:244-9.	Japan	2016	MCL - Action tremor, MCL, ATX	1	65	Female	BD type 1
Hellmann MJ	Hellmann MJ, Gupta N. Silent danger: Lithium toxicity and associated neurologic sequelae. Am J Respir Crit Care Med 2017;195:A3799.	US	2017	MCL	1	66	Male	BD

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Kayipmaz S	Kayipmaz S, Altınöz AE, Ok NEG. Lithium intoxication: A possible interaction with moxifloxacin. Clin Psychopharmacol Neurosci 2017;15:407-9.	Turkey	2017	MCL - Tremor	1	74	Female	BD
Stetkarova I	Stetkarova I, Bocek V, Gismatullina A, Svobodova Z, Peisker T. Severe chronic lithium intoxication in patient treated for bipolar disorder. Neuro Endocrinol Lett 2017;38:397-400.	Czech Republic	2017	MCL - Tremor, ATX, dysarthria, generalized MCL	1	72	Female	BD
Jacobson JC	Jacobson JC, Garcia-Pittman EC. Case of a patient with bipolar disorder and delayed subcortical dementia onset following acute lithium toxicity. Am J Geriatr Psychiatry 2018;26:S97.	US	2018	MCL - Tremor, aphasia	1	...	Female	BD
Orleans RA	Orleans RA, Dubin MJ, Kast KA. The effect of a therapeutic lithium level on a stroke-related cerebellar tremor. BMJ Case Rep 2018;2018:bcr2017222920.	US	2018	MCL - Generalized MCL, coarse tremor	1	...	...	...
Sarrigiannis PG	Sarrigiannis PG, Zis P, Unwin ZC, Blackburn DJ, Hoggard N, Zhao Y, *et al*.. Tremor after long term lithium treatment; is it cortical myoclonus? Cerebellum Ataxias 2019;6:5.	UK	2019	MCL - Action and stimulus reflex cortical MCL	1 (8)	77	Female	…
				MCL - Cortical source	1 (8)	63	Female	…
				MCL - Cortical source	1 (8)	57	Male	…
				MCL - Cortical source	1 (8)	47	Female	…
				MCL - Cortical source	1 (8)	55	Female	…
				MCL - Cortical source	1 (8)	70	Female	…
				MCL - Cortical source	1 (8)	42	Female	…
				MCL - Central tremor	1 (8)	66	Male	…
Vallianou N	Vallianou N, Konstantinou F, Gennimata V, Micha P, Geladari E, Kounatid D. A case of Syndrome of Irreversible Lithium Effectuated Neurotoxicity (SILENT). Neth J Med 2019;77:301-2.	Holland	2019	MCL - Coarse tremor	1	74	Male	BD

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Kiziltan ME	Kiziltan ME, Gündüz A, Ser MH, Yeni SN, Özkara C, Demirbilek V, *et al*. The association between causes and electrophysiology in myoclonus: When and why electrophysiology? Neurol Sci Neurophysiol 2020;37:176-82.	Turkey	2020	MCL	...	26.3 (SD=11.4)	...	...
Nagamine T	Nagamine T. Lithium intoxication in the elderly: A possible interaction between azilsartan, fluvoxamine, and lithium. Innov Clin Neurosci 2020;17:45-6.	Japan	2020	MCL - Tremor	1	82	Male	BD
Burton C	Burton C, Mathys M, Gutierrez E. Comparison of lithium to second generation antipsychotics for the treatment of bipolar disorder in older veterans. Psychiatry Res 2021;303:114063.	US	2021	MCL - Tremor	1	...	...	...
Hyder S	Hyder S, Hundal J, Rasheed A. 817: Lethal lithium: A rare case of persistent neurotoxicity. Crit Care Med 2021;49:405.	US	2021	MCL - Tremor	1	54	Female	BD
				PKN				
Dalén P	Dalén P, Steg G. Lithium and levodopa in Parkinsonism. Lancet 1973;1:936-7.	Sweden	1973	PKN	1 (2)	...	Male	Reduce hyperkinetic phenomena (caused by Parkinson's disease) without a considerable increase of parkinsonian symptoms
				PKN	1 (2)	...	Female	Reduce hyperkinetic phenomena (caused by Parkinson's disease) without a considerable increase of parkinsonian symptoms
Cohen WJ	Cohen WJ, Cohen NH. Lithium carbonate, haloperidol, and irreversible brain damage. JAMA 1974;230:1283-7.	US	1974	PKN - ATX	1 (4)	34	Female	Manic-depressive psychosis

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Shopsin B	Shopsin B, Gershon S. Cogwheel rigidity related to lithium maintenance. Am J Psychiatry 1975;132:536-8.	US	1975	PKN - Cogwheel rigidity	1 (16)	57	Male	BD
				PKN - Cogwheel rigidity	1 (16)	75	Female	BD
				PKN - Cogwheel rigidity	1 (16)	38	Female	BD
				PKN - Cogwheel rigidity	1 (16)	55	Female	BD
				PKN - Cogwheel rigidity	1 (16)	74	Female	BD
				PKN - Cogwheel rigidity	1 (16)	57	Female	Unipolar disorder
				PKN - Cogwheel rigidity	1 (16)	35	Female	Unipolar disorder
				PKN - Cogwheel rigidity	1 (16)	38	Female	Unipolar disorder
				PKN - Cogwheel rigidity	1 (16)	28	Female	Unipolar disorder
				PKN - Cogwheel rigidity	1 (16)	60	Female	Unipolar disorder
				PKN - Cogwheel rigidity	1 (16)	37	Female	BD
				PKN - Cogwheel rigidity	1 (16)	65	Female	BD
				PKN - Cogwheel rigidity	1 (16)	51	Male	BD
				PKN - Cogwheel rigidity	1 (16)	56	Female	Unipolar disorder
				PKN - Cogwheel rigidity	1 (16)	54	Female	Unipolar disorder
				PKN - Cogwheel rigidity	1 (16)	45	Male	Schizoaffective
Branchey MH	Branchey MH, Charles J, Simpson GM. Extrapyramidal side effects in lithium maintenance therapy. Am J Psychiatry 1976;133:444-5.	US	1976	PKN - Cogwheel rigidity, limb rigidity, tremor of extremities	3 (36)	46.1 (mean)	... (11 male 25 female)	... (33 manic-depressive and 3 schizoaffective)
Loudon JB	Loudon JB, Waring H. Toxic reactions to lithium and haloperidol. Lancet 1976;2:1088.	Scotland	1976	PKN - DTN, DKN	6	36-63	...	Manic-depressive illness for 2-20 years
Lutz EG	Lutz EG. Acute lithium-induced Parkinsonism precipitated by liquid protein diet. J Med Soc N J 1978;75:165-6.	US	1978	PKN	1	...	...	...
Asnis GM	Asnis GM, Asnis D, Dunner DL, Fieve RR. Cogwheel rigidity during chronic lithium therapy. Am J Psychiatry 1979;136:1225-6.	US	1979	PKN - Cogwheel rigidity, tremor	38 (97)	47.2 (mean)	... (41 male 56 female)	Manic-depressive illness
Tyrer P	Tyrer P, Alexander MS, Regan A, Lee I. An extrapyramidal syndrome after lithium therapy. Br J Psychiatry 1980;136:191-4.	England	1980	PKN - Tremor, cogwheel rigidity, mask-like face	1 (2)	56	Female	Manic-depressive psychosis
				PKN - Tremor, cogwheel rigidity	1 (2)	66	Female	Manic-depressive illness

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Reches A	Reches A, Tietler J, Lavy S. Parkinsonism due to lithium carbonate poisoning. Arch Neurol 1981;38:471.	US	1981	PKN - Tremor, muscular rigidity, bradykinesia, cogwheel rigidity	1	62	Male	Depression
Spring G	Spring G, Frankel M. New data on lithium and haloperidol incompatibility. Am J Psychiatry 1981;138:818-21.	US	1981	PKN - Rigidity, dysarthria, DKN, cogwheeling	1	53	Male	Manic-depressive illness, severe manic attacks, depressive episodes
Apte SN	Apte SN, Langston JW. Permanent neurological deficits due to lithium toxicity. Ann Neurol 1983;13:453-5.	US	1983	PKN - Rigidity, ATX, dysmetria	1 (2)	46	Female	Manic depressive illness
Donaldson IM	Donaldson IM, Cuningham J. Persisting neurologic sequelae of lithium carbonate therapy. Arch Neurol 1983;40:747-51.	US	1983	PKN - ATX, rigidity, tremor, incoordination, dysarthria	1 (2)	53	Female	Manic-depressive illness
				PKN - Cogwheel rigidity, DKN	1 (2)	53	Female	Manic-depressive illness
Perényi A	Perényi A, Rihmer Z, Bánki CM. Parkinsonian symptoms with lithium, lithium-neuroleptic, and lithium-antidepressant treatment. J Affect Disord 1983;5:171-7.	Hungary	1983	PKN - Tremor, rigidity, AKT, and akinesia	5 (24)	45.2 (average). The youngest being 23, and the oldest being 71 years old	Female	BD I (n=35), BD II (n=27), unipolar (n=7) and schizoaffective (n=12)
Lang AE	Lang AE. Lithium and Parkinsonism. Ann Neurol 1984;15:214.	Canada	1984	PKN - Tremor, rigidity, bradykinesia	1	71	Female	...
Addonizzio G	Addonizio G. Rapid induction of extrapyramidal side effects with combined use of lithium and neuroleptics. J Clin Psychopharmacol 1985;5:296-8.	US	1985	PKN - Tremor, rigidity	1 (2)	23	Female	BD, manic with psychotic features
				PKN - Tremor, rigidity and stiffness	1 (2)	24	Male	BD, manic with psychotic features
Dyson EH	Dyson EH, Simpson D, Prescott LF, Proudfoot AT. Self-poisoning and therapeutic intoxication with lithium. Hum Toxicol 1987;6:325-9.	UK	1987	PKN - Prolonged PKN, tremor, rigidity, bradykinesia	1 (28)	…	... (22 males, 38 females, 6 unknown)	Intoxication

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Gajkowski K	Gajkowski K, Werkowicz-Pelczyk D, Masiak I, Rysz A. Neurologic symptoms in lithium poisoning. Neurol Neurochir Pol 1987;21:412-4.	Poland	1987	PKN	1	69	Female	BD
Chouinard G	Chouinard G. The use of benzodiazepines in the treatment of manic-depressive illness. J Clin Psychiatry 1988;49 Suppl:15-20.	Canada	1988	PKN	1	…	…	…
Sandyk R	Sandyk R, Pardeshi R. Pyridoxine improves drug-induced Parkinsonism and psychosis in a schizophrenic patient. Int J Neurosci 1990;52:225-32.	US	1990	PKN	1	42	Male	Schizophrenia
Scappa S	Scappa S, Teverbaugh P, Ananth J. Episodic tardive dyskinesia and Parkinsonism in bipolar disorder patients. Can J Psychiatry 1993;38:633-4.	Canada	1993	PKN	1 (3)	63	Male	Depression, hypomania
Lecamwasam D	Lecamwasam D, Synek B, Moyles K, Ghose K. Chronic lithium neurotoxicity presenting as Parkinson's disease. Int Clin Psychopharmacol 1994;9:127-9.	New Zealand	1994	PKN	1	71	Male	Manic depressive psychosis
Holroyd S	Holroyd S, Smith D. Disabling Parkinsonism due to lithium: A case report. J Geriatr Psychiatry Neurol 1995;8:118-9.	US	1995	PKN	1	78	Female	Depression, hypomania

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Northcott C	Northcott C, Lunn V, Yatham LN. Parkinsonism and bipolar affective disorder. Can J Psychiatry 1995;40:159-60.	Canada	1995	PKN - Tremor, akinesia	1	66	Male	Manic state
Aguilar M	Aguilar M, Valles V, Garolera M, Delgado L, Alberni J. Drug induced progressive supranuclear palsy (PSP) syndrome. Mov Disord 1996;11:142.	Spain	1996	PKN - PSP syndrome	1	46	Male	BD
Jimenez F	Jiménez-Jiménez FJ, Ortí-Pareja M, Ayuso-Peralta L, Gasalla T, Cabrera-Valdivia F, Vaquero A, *et al*. Drug-induced Parkinsonism in a movement disorders unit: A four-year survey. Parkinsonism Relat Disord 1996;2:145-9.	Spain	1996	PKN - DTN, DKN	1 (646)	...	...	...
Fallgatter AJ	Fallgatter AJ, Strik WK. Reversible neuropsychiatric side effects of lithium with normal serum levels. A case report. Nervenarzt 1997;68:586-90.	Germany	1997	PKN	1	56	Female	Manic depressive illness
Wils V	Wils V, Golüke-Willemse G. Extrapyramidal syndrome due to valproate administration as an adjunct to lithium in an elderly manic patient. Int J Geriatr Psychiatry 1997;12:272.	Netherlands	1997	PKN	1	70	Female	BD
Dallocchio C	Dallocchio C, Mazzarello P. A case of Parkinsonism due to lithium intoxication: Treatment with Pramipexole. J Clin Neurosci 2002;9:310-1.	Italy	2002	PKN	1	72	Female	BD
Luby ED	Luby ED, Singareddy RK. Long-term therapy with lithium in a private practice clinic: A naturalistic study. Bipolar Disord 2003;5:62-8.	US	2003	PKN	1 (3)	74	Female	BD
				PKN	1 (3)	78	Male	BD
				PKN	1 (3)	89	Female	BD

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication	
Kaplan PW	Kaplan PW, Birbeck G. Lithium-induced confusional states: Nonconvulsive status epilepticus or triphasic encephalopathy? Epilepsia 2006;47:2071-4.	US	2006	PKN	1	73	Female	BD	
Koener B	Koener B, Hermans E, Maloteaux JM, Jean-Jean A, Constant EL. Paradoxical motor syndrome following a switch from atypical neuroleptics to aripiprazole. Am J Psychiatry 2007;164:1437-8.	Belgium	2007	PKN	1	54	Female	BD	
Shen HC	Shen HC, Li JY, Lo YK. Lithium intoxication-induced acute Parkinsonism complicated with hyperparathyroidism and nephrogenic diabetes insipidus: Report of a case. Acta Neurol Taiwan 2007;16:231-3.	Taiwan	2007	PKN	1	67	Female	BD	
Aguilar LG	Aguilar LG, Ondo WG. Exploring the relationship between drug-induced Parkinsonism and tardive dyskinesias. Mov Disord 2008;23:275.	US	2008	PKN	13	63.2 (mean)	...	...	
Sarma GR	Sarma GR, Thomas M, R AK. Drug induced reversible Parkinsonism: A report of 5 cases: 723. Mov Disord 2008;23:237-8.	India	2008	PKN	1	72	Male	BD	
Huang YC	Huang YC, Lee Y, Lin PY. Reversible Pisa syndrome associated with switching from haloperidol to aripiprazole during lithium treatment. Prog Neuropsychopharmacol Biol Psychiatry 2009;33:1284-5.	Taiwan	2009	PKN	1	46	Female		Schizoaffective disorder, BD

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Munhoz R	Munhoz R, Teive H, Werneck L. Class specific manifestation in drug induced Parkinsonism: We-41. Mov Disord 2009;24:69.	Brazil	2009	PKN	2	66.3 (mean)	...	...
Walrave TRWM	Walrave TR, Bulens C. Parkinsonism during lithium use. Tijdschr Psychiatr 2009;51:123-7.	Netherlands	2009	PKN	2	...	...	BD
Palma JA	Palma JA, Fernandez-Torron R, Gallego Perez-Larraya J. Extrapyramidal syndrome related to lithium-carbamazepine combination therapy at therapeutic serum levels. Clin Neuropharmacol 2010;33:102-3.	Spain	2010	PKN - ATX, imbalance	1	62	Male	BD
Shprecher D	Shprecher D, Evans R. Dysphagia as a presenting symptom of progressive supranuclear palsy: 971. Mov Disord 2010;25:508.	US	2010	PKN	1	71	Female	BD
Bondon-Guitton E	Bondon-Guitton E, Perez-Lloret S, Bagheri H, Brefel C, Rascol O, Montastruc JL. Drug-induced Parkinsonism: A review of 17 years' experience in a regional pharmacovigilance center in France. Mov Disord 2011;26:2226-31.	France	2011	PKN	4	...	...	...
Caykoylu A	Caykoylu A, Ekinci O, Ugurlu GK, Albayrak Y. Aripiprazole-associated bruxism, akathisia, and Parkinsonism in a bipolar patient. J Clin Psychopharmacol 2011;31:134-5.	Turkey	2011	PKN - AKT, bruxism	1	20	Female	BD
Mazzini L	Mazzini L, Oggioni GD, Nasuelli N, Servo S, Testa L, Monaco F. Disabling Parkinsonism following brief exposure to lithium carbonate in amyotrophic lateral sclerosis. J Neurol 2011;258:333-4.	Italy	2011	PKN - ALS	1	46	Male	ALS

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Sarna JR	Sarna JR, Pringsheim T. Progressive supranuclear palsy-like phenotype associated with concomitant exposure to mood stabilizer and neuroleptic: 135. Mov Disord 2011;26:45.	Canada	2011	PKN	1 (2)	59	Male	BD
				PKN	1 (2)	63	Female	BD
Babinsky E	Babinsky E, Levene RS. Multisystem atrophy made worse by lithium treatment in a hospice patient: A case report. Am J Hosp Palliat Care 2012;29:570-3.	US	2012	PKN	1	65	Male	BD type I
Bhattacharjee S	Bhattacharjee S, Yela R, Chadwick G. Can lithium unmask the preclinical Parkinsonian features? Ir Med J 2013;106:254.	Ireland	2013	PKN	1	67	Male	BD
Alonso-Canovas A	Alonso-Canovas A, Lopez-Sendon JL, DeFelipe-Mimbrera A, Matute-Lozano MC, Sainz de la Maza-Cantero S, Buisan J, *et al*. Drug induced parkinsonism: Can transcranial ultrasound predict response to withdrawal of the offending drug? Mov Disord 2015;29:303.	Spain	2014	PKN	1	73.5 (mean)	...	...
Basile G	Basile G, Epifanio A, Mandraffino R, Trifirò G. Parkinsonism and severe hypothyroidism in an elderly patient: A case of lithium toxicity due to pharmacological interactions. J Clin Pharm Ther 2014;39:452-4.	Italy	2014	PKN	1	74	Female	BD
Cilia R	Cilia R, Marotta G, Belletti A, Siri C, Pezzoli G. Reversible dopamine transporter reduction in drug-induced Parkinsonism. Mov Disord 2014;29:575-7.	Italy	2014	PKN	1	71	Female	BD

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Irons R	Irons R, Joanna B, Apurba C. The role of DaT scan in drug induced Parkinsonism: 986. Mov Disord 2015;30:382.	UK	2015	PKN	1	80	Female	...
Vandewalle W	Vandewalle W, Boon E, Sienaert P. Movement disorders due to modern antidepressants and mood stabilizers. Tijdschr Psychiatr 2015;57:132-7.	Belgium	2015	PKN	2	...	...	...
Glass OM	Glass OM, Janjua AU, Hermida AP. Lithium-induced Parkinsonism in a bipolar patient. Am J Geriatr Psychiatry 2016;24:90.	US	2016	PKN	1	65	Female	BD
Hermida AP	Hermida AP, Janjua AU, Glass OM, Vaughan CP, Goldstein F, Trotti LM, *et al*. A case of lithium-induced Parkinsonism presenting with typical motor symptoms of Parkinson's disease in a bipolar patient. Int Psychogeriatr 2016;28:2101-4.	US	2016	PKN	1	65	Female	BD
Noyce AJ	Noyce AJ, Schrag A, Masters J, Bestwick JP, Giovannoni G, Lees AJ. Blinded video assessment of subtle Parkinsonian signs in PREDICT-PD participants: 1539. Mov Disord 2016;31:506.	UK	2016	PKN	1	...	...	...
Kumar N	Kumar N, Mendonça DA, Jog M. Teaching video NeuroImages: Lithium-induced reversible Pisa syndrome. Neurology 2017;88:e184.	US	2017	PKN - DTN (Pisa syndrome)	1	49	Male	BD
Aikoye SA	Aikoye SA, Parashar SD, Mann GS, Tinklepaugh M. Lithium toxicity misdiagnosed and treated as Parkinson's disease. Neurol Clin Therapeut J 2018;2:1-2.	US	2018	PKN - Subacute severe reversible	1	60	Female	BD

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Chandana G	Chandana G, Saijyothi D, Saranya PV, Nirmala G, Madhavl V, Ranganayakulu D. Lithium induced extrapyramidal symptoms - A Parkinson's disease in elderly patient. EC Pharmacol Toxicol 2018;6:375-7.	India	2018	PKN	1	70	Male	BD
Cruz CC	Cruz CC, Dafonte AA, Melero PV. Lithium Neurotoxicity: A Case Report: 1173. 31st ECNP Congress 2018. Barcelona, Spain; 2018.	Spain	2018	PKN	1	54	Male	BD
Florescu A	Florescu A, Whitney D, Bhatti D, Bertoni JM, Torres-Russotto D. Paradoxical worsening of Parkinsonism upon neuroleptic withdrawal: More common than we think? Parkinsonism Relat Disord 2018;52:115-6.	US	2018	PKN	1	68	Male	BD
Yomtoob J	Yomtoob J, Koloms K, Bega D. DAT-SPECT imaging in cases of drug-induced Parkinsonism in a specialty movement disorders practice. Parkinsonism Relat Disord 2018;53:37-41.	US	2018	PKN	...	...	...	...
Shingavi S	Shingavi S, Singaravelan RM, Bhalerao S. Use of therapeutic exercises in drug induced Parkinsonism: A case report. Int J Sci Dev Res 2019;4:537-9.	India	2019	PKN - Physiotherapy	1	62	Male	BD
				DKN				
Peters HA	Peters HA. Lithium intoxication producing chorea athetosis with recovery. Wis Med J 1949;48:1075.	US	1949	DKN - Choreoathetosis	1	...	...	...
Crews EL	Crews EL, Carpenter AE. Lithium-induced aggravation of tardive dyskinesia. Am J Psychiatry 1977;134:933.	US	1977	DKN - Aggravation of TD	1	46	Female	BD, maniac phase

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Beitman BD	Beitman BD. Tardive dyskinesia reinduced by lithium carbonate. Am J Psychiatry 1978;135:1229-30.	US	1978	DKN - TD, orofacial	1	56	Female	Recurrent depressive episodes
Stancer HC	Stancer HC. Tardive dyskinesia not associated with neuroleptics. Am J Psychiatry 1979;136:727.	US	1979	DKN - TD	1 (2)	62	Female	DPS (sister was bipolar)
				DKN - TD	1 (2)	38	Male	Manic-depressive disorder
Thomas CJ	Thomas CJ. Brain damage with lithium/haloperidol. Br J Psychiatry 1979;134:552.	England	1979	DKN - Orofacial	1	58	Female	Manic-depressive psychosis
Himmelhoch JM	Himmelhoch JM, Neil JF, May SJ, Fuchs CZ, Licata SM. Age, dementia, dyskinesias, and lithium response. Am J Psychiatry 1980;137:941-5.	US	1980	DKN - PKN	15 (81)	63.27 (mean)	...	BD, manic-depressive episodes
Sachdeva JR	Sachdeva JR, Paruthi SC. Chorea-a complication of lithium. J Indian Med Assoc 1980;75:37-8.	India	1980	DKN - Chorea	1	…	…	…
Heim J	Heim J, Pinel JF, Allannic H, Ferrand P, Sabouraud O, Lorcy Y. A case of permanent neurological sequelae by lithium intoxication during a thyrotoxicosis. Sem Hop 1981;57:1349-52.	France	1981	DKN	1	…	…	…
Weiner WJ	Weiner WJ, Nausieda PA, Glantz RH. Meige syndrome (blepharospasm-oromandibular dystonia) after long-term neuroleptic therapy. Neurology 1981;31:1555-6.	US	1981	DKN - Meige-like syndrome	1 (2)	...	...	...
				DKN - Meige-like syndrome	1 (2)	...	...	Intermittent psychosis
Lieberman A	Lieberman A, Gopinathan G. Treatment of “on-off” phenomena with lithium. Ann Neurol 1982;12:402.	US	1982	DKN - Increase on-off phenomena of PKN	1	62 (mean)	...	Treatment of on-off syndrome
Lewis DA	Lewis DA. Unrecognized chronic lithium neurotoxic reactions. JAMA 1983;250:2029-30.	US	1983	DKN	1	58	Male	BD

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Mann SC	Mann SC, Greenstein RA, Eilers R. Early onset of severe dyskinesia following lithium-haloperidol treatment. Am J Psychiatry 1983;140:1385-6.	US	1983	DKN - Axial DTN, tics, choreoathetosis, AKT	1	39	Male	BD
Manor E	Manor E. A case of reversible tachy-bradycardia syndrome and permanent neurological sequelae in lithium intoxication. In: Chambers CM, Chambers PL, Gitter S, editors. Toxicology in the Use, Misuse, and Abuse of Food, Drugs, and Chemicals. Archives of Toxicology (Supplement). Vol. 6. Berlin, Heidelberg: Springer; 1983.	Israel	1983	DKN	1	28	Female	Manic depressive illness
Rao AV	Rao AV, Hariharasubramanian N, Sugumar A. A study of side effects of lithium. Indian J Psychiatry 1983;25:87-93.	India	1983	DKN	4 (120)	39.5 (mean)	...	BD, unipolar disorder
Standish-Barry HMAS	Standish-Barry HM, Shelly MA. Toxic neurological reaction to lithium/ thioridazine. Lancet 1983;1:771.	England	1983	DKN - AKT, choreoathetosis, oromandibular DTN	1	45	Female	Manic-depressive psychosis for 24 years
Zorumski CF	Zorumski CF, Bakris GL. Choreoathetosis associated with lithium: Case report and literature review. Am J Psychiatry 1983;140:1621-2.	US	1983	DKN - ATX, dysarthria, choreoathetosis	1	58	Female	BD
Coffey CE	Coffey CE, Ross DR, Massey EW, Olanow CW. Dyskinesias associated with lithium therapy in Parkinsonism. Clin Neuropharmacol 1984;7:223-9.	US	1984	DKN - Choreoathetosis, hemiballismus, axial DTN, oromandibular DTN	1 (5)	60	Male	Reduce Parkinson's akinesia (trial)
				DKN - Choreoathetosis, hemiballismus, axial DTN, oromandibular DTN	1 (5)	55	Male	Reduce Parkinson's akinesia (trial)
				DKN - Choreoathetosis, hemiballismus	1 (5)	37	Female	Reduce Parkinson's akinesia (trial)
				DKN - Axial DTN, choreoathetosis	1 (5)	67	Female	Reduce Parkinson's akinesia (trial)
				DKN - Oromandiublar DTN	1 (5)	69	Male	Reduce Parkinson's akinesia (trial)

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Perényi A	Perényi A, Szücs R, Frecska E. Tardive dyskinesia in patients receiving lithium maintenance therapy. Biol Psychiatry 1984;19:1573-8.	Hungary	1984	DKN	1	…	…	…
Campbell WG	Campbell WG, Raskind MA, Gordon T, Shaw CM. Iron pigment in the brain of a man with tardive dyskinesia. Am J Psychiatry 1985;142:364-5.	US	1985	DKN	1	64	Male	BD
Walevski A	Walevski A, Radwan M. Choreoathetosis as toxic effect of lithium treatment. Eur Neurol 1986;25:412-5.	Israel	1986	DKN	1 (2)	62	Female	Maniform psychotic state
				DKN	1 (2)	73	Female	BD
Haggerty JJ Jr.	Haggerty JJ Jr., Bentsen BS, Gillette GM. Neuroleptic malignant syndrome superimposed on tardive dyskinesia. Br J Psychiatry 1987;150:104-5.	UK	1987	DKN - TD, choreoathetosis	1	30	Male	Paranoid psychosis
Nagaraja D	Nagaraja D, Taly AB, Sahu RN, Channabasavanna SM, Narayanan HS. Permanent neurological sequelae due to lithium toxicity. Clin Neurol Neurosurg 1987;89:31-4.	India	1987	DKN	1 (6)	35	Male	Manic-depressive psychosis
				DKN	1 (6)	32	Female	Manic-depressive psychosis
				DKN	1 (6)	56	Male	Manic-depressive psychosis
Nasrallah HA	Nasrallah HA, Churchill CM, Hamdan-Allan GA. Higher frequency of neuroleptic-induced dystonia in mania than in schizophrenia. Am J Psychiatry 1988;145:1455-6.	US	1988	DKN - DTN	12 (46)	...	Male	BD
Dinan TG	Dinan TG, Kohen D. Tardive dyskinesia in bipolar affective disorder: Relationship to lithium therapy. Br J Psychiatry 1989;155:55-7.	UK	1989	DKN - TD	9(40)	…	…	…
Helmuth D	Helmuth D, Ljaljevic Z, Ramirez L, Meltzer HY. Choreoathetosis induced by verapamil and lithium treatment. J Clin Psychopharmacol 1989;9:454-5.	US	1989	DKN - Choreoathetosis	1	66	Male	BD

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Matsis PP	Matsis PP, Fisher RA, Tasman-Jones C. Acute lithium toxicity-chorea, hypercalcemia and hyperamylasemia. Aust N Z J Med 1989;19:718-20.	New Zealand	1989	DKN - Choreiform movements	1	71	Female	BD
Reed SM	Reed SM, Wise MG, Timmerman I. Choreoathetosis: A sign of lithium toxicity. J Neuropsychiatry Clin Neurosci 1989;1:57-60.	US	1989	DKN - Choreoathetosis	1 (2)	61	Male	BD
				DKN - Choreoathetosis	1 (2)	73	Male	BD
Sternbach H	Sternbach H, Jordan S. Lithium-associated tardive dyskinesia. J Clin Psychopharmacol 1990;10:143-4.	US	1990	DKN - TD, oromandibular DTN	1	63	Female	Manic-depressive illness
Scappa S	Scappa S, Teverbaugh P, Ananth J. Episodic tardive dyskinesia and Parkinsonism in bipolar disorder patients. Can J Psychiatry 1993;38:633-4.	Canada	1993	DKN - PKN, choreoathetosis	1 (3)	41	Male	Mania, DPS
				DKN - Choreoathetosis, DTN	1 (3)	29	Female	BD
Lazarus A	Lazarus A. Tardive dyskinesia-like syndrome associated with lithium and carbamazepine. J Clin Psychopharmacol 1994;14:146-7.	US	1994	DKN - TD, DTN, MCL	1	36	Female	BD
Trugman JM	Trugman JM, Leadbetter R, Zalis ME, Burgdorf RO, Wooten GF. Treatment of severe axial tardive dystonia with clozapine: Case report and hypothesis. Mov Disord 1994;9:441-6.	US	1994	DKN - DTN; history of PKN, AKT	1	33	Male	Schizophrenia
Podskalny GD	Podskalny GD, Factor SA. Chorea caused by lithium intoxication: A case report and literature review. Mov Disord 1996;11:733-7.	US	1996	DKN - Choreoathetosis, dysarthria, gait ataxia	1	78	Female	BD

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Meyer-Lindenberg A	Meyer-Lindenberg A, Krausnick B. Tardive dyskinesia in a neuroleptic-naive patient with bipolar-I disorder: Persistent exacerbation after lithium intoxication. Mov Disord 1997;12:1108-9.	Germany	1997	DKN - Chorea, tremor, ATX gait	1	72	Female	BD type 1
Higes-Pascual F	Higes-Pascual F, de Arriba de la Fuente G, de Pedro-Esteban F. Choreoathetosis: An uncommon sign of lithium poisoning. Rev Neurol 1998;26:841.	Spain	1998	DKN - Choreoathetosis	1	64	Female	Manic-depressive, hypomania, psychosis
Normann C	Normann C, Brandt C, Berger M, Walden J. Delirium and persistent dyskinesia induced by a lithium-neuroleptic interaction. Pharmacopsychiatry 1998;31:201-4.	Germany	1998	DKN - Choreoatheosis, PKN	1	62	Female	BD
Gerding LB	Gerding LB, Labbate LA. Use of clonazepam in an elderly bipolar patient with tardive dyskinesia: A case report. Ann Clin Psychiatry 1999;11:87-9.	US	1999	DKN - TD, choreoathetoid movements, DTN	1	81	Male	BD type 1
McGavin CL	McGavin CL, John V, Musser WS. Levetiracetam as a treatment for tardive dyskinesia: A case report. Neurology 2003;61:419.	US	2003	DKN - TD, choreic, DTN	1	60	Female	Chronic DPS and borderline
Stemper B	Stemper B, Thürauf N, Neundörfer B, Heckmann JG. Choreoathetosis related to lithium intoxication. Eur J Neurol 2003;10:743-4.	Germany	2003	DKN - Choreoathetosis	1	76	Female	Recurrent depressive episodes
Wada K	Wada K, Sasaki T, Yoshimura Y, Erabi H. Reversible choreoathetosis associated with lithium intoxication. Seishin Shinkeigaku Zasshi 2003;105:1206-12.	Japan	2003	DKN - Choreoathetosis	1	65	Female	BD type 2

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Bender S	Bender S, Linka T, Wolstein J, Gehendges S, Paulus HJ, Schall U, *et al*. Safety and efficacy of combined clozapine-lithium pharmacotherapy. Int J Neuropsychopharmacol 2004;7:59-63.	Germany	2004	DKN - Orofacial	3	39.5	...	...
Mendhekar DN	Mendhekar DN, Subhash KR. Successful treatment of senile dyskinesia with risperidone. Indian J Pharmacol 2004;36:102.	India	2004	DKN - Senile spontaneous DKN	1	72	Male	Severe major DPS
Mendhekar DN	Mendhekar DN. Rabbit syndrome induced by combined lithium and risperidone. Can J Psychiatry 2005;50:369.	India	2005	DKN - AKT, rabbit syndrome	1	42	Female	BD
Ozsoy S	Ozsoy S, Basturk M, Esel E. Cerebellar syndrome in a patient with pneumonia under lithium treatment: A case report. Prog Neuropsychopharmacol Biol Psychiatry 2006;30:1532-4.	Turkey	2006	DKN - Dysarthria, ATX	1	31	Male	BD
Hunter CB	Hunter CB, Kenney C, Mejia N, Davidson A, Jankovic J. Medications Associated with the Onset of Tardive Dyskinesia. Baylor College of Medicine; 2008.	US	2008	DKN	9	63.8 (mean)	...	...
Lloyd RB	Lloyd RB, Perkins RE, Schwartz AC. Choreoathetosis in the setting of lithium toxicity. Psychosomatics 2010;51:529-31.	US	2010	DKN - Choreoathetosis	1	69	Female	Schizoaffective disorder and BD
Chung AK	Chung AK. Atypical presentation of tardive dyskinesia associated with risperidone long-acting injection as maintenance treatment in bipolar affective disorder: A case report. Curr Drug Saf 2012;7:21-3.	China	2012	DKN - Oromandibular DTN	1	55	Male	BD

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Arambewela MH	Arambewela MH, Palangasinghe DR, Katulanda P. A patient with neuropsychiatric manifestations and thyrotoxicosis in a background of lithium toxicity. Thyroid Disorders Ther 2015;4:3.	Sri Lanka	2015	DKN - Chorea, ATX, dysarthria	1	70	Male	...
Cobb A	Cobb A, Messerli A, Klingeman H, Aakre C, Mohabbat AB. A rare complication of lithium toxicity. Minn Med 2015;98:42.	US	2015	DKN - Chorea, ATX, PKN	1	75	Female	BD type 1
Vandewalle W	Vandewalle W, Boon E, Sienaert P. Movement disorders due to modern antidepressants and mood stabilizers. Tijdschr Psychiatr 2015;57:132-7.	Belgium	2015	DKN - Not specified the DKN type	4	...	...	...
Amamou B	Amamou B, Essid N, Mrad A, Mhalla A, Gaha L. Resolution of tardive dyskinesia with clozapine: A case report. Dual Diagn Open Access 2016;1:19.	Tunisia	2016	DKN - TD, DTN	1	43	Male	BD
Huang SS	Huang SS. Prolonged dyskinesia following lithium intoxication in an elderly patient with bipolar I disorder. Kaohsiung J Med Sci 2016;32:278-9.	China	2016	DKN - Chorea	1	67	Female	BD type I
Rachamallu V	Rachamallu V, Haq A, Song MM, Aligeti M. Clozapine-induced microseizures, orofacial dyskinesia, and speech dysfluency in an adolescent with treatment resistant early onset schizophrenia on concurrent lithium therapy. Case Rep Psychiatry 2017;2017:7359095.	US	2017	DKN - Orofacial	1	16	Male	Schizoaffective disorder

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Fountoulakis KN	Fountoulakis KN, Tegos T, Kimiskidis V. Lithium monotherapy-induced tardive dyskinesia. J Affect Disord 2019;244:78-9.	Greece	2019	DKN - TD	1	68	Female	BD
Silva DG	Silva GD, Parmera JB, Haddad MS. Acute chorea: Case series from the emergency room of a Brazilian tertiary-level center. Arq Neuropsiquiatr 2021;79:233-7.	Brazil	2020	DKN - Chorea	1	61	Female	...
				AKT				
Loudon JB	Loudon JB, Waring H. Toxic reactions to lithium and haloperidol. Lancet 1976;2:1088.	Scotland	1976	AKT - Haloperidol + LTM	1	37	Male	Manic-depressive illness
Channabasavanna, SM	Channabasavanna SM, Goswami U. Akathisia during lithium prophylaxis. Br J Psychiatry 1984;144:555-6.	India	1984	AKT - PKN	1	52	Male	BD
Price WA	Price WA, Zimmer B. Lithium-induced akathisia. J Clin Psychiatry 1987;48:81.	US	1987	AKT	1	66	Female	BD
Zubenko GS	Zubenko GS, Cohen BM, Lipinski JF Jr. Antidepressant-related akathisia. J Clin Psychopharmacol 1987;7:254-7.	US	1987	AKT - Trazodone + LTM	1	63	Male	BD, DPS
Patterson JF	Patterson JF. Lithium-induced akathisia. J Clin Psychopharmacol 1988;8:445.	US	1988	AKT - Restless legs syndrome	1	54	Male	Manic episode
Yassa R	Yassa R, Groulx B. Lorazepam in the treatment of lithium-induced akathisia. J Clin Psychopharmacol 1989;9:70-1.	Canada	1989	AKT - Lorazepam therapy	1	64	Male	BD
Poyurowsky M	Poyurovsky M, Kreinin A, Modai I, Weizman A. Lithium-induced akathisia responds to low-dose mianserin: Case report. Int Clin Psychopharmacol 1995;10:261-3.	Israel	1995	AKT - Mianserin therapy	1	34	Male	BD

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Muthane UB	Muthane UB, Prasad BN, Vasanth A, Satishchandra P. Tardive Parkinsonism, orofacial dyskinesia and akathisia following brief exposure to lithium carbonate. J Neurol Sci 2000;176:78-9.	India	2000	AKT - PKN, orofacial DKN	1	65	Female	DPS and pathological sexual desire
Scorr L	Scorr L, Factor S. Non-tardive orofacial akathisia with dental sensory phenomenon. Mov Disord 2015;30:285.	US	2015	AKT - Orofacial AKT	1	73	Male	BD
Vandewalle W	Vandewalle W, Boon E, Sienaert P. Movement disorders due to modern antidepressants and mood stabilizers. Tijdschr Psychiatr 2015;57:132-7.	Belgium	2015	AKT	1	...	...	...
Demir B	Demir B, Sancaktar M, Altindag A. Lithium-induced treatment-resistant akathisia: A case report and literature overview. Clin Neuropharmacol 2021;44:112-3.	Turkey	2021	AKT	1	49	Female	Maniac episode
				RLS				
Heiman EM	Heiman EM, Christie M. Lithium-aggravated nocturnal myoclonus and restless legs syndrome. Am J Psychiatry 1986;143:1191-2.	US	1986	RLS - Aggravated by LTM	1	48	Female	BD
Terao T	Terao T, Terao M, Yoshimura R, Abe K. Restless legs syndrome induced by lithium. Biol Psychiatry 1991;30:1167-70.	Japan	1991	RLS	1	18	Male	Obsessive-compulsive disorder
Kauta S	Kauta S, Antoniou M. An atypical case of restless legs syndrome affecting only the toes and exacerbated by lithium. J Sleep Disorders Ther 2013;2:1000107.	US	2013	RLS - Aggravated by LTM	1	51	Female	Mood disorder

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Demirci K	Demirci K, Sert H. Does using quetiapine and lithium at the same time create restless leg syndrome? A case report. Klinik Psikofarmakoloji Bulteni 2014;24:149-50.	Turkey	2014	RLS - Quetiapine + LTM	1	...	Female	BD
Chen PH	Chen PH. Restless leg syndrome induced by escitalopram and lithium combined with quetiapine treatment in bipolar II disorder: A case report. Clin Neuropharmacol 2016;39:118-9.	China	2016	RLS - Quetiapine + LTM	1	46	Male	BD type 2
Öhlund L	Öhlund L, Ott M, Oja S, Bergqvist M, Lundqvist R, Sandlund M, *et al*. Reasons for lithium discontinuation in men and women with bipolar disorder: A retrospective cohort study. BMC Psychiatry 2018;18:37.	Sweden	2018	RLS	5	...	...	BD
				Stutter				
Netski AL	Netski AL, Piasecki M. Lithium-induced exacerbation of stutter. Ann Pharmacother 2001;35:961.	US	2001	Stuttering	1	48	Male	BD
Gulack BC	Gulack BC, Puri NV, Kim WJ. Stutter exacerbated by lithium in a pediatric patient with bipolar disorder. Ann Pharmacother 2011;45:e57.	US	2011	Stuttering	1	10	Male	BD
Sabillo S	Sabillo S, Samala RV, Ciocon JO. A stuttering discovery of lithium toxicity. J Am Med Dir Assoc 2012;13:660-1.	US	2012	Stuttering	1	86	Female	BD
				CJLS				
Helmchen H	Helmchen H, Kanowski S. EEG-changes during lithium therapy. Nervenarzt 1971;42:144-8.	Germany	1971	CJLS	1	...	...	...

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Kemperman CJ	Kemperman CJ, van Gent EM, de Rooij JA, Notermans SL. Neurotoxicity of lithium with normal lithium levels. Ned Tijdschr Geneeskd 1988;132:2066-70.	Netherlands	1988	CJLS	1	72	Female	…
Smith SJ	Smith SJ, Kocen RS. A Creutzfeldt-Jakob like syndrome due to lithium toxicity. J Neurol Neurosurg Psychiatry 1988;51:120-3.	UK	1988	CJLS - PKN	1 (2)	72	Female	DPS
				CJLS - MCL	1 (2)	69	Female	DPS
Broussolle E	Broussolle E, Setiey A, Moene Y, Trielett M, Chazot G. Reversible Creutzfeldt-Jakob like syndrome induced by lithium plus levodopa treatment. J Neurol Neurosurg Psychiatry 1989;52:686-7.	France	1989	CJLS - PKN	1	70	Female	DPS
Primavera A	Primavera A, Brusa G, Poeta MG. A Creutzfeldt-Jakob like syndrome due to lithium toxicity. J Neurol Neurosurg Psychiatry 1989;52:423.	Italy	1989	CJLS	1 (2)	...	...	...
				CJLS - Choreoathetosis	1 (2)	...	...	...
Waldman AJ	Waldman AJ. A Creutzfeldt-Jakob-like syndrome due to polypharmacy. South Med J 1990;83:1493.	US	1990	CJLS - Tremor	1	68	Female	DPS
Fineli PF	Finelli PF. Drug-induced Creutzfeldt-Jakob like syndrome. J Psychiatry Neurosci 1992;17:103-5.	US	1992	CJLS - MCL	1	63	Male	DPS
Casanova B	Casanova B, de Entrambasaguas M, Perla C, Gómez-Siurana E, Benetó A, Burguera JA. Lithium-induced Creutzfeldt-Jakob syndrome. Clin Neuropharmacol 1996;19:356-9.	Spain	1996	CJLS - MCL, PKN	1	67	Male	BD

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Masmoudi K	Masmoudi K, Rosa A, Canaple S, Andrejak M. Pseudo-Creutzfeldt-Jakob syndrome with long-term lithium use. Therapie 1996;51:688-90.	France	1996	CJLS	1	…	…	…
Laasonen-Balk T	Laasonen-Balk T, Paukkala E, Koponen H. Creutzfeldt-Jacob like syndrome due to lithium intoxication. Duodecim 1997;113:323-5.	Finland	1997	CJLS	1	…	…	…
Takahashi M	Takahashi M, Hashimoto S, Suenaga T, Nakamura M, Takahashi K. Creutzfeldt-Jakob like syndrome due to lithium intoxication - A case report. Rinsho Shinkeigaku 1997;37:338-40.	Japan	1997	CJLS - MCL	1	76	Female	…
Kikyo H	Kikyo H, Furukawa T. Creutzfeldt-Jakob-like syndrome induced by lithium, levomepromazine, and phenobarbitone. J Neurol Neurosurg Psychiatry 1999;66:802-3.	Japan	1999	CJLS - MCL	1	65	Female	Manic-depressive disease
Slama M	Slama M, Masmoudi K, Blanchard N, Andréjak M. A possible case of lithium intoxication mimicking Creutzfeld-Jakob syndrome. Pharmacopsychiatry 2000;33:145-6.	France	2000	CJLS - MCL	1	66	Female	BD
Mouldi S	Mouldi S, Le Rhun E, Gautier S, Devemy M, Destée A, Defebvre L. Lithium-induced encephalopathy mimicking Creutzfeldt-Jakob disease. Rev Neurol (Paris) 2006;162:1118-21.	France	2006	CJLS - MCL, CS	1	67	Male	BD
Isikay CT	Işikay CT, Yığıt A, Çelık T. Creutzfeldt-Jakob-like EEG changes in a case of fatal lithium toxicity. J Neurol Sci 2011;28:604-8.	Turkey	2011	CJLS	1	52	Female	BD

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Kim SW	Kim SW, Sunwoo MK, Hong JY, Lee JD, Lee PH. The perfusion pattern in a patient with lithium intoxication mimicking Creutzfeldt-Jakob disease. J Clin Psychiatry 2013;74:e1134-5.	Korea	2013	CJLS - MCL	1	…	…	…
Fernández-Torre JL	Fernández-Torre JL, Oterino A, Marcelino-Salas K, Riesco-Pérez N. Creutzfeldt-Jakob-like syndrome secondary to severe lithium intoxication: A detailed follow-up electroencephalographic study. Clin Neurophysiol 2014;125:2315-7.	Spain	2014	CJLS - MCL, PKN	1	78	Female	Schizoaffective disorder
Madhusudhan BK	Madhusudhan BK. Nonconvulsive status epilepticus and Creutzfeldt-Jakob-like EEG changes in a case of lithium toxicity. Epilepsy Behav Case Rep 2014;2:203-5.	India	2014	CJLS	1	63	Female	BD
				DTN				
Aronson TA	Aronson TA. Persistent drug-induced Parkinsonism. Biol Psychiatry 1985;20:795-8.	US	1985	DTN - LTM, haloperidol	1	45	Male	DPS
Goetting MG	Goetting MG. Acute lithium poisoning in a child with dystonia. Pediatrics 1985;76:978-80.	US	1985	DTN - Intoxication	1	3.5	Female	Intoxication
Yazici O	Yazici O, Kantemir E, Taştaban Y, Uçok A, Ozgüroğlu M. Spontaneous improvement of tardive dystonia during mania. Br J Psychiatry 1991;158:847-50.	UK	1991	DTN - Tardive DTN, laterocollis	1 (2)	30	Female	Manic disorder
			1991	DTN - Tardive DTN	1 (2)	33	Female	Depressive syndrome (with a suicide attempt) and a paranoid component. Hypomania in the past
Manji H	Manji H, Howard RS, Miller DH, Hirsch NP, Carr L, Bhatia K, *et al.* Status dystonicus: The syndrome and its management. Brain 1998;121:243-52.	UK	1998	DTN - Status dystonicus	1	23	Female	...

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Durrenberger S	Durrenberger S, de Leon J. Acute dystonic reaction to lithium and risperidone. J NeuropsychiatryClinNeurosci 1999;11:518-9.	US	1999	DTN - LTM + risperidone	1	...	...	...
Chakrabarti S	Chakrabarti S, Chand PK. Lithium - Induced tardive dystonia. Neurol India 2002;50:473-5.	India	2002	DTN - Tardive DTN, laterocollis, retrocollis	1	38	Male	BD
Rosebush PI	Rosebush PI. Tardive dystonia and its treatment. J Psychiatry Neurosci 2003;28:240.	Canada	2003	DTN - Tardive DTN, torticollis	1	45	Male	Manic episodes
Silva MC	Silva MC, Ramani MK, Murthy P. Lithium withdrawal induced dystonia - A case report. Priory Psych 2003; Available from: https://www.priory.com/psych/lithdystonia.htm. [Last accessed on 2021 Nov 23].	India	2003	DTN - Axial DTN	1	43	Male	Dementia, mood swings, behavioral disturbances
Oommen E	Oommen E, Chand PK, Sharma PS. Aripiprazole-induced tardive dystonia. Prim Care Companion J Clin Psychiatry 2006;8:378-9.	India	2007	DTN - LTM + aripiprazole	1	25	Female	Schizoaffective disorder
Kwan Y	Kwan Y, Sim K. Resolution of tardive dystonia in a patient with bipolar disorder treated with clozapine: A case report. Prog Neuropsychopharmacol Biol Psychiatry 2010;34:238-9.	China	2010	DTN - LTM + haloperidol	1	34	Male	BD
Mclaren JL	McLaren JL, Cauble S, Barnett RJ. Aripiprazole induced acute dystonia after discontinuation of a stimulant medication. J Clin Psychopharmacol 2010;30:77-8.	Lebanon	2010	DTN - Oromandibular DTN	1	11	Male	BD
Vandewalle W	Vandewalle W, Boon E, Sienaert P. Movement disorders due to modern antidepressants and mood stabilizers. Tijdschr Psychiatr 2015;57:132-7.	Belgium	2015	DTN - Not specific type of DTN	1	...	...	...

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Chandar P	Chandar P, Kulandaisamy S, Malhotra I, Kupfer Y, Shamian B, Rai AK, *et al*. 1749: Lithium-induced angioedema. Crit Care Med 2016;44:512.	US	2016	DTN - Oromandibular DTN	1	46	Male	DPS
Engel A	Engel A, Bilbruck T, Hossain S, Leahy R. Lithium-induced acute intermittent dystonia in a patient with schizoaffective disorder. Eur Psychiatry 2016;33:539.	US	2016	DTN - Intermittent	1	69	Male	Schizoaffective disorder
Huang SY	Huang SY, Huang MW, Tseng SY, Huang LC. Reversible Pisa syndrome related to the interaction between lithium and clotiapine: Case report. Kaohsiung J Med Sci 2018;34:707-8.	China	2018	DTN - Pisa syndrome	1	31	Female	BD
Aggarwal R	Aggarwal R, Garg D, Dhamija RK. Lithium-induced lingual dystonia. Ann Indian Acad Neurol 2020;23:383-4.	India	2019	DTN - Lingual DTN	1	60	Male	BD
Yildiz MÇ	Yildiz MÇ, Arslan M, Gökçenoğlu Y, Çalışkan AM, Çalışkan S, Eren I. Dystonia as an unexpected interaction of ciprofloxacin and clozapine: A case report. Klinik Psikofarmakoloji Bulteni 2019;29:182.	Turkey	2019	DTN - LTM + clozapine + ciprofloxacin	1	55	Male	Complaints of excessive and rapid speech, irritability, aggression, sleep disturbances, increased appetite and libido
Pikard JL	Pikard JL, Oliver D, Saraceno J, Groll D. Lithium: Contributor to movement disorder sensitivity after anoxic brain injury? SAGE Open Med Case Rep 2019;7:2050313X18823101.	Canada	2019	DTN - Segmental DTN	1	35	Male	BD type 1
Chaudhari P	Chaudhari P, Karia S, Shah N, De Sousa A. Lithium induced bruxism: A case report. Indian J Ment Health 2020;7:384-6.	India	2020	DTN - Bruxism	1	18	Female	BD type 1

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Hsieh H	Hsieh HT, Yeh YW. Dose-dependent effects of lithium treatment on the aggravation of antipsychotic-induced Pisa syndrome. Clin Neuropharmacol 2020;43:90-1.	Taiwan	2020	DTN - Pisa syndrome	1	62	Male	BD type 1
Kumar A	Kumar A, Grover S. A rare association of lithium carbonate with blepharospasm: A case report. Indian J Psychiatry 2020;62:743-5.	India	2020	DTN - Blepharospasm	1	41	Male	BD
				Tics				
Kerbeshian J	Kerbeshian J, Burd L. Differential responsiveness to lithium in patients with Tourette disorder. Neurosci Biobehav Rev 1988;12:247-50.	US	1988	LTM worsening Tourette disorder symptoms	5	9.6	Male	BD
Potter PO	Potter PO, John N, Coffey DB. Onset of abnormal movements and cardiovascular symptoms after acute change in complex polypharmacy in a child with attention-deficit/hyperactivity disorder and mood symptoms. J Child Adolesc Psychopharmacol 2012;22:388-92.	US	2012	Tic aggraveted by LTM	1	8	Male	Aggressive behavior
				Cerebellar syndrome				
Nagaraja D	Nagaraja D, Taly AB, Sahu RN, Channabasavanna SM, Narayanan HS. Permanent neurological sequelae due to lithium toxicity. Clin Neurol Neurosurg 1987;89:31-4.	India	1987	Cerebellar syndrome	1 (6)	32	Male	Manic-depressive psychosis
				Cerebellar syndrome	1 (6)	33	Female	Manic-depressive psychosis
				Cerebellar syndrome	1 (6)	41	Male	Manic-depressive psychosis
Tesio L	Tesio L, Porta GL, Messa E. Cerebellar syndrome in lithium poisoning: A case of partial recovery. J Neurol Neurosurg Psychiatry 1987;50:235.	Italy	1987	Cerebellar syndrome - Intoxication, coma	1	51	Male	Suicide attempt. Intoxication

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Yoshimoto Y	Yoshimoto Y. A case of lithium intoxication with downbeat vertical nystagmus. Auris Nasus Larynx 1987;14:71-5.	Japan	1987	Cerebellar syndrome	1	56	Male	Mania
Others not clearly defined - EPSs without clearly stating other of the above, or unclear relation to lithium								
Shopsin B	Shopsin B, Johnson G, Gershon S. Neurotoxicity with lithium: Differential drug responsiveness. Int Pharmacopsychiatry 1970;5:170-82.	US	1970	EPS - Motor stereotype	1 (4)	28	Female	Schizophrenic reaction, schizoaffective type, with marked elation
				EPS - Motor stereotype	1 (4)	43	Male	Prophylaxis against manic and depressive relapses
McCaul JA	McCaul JA, Stern GM. Letter: Lithium in Parkinson's disease. Lancet 1974;1:1117.	England	1974	PKN - Does not change PKN disabilities	21	...	...	Parkinson's disease
Gabriel E	Gabriel E, Karobath M, Lenz G. The extrapyramidal symptoms in the combination of lithium long-term lithium therapy with nortriptyline. A case report on the formation of a pathogenesis hypothesis. Nervenarzt 1976;47:46-8.	Austria	1976	EPS - LTM + nortriptyline	1	...	...	...
Johnels B	Johnels B, Wallin L, Wålinder J. Extrapyramidal side effects of lithium treatment. Br Med J 1976;2:642.	Sweden	1976	EPS	1 (2)	57	Female	BD
				EPS	1 (2)	59	Male	BD
Kane J	Kane J, Rifkin A, Quitkin F, Klein DF. Extrapyramidal side effects with lithium treatment. Am J Psychiatry 1978;135:851-3.	US	1978	EPS	38	36 (mean)	Male and Female	36 bipolar manic-depressive patients and 2 schizoaffective patients
Bone S	Bone S, Roose SP, Dunner DL, Fieve RR. Incidence of side effects in patients on long-term lithium therapy. Am J Psychiatry 1980;137:103-4.	US	1980	EPS	125	...	Male and Female	Acute mania, BD

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Miller F	Miller F, Menninger J, Whitcup SM. Lithium-neuroleptic neurotoxicity in the elderly bipolar patient. J Clin Psychopharmacol 1986;6:176-8.	US	1986	EPS	1 (3)	70	Female	BD, depressed type
				EPS	1 (3)	70	Female	BD, depressed type
				EPS	1 (3)	72	Female	BD, depressed type
Sachdev PS	Sachdev PS. Lithium potentiation of neuroleptic-related extrapyramidal side effects. Am J Psychiatry 1986;143:942.	New Zealand	1986	EPS - PKN	1	27	Female	Manic illness
Miller F	Miller F, Menninger J. Lithium-neuroleptic neurotoxicity is dose dependent. J Clin Psychopharmacol 1987;7:89-91.	US	1987	EPS related to LTM-dose	6 (22) - only 6 developed neurotoxicity	Unclear	Unclear	BD
Morgenstern H	Morgenstern H, Glazer WM, Gibowski LD, Holmberg S. Predictors of tardive dyskinesia: Results of a cross-sectional study in an outpatient population. J Chronic Dis 1987;40:319-27.	US	1987	DKN - TD	12 (180)	55 (mean)	...	...
Addonisio G	Addonizio G, Roth SD, Stokes PE, Stoll PM. Increased extrapyramidal symptoms with addition of lithium to neuroleptics. J Nerv Ment Dis 1988;176:682-5.	US	1988	EPS	10	37.2 (18-59)	9 female and 1 male	5 BD, 2 schizoaffective disorder, 3 schizophrenic disorders
Nasrallah HA	Nasrallah HA, Churchill CM, Hamdan-Allan GA. Higher frequency of neuroleptic-induced dystonia in mania than in schizophrenia. Am J Psychiatry 1988;145:1455-6.	US	1988	Acute DTN	135	...	...	...
Waddington JL	Waddington JL, Youssef HA. Tardive dyskinesia in bipolar affective disorder: Aging, cognitive dysfunction, course of illness, and exposure to neuroleptics and lithium. Am J Psychiatry 1988;145:613-6.	US	1988	DKN - Prognostic factors	25	...	...	...

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Axelsson R	Axelsson R, Nilsson A. On the pathogenesis of abnormal involuntary movements in lithium-treated patients with major affective disorder. Eur Arch Psychiatry Clin Neurosci 1991;241:1-7.	Sweden	1991	Abnormal involuntary movements	37 Literature review	...	...	...
Moskowitz AS	Moskowitz AS, Altshuler L. Increased sensitivity to lithium-induced neurotoxicity after stroke: A case report. J Clin Psychopharmacol 1991;11:272-3.	US	1991	Stroke symptoms worsening with LTM	1	49	Male	BD
Kohler J	Kohler J, Mergner T, Bohle M, Neumann-Haefelin D. Neurologic complications of Q-fever (*Coxiella burnetii*). Fortschr Neurol Psychiatr 1992;60:110-3.	Germany	1992	Neurological complications associated with *Coxiella* and LTM	…	…	…	…
Holroyd S	Holroyd S, Rabins PV. A retrospective chart review of lithium side effects in a geriatric outpatient population. Am J Geriatr Psychiatry 1994;2:346-51.	US	1994	LTM side effects in a geriatric outpatient population	114	...	...	...
Arya DK	Arya DK. Lithium-induced neurotoxicity at serum lithium levels within the therapeutic range. Aust N Z J Psychiatry 1996;30:871-3.	New Zealand	1996	EPS - PKN	1	73	Female	BD
Ghardirian AM	Ghadirian AM, Annable L, Bélanger MC, Chouinard G. A cross-sectional study of Parkinsonism and tardive dyskinesia in lithium-treated affective disordered patients. J Clin Psychiatry 1996;57:22-8.	Canada	1996	EPS	130	20-68	…	110 - BD, 18 - Unipolar (major) depression, and 2 - Atypical affective disorder
Tuglu C	Tuglu C, Erdogan E, Abay E. Delirium and extrapyramidal symptoms due to a lithium-olanzapine combination therapy: A case report. J Korean Med Sci 2005;20:691-4.	Turkey	2005	EPS - Walking tremor in limbs	1	62	Female	BD

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Brandt-Christensen M	Brandt-Christensen M, Kvist K, Nilsson FM, Andersen PK, Kessing LV. Treatment with antidepressants and lithium is associated with increased risk of treatment with antiparkinson drugs: A pharmacoepidemiological study. J Neurol Neurosurg Psychiatry 2006;77:781-3.	Denmark	2006	EPS	…	…	…	…
Galpern WR	Galpern WR. Lithium in progressive supranuclear palsy and corticobasal degeneration. Mov Disord 2010;25:498.	US	2010	PKN - Corticobasal degeneration and supranuclear gaze palsy	…	...	...	...
Lyell VR	Lyell VR, Henderson EJ, Ahearn DJ, MacMahon DG. Multi-centre survey of new patients referred from primary care with parkinsonism-what proportion are on medications which can cause drug induced parkinsonism?: 113. Mov Disord 2010;25:224.	UK	2010	PKN	…	...	...	...
Guillan M	Guillan M, Alonso-Canovas A, Garcia-Caldentey J, Hernandez-Medrano I, DeFelipe A, Martinez-Castrillo JC, *et al*. Inpatient movement disorders: Beware of the drugs! Mov Disord 2012;27:431.	Spain	2012	EPS	…			
Vandewalle W	Vandewalle W, Boon E, Sienaert P. Movement disorders due to modern antidepressants and mood stabilizers. Tijdschr Psychiatr 2015;57:132-7.	Belgium	2015	General	29	…	…	…

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Supplemental Table 2: Contd...

Main author	Reference	Country	Year	Type	Number of patients reported	Age	Sex	LTM indication
Marras C	Marras C, Herrmann N, Fischer HD, Fung K, Gruneir A, Rochon PA, *et al*. Lithium use in older adults is associated with increased prescribing of Parkinson medications. Am J Geriatr Psychiatry 2016;24:301-9.	Canada	2016	PKN	…	…	…	…
Rey *et al*.	Rey M, Molina L, Recinos B, Paz B, Rovelo M, Elias R, *et al*. Risk of movement disorders with antipsychotic drugs in patients with schizophrenia or depressive disorders: 901. Mov Disord 2016;31:290.	Argentina	2016	EPS	…	…	…	…
Thi Truong BE	Thi Truong BE, Sung FC, Lin CL, Hang LW, Teng YK, Tzeng YL. A follow-up study on restless legs syndrome in chronic obstructive pulmonary disease population. Sleep Med 2021;80:9-15.	Taiwan	2021	RLS	7	…	…	…

Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
						MCL			
Coats DA	…	...	3.6 mEq/L	...	24-48 h	...	Lost a lot of weight. Treated with IV solution containing 5% glucose and 40 mEq of potassium chloride per liter of 9% saline	Confusion, urine and fecal incontinence, ataxia, twitches of the small muscles of the hands and face, and occasional muscular jerks of the arms and legs	…
	...	21 mEq, 3×/day LTM citrate	2.9 mEq/L	...	24-48 h	...	Symptoms started after chlorpromazine hydrochloride 75 mg 2×/day IM had been given in addition. Grossly dehydrated with poor peripheral circulation at hospital admission. Treated with IV infusions of distilled water with glucose, insulin, and potassium chloride	Drowsiness, coma, urine and fecal incontinence. Muscular twitches of forearms and legs, with fasciculation of the small muscles of the hands and face	…

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Supplemental Table 2: Contd...

Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
	...	14 mEq LTM citrate 3×/day	3.5 mEq/L	6 months	5 days	...	Treated with IV infusions of Darrow's solution, glucose solution (5%), and 20 units of insulin	Confusion, coma, urine and fecal incontinence, no response to painful stimuli; the knee and plantar responses were weak, and she had a sluggishly reacting pupillary light reflex. Cheyne-Stokes breathing	...
	...	21 mEq LTM citrate, 3×/day	4.2 mEq/L	...	5 days	...	Treated with 0.9% saline solution with glucose and potassium chloride	Confusion, ataxia, muscular twitching of hands and face	...
	...	...	4.2 mEq/L	...	7 days	...	Malnutrition, apparently lost about 30 pounds in weight (cachectic). Prefrontal leucotomy 7 years previously, no benefit; Treatment: Oral potassium chloride, IV glucose, and Darrow' s solutions	Fibrillation of the small muscles of the hands and face was present, but there were no gross jerks	…
	...	14 mEq/L LTM citrate, 3×/day	2.3 mEq/L	Several months	4 days	...	During a period of hot weather, she began to vomit and became ataxic, and she was sent to hospital. Treated with oral glucose (fruits), soluble insulin, and potassium chloride	Confusion, ataxia, fasciculation of the small muscles of the hands and face	...
Verbov JL	DPS, anorexia	250 mg LTM carbonate 4×/day	4.5 mEq/L	8 years	80 days. On discharge, she was still euphoric, with some dysarthria, slightly ataxic gait, intention tremor of her right upper limb, equally brisk limb reflexes and normal plantar responses	Reevaluated 25 days later, further improving	Recent weight loss. Treated with IV fluid reposition according to serum electrolyte values	Coma, increased limb reflexes, and an extensor left plantar response. There was no neck stiffness and fundi were normal. Lower limbs spasticity, dysarthria, ataxic gait, intention tremor of her right upper limb	Normal EEG
Shopsin B	…	1500 mg/ day	0.8-1.25 mEq/L	1 week	Patient was transferred to state-hospital	...	Medication discontinued	1st week: Hand tremor (0.8 mEq/L) 2nd week (1.25 mEq/L): Extremely hyperactive, fidgety, unable to sit still, tense, with a mask-like facies and peculiar grimacing gesticulations.	EEG indicated bilateral cerebral dysfunction with considerable eye movement and abnormal activity. There was 2-3 cps reported, up to 50 mV waves bilaterally in the temporal regions, an increase in bilateral slow-wave alpha-activity as well as bilateral low-voltage beta activity.

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Supplemental Table 2: Contd...

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								Her behavior was strange, apparently irrelevant, with hyperactive movements of her hands, arms, and head that were seemingly purposeless and nondirectional. Mild to moderate hypotonia, hyperreflexia, diffuse choreoathetotic manifestations (resembling movements of Huntington's chorea), ataxia, a positive Romberg dysdiadochokinesia, dyssynergia, and mild nystagmus	Blood LTM taken at the time of EEG was 1.1 mEq/1. Repeat-EEG revealed bilateral cerebral dysfunction; this time, the alpha and beta activity was even slower, with no countable alpha-rhythm bilaterally and extremely low-voltage beta activity on both sides. Lithemy in the morning of EEG was 1.28 mEq/L
								After 2.5 weeks: Confusion, disorientation, drowsiness, impaired memory, cognition, and mentation. Tremor and hyperactivity disappeared, and the choreoathetotic picture dissipated significantly	
	…	1250 mg/day	1.4 mEq/L	4 weeks	Patient was transferred to state hospital	…	Medication discontinued	Lethargy, confusion, reduced comprehension, cognitive impairment, memory loss, disorientation, slurring of speech, ataxia, dysarthria	EEG at the end of 4th week: Bilateral cerebral dysfunction, generalized slow wave activity
Castaing R	...	Intoxication	...	...	...	...	...	...	...
Itil TM	...	...	...	...	...	...	...	...	...

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Favarel-Garrigues B	...	Intoxication	...	...	...	...	...	...	...
Setiey A	...	...	...	...	...	...	...	...	...
Von Hartitzsch B	…	800-2400 mg daily (mainly 1600 mg divided in 4 doses daily)	5 mEq/L	1 week	...	Reevaluated 1 year later, she was ataxic with frequent choreoathetosis movements	Had 3 grand mal seizures during internation. Treated with peritoneal dialysis. Other medication: Chlorpromazine 100-200 mg daily	4th day: She was drowsy, nauseated, and vomiting; 5th day: She was lethargic, ataxic, and had difficulty in walking; 7th day: She could not sit unaided, became unresponsive, and had three grand mal seizures. She was stuporous, responding to painful stimuli only by opening her eyes and showed generalized hyperreflexia and bilateral extensor plantar responses. After peritoneal dialysis: A flapping tremor of her left hand, constant fluttering of her eyelids, pursing of her lips, and frequent involuntary movements of extrapyramidal type involving both right and left arms, bilateral nystagmus, and features suggesting some cerebellar ataxia involving the right side	...
	...	1600 mg daily	2.3 mEq/L	4 weeks	...	6 months later, she remained very ataxic when walking on a wide base and needed the support of two people. She had choreiform movements involving head, tongue, and limbs with a compound rhythmic tremor affecting particularly the right hand	Hemodialysis using an Ultraflo 100 coil	Vomit, disorientation, slurred speech, grand mal seizure, stupor, coma, hyperreflexia, and bilateral extensor plantar responses.	An electroencephalogram, a skull X-ray picture, and a cerebrospinal fluid examination were normal

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Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
								Coarse tremor, ataxia, muscular twitches, choreiform movements involving head, tongue, and limbs with a compound rhythmic tremor affecting particularly the right hand. Incoordination in the heel-shin test	
Juul-Jensen P	…	...	5.6 mEq/L	...	...	Neurological examination 5 years later showed dysarthria, nystagmus, ataxic knee-heel and finger-nose tests, and bilateral dysdiadochokinesia. Positional and vibrational senses were normal. Deep reflexes hyperreactive. The patient had no permanent mental after-effect of the LTM intoxication	Cardiac arrest during forced diuresis, normal activity obtained from external heart massage; She survived with severe neurological defects. Phenytoin	Bilateral nystagmus and hyperactive deep reflexes of the extremities, normal plantar responses, grand mal seizures. Spasticity, myoclonic jerks	...
	…	900 mg daily	2.9 mEq/L	1 week after a major gynecological operation (suffered dehydration)	1 month	3 years later, the patient still showed slight signs of cerebellar affection	...	Clouding of consciousness, bilateral nystagmus, and rigidity. Knee-heel and finger nose tests ataxic. Tremor	...
Cohen WJ	…	1500 mg/day	11th day: 1.37 mEq/L. 14th day: 1.48 mEq/L	11 days	40 days	Up to 10 months after admission, the patient was demented, with a mask-like facies and occasional opsoclonus. Speech was dysarthric, monotonous, and low-pitched.	On 14th day all medications including haloperidol (45 mg/day) and benztropine mesylate (5 mg/day) were discontinued Haloperidol (average dosage, 45 mg/day; range, 20-70 mg/day) and benztropine mesylate, 5 mg/day	Fever, vertical nystagmus, opsoclonus, and purposeless, incessant, ataxic limb movements. Decreased activity, flutter-like oscillations of the globes, confusion, lethargy, and somnolescence	EEG showed an excess of bilaterally symmetrical slow-wave activity that gradually subsided during the 4 weeks following cessation of drug therapy. EEGs were normal by the 40th day after drug treatment was withdrawn. A pneumoencephalogram showed slight dilation of the lateral ventricles and areas of focal atrophy over the convexities

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Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
						Generalized weakness, diffuse hypotonia, hyperreflexia, and a pill-rolling tremor of the upper extremities were present. Limb and truncal ataxia, dyssynergia, dysdiadochokinesia, and dysmetria were notable			
	…	600-1800 mg/day (1.165 average)	11th day: 1.38 mEq/L. 13th day: 0.81 mEq/L. 19th day: 1.47 mEq/L. 20th day: 1.58 mEq/L	13 days	1 week after discontinuation of LTM (27 days of internment)	Repeated examinations during the next 5 months showed a buccofacial dyskinesia and choreoathetotic movements, resting tremor, and cogwheel movements persisted	13th day: Benztropine mesylate, 4 mg/day, was given. 19th day: Haloperidol and benztropine mesylate administration was discontinued. (38°C fever) 20th day: LTM was discontinued	On the 16th day of treatment, tremulousness, ataxia, intention tremor, and increased rigidity were noted. By the 19th day of LTM carbonate therapy, the patient exhibited a clouded sensorium, impaired upward gaze, generalized hyperreflexia, marked cogwheel rigidity, and a static, coarse tremor. On 27th day: A prominent buccofacial dyskinesia, never before observed, was present, as well as gross tremor at rest. Generalized hyperreflexia, unsteady gait, cogwheel rigidity, and mild, diffuse muscle weakness were also present	EEG obtained 3 weeks later was normal

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	Past diagnoses had included "manic-depressive psychosis," "schizophrenia," and "depressive neurosis"	1800 mg/day	6th day: 2.45 mEq/L. 7th day: 1.40 mEq/L. 8th day: 1.29 mEq/L. 10th day: 0.55 mEq/L	4 days	2 days after, LTM discontinuation 9 days	Repeated examinations during the next 6 months showed persistent tremor at rest and cogwheel rigidity in the upper extremities, buccofacial dyskinesia, and choreoathetotic movements in both feet	4th day, she became febrile. On day 7, all medication was discontinued (haloperidol and LTM). Previous phenothiazine therapy	4th day: Tremor and signs of cerebellar dysfunction. 5th day: She was obtunded, diaphoretic, and weak and tremulous. 6th day: Pyrexia and progression of the neurologic syndrome were accompanied by an elevated WBC (13,500/cumm). Days 8-10 showed a severely dysarthric, demented, lethargic woman, exhibiting palilalia and a mask-like facies and paucity of eye movements. A postural tremor, cogwheel movements, and lead-pipe rigidity were present. 9th day: A striking buccofacial dyskinesia and a parkinsonian tremor of both upper extremities were present, choreiform movements were observed, and the patient walked with a marche à petit pas	A waking EEG obtained on the 9th hospital day showed a generalized excess of theta (5-7 cycles per second) activity. A waking EEG obtained on the 14th hospital day showed definite improvement with only a slight excess of theta activity
Dyksen MW	Primary hyperparathyroidism, diagnosed after starting ECT treatment	300 mg, 3×/day, than 1500 mg/day	1.04 mEq/L	Immediately after 7th and 10th ECT sessions	2 self-limited episodes lasting about 2 h each	18 months later had no depressive or maniac episodes, no mention on movement disorders	Because of nausea and vomiting, LTM was discontinued after 10 days, and she was given trifluoperazine, elevated mood returned to normal over the next 3 weeks, and then, she was discharged on 50 mg fluphenazine decanoate every 2 weeks. After 10 days at home, depressive symptoms started, she was re-hospitalized 14 days after discharge, and LTM 300 mg 3×/day was reintroduced.	Psychomotor retardation, tension, and frequent periods of wakefulness during the night. Post-ECT bilateral upper limb asterixis related to primary hyperparathyroidism, during LTM treatment	The EEG showed generalized slowing, a pattern consistent with the presence of a metabolic encephalopathy. Skull films and a brain scan were normal

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							After last ECT, she was referred to endocrinologist. She was discharged on thioridazine, desipramine (150 mg/day), and LTM, discontinued the two former in the following months Other medications: Fluphenazine, trimethobenzamide, atropine, thiopental, succinylcholine, thioridazine		
Dyksen MW	…	900 mg/day after 2 week washout period. LTM was raised to 1800 mg/day 5 days later, due to low lithemy and persistent symptoms	0.29 mEq/L, then 1.27 mEq/L, then 0.73 mEq/L, then 0.39 mEq/L	17 days after raising dose to 1800 mg/day, 22 days after starting LTM	4-5 days	…	The patient was prescribed 900 mg/day LTM and 20 mg/day of haloperidol. She stopped taking her medications 3 days before hospital admission. LTM was discontinued 4 days after dose was increased, or 9 days after LTM was started in hospital	Only asterixis is described	…
Uchigata M	…	1800 mg daily	1.4 mEq/L	4 years	…	…	Medications were stopped and infusion of normal saline and lactated Ringer's solutions was started. 3 months later, dysarthria, truncal ataxia with mild limb ataxia, vertical nystagmus, mild weakness of the extremities, diminished DTRs of the lower extremities, and decreased vibratory sense in the feet remained Other medications: Chlorpromazine (150 mg daily) and levomepromazine (150 mg daily)	Drowsiness, dysarthria, tremor, and unsteady gait, followed by muscle twitching, increased muscle tone, sweating, fever to 38°C, coma, rigidity, and MCL-like involuntary movement were observed in the extremities. Miotic pupils with the absence of light reflexes. DTRs were normal in the arms and diminished in the legs	EEG transiently showed moderate frontal theta excess but returned to normal. NCV in the sural nerve was mildly slowed (46 ml s), but NCVs of the median and posterior tibia 1 nerves were 66 and 48 m/s, respectively. A biopsy of the left peroneal muscle showed features of neurogenic atrophy, including scattered small angulated fibers and small group atrophy associated with mild myopathic changes, i.e., central nuclei and round fibers. On histochemical examination, target fibers and type I fiber atrophy were observed. Left sural nerve biopsy disclosed mild diminution in the number of myelinated fibers, slight demyelination, and endoneurial fibrosis. Electron microscopic examination revealed some myelin figures

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Apte SN	...	300 mg 3×/day	5.7 mEq/L	3 days (3 h after he ingested 27 LTM tablets)	...	1½ years later: Coarse bilateral gaze-dependent nystagmus and striking ocular dysmetria were present. He exhibited scanning speech, and there was bilateral dysmetria on finger-to-nose and heel-to-shin maneuvers. Rapid alternating movements were bilaterally impaired, and he demonstrated an ataxic gait. Continuous low-amplitude choreiform and athetoid movements affected the extremities, mostly the hands and arms	Aggressive intravenous hydration, hemodialysis was initiated (4-h sessions for 4 consecutive days). CTI care was necessary	Nausea and vomiting, dehydration and oliguria, confused and had a slightly lower blood pressure (92/50 mmHg), unintelligible speech, tremor, fever and peripheral leukocytosis, mask-like facies, decerebrate posturing, deficit in recent memory, scanning speech, both truncal and appendicular ataxia, intermittent decerebrate posturing were observed. Choreiform and athetoid movements	CT scan and EEG were normal, as were the serum ceruloplasmin level and liver function tests
Rosen PB	...	...	>7.4 mEq/L	1 day	2 weeks	...	Hemodialysis. The patient was treated with clonazepam, which reduced the myoclonic activity	Psychomotor retardation and decreased DTRs. Pupils were 3 mm and sluggishly reactive to light. Corneal reflexes were intact.Deep coma and DTRs decreased, and plantar reflexes were absent. Voluntary movements of her extremities induced repetitive action MCL of the face, arms, and legs, more pronounced on the left.	EEG demonstrated diffuse 4-5 Hz theta rhythm bilaterally with paroxysmal high-voltage spike discharges in both hemispheres, more marked on the left. A repeat EEG 6 days later showed only intermittent 5-6 Hz symmetrical theta rhythm with 8-9 Hz alpha waves present in the posterior quadrants

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								MCL also could be precipitated by passive movement of the extremities, Babinski responses bilaterally, convulsions, and coma	
Sandyk R	…	...	Not high	...	...	...	Leukocytosis and elevated serum enzyme, blood urea nitrogen, creatinine, and fasting blood glucose levels One patient suffered widespread irreversible brain damage; the other was left with persistent dyskinesia Other medication: Haloperidol	Lethargy, fever, tremulousness, confusion, and extrapyramidal and cerebellar dysfunction	...
Julius SC	Mildly mentally retarded woman	1200 mg/day	1.57 mEq/l; 0.94 mEq/L; 0.77 mEq/L	5 days	4 days	Midline epileptiform abnormalities were not present on subsequent EEGs (6 days and 3 weeks later), and she has remained seizure free for 18 months on no anticonvulsant medications	No prior history of seizures	On examination, she was alert and oriented. Except for mild cognitive impairment, neurological examination was otherwise unrevealing. She had four generalized tonic-clonic seizures within 2 h, which were terminated with intravenous benzodiazepines. Postictally, she was somnolent and mildly dysarthric, without focal findings	Before LTM administration, EEG showed moderate diffuse abnormalities (increased theta and delta activity). CT scan, with and without contrast, was normal. After LTM use, EEG showed nearly continuous repetitive sharp waves, maximal at the midline vertex electrode
	Generalized seizures related to alcohol withdrawal	1800 mg/day, 3 days later 1200 mg/day	2.15 mEq/L	8 days	9 days	…	Postpartum seizures 30 years earlier	DTRs were hyperactive and symmetrical, and plantar responses were extensor. General medical and neurological examinations were otherwise unremarkable	EEG 9 days after admission showed intermittent repetitive sharp waves, maximal at the midline vertex (Cz), often associated with myoclonic jerks of the legs

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Devanand DP	…	600 mg/day	...	6 days	1 week	She was discharged a month later on injection fluphenazine decanoate and desipramine, and there is no recurrence of MCL	Medications at admission were imipramine 200 mg/day, haloperidol 2 mg 3 times/day, and triazolam 0.5 mg/day. After drug washout, she received 20 bilateral ECT treatments with chlorpromazine added late in the course of treatment. 3 days after ECT ended, nortriptyline was added to chlorpromazine 2400 mg/day and increased to 75 mg/day. LTM carbonate 300 mg twice a day was added to treat depression. Benztropine was added to treat EPS 3 mg/day with chlorpromazine reduced to 1600 mg/day over the next 5 days. Myoclonic jerks was observed, and LTM was stopped. MCL disappeared in the next week on desipramine 75 mg/day	MCL jerks on both upper and lower limbs with gait abnormality consistent with MCL	EEG was normal
	…	900 mg/day	0.93 mEq/L	1 week	…	LTM was then decreased to 600 mg/day and myoclonic jerks did not occur thereafter	At admission, for treatment of depression, imipramine 100 m/day, fluphenazine 5 mg/day, and lorazepam 3 mg/day were given. She received 14 ECT with good response and then started with nortriptyline 25 mg/day and LTM carbonate 600 mg/day. Nortriptyline was increased over the next 10 days to 125 mg/day, and LTM was increased to 900 mg/day with propranolol 40 mg/day to control LTM-induced tremor. Over the next few days, myoclonic jerks of both upper and lower limbs developed. The patient reported she had similar symptoms with imipramine and LTM combined but not on imipramine alone. LTM was then decreased to 600 mg/day and myoclonic jerks did not occur thereafter	Myoclonic jerks on both upper and lower limbs with gait abnormality consistent with MCL	EEG was normal
Lemus CZ	…	…	LTM toxicity was ruled out	…	…	After 10 months, there was no reemergence of MCL	Clozapine and LTM combined	Paroxysmal jerky movements of the extremities	…

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Simon LT	Hypertension, diabetes, right hemiparesis from stroke	300 mg/3 times day	0.85 mmol/L	Not clear - 2.5 months after starting carbamazepine	2 days after withdrawal	…	The patient's medications at that time were LTM carbonate, 300 mg three times daily; disulfiram, 250 mg daily; and carbamazepine, 100 mg three times daily. Carbamazepine had been started 2.5 months earlier for the management of mania. He had been taking disulfiram for 8 years to treat alcoholism. When carbamazepine was withdrawn, all symptoms resolved within 2 days. The patient was discharged on LTM, 300 mg three times daily, and disulfiram, 250 mg daily, without return of symptoms. The administration of carbamazepine was temporally related to the patient's symptoms, which abated with withdrawal of carbamazepine and recurred with its readministration	Confusion, left-sided MCL, temperature of 39°C, and a diffuse erythematous maculopapular rash	EEG was diffusely slow without focal or paroxysmal abnormalities
Vanhooren G	Bronchopneumonia with respiratory failure, hypothyroidism, and renal diabetes insipidus	900 mg/day	3.5 mEq/L (2 days after withdrawal)	…	…	1 year after, the intoxication normal muscle strength, weak tendon reflexes, and normal sensation in arms and legs were found, but ataxia remained unchanged	Besides LTM, the patient was on levomepromazine 150 mg/day for 2 weeks. Bronchopneumonia with respiratory failure, hypothyroidism, and renal diabetes insipidus were treated. 3 weeks after admission, the patient could be weaned from the ventilator. The clinical findings did not change	Hospitalized with progressive obtundation with rigidity and fever. The days following admission, the patient became comatose. There was generalized hypertonia, bilateral Babinski sign and conjugate left-sided deviation of the eyes. Subsequently, there was right-sided hemiparesis. The plantar responses were flexor. In the following 2 weeks, the patient regained consciousness. A predominantly proximal paraparesis was noted. Tendon reflexes were normal.	EEG showed a low-voltage alpha rhythm with bilateral, polymorphous delta paroxysms without lateralization. CT scan of the head did not show any abnormalities. MNCV in the peroneal, tibial, and median nerve were moderately slowed. The CMAP was of low amplitude. The SNAP of the sural nerve could not be elicited. EMG showed resting activity and polyphasic MUPs in the muscles of the lower extremities

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								Further - proximal paraparesis, distal paresis of the upper extremities, generalized areflexia, severe ataxia were noted	
	…	1250 mg/day	0.75 mEq/L	3 months	…	11 months later, some symptoms persisted	Because of deterioration of the mental status, haloperidol, 100 mg/day, and levomepromazine, 500 mg/day, were added to the LTM carbonate therapy From the 10th day on and even after dose reduction of the neuroleptics, encephalopathy with generalized rigidity, hyperthermia, and leukocytosis ensued. Intubation, myorelaxation, and artificial ventilation were necessary	Extrapyramidal rigidity and bulbar symptoms developed progressively. Coma, with reaction to painful stimuli, right arm paresis, generalized hypertonia with conjugate right-sided deviation of the eyes, and oral dyskinesia were noted. Generalized MCL 10 days later 2 weeks after intoxication, the patient regained consciousness. Speech was dysarthric. Complete flaccid paralysis of the legs with areflexia and moderate asymmetric arm paresis with weak tendon reflexes were found	CT scan of the head showed no abnormalities. Needle EMG showed fibrillation potentials and PSW in all muscles examined, including paravertebral muscles. MNCV of the median, ulnar, and peroneal nerve and SNCV of the sural nerve were normal. The amplitude of the CMAP of the thenar, hypothenar, and short extensor of the toes was diminished At 5 months, CT scan of the head showed cerebellar, vermian atrophy. A slow increase of leg muscle strength was noted. The MNCV and SNCV were normal or slightly slowed, and the CMAP in the median and ulnar nerve had increased. 8 months after clinical diagnosis, sural nerve biopsy revealed moderate loss of myelinated fibers and mild endoneural fibrosis. Characteristics were several clusters of small thinly myelinated axons. There were scattered vacuolated macrophages in which some myelin debris was noted electromicroscopically. A few isolated, thinly myelinated, regenerated large axons were found

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Kojima H	Mild hypertension and mild diabetes mellitus were well controlled without medication	600-1000 mg/day	1.6 mEq/L	After increased dosage of LTM	…	Thereafter, he responded well to LTM alone (600 mg/day, serum level of 1.0 mEq/L) without developing serotonin syndrome. About 7 months after admission, he was discharged with a Hamilton depression rating score of 3	Episode of depression 2 years before, with tonic seizure. Used clomipramine, 30 mg/day, plus levomepromazine, 25 mg/day at the time, his depression did not improve sufficiently Severely depressed when admitted (Hamilton depression rating score of 39). A regimen of clomipramine, 25 mg/day; levomepromazine, 25 mg/day; and flunitrazepam, 2 mg/day, was started. The clomipramine dose was gradually increased to 175 mg/day over a month, but the dosages of levomepromazine and flunitrazepam remained unchanged throughout this hospitalization. Subsequently, a regimen of LTM, 600 mg/day, was added. A week later, the LTM dose was increased to 1000 mg/day. Thereafter, he suffered from MCL, shivering, tremors, incoordination, and elated mood, i.e., serotonin syndrome. LTM was then discontinued, with the result that MCL, shivering, and incoordination were dramatically reduced. For the next 2 months, the clomipramine dose was gradually decreased to SO mg/day, but there remained slight MCL, shivering, and tremor. Finally, the clomipramine regimen was discontinued, with complete remission of the serotonin syndrome	MCL, shivering, tremors, incoordination, slight dysarthria, tonic seizure	Brain MRI revealed lacunar infarction at the right basal ganglia. EEG revealed no abnormalities
Prettyman R	Idiopathic epilepsy (controlled on carbamazepine)	800 mg/day	0.55 mmol/l	18 days	…	…	On the basis of a previously satisfactory response to LTM, he was commenced on lithium carbonate (priadel, 800 mg daily) in addition to oral (haloperidol and chlorpromazine) and depot (fluphenazine) neuroleptics which had previously been tolerated well with only mild parkinsonian side effects. LTM was subsequently discontinued and the patient's neurological status reverted to normal. 3 months later, LTM carbonate was prescribed again, this time at a dose of 400 mg daily. 4 days later, a similar pattern of neurological abnormalities were observed. Several lithium trials	MCL, ataxia	Cranial CT scan was normal

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Rittmannsberger H	…	1350 mg/day	…	Unclear, 4 days after admission	Symptoms regressed completely after clozapine was reduced	…	Also used zuclopenthixol with LTM. On admission, clozapine 250 mg/day was added. Biperiden was given for the EPSs	Rigor, akinesia. Unsteadiness, tremor, asterixis (flapping tremor)	…
Loza B	…	…	…	…	…	…	Serotonin syndrome in patient using fluoxetine and LTM	The patient presented nearly all Sternbach's diagnostic criteria for symptoms of serotonin syndrome - Changes in mental status, restlessness, MCL, hyperreflexia, tremor, shivering, incoordination, hyperthermia, diaphoresis, and diarrhea	…
Nisijima K	Serotonin syndrome	400 mg/day. In early 1995, he doubled the dosage by himself taking 800 mg/day	…	Not specified (around 7 days)	…	…	He was on treatment of LTM 400 mg/day and trazodone 125 mg/day and also levomepromazine 20 mg and nitrazepam 10 mg to sleep. In the early May 1995, he became depressed and doubled the dosage of LTM and trazodone by himself. On May 19, he was admitted to the hospital in comatose. Further, he took trazodone and amitriptyline, dantrolene, and bromocriptine	Comatose, tremor, incoordination, muscle rigidity, hyperreflexia, delirium, MCL, diaphoresis	Cranial CT scan showed no abnormalities
Rittmannsberger H	Severe obesity	1125 mg/day	…	…	…	…	20 years the duration of the illness	…	Cranial CT scan mild atrophy
	Obesity	1350 mg/day	…	…	…	…	2 years the duration of the illness	…	Cranial CT scan was normal
	Severe obesity	1125 mg/day	1.12 mVal/L	…	…	…	22 years the duration of the illness	…	Cranial CT scan was normal
	None	1800 mg/day	1.04 mVal/L	…	…	…	11 years the duration of the illness	…	Cranial CT scan was normal
	Obesity	1350 mg/day	…	…	…	…	20 years the duration of the illness	…	Cranial CT scan was normal
	Obesity	675 mg/day	…	…	…	…	21 years was the duration of the illness	…	Cranial CT scan mild atrophy
	None	675 mg/day	…	…	…	…	2 years was the duration of the illness	…	Cranial CT scan was normal

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Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
Evidente VG	…	900 mg/day	0.3 mEq/L	…	…	No	He was diagnosed 13 years before presentation with bipolar disorder and had been treated with LTM (900 mg/day) and doxepin (200 mg/day) since then. 1 year before presentation, he decreased the LTM to 450 mg/day. About 6 months before presentation, the patient increased the dose of LTM to 900 mg/day, and within a few weeks, he developed shaking and jerking of the hands during activity. There was no bradykinesia, change in muscle tone, or rest tremor	Moderately severe multidirectional myoclonic jerking of both arms was seen on sustained posture and arm movement	EEG-EMG polygraphy showed almost continuous, irregular, multifocal, short-duration (<50-100 ms) discharges in both upper extremities (most prominent in the left deltoid) during sustained arm posture and finger-to-nose testing. The myoclonic activity in the left deltoid occurred both synchronously and asynchronously with that of the other upper extremity muscles. Left median nerve SEPs were not enlarged. No exaggerated LLRs were seen. Back averaging of 216 myoclonic discharges of the left deltoid yielded a reproducible positive-negative focal EEG transient over the contralateral sensorimotor region. EEG transient was maximal at CP4 and had a field spread to CP3, PO3, and PO4. The amplitude of the positive transient was 2.2 V from baseline and preceded the averaged EMG myoclonic discharge by 15 ms
Lee SH	…	…	<0.5 mEq/L	…	…	…	…	Ataxia, coarse tremor, MCL, facial spasm, and increased DTR	…
Stewart JT	Mild vascular dementia, diabetes mellitus with peripheral neuropathy, hypertension, and benign prostatic hypertrophy	300 mg daily	0.7 mEq/L	Uncertain (<16 months)	2 weeks	…	Admission 16 months after LTM was introduced. The patient related that the tremor had been present for many months, clearly antedating the hip fracture, and that it interfered with his ability to eat and resulted in his frequently dropping things. There was a remote history of alcohol abuse, but he had been abstinent for 19 years. Medications included LTM carbonate 300 mg qhs, levothyroxine 50 mcg/d, clopidogrel, diltiazem, fosinopril, ranitidine, insulin, a variety of vitamins and laxatives, and oxycodone/acetaminophen prn.	Coarse, nonrhythmic, flapping tremor in both arms, best described as frequent momentary loss of muscle tone and clearly exacerbated by dorsiflexion of the wrists	…

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							Serum LTM level was 0.7 mEq/L. Discontinuation of oxycodone did not result in any appreciable improvement of the movement disorder. At this point, LTM was discontinued. The MD began to improve within several days and had resolved completely within 2 weeks		
Roccatagliata L	Hypertension	…	0.9 mEq/L	2 days	4 days	…	Accidental ingestion of at least 10 tablets of LTM (i.e., 3000 mg) over 2 consecutive days	Abrupt onset of altered mental state and postural tremor. Neurological status indicated confusion and decreased spontaneous speech. She became mutacic, and facial and limb MCL was evident	EEG performed 48 h later showed spike-wave discharges occurring every 2-4 s, consistent with continuous seizure activity. After 10 mg IV diazepam, the epileptic discharges subsided and the mental state improved
Caviness JN	…	600 mg	…	…	…	…	…	MCL	EEG 10.0 Hz
	…	300 mg	…	…	…	…	…	MCL	EEG 12.0 Hz
	…	300 mg	1.2 mEq/L	…	3 weeks	CR	…	MCL	EEG 10.0 Hz w/paroxysmal theta
	…	900-1200 mg	1.4 mEq/L	…	3 weeks	CR	…	MCL	EEG 9.0 Hz w/paroxysmal theta
	…	300 mg	0.5 mEq/L	…	…	…	He was receiving LTM, sertraline hydrochloride, and nefazodone hydrochloride. After withdrawal of nefazodone therapy, MCL showed marked clinical improvement	MCL	EEG 8.0 Hz w/paroxysmal theta
Smith D	Diabetes mellitus type 2	400 mg twice daily	0.35-2.02 mmol/L	…	After three sessions of hemodialysis with a blood flow of 170 ml/min, in the following week	…	Besides LTM, he was taking low-dose venlafaxine. Initially, he was treated for symptomatic hypoglycemia. 8 days later, he returned, having experienced confusion, anorexia, and generalized shaking for 3 days. He was judged to have symptomatic hypoglycemia and was treated with oral lucozade and a maintenance infusion of 5% dextrose. The hypoglycemic medications were stopped. Next day, his blood glucose concentrations were in the normal range, but his symptoms were worse.	Confusion, anorexia and generalized shaking. Drowsy, obtunded, and abulic, and he had developed a coarse tremor with myoclonic jerks	Cranial CT scan was normal. A transient ischemic attack was diagnosed. On readmission, repeat CT and MRI of the brain were normal. EEG showed diffuse slowing throughout the brain with no epileptiform activity

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							He was increasingly drowsy, obtunded, and abulic, and he had developed a coarse tremor with myoclonic jerks of his arms and legs. Encephalopathy secondary to LTM intoxication was diagnosed, and all his psychotropic medications were stopped. He was treated with isotonic saline as fluid replacement and with three sessions of hemodialysis with a blood flow of 170 ml/min. LTM levels fell to undetectable. His tremor and myoclonic jerks stopped, and over the following week, his toxic encephalopathy resolved		
Bender S	...	...	...	...	...	...	Study that assessed the safety and efficacy of combined clozapine-LTM pharmacotherapy. Of 44 patients, 2 developed reversible MCL	...	...
Reif A	Obesity and mild diabetes mellitus	...	0.67-0.87 mmol/L	7 days after, VPA was started	2 days after, VPA was discontinued	14 days after VPA discontinuation, EEG was only slightly altered (background rhythm, 7-8 Hz) with intermittent, generalized theta waves. Another 2 weeks later, EEG was normal (basal frequency, 8-9 Hz) and similar to baseline	There was no history for head trauma or neurological disorders. He had no psychiatric history except for potentially harmful alcohol abuse. On admission, he was treated with LTM, risperidone and amitriptyline. We increased risperidone dosage to 4 mg/day, added flupentixol (10 mg) and substituted amitriptyline by clomipramine (225 mg), which slightly improved his condition. All drugs were well tolerated. As he continuously suffered from an atypical depression with persecutory delusions, a treatment attempt with VPA was initiated (day 1, 500 mg; day 2, 1000 mg; day 3 and thereafter, 2000 mg corresponding to 20 mg/kg). History of use of acarbose, amitriptyline, flupentixol, mirtazapine, risperidone, and clomipramine	Tremor and symmetric MCL of the upper extremities	EEG showed a prominent, generalized slowing with theta-/delta-rhythm (basal frequency, 2.5 Hz) during the whole recording of 13 min
Kaplan PW	...	...	2.8 µg/mL	...	...	Returned to baseline in 3 days	Hydration, stopped LTM. In use of haloperidol, VPA, sertraline	Obtunded, confused, dysarthria, mutism, rigidity, corticospinal sign/brisks reflexes, MCL twitches	EEG showed triphasic waves

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	...	...	4.6 µg/mL	...	...	Recovery over 3 months	ICU hemodialysis, lorazepam, stop LTM. In use of prolixin, VPA, aminophylline	Lethargic, dysarthria, mutism, rigidity, corticospinal sign/ brisks reflexes, MCL twitches, ataxia/ tremor	EEG showed triphasic waves
	...	...	1.5 µg/mL	...	...	Returned to baseline in 6 months	Hydration, stopped LTM. In use of perphenazine	Drowsy, confused, dysarthria, mutism, rigidity, corticospinal sign/brisks reflexes, MCL twitches, ataxia/ tremor	EEG showed triphasic waves theta/delta
	...	...	3.1 µg/mL	...	...	Returned to baseline in 4 months	Lorazepam, stopped LTM. In use of haloperidol	Lethargic, unresponsive, dysarthria, mutism, rigidity, corticospinal sign/brisks reflexes, MCL twitches, ataxia/ tremor	EEG showed triphasic waves
	...	...	2.7 µg/mL	...	...	Improved over 12 days	Stopped LTM and treated an infection. In use of risperidone, thiothixene, and benztropine	Confused, unresponsive, hallucination dysarthria, mutism, rigidity, corticospinal sign/brisks reflexes, MCL twitches, ataxia/ tremor	EEG showed triphasic waves
Grueneberger EC	…	450-1200 mg nightly	0.3-0.8 mEq/L	Approximately, 9 days after hospitalization	Approximately, 1 day	…	He was treated with quetiapine titrated to 600 mg/day without complications. The patient's outpatient LTM dose had been 450 mg nightly. His LTM levels on the 1st day of the hospitalization were below therapeutic levels at 0.3 mEq/L, and his LTM was subsequently titrated to 300 mg in the morning and 600 mg at night. The patient's LTM level 5 days later was 0.5 mEq/L. The LTM dose was then increased to 1200 mg nightly. Mr. C seemed to be tolerating all medications, and his LTM levels were scheduled to be checked again 5 days after the increase to 1200 mg.	MCL, sedation, and confusion. Poverty of thought, sparse, and soft speech. Muscle fasciculation in his hands, arms, and face, which progressed to bilateral myoclonic jerks. <5 min later, the treatment team witnessed having a generalized tonic-clonic seizure that lasted for approximately 1 min.	Sleep-deprived EEG was obtained and found to be within normal limits

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							On the 9th day of his hospitalization, Mr. C's speech became sparse and soft, he displayed poverty of thought, delayed verbal responses to questions, and appeared more disorganized than he previously had been. He suddenly began to experience muscle fasciculation in his hands, arms, and face, which progressed to bilateral myoclonic jerks. <5 min later, the treatment team witnessed Mr. C having a generalized tonic-clonic seizure that lasted for approximately 1 min. He was initially unresponsive following the seizure, with blood-tinged secretions coming from his mouth. He quickly became lethargic and was arousable only to pain and auditory stimuli. He was immediately transferred to the emergency department for further evaluation. His medications were discontinued. Mr. C's LTM level after the onset of the seizure was 0.8 mEq/L. The following day, a sleep-deprived EEG was obtained and found to be within normal limits. His mental status returned to baseline alertness and orientation, but he did not recall much of the prior morning	He quickly became lethargic and was arousable only to pain and auditory stimuli	
Mahasuar R	…	…	0.57 mmol/L	6 years	3 months	Over the next 3 months of follow-up, our patient reported a periodic fluctuation in the intensity of his symptoms but with no further sustained improvement	He had been taking a combination of LTM and carbamazepine continuously. They considered a diagnosis of tardive PT, so his LTM dosage was tapered off and then stopped. They continued his carbamazepine dosage and started him on a therapy of clonazepam at 0.25 mg twice daily. Subsequently, his visible tongue tremors were reduced in a week, and by the end of 1 month, he subjectively reported an improvement of about 60% in his tremors and clicking sound	Bilateral rhythmic oscillations of his soft palate associated with a clicking sound and tremors of the tongue, which were not synchronous with his palatal movements. With distraction, his tongue tremors reduced in intensity, but no obvious change in the clicking sound was noticed	Brain MRI, EEG, EMG, and a laboratory work-up for Wilson's disease were within normal limits

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Almeida AG	Diabetes mellitus type 2	…	3.1 mmol/L	…	…	…	The patient was hydrated, and although there is an improvement trend of the serum LTM concentrations, she developed hypernatremia (160 mmol/L), hyperglycemia (400 mg/dl) and oligoanuria (6 cc/h). The neurologic status aggravated into coma, with global respiratory insufficiency and need for invasive ventilatory support	On admission: Lethargic behavior, tremor, and disorientation. After 12 days, on readmission: Diarrhea, alternating lethargic with agitated behavior, muscular rigidity, extrapyramidal tremors, dehydration, and bradycardia, aggravating to coma. 21 days after hospital admission, on the critical care unit. Neurologic examination showed depressed level of consciousness on a low diencephalic level compatible with toxic or metabolic dysfunction (vertical bilateral nystagmus and slight ocular roving, muscular hypotonia and hyporeflexion)	EEG revealed moderate diffuse sluggishness. Brain MRI excluded desmielinization syndrome. Electrocardiogram showed sinusal bradycardia and prolonged QT interval with flattened T waves
Bakelants E	Diabetes mellitus type 2 (noninsulin dependent)	…	2.09 mmol/L	…	…	…	Acute neurologic deterioration due to LTM intoxication. The woman, whose medical history included bipolar disorder and noninsulin-dependent diabetes mellitus, presented with hypoglycemia, confusion, and alternating agitation and apathy. Her current medications included LTM, diclofenac, olanzapine, sertraline, trazodone, and glibenclamide/metformin. LTM was discontinued, and the woman received saline. She gradually recovered and was discharged from the ICU. LTM was subsequently restarted at a reduced dose	Stuporous upon arrival, with a Glasgow coma scale score of 8/15. Persistent MCL of the left foot	EEG was moderately decelerated with triphasic waves

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Chen WY	…	600 mg daily	3.43 mEq/L	1 day after admission, he developed irregular, slow, choreiform protruding, and twisting movements of his tongue	In 3 years of follow-up with medical care, he had normal neurological presentation without any involuntary movements. His serum LTM remained in the normal therapeutic range	…	He had a history of bipolar disorder and had been using LTM carbonate (600 mg/day) medications and sedative agents for at least 20 years. LTM carbonate was discontinued since detection of high serum LTM level	He had acute conscious disturbance, atrial flutter, MCL of limbs, and orolingual DKN. Neurological examination revealed Glasgow coma scale of E2M4V2, intact cranial reflexes, four limbs symmetrical response to pain stimuli, and generalized increased DTRs. Besides, positive and negative MCL involving four limbs was observed	…
Mignarri A.	…	600 mg daily	2.45 mmol/L	In the last 2 months, the patient was noted to have decreased cognitive function associated with worsening ataxia and involuntary movements	After LTM withdrawal, the patient was released on the 10th day, with normal neurological examination	…	She had been affected by bipolar disorder since adolescence and had been receiving treatment with LTM carbonate (600 mg/day) for 15 years and olanzapine (5 mg/day) for 5 years. Apart of the psychiatric illness, her clinical history was unremarkable. In the last 2 months, the patient was noted to have decreased cognitive function associated with worsening ATX and involuntary movements. Further, relatives referred that the patient had become distractible, dysphoric, and irritable. With the discontinuation of LTM, there was a marked normalization serum LTM levels and rapid improvement in cognitive levels function and ataxia, as well as disappearance of MCL pushes	Neurological examination revealed ideomotor apraxia, gait ATX, limb dysmetria, and hand myoclonic movements	…

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Kitami M	Hypertension	600 mg daily	2.9 mEq/L	2 years	3 weeks (not clear)	…	Developed ATX, tremor, and MCL. After admission, she suddenly threw up and lost consciousness; dehydration and renal dysfunction have been recognized, and serum LTM concentration was very (2.9 mEq/L), her condition was diagnosed as having severe LTM poisoning, and her treatment with LTM was stopped. She was treated with IV crystalloids restore proper hydration and tissue perfusion. Subsequent echocardiography showed left ventricular dysfunction (its ejection fraction was reduced to 0.30) caused by apical and basal kinesia hyperkinesia (which resulted in a characteristic shape of the left ventricle, similar to round-bottomed Japanese with narrow neck "Takotsubo" pot to hold octopuses), and his condition was diagnosed as having Takotsubo's cardiomyopathy. 8 days later, we confirmed that their serum LTM concentration was not high (0.06 mEq/L). All the neurological and cardiac abnormalities disappeared in 3 weeks, and she had no manic during that period	ATX, tremor, and MCL	The results of brain MRI and cerebrospinal fluid investigations were normal. EEG demonstrated diffuse slowing
Fitzgerald RT	Hypertension, hypothyroidism	LTM ER 3-4 times daily	>4 mEq/L	...	On day 33 of hospitalization, the patient had returned to baseline and was discharged to home	Subsequent brain MRI, 5 months later, the patient showed complete resolution of parenchymal signal abnormalities of PRES	On arrival, the patient was hypoxic (pulse oximetry 80%-85%) and subsequently intubated. Medicines at the time of admission included: Clonazepam QD (unknown dose), quetiapine 300 mg QD, gabapentin 200 mg QD, LTM ER 3-4 times a day, levothyroxine 0.075 mg QD, duloxetine 60 mg BID, dicyclomine 20 mg QD, olmesartan 40 mg/25 mg QD, and carisoprodol 350 mg Q 6 h. The initial serum LTM level was >4 mEq/L. LTM was discontinued on admission. On the second hospital day, LTM levels trended down and were <1 mEq/L. The patient was extubated on hospital day 6 but remained noncommunicative and somnolent. On hospital day 10, the patient complained of headache and was then witnessed to have three separate tonic-clonic seizures with loss of bladder/bowel continence	She exhibited tremulousness on movement, myoclonic jerks, and 4+ reflexes with clonus	EEG showed moderate generalized slowing and epileptiform sharp waves reversing at the P3 derivation. A cranial CT scan showed new, symmetric areas of hypoattenuation involving subcortical white matter of the parieto-occipital regions suggestive of PRES. Subsequent brain MRI on 14 admission's day confirmed findings of PRES as manifested by symmetric parietal and posterior frontal subcortical FLAIR hyperintensities without corresponding reduced diffusivity. EEG showed bilateral posterior quadrant ictal discharges

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	Diabetes mellitus, hypertension	…	1.7 mEq/L	…	Throughout the remainder of the admission, the patient's mental status never returned to baseline	…	Home medications included amitriptyline, sertraline, levothyroxine, and LTM (doses unknown). LTM was discontinued on admission. On the 12th hospital day, the patient aspirated and developed acute respiratory failure with rapid clinical decline requiring intubation	Complaints of weakness and syncope accompanied by "jerking" movements of his extremities	An initial cranial CT scan was normal and initial EEG revealed background slowing. A brain MRI showed symmetric subcortical parieto-occipital and temporal lobe vasogenic edema characteristic of PRES and without evidence of hemorrhage. EEG after intubation (day 13) revealed worsening, severe diffuse disturbance of the cortical activity without epileptic activity
Loens S	Hypertension, hypothyroidism, diabetes mellitus, and COPD	…	1.7 mmol/L	...	25 days	…	Her medication consisted of hydrochlorothiazide, valsartan, L-thyroxin, glimepiride, quetiapine, pipamperone, chlorprothixene, and LTM. 4 days before admittance, she had been discharged from another hospital to her regular nursing home after being treated for LTM intoxication. On admission, the serum LTM was 1.7 mmol/L (0.6-0.8 mmol/L). The patient was admitted to the ICU. LTM therapy was stopped. Hydrochlorothiazide and valsartan were withdrawn as well, considering their potential to increase LTM levels, as were quetiapine, pipamperone and chlorprothixene. Despite nearly normalized laboratory parameters, including LTM levels, after 3 days of treatment, the patient still did hardly respond to pain. The antihypertensive therapy was intensified, and MAP held in a range of 70-105 mmHg. Nevertheless, the patient remained unconscious for 10 days. When her vigilance improved, antipsychotic medication with quetiapine was reinstalled since the patient showed severe disorientation, restlessness, agitation and rapid mood swings. Furthermore, cortical blindness was evident. Finally, after 25 days, the patient fully recovered	Somnolence, disorientation, dysarthria, and generalized MCL	Second cranial CT scan showed bilateral posterior hypointensities suggestive of PRES. The diagnosis was confirmed by brain MRI

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Vandewalle W	...	...	...	...	...	...	Study that assessed the MDs caused by different antidepressants. MCL was associated with LTM in 2 individuals	...	...
Hayashi Y	Hypertension	600 mg daily	3.28 mEq/L	Her symptoms started after 3 weeks of azilsartan administration. She was diagnosed to have LTM intoxication based on an elevated serum LTM concentration of 3.28 mEq/L. Took LTM for the last 10 years	…	…	…	Action tremor and showed a gradual deterioration of her physical state. Mild consciousness disturbances, MCL, truncal ATX, and appetite loss	…
Hellmann MJ	COPD	...	5.17 mmol/L	1 month prior, he was hospitalized for a COPD exacerbation and started on lisinopril for hypertension. Days after discharge, his family noticed progressive confusion, ATX, and dysarthria; he became incontinent and lethargic	...	At 1 year follow-up, the patient had residual memory impairment and required walking aids for ambulation	1 month prior, he was hospitalized for a COPD exacerbation and started on lisinopril for hypertension	Days after discharge, his family noticed progressive confusion, ATX, and dysarthria. He became incontinent and lethargic and was brought to an outside facility for evaluation. On arrival, he was agitated, withdrawing to painful stimulation and moaning incoherently. He exhibited coarse tremors, hyperreflexia, fasciculation, and myoclonic jerks	...

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Kayipmaz S	Bronchiolitis	300 mg twice a day	1.7 mEq/L	Her symptoms began the day after she started using moxifloxacin 400 mg/day for the treatment of bronchiolitis	After removal of the LTM and moxifloxacin, the tremors and myoclonic jerks were diminished. On the 2nd day, drowsiness and disorientation were still evident, but these remaining neurological signs were resolved 1 week later	…	5-year history of BD. She started on LTM carbonate 600 mg/day, haloperidol 10 mg/day, and risperidone 2 mg/day at her first manic episode in 2010. After she had a depressive episode in 2011, sertraline 25 mg/day added to treatment, and from then until January 2016, her serum LTM concentration ranged from 0.60 to 0.80 mmol/L. She had been maintained on LTM carbonate 300 mg twice a day. Her symptoms began the day after she started using moxifloxacin 400 mg/day for the treatment of bronchiolitis	Severe tremor in both hands, myoclonic jerks of the upper extremities, exhaustion, and slurred speech. On her mental state examination, she was slightly drowsy and disoriented. Her speech was slurred	Brain MRI and EEG were normal
Stetkarova I	Hypertension, rheumatoid arthritis, autoimmune thyroiditis	900 mg daily	2.7 mmol/L	10 years after starting LTM (not clear)	3 months after the intoxication, she was able to walk 40-50 m alone with a cane. Her condition significantly improved	…	The patient had a history of surgery for uterine adenocarcinoma 1 year ago. She was treated for hypertension (beta-blockers: Bisoprolol 5 mg daily, ACE inhibitors: Perindopril 4 mg daily). She was further treated with quetiapine (400 mg daily) due to psychiatric indications. She has been followed up for rheumatoid arthritis and previously treated with biological treatment, and autoimmune thyroiditis, atypical form of lymphocytic thyroiditis. The patient was asked about gastrointestinal difficulties before the current disease. She mentioned diarrhea and abdominal pain 2 months before the hospitalization. During the hospitalization, the patient developed bulbar symptoms with dysarthria and dysphagia and worsening of cerebellar symptoms	Admitted to the neurological department for gait impairment lasting for 2 days with muscle weakness, MCL, impaired speech, and in particular short-term memory disorders. Neurological examination revealed remarkable generalized MCL in the upper and lower extremities and mild memory impairment. Severe tremor was present in the upper extremities with mild ATX; tendon reflexes were symmetrical and normally elicitable, spastic pyramidal signs were negative with generalized muscle weakness. Bulbar symptoms with dysarthria	EEG revealed abnormal pattern with diffusely irregular delta frequency of 3-4 Hz, presence of occasional sharp waves and theta triphasic isolated complexes. CT scan of the chest and abdomen revealed a focal lesion in the right mediastinum, suspected tumor, or enlarged lymph nodes. Brain MRI revealed no clear pathology, only findings of minor diffuse atrophy, and a few nonspecific lesions in both hemispheres. EMG examination showed low amplitude of motor responses (CMAP) in the lower and upper extremities; the histogram provided a higher percentage of myogenic units in the right tibialis anterior muscle. No myoclonic jerks were found in the vasus lateralis muscle, MUPs were normal in size and shape

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Jacobson JC	Delayed subcortical dementia	...	2.2 mmol/L	...	After 2 years of poisoning by LTM, she still shows signs of profound cognitive decline, including inattention, marked apathy, and decline in group and independent activities	Follow-up brain MRI investigation was unrevealing	In its history, there an event of acute LTM poisoning	Myoclonic jerks, tremors, and expressive aphasia	Brain MRI was normal
Orleans RA	...	...	...	...	...	...	A case of dose-dependent LTM effects of stroke-related and chronic cerebellar tremor	...	...
Sarrigiannis PG	...	400 mg daily	0.4-1.0 mmol/L	40 years on LTM (uncertain)	...	…	...	ATX on finger-nose and heel to sheen examination, evidence of gait ATX, and an irregular upper limb postural and action tremor that tended to persist at rest	Cerebellar MRI spectroscopy: Reduced NAA/Cra vermis 0.91 hemispheres 0.78. EEG showed background rhythms lying within normal limits with no clear focal or epileptiform discharges
	...	400 mg daily	0.4-1.0 mmol/L	10 years on LTM (uncertain)	...	…	History of excessive alcohol intake	ATX on finger-nose and heel to sheen examination, evidence of gait ATX, and an irregular upper limb postural and action tremor that tended to persist at rest	Cerebellar MRI spectroscopy: Reduced NAA/Cr vermis 0.87 hemispheres 1.04; EEG showed background rhythms lying within normal limits with no clear focal or epileptiform discharges
	...	400 mg daily	0.4-1.0 mmol/L	7 years on LTM (uncertain)	...	…	History of excessive alcohol intake	ATX on finger-nose and heel to sheen examination, evidence of gait ATX, and an irregular upper limb postural and action tremor that tended to persist at rest	Cerebellar MRI spectroscopy: Reduced NAA/Cr vermis 0.79 hemispheres 1.04; EEG showed background rhythms lying within normal limits with no clear focal or epileptiform discharges

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	...	800 mg daily	0.4-1.0 mmol/L	10 years on LTM (uncertain)	...	...	...	Jerky upper limb tremor, gaze evoked nystagmus, brisk reflexes, and gait ATX	Cerebellar MRI spectroscopy: Reduced NAA/Cr vermis 0.75 hemispheres 0.8; EEG showed background rhythms lying within normal limits with no clear focal or epileptiform discharges
	History of thyrotoxicosis treated with carbimazole but was euthyroid at presentation	675 mg daily	0.4-1.0 mmol/L	30 years on LTM (uncertain)	...	...	...	ATX on finger-nose and heel to sheen examination, evidence of gait ATX, and an irregular upper limb postural and action tremor that tended to persist at rest	Cerebellar MRI spectroscopy: Reduced NAA/Cr vermis 0.89 hemispheres 0.85; EEG showed background rhythms lying within normal limits with no clear focal or epileptiform discharges
	...	400 mg daily	0.4-1.0 mmol/L	20 years on LTM (uncertain)	...	...	...	Upper limb jerky postural/action tremor	EEG showed occasional sharp/spike and slow-wave discharges with a right frontotemporal and parietal emphasis
	Previous gastric bypass surgery, hypothyroidism	1000 mg daily	0.4-1.0 mmol/L	10 years on LTM (uncertain)	...	...	...	Upper limb jerky postural/action tremor; gait ATX, occasional jerks of the right leg	EEG showed a single spike/slow-wave discharge occurred in the left frontotemporal region
	...	800 mg daily	0.4-1.0 mmol/L	29 years on LTM (uncertain)	...	...	...	Upper limb jerky postural/action tremor	EEG showed some nonspecific bursts of slow-wave activity, mainly theta
Vallianou N	Ischemic heart disease and hypothyroidism	900 mg daily	2.03 mEq/L	The patient has been using LTM for 37 years, and the current symptoms started 5 days before he sought medical help	LTM was immediately discontinued and vigorous hydration introduced, which resulted in subsequent normalization of serum LTM levels 2 days later. However, the patient still had ATX and memory deficits, and nystagmus was still present, together with extrapyramidal signs	...	The patient uses others medications (irbesartan/hydrochlorothiazide 300/12 mg , betaxolol 10 mg, triflusal 600 mg, ezetimibe/simvastatin 10/40 mg, thyroxin 50 μg); and there also records that the patient had LTM poisoning 11 years ago	Admitted for dysarthria, agitation, and confusion. On clinical examination, the patient was agitated with sluggishness, coarse tremors, and MCL	Two cranial CT scans were negative for stroke

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Supplemental Table 2: Contd...

Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
Kiziltan ME	...	...	...	...	...	...	The manuscript does not clearly define the number of patients in use of LTM. However, they report that all patients with VPA or LTM-related MCL had subcortical subtype	...	...
Nagamine T	Hypertension	600 mg	3.2 mEq/L	...	2 weeks	Complete recovery	Possible interaction among fluvoxamine, azilsartan, and LTM. CM: All prescribed drugs were discontinued. Fluid resuscitation with 0.9% saline solution was started	Severe tremor in both hands and myoclonic jerks of the upper extremities	Brain MRI was normal
Burton C	...	...	...	...	...	...	...	MCL, ataxia, and hyperreflexia	
Hyder S	...	...	3.0 mEq/L	...	...	Complete recovery	LTM discontinued. Persistent reversible encephalopathy syndrome versus syndrome of irreversible LTM-effectuated neurotoxicity	Tremors, MCL and hyperreflexia	Cranial CT scan was normal. Brain MRI showed subcortical hyperintensities symmetrically distributed in the parietal and parieto-occipital region
						PKN			
Dalén P	Parkinson's disease	2 mEq/day	0.2 mEq/L	...	...	Hyperkinetic movements were significantly reduced	...	Increased PKN symptoms, and hyperkinetic movements were significantly reduced	...
	Parkinson's disease	12-16 mEq/day	0.6 mEq/L	...	...	During this treatment, her involuntary movements have completely disappeared	...	Cogwheel rigidity. Hyperkinetic involuntary movements have completely disappeared	...
Cohen WJ	...	1800 mg/day	1.63-1.81 mEq/L	5 days after LTM introduction	18 days after LTM discontinuation (28 days total hospital stay)	After 10 months, she continued with mask-like facies, totally demented, and incontinent and did not respond to any commands or speak. Snout, palmomental, and bilateral grasp reflexes were present	Admission: She was euphoric, agitated and hyperactive, talking to God, and had pressured speech and flight of ideas. First 2 days: She was uncooperative, with inappropriate behavior, delusions, and hallucinations. In the next 2 days, the condition improved. In the 5th day: She became confused, tremulous, weak, and lethargic, with an immobile facies, cogwheel rigidity, and sialorrhea. Haloperidol dosage was decreased to 20 mg/day; benztropine mesylate 2 mg/day was given. At the 8th day:	Confusion, tremor, dysmetric ATX of the globes, vertical nystagmus, and urinary and fecal incontinence were observed. Involuntary, purposeless movements of all limbs and trunk, oculogyric crisis, and lead-pipe and cogwheel rigidity were noted.	Serial EEGs showed generalized slowing (without focal or epileptogenic abnormalities). A pneumoencephalogram showed a large cisterna magna, prominent spaces in the superior cerebellar region and widened cortical sulci

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							Her temperature was 39.3°C, Haloperidol and benztropine mesylate treatment were discontinued; she was prostrate, stuporous, and restless, with involuntary, purposeless movements of all limbs and trunk, oculogyric crisis, and lead-pipe and cogwheel rigidity; she was extremely confused and disoriented, with unintelligible, dysarthric speech. Dysmetric ataxia of the globes, vertical nystagmus, and urinary and fecal incontinence were observed. 8th day: Haloperidol and benztropine mesylate treatment was discontinued. 10th day: LTM carbonate therapy was discontinued	Opsoclonus, cogwheel and lead-pipe rigidity, wildly uncoordinated movements of all extremities, rolling movements of the head and trunk, hypotonic muscles and joints were observed	
Shopsin B	...	...	...	Evaluated after 11 months of treatment	...	...	...	Severity of cogwheel rigidity: 1	...
	...	...	...	Evaluated after 18 months of treatment	...	...	This symptom does not subside with the use of intravenously administered antiparkinsonian drugs. Used benztropine	Severity of cogwheel rigidity: 1-2	...
	...	...	...	Evaluated after 60 months of treatment	...	...	This symptom improve with intravenously administered benztropine	Severity of cogwheel rigidity: 4	...
	...	...	...	Evaluated after 60 months of treatment	...	...	...	Severity of cogwheel rigidity: 1-2	...
		...		Evaluated after 48 months of treatment		...	This symptom does not subside with the use of intravenously administered antiparkinsonian drugs. Other medication: Benztropine	Severity of cogwheel rigidity: 4	...
	...	...	...	Evaluated after 14 months of treatment	...	...	...	Severity of cogwheel rigidity: 1-2	...
	...	...	...	Evaluated after 36 months of treatment	...	...	...	Severity of cogwheel rigidity: 2	...
	...	...	...	Evaluated after 60 months of treatment	...	...	...	Severity of cogwheel rigidity: 4	...
	...	...	...	Evaluated after 16 months of treatment	...	...	This symptom does not subside with the use of intravenously administered antiparkinsonian drugs	Severity of cogwheel rigidity: 1-2	...

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Supplemental Table 2: Contd...

Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
	...	...	...	Evaluated after 36 months of treatment	...	...	This symptom does not subside with the use of intravenously administered antiparkinsonian drugs	Severity of cogwheel rigidity: 3	...
	...	...	...	Evaluated after 24 months of treatment	...	...	...	Severity of cogwheel rigidity: 1-2	...
	...	...	...	Evaluated after 36 months of treatment	...	...	This symptom does not subside with the use of intravenously administered antiparkinsonian drugs	Severity of cogwheel rigidity: 2-3	...
	...	...	...	Evaluated after 48 months of treatment	...	...	This symptom improved with the use of intravenously administered benztropine	Severity of cogwheel rigidity: 2-3	...
	...	...	...	Evaluated after 48 months of treatment	...	...	This symptom does not subside with the use of intravenously administered antiparkinsonian drugs	Severity of cogwheel rigidity: 2	...
		...	...	Evaluated after 36 months of treatment	...	...	This symptom does not subside with the use of intravenously administered antiparkinsonian drugs	Severity of cogwheel rigidity: 3	...
		...	...	Evaluated after 16 months of treatment	...	...	...	Severity of cogwheel rigidity: 1	...
Branchey MH	...	...	0.6-1.2 mEq/L	About 2 years (patients used LTM from 6 moths to 7 years before evaluation)	...	...	...	A total of 36 individuals were studied, 3 developed some degree of cogwheel rigidity, with limb rigidity and tremor of extremities. These 3 have been taking LTM for 2 years or more. 6 other patients had rigidity and tremor, 15 had only tremor, and 2 had only rigidity. 4 patients responsive to the glabella tap (positive) where between the group with evidence of tremor. The degree if rigidity shown in the 11 patients was very low	...

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Loudon JB	...	...	0.6-1.5 mEq/L	…	...	...	...	Rigidity, tremor, DTN, TD, restless legs, bruxism. Possible interaction with haloperidol. The PKN symptoms only alleviate after LTM withdrawal	...
Lutz EG	...	...	...	...	...	...	Acute LTM-induced PKN precipitated by liquid protein diet	...	...
Asnis GM	…	...	0.81-1.0 mEq/L	Different groups used LTM for about 44-73.5 months before evaluation	...	...	Of the 97 patients, 79 were receiving LTM without concomitant antipsychotic or dopamine-depleting agents, although 19 of these 79 patients had concomitant use of tricyclic antidepressants. There were no significant differences between the group with slight cogwheel rigidity and the group with no cogwheel rigidity in regard to age, duration of lithium treatment, or serum LTM level	Of the total of 22 patients with bilateral cogwheel rigidity, severity was rated as slight in 10 cases and moderate in 12, whereas all 16 patients with unilateral cogwheel rigidity were given slight severity ratings. Patients treated with LTM alone - slight (*n*=22) and moderate (*n*=6) cogwheel rigidity. Patients treated with lithium + dopamine blocker/ depleter - slight (*n*=4) and moderate (*n*=6) cogwheel rigidity. 34 individuals presented tremor	
Tyrer P	Episodic affective and schizophreniform symptoms	400-800 mg daily (sustained release)	0.6-1.5 mmol/L	2 weeks	2 months	Her symptoms persisted after discharge from hospital and only improved when orphenadrine was stopped 2 months later	She was prescribed the antiparkinsonian drug (orphenadrine) to facilitate improvement	Mask-like facies with no spontaneous movement of face or limbs, tremor of arms and legs, marked salivation with dribbling, and severe cogwheel rigidity	...

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	...	...	0.5-1.4 mMol/L	8 years	...	...	During different acute episodes, she had been treated with ECT, amitriptyline, haloperidol, and chlorpromazine	Positive glabellar tap and a coarse tremor of hands and feet. On the Simpson-Angus Rating Scale, her mean score was 1.4. Tremor, difficulty in walking, and cogwheel rigidity	...
Reches A	...	1200 mg/day	1.8 mEq/L	Approximately 1 year later, a diagnosis of Parkinson's disease was made because of progressive hypokinesia and increased muscular tone. Approximately 4 years after the beginning of his therapy with LTM carbonate, the patient was referred to our department with the diagnosis of atypical, unresponsive Parkinson's disease	Withdrawing the LTM carbonate resulted in dramatic improvement of his condition over several days	The patient became well oriented and the motor disturbances completely regressed; antiparkinsonian medications were no longer needed. The patient has been followed up for 1 year after his discharge. During this period, repeated neurological examinations gave normal results, with no signs of extrapyramidal dysfunction	Anticholinergic agents and a combination of levodopa + carbidopa, amantadine hydrochloride (300 mg/day)	Disoriented and slightly dysarthric patient. Fine postural tremor of the hands and fine muscular twitches in most muscles were observed. Marked cogwheel rigidity was found in all four extremities, along with hyperactive muscle stretch reflexes. No pathological reflexes were elicited. Dystonic posturing of the toes and dyskinetic movements of the tongue, face, and both hands were frequently observed. The respirations were disturbed by irregular contractions of the diaphragm. He was very bradykinetic. His gait was slow, shuffling, unsteady, and unaccompanied by any associated movements	...

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Spring G	…	1500 mg/day	0.8 mEq/L (1st hospitalization). 1.5 mEq/L (2nd hospitalization)	...	1 month (unclear)	Needed ICU care	Required physical restraint for 14 days. 1st hospitalization: Chlorpromazine was discontinued and the EPSs completely cleared. 1.5 years after in the 2nd hospitalization: LTM was discontinued. When EPSs appeared, chlorpromazine was immediately discontinued and the symptoms disappeared	Severe EPSs, especially marked rigidity. Difficulty initiating voluntary movements, swallowing, fever of 104°F, his speech was dysarthric and not intelligible, involuntary movements of the tongue and lips, DKN. Parkinsonian gait, cogwheeling, festinating gait	EEG was mildly abnormal, with diffuse, slight slowing 7-8 cycles/s. It was read as showing diffuse bilateral cerebral dysfunction of a nonspecific degree consistent with toxic or metabolic encephalopathy. Repeat EEGs showed an initial slight deterioration, then a gradual improvement and return to normal over a period of approximately 1 month
Apte SN	...	1200 mg/day	2.8 mEq/L	3 weeks	...	4 years later, the patient was evaluated on neurobehavioral unit	The medication was discontinued, and she was treated with IV fluids. Other medication: Tetracycline	Bilateral gaze-dependent nystagmus, saccadic pursuit, scanning speech, and lead-pipe rigidity of all extremities were noted. Finger-to-nose and heel-to-shin tests revealed dysmetria; rapid alternating movements were poorly performed in all extremities, and she had a broad-based ataxic gait. Reflexes were brisk throughout except in the right arm, where she had findings consistent with a previously diagnosed radial nerve compression palsy. Plantar responses were flexor	...

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Donaldson IM	…	1500 mg/day. 1000 mg/day 4 days later	1.9 mEq/L	5 weeks	…	When assessed at the neurology department of Christchurch (New Zealand) Hospital, 5 months later, she was markedly. She had mild anisocoria, lid retraction, lid lag, and severe dysarthria with slurred monosyllabic speech. There was resting tremor of the head and all limbs, of approximately 3 Hz. She had mild generalized hypertonia, hyperreflexia with flexor plantar responses, and gross incoordination in all limbs with intention tremor. She was unable to walk without the support of one person. Follow-up examination after 2 years showed no change in her signs	WBC count of 13,200/cumm with 74% neutrophils. LTM carbonate therapy was discontinued the day after admission, and benztropine mesylate (2 mg twice daily) was given for 8 days. The patient also received IV ampicillin sodium (3200 mg/day). Other med: Haloperidol (30 mg/day) and procyclidine hydrochloride (10 mg/day), benztropine mesylate (2 mg twice daily)	Kernig's sign was questionably positive, she was akinetic and mute and had generally increased tone, sialorrhea, and a positive response to glabellar tap, she was disoriented, dysarthric, and dysphagic; mild anisocoria, lid retraction, lid lag, and severe dysarthria with slurred monosyllabic speech, tremor, ATX	Pneumoencephalogram showed widening of the cerebellar sulci suggestive of cerebellar atrophy but was otherwise normal
	…	1000 mg/day	3.9 mEq/L	2 years	…	1 year after, she had ocular dysmetria and markedly slurred, monosyllabic, scanning speech. She was generally hyperreflexic, with absent ankle jerks and flexor plantar responses, and had markedly incoordinated limbs and intention tremor. She was very ataxic and unable to walk unassisted	On admission, her temperature was 38.8°C. She had tachycardia of 100 beats/min, and her BP was 160/110 mmHg. She was given 2 mg of benztropine mesylate, without improvement. Alkaline phosphatase level of 498 IU/L. Both drugs were discontinued. The patient was treated with IV fluids at a rate of 4 L/day. Other medication: Haloperidol (10-20 mg/day)	Speech incomprehensible, motor perseveration, involuntary facial movements, tone generally increased, cogwheel rigidity, hyperreflexia present in the arms, oral DKN	…

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Perényi A		...	0.3-1.5 mMol/L	3-168 months (unclear)	...	...	24 patients were receiving treatment with LTM alone, 30 with LTM and 1 or more neuroleptics, and 27 with LTM and antidepressant	Severe tremor, salivation, blepharospasm, cogwheel rigidity, AKT, and akinesia	...
Lang AE	...	600 mg/day	1.35 mmol/L	Early in treatment to 10 years	5 weeks	...	LTM was discontinued, and 5 weeks later, aside from a mild postural tremor and poor postural stability, all signs of PKN had resolved. Performance on timed maneuvers of finger and hand dexterity, foot tapping, and walking had improved markedly	Intermittent rest tremor in the right arm and a bilateral postural tremor in the outstretched arms. She had rigidity in all limbs and in her neck and trunk, and she demonstrated moderately severe bradykinesia of both hands and feet. Her posture was flexed, gait was slowed, and postural stability was poor	...
Addonizzio G	...	1200 mg/day divided in 4 doses	0.46-1.15 mEq/L	1 day	8 weeks	Tremor and rigidity disappeared, and the patient continued to receive 10 mg of trifluoperazine	Haloperidol 10 mg/day in the admission. After 8 days, benztropine was added 3 mg/day, Haloperidol was discontinued and trifluoperazine 20 mg/day was added. LTM was tapered and discontinued 15 days after initiation. History of occasional cocaine abuse	Coarse parkinsonian tremor in both arms, head tremor, sialorrhea, marked rigidity, confusion	Sleep EEG was normal
	5-year history of paranoid psychotic episodes	900-1800 mg/day	0.5-1.17 mEq/L	1 day	...	He still complained of stiffness and had a persistent hand tremor upon discharge	LTM was increased to 1800 mg/day during 4 weeks, chlorpromazine was tapered to 200 mg/day, benztropine was maintained at 2 mg/day. Under this regimen, tremor and rigidity improved, but stiffness and hand tremor persisted. 200-600 mg daily of chlorpromazine for 5 years	Stiffness in his face, arms and legs. Mild rigidity in his arms and coarse parkinsonian tremor in both hands	...
Dyson EH	....	...		6 days-5 years	...	...	Of the patients with therapeutic intoxication, 19 were also receiving psychotropic drugs including benzodiazepines (7), phenothiazines (6), tricyclic antidepressants (5), monoamine oxidase inhibitors (3), antiparkinsonian drugs (3) haloperidol (2), tryptophan (2), and mianserin (1). However, only 5 had had any recent change in psychotropic medication (other than LTM) before admission.	Hyperreflexia, increased muscle tone (usually cogwheel in type), ataxia, tremor, confusion, agitation, and drowsiness	...

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							Gastric lavage was carried out in 23 patients, and emesis induced in 3 following acute overdose. 21 patients with features of toxicity were given IV saline and 5% dextrose (14) or forced alkaline diuresis (7) for periods of 1-7 days at rates of 2-14 1/day. One other patient in whom forced alkaline diuresis was attempted developed acute renal failure which required hemodialysis on 2 successive days. Five others were given increased oral fluids only and one in whom toxicity was probably precipitated by previously undiagnosed hypothyroidism was started on thyroxin		
Gajkowski K	Myocardial infarction	…	…	…	…	…	After withdrawal of LTM and correction of water and electrolyte disturbances as well as pharmacological treatment, gradual disappearance of neurological abnormalities was observed, with full normalization of EEG tracings	PKN + amnesia	EEG was abnormal
Chouinard G	…	…	…	…	…	…	…	…	…
Sandyk R	...	600 mg/day	...	...	14 days after pyroxene therapy (100 mg/day)	...	He has been receiving neuroleptic therapy since 1975 and recent medications included haloperidol (40 mg/day), and for episodic dyscontrol syndrome, LTM carbonate (600 mg/day) and carbamazepine (800 mg/day). Besides LTM and haloperidol, he was prescribed carbamazepine (800 mg/day). Following 7 days of pyridoxine therapy (100 mg/day) (in conjunction with his current medication), there was a dramatic reduction (approximately 80%) in the severity of the tremor with complete absence noted following 14 days of therapy	Examination revealed severe bilateral upper limb PKN resting tremor with slight predominance on the right, “masked-like” face with extensive seborrheic dermatitis of the nasolabial folds and forehead, stooped posture, and absence of arm swing on walking. Blinking was generally diminished, but increased spontaneously during hallucinatory activity. The glabellar tap was positive.	Cranial CT scan showed mild cortical atrophy with slightly enlarged lateral and third ventricles with no focal lesions

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								He also had mild involuntary movements of the tongue associated with choreoathetoid movements in the upper and lower extremities. Cogwheel rigidity was noted in the wrists bilaterally and neck muscles. He hand frequent visual hallucinations during the examination which were associated with further augmentation of his involuntary movements, particularly tremor	
Scappa S	...	1500 mg/day	...	...	...	...	He was admitted for full-blown mania for the first time in January 1974. This was followed by further admissions in 1975. During the final admission, the administration of LTM and chlorpromazine rapidly improved his behavior, but severe PKN symptoms also occurred. An acute manic episode occurred on February 14, 1978, resulting in another admission to the hospital. Mania was controlled by administering 1500 mg of LTM, 50 mg of haloperidol, and 15 mg of procyclidine per day. He was discharged within 2 weeks. However, he was readmitted 1 month after discharge for a severe depression accompanied by TD and marked PKN. He became manic, while in the hospital, the TD and PKN disappeared	Parkisonian symptoms	...

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Lecamwasam D	Congestive cardiac failure	550 mg (divided 2×/day); 1500-2000 mg	0.5-0.7 mmol/L; 3 mmol/L; 0.85 and 0.99 mmol/L	…	…	He died	1983 - Became confuse and agitated. Received high doses of LTM (1500-2000 mg). Became comatose, generalized muscle tremor. Slurred speech, paraparesis 1989 - Swelling of feet, deterioration of speech, difficulty swallowing, poor mobility, gait disorder. LTM within normal range 1993 - Looked "parkinsonian," congestive cardiac failure, gross dysarthria, hardly intelligible speech, gait, stooped posture, parkinsonian facial expression with dribbling of saliva. Increased tone in upper and lower limbs, hyperreflexia and coarse resting tremor	Deterioration of mobility, speech and difficulty swallowing. Gross dysarthria, gait, stooped posture. Increased tone in uper and lower lymbs, hyperreflexia and coarse resting tremor	...
Holroyd S	Glaucoma, degenerative arthritis of the left knee	900 mg/day; 300 mg/day	0.6-1.0 mmol/L; 1.1 mmol/L; 0.3-0.78 mmol/L; 0.3-0.5 mmol/L	…	5 days	...	Recurrent major depression for over 30 years. She had received various antidepressants as well as ECT. Following a successful course of ECT, she was placed on LTM in combination with nortriptyline. Start of symptoms with bradykinesia and difficulty standing over. LTM was immediately discontinued resulting in a resolution of all symptoms over a 5-day period. She then suffered a relapse of major depression requiring hospitalization and ECT. LTM was then resumed, with serum levels maintained in a range of 0.3-0.78 mmol/L. During assessment, it was noticed that she had a recurrence of micrographia, mild upper extremity tremor, and shuffling gait when the LTM level rose above 0.7 mmol/L. For this reason, LTM levels were then maintained in the 0.3-0.5 mmol/L range of 300 mg per day	Patient had the onset of bradykinesia and difficulty standing. The neurologic examination revealed severe PKN with tremor, cogwheel rigidity, bradykinesia, micrographia, and difficulty standing	EEG was normal

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Northcott C	...	600-900 mg/day	...	...	...	At the time of his discharge, there was a significant reduction in his PKN symptoms but not to a premorbid level	28-year history of BD characterized by 3 previous manic episodes in 1966, 1968, 1981, but no depressions. Presented in January 1994 in a manic state and was near immobilizing bradykinesia. His euthymic mood had been maintained from 1981 to 1990 on prophylactic chlorpromazine (150 mg per day) and from 1990 to June 1993 with LTM carbonate (300 mg/day). In the early December 1993, he began to exhibit elevated mood which progressed over the next 4 weeks to mania with grandiose delusions despite a decrease in Sinemet CR (one tablet per day). His bradykinesia and rigidity worsened, but he was still feeding himself and mobile without aids. Because of worsening manic symptoms, he was hospitalized in early January 1994 and started on LTM carbonate (600 mg increased to 900 mg per day over 1 week), clonazepam (4 mg/day), and Sinemet CR 200/150 was increased to two tablets per day	Unilateral hand tremor and generalized rigidity. He was diagnosed with Stage III Parkinson's disease in October 1993 and commencement of Sinemet CR 200/150 (2.5 tablets per day) led to an attenuation of his Parkinson's symptoms within a few days	...
Aguilar M	...	1200 mg/day	0.63 mmol/L	3 weeks	2 weeks	...	He was treated with neuroleptic drugs (haloperidol 40 mg/day, chlorpromazine 300 mg/day) and LTM carbonate 1200 mg/day. 3 weeks later he developed PSP syndrome	Rigidity with axial predominance, bradykinesia, supranuclear vertical gaze palsy, pseudobulbar palsy together with subcortical dementia (memory disturbance, visuospatial deficits, impairment of executive functions, and bradyphrenia), and AKT	...
Jimenez F	...	...	...	...	...	...	...	Several medications about drug-induced PKN were analyzed. There were no specified data about those patients who used LTM	...

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Fallgatter AJ	…	…	... (therapeutic serum levels)	…	…	…	In contrast to previous reports, the casual role LTM was underscored by symptom increase after LTM re-exposure at therapeutic serum levels. The patient recovered completely after cessation of the LTM	Disorientation, aphasia, ideational apraxia, restlessness, and severe sleep disorder	…
Wils V		...	0.6-0.8 mEq/L	10 days	…	…	VPA was started and titrated to 750 mg/day (blood levels 48-52 mg/L, with 50-90 mg/L being the therapeutic range for anticonvulsant activity). Other prescribed drugs were acetylsalicylic acid, captopril, metformin, and lormetazepam. Doses of all comedication were kept unchanged, and no antipsychotics were administered. 10 days after reaching the final dose of VPA, sedation, cogwheel rigidity, shuffling gait, dysarthria, drooling, and dysphagia were noted. PKN increased in severity over the next 10 days, eventually necessitating the withdrawal of VPA. The EPSs proved reversible, but mania relapsed	Sedation, cogwheel, rigidity, shuffling gait, dysarthria, drooling, and dysphagia	...
Dallocchio C	…	600 mg/day	3.7 mmol/L	…	2 weeks	…	Treated with LTM 600 mg/day for 1 year (a month before the serum LTM concentration was 0.8 mmol/L) was referred to our hospital service because of the recent appearance of psychomotor slowness, difficulty in walking, and tremor of the limbs. LTM was withdrawn, and 3 months later, it was resumed with lower doses	Psychomotor slowness, difficulty in walking, and tremor of the limbs. Psychic slowness without significant cognitive impairment, a clear upward gaze palsy (without a supranuclear component), severe bradykinesia, and severe rigidity of the fore limbs with positive cogwheel phenomenon, rest, and postural tremor with mild amplitude and frequency of 4-5 Hz in all limbs, predominantly on the left side	EEG, chest X-rays, electrocardiograph, and cranial CT scan were normal

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Supplemental Table 2: Contd...

Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
Luby ED	Carcinoma of the breast, sick sinus syndrome, parathyroid adenoma	900-1500 mg qd	0.6-0.9 mEq/L	...	...	...	History of BD and LTM intolerance. During another trial with LTM, she became depressed, disoriented, and confused	Unsteady gait, psychomotor retardation, coarse tremor, and positive Romberg sign	...
	Hypothyroidism secondary to LTM therapy. Colon cancer and chronic lymphocytic leukemia	900 mg	0.5-1.0 mEq/L	19 years approximately	...	...	Following this taper with LTM, he cycled into a major depressive episode, and he was started on bupropion 300 mg qd and VPA 750 mg qd. Subsequently, his neurologist added amantadine 100 mg tid for his PKN symptoms. The discontinuation of LTM did not result in a remission in his PKN	PKN symptoms as shuffling gait, hand tremor, and mask-like facies	...
	LTM-induced interstitial nephritis	900 mg	0.4-1.0 mEq/L	...	...	...	At the initiation of treatment, she presented with symptoms of mania with pressured speech and irritability. She was on imipramine 75 mg qd. She was started on LTM 900 mg qd and imipramine was discontinued. She developed ATX with hand tremor while on 900 mg, and the dose was reduced to 600 mg qd and has been maintained since that time. During the past 2 years, her creatinine level has gradually been increasing, and her nephrologist diagnosed a LTM-induced interstitial nephritis	ATX, hand tremor	...
Kaplan PW	...	....	1.5 mEq/L	...	8 days	Improved over 8 days	Management was ICU hydration treated infection. Other medications: Synthroid	Dysarthria, mutism, rigidity, corticospinal signs, tremor	EEG showed rhythmic anterior delta
Koener B	...	...	...	...	3 months	...	The patient was treated with LTM at therapeutic rates for 25 years and olanzapine for 1 year. 3 years before, she received risperidone for several months. Because the patient reported being unsatisfied, diurnal tiredness, increase of appetite, and weight gain, olanzapine was substituted to amisulpride up to 200 mg/day. 1 month later, amisulpride was progressively discontinued, since weight gain was persistent, and aripiprazole (5 mg and then 10 mg) was started. Rapidly, an akineto-hypertonic parkinsonian syndrome developed in the patient, with shaking of her upper limbs and stiffness of her four limbs, impeding her from lying down, getting up, walking, and feeding herself	Akineto-hypertonic parkinsonian syndrome with shaking of the upper limbs and stiffness of her four limbs, impeding her from lying down, getting up, walking, and feeding herself	...

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Supplemental Table 2: Contd...

Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
Shen HC	Renal insufficiency, urinary tract infarction, hyperparathyroidism, nephrogenic diabetes insipidus	400 mg/day	3.6 mEq/L	10 years	…	1 month later, apart from the residual EPSs and mania, her condition was otherwise stationary	She was treated with LTM for 10 years. She was found to have a high serum level of intact parathyroid hormone: 135.0 pg/ml and a suspicious parathyroid adenoma. Polyuria with hypernatremia was also noted. A water deprivation test confirmed nephrogenic diabetes insipidus. After correction of electrolyte imbalance and reduction of LTM level, her consciousness recovered. Her PKN features were responsive to levodopa 400 mg/day in 2 divided doses	Hand tremor, psychomotor slowness, and difficulty walking. On arrival, she presented psychic slowness with significant cognitive impairment, masked face, severe bradykinesia, severe rigidity of four limbs, and postural tremor in all limbs	Cranial CT scan was normal
Aguilar LG	...	...	...	71.4 months (mean)	...	...	...	Study that assessed drug-induced PKN. Of 55 individuals reported, 13 used LTM. No specific details are described	...
Sarma GR	…	…	…	12 years	…	…	His LTM levels were normal, and he was given ropinirole, levodopa, and amantadine with no relief. His LTM levels after 3 months were found elevated. His PKN completely resolved after stopping LTM	Postural tremors, rigidity, postural imbalance, and bradykinesia	…
Huang YC	Diabetes mellitus	900 mg/day	0.7 mEq/L	2 days	3 days later after discontinuation of aripiprazole, 9 days after discontinuation of LTM	There was no more EPS in the following 9 months	She had a history of risperidone-induced PKN, which was subsided after the drug was discontinued. This time, she was hospitalized due to agitation, outside wandering, irritable mood, auditory hallucination, and referential delusion. Haloperidol was administered on the day of hospitalization, gradually titrated to 7.5 mg/day. Trihexyphenidyl 6 mg/day was also used to prevent EPSs. Eight days after hospitalization, LTM 900 mg/day was added due to incessant irritability and hyperactivity. However, mild muscle rigidity, bilateral hands and right leg tremor, and bradykinesia were observed 2 days after LTM was added. In addition, polyuria and polydipsia were observed 7 days after the use of LTM.	Mild muscle rigidity, bilateral hands and right leg tremor, and bradykinesia. Tonic lateral flexion of trunk. Mild retrocolis was also noted while standing or sitting	Cranial CT scan was normal

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Supplemental Table 2: Contd...

Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
							The serum level of LTM was maintained at 0.7 mEq/L. Her manic and psychotic symptoms were persistent, so as PKN even though trihexyphenidyl 6 m/day or later biperiden 4 mg/day was used. Then, we shifted haloperidol 7.5 mg/day to aripiprazole 10 mg/day at the 15th day after hospitalization. 3 days later, her head and trunk deviated to the left side with about 10° away from midline, while bradykinesia and rigidity were still noted. LTM was discontinued 4 days after the appearance of the trunk deviation. Polyuria and polydipsia improved 5 days after the interruption of LTM. Her psychotic symptoms were well controlled by combined clozapine, haloperidol, and carbamazepine treatment		
Munhoz R	...	...	...	2.51 years	...	...	...	Study that assessed drug-induced PKN. Of 120 individuals reported, 2 used LTM. No specific details are described	...
Walrave TRWM	…	…	In both patients, LTM levels were within the therapeutic range	...	Few months, not specified	…	The LTM dosage was reduced gradually, and within a few months later, all neurological symptoms subsided completely	Symptoms of rigidity and an altered gait, namely symptoms compatible with a diagnosis of PKN with an action tremor	…
Palma JA	…	800 mg/day	0.65 mEq/L	…	14 days. Reduction of carbamazepine dose to 200 mg/day led to a progressive improvement of the symptoms within the 1st days, with a complete resolution at day 14. LTM dose was unchanged	…	Besides LTM, he was taking carbamazepine 600 mg/day. After resolution of symptoms with carbamazepine reduction, the patient was rechallenged with carbamazepine a week later at a dose of 600 mg/day. 5 days later, ataxia and imbalance were again observed with a serum carbamazepine level (12 h postdose) of 4.98 kg/mL. Carbamazepine was held up, and 6 days later, the disturbances had again disappeared	On clinical examination, reflexes were extremely brisk, with bilateral Achilles clonus. He could stand by himself, albeit barely, and the gait was ATX and unstable. A mild bradykinesia was present. He was unable to walk with a tandem gait, and Romberg sign was positive.	Electromyography, transcranial magnetic stimulation, MRI of the brain and spine were normal

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Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
								There was no Babinski sign, and tone and strength appeared to be preserved in all muscle groups. He exhibited bilateral upper limb distal intention tremor, predominantly in the right extremity in finger-to-nose testing. Finger numbness or limb paresthesias were absent	
Shprecher D	…	…	…	…	…	At 6- and 12-month follow-up, dysphagia and dysarthria were markedly improved. Gait improved modestly after intensive physical therapy, though she remained unstable on pull testing	She was found to have a toxic LTM level and had dramatic improvement of all symptoms, except postural instability, after LTM was discontinued in favor of VPA	Dysphagia, dysarthria, incontinence, and postural instability. Initial examination showed impaired vertical gaze and symmetric PKN with marked postural instability	Cranial CT scan showed significant bilateral frontotemporal atrophy
Bondon-Guitton E	...	...	...	...	...	...	...	Study that assessed spontaneous notifications of drug-induced PKN to a French regional pharmacovigilance center between 1993 and 2009. Of 155 notifications, 4 were about LTM. No specific details are described	...

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Supplemental Table 2: Contd...

Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
Caykoylu A	…	600-1200 mg/day	0.83 mEq/L	1 week	1 week after stopping aripiprazole	During the follow-up, after stopping aripiprazole and biperiden, there was no reemergence of EPS including PKN, AKT, and bruxism	Admitted in first mania episode. Aripiprazole was started at a dosage of 5 mg/day, which was titrated up to 15 mg/day in 2 weeks. Concomitantly, LTM carbonate was started at a dosage of 600 mg/day, which was gradually titrated up to 1200 mg/day. Developed bruxism of mixed typed - both grinding and clenching. Subsequently, aripiprazole was reduced to 10 mg/day and lorazepam 2.5 mg/day (per os) was added to ongoing medication. After 3 days under this treatment, the patient noted partial improvement in her AKT and bruxism. Subsequently, biperiden, per os at a dose of 2 mg/day, was added to her treatment regimen, aripiprazole was reduced to 5 mg/day, and lorazepam was gradually stopped. On the 5th day of treatment with aripiprazole at 5 mg/day, biperiden at 2 mg/day, and LTM at 1200 mg/day, there was a significant improvement in her PKN, bruxism, and AKT symptoms. It was decided to completely stop administration of aripiprazole. At the end of the 1st week after stopping the aripiprazole, we observed that her bruxism, PKN, and AKT symptoms had been completely resolved	Bruxism of mixed typed (both grinding and clenching). Her complaints included masseter tightness, headaches, and tooth pain. These involuntary movements were observed only while she was awake. They were regular and rhythmic and would disappear while eating and speaking. Increased leg movements and body rocking. The patient was diagnosed as having bruxism accompanied with drug-associated AKT. Her total score on the BARS was 11. PKN symptoms such as bilateral resting hand tremor, parkinsonian gait, bradykinesia, and rigidity were found in her clinical examination. Her SAS score was 14	Brain MRI and EEG were normal

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Supplemental Table 2: Contd...

Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
Mazzini L	…	300 mg/day	0.31 mEq/L	3 months	8 months after LTM discontinuation, the extrapyramidal features significantly improved, only festinating gait persisted. However, spasticity severely worsened and functional status was largely impaired	…	Associated medications were riluzole 100 mg/day, α-tocopherol 900 mg/day, and trihexyphenidyl 4 mg/day (symptomatic of sialorrhea). LTM was immediately discontinued. A therapeutic attempt with L-dopa was unsuccessful	Before starting LTM, on neurological examination, we found mild atrophy and fasciculation of the tongue, severe dysarthria, and mild dysphagia. Jaw jerk and glabellar tap were absent. Light lower limb muscle weakness, rare diffused fasciculations, and normal muscle tone were detected. After 3 months of starting LTM, neurological examination showed festinating gait, diffuse bradykinesia, severe stiffness, and positive cogwheel phenomenon both in the upper and lower limbs. No LTM-induced postural tremor was detected	Brain MRI showed hyperintensities of the corticospinal tract were detected bilaterally (as expected in ALS). SPECT with 1231-ioflupano (DAT-scan) showed normal dopaminergic function in the basal ganglia. The patient also tested negative for SOD1, TDP-43, and FUS gene mutations
Sarna JR	…	…	…	…	…	Follow-up 4 months later, disclosed significant improvement in rigidity was noted although he had residual slowing of saccades and new left-sided intermittent resting tremor	Being treated with LTM and olanzapine. Based on the findings, olanzapine was discontinued and treatment with quetiapine was initiated	Bilateral postural tremor, rigidity, and stooped posture were noted. On initial neurological examination, he was also noted to have slow vertical saccades	…

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Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
	Diabetes mellitus	...	...	1-2 years	...	...	PKN after approximately 1-2 years of treatment with VPA, LTM, and olanzapine. Substitution of VPA and olanzapine for tegretol and quetiapine resulted in a slow but significant improvement of PKN. Vertical saccades remained slow but substantially improved	Slowly progressive akinesia, rigidity, and shuffled gait were noted. During her assessment, she was also noted to have a stare, slow vertical saccades, axial stiffness, and positive applause sign	Brain MRI was normal
Babinsky E	MSA, coronary artery disease, hypercholesterolemia, hypothyroidism, COPD, history of cholecystectomy, and sleep apnea	900 mg/day	1.1 mEq/L	Over the past 2 years, the patient had complained of worsening ATX, weakness, feeling dizzy, and intractable vomiting for which he was seen at a local tertiary hospital. The patient had also complained of a 30-pound weight loss over the prior 6 months, as well as some dysphasia	Within 3 months after discontinuation of LTM, his symptoms disappeared to the point that he was able to walk independently and had a significant improvement with his intractable vomiting	...	He reported a significant adverse reaction to olanzapine when it was given in its combination form, Symbyax, a combination drug of olanzapine and fluoxetine manifested by difficulty walking and feeling weak. These symptoms had resolved following discontinuation of Symbyax. He used: Levothyroxine 0.175 mg/day, ezetimibe 10 mg/day, celecoxib 200 mg PRN daily (headache), dutasteride 0.5 mg/day, atorvastatin 40 mg/day, tamsulosin 0.4 mg/day, LTM 900 mg/day, fluoxetine 40 mg/day, aspirin 81 mg/day, bupropion 200 mg twice daily, and esomeprazole 40 mg/day. On realizing the toxicity of LTM, the medication was stopped	Gait ataxia, postural-kinetic tremor of the upper extremities, unsteady gait. He had reduced DTRs throughout, without a Babinski or Chaddock sign. His hospice intake examination revealed scattered rhonchi, right-sided hyperreflexia, masked facies, and cogwheel rigidity in both upper and lower extremities, more marked on the left	Brain MRI and EEG were normal
Bhattacharjee S	...	...	...	2 months	...	The patient showed signs of tremor in the hands for 6 years, but it worsened in the last 6 months; tremors started after 2 months of the use of LTM	...	On examination, he had asymmetrical (left > right), rest and postural tremor in both of his hands, with rigidity and bradykinesia in both hands (left > right). There was no gauze restriction, autonomic dysfunction, or focal neurological deficit	...

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Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
Alonso-Canovas A	...	...	...	...	...	...	...	Study that determines whether transcranial ultrasound may help predict response to withdrawal of the offending drug in drug-induced PKN. Of 74 individuals, 1 was about LTM	...
Basile G	Severe hypothyroidism, hypertension, and diabetes mellitus	600 mg/day	…	…	5 months	…	She was affected by mild mental retardation, with a BD for the past about 40 years and was treated chronically with carbonate LTM 600 mg/day and clomipramine 75 mg/day. For the past 20 years, she was also affected by hypertension and diabetes mellitus, which were treated, respectively, with valsartan/hydrochlorothiazide 160/125 mg/day and glimepiride 2 mg/day. LTM treatment was gradually reduced and, after short period, discontinued. Treatment with levothyroxine and saline solution IV was readily performed, and valsartan/hydrochlorothiazide was replaced with amlodipine 5 mg/day as they were identified as potential interactants with LTM	Tremor, bradykinesia, rigidity, postural instability/ATX, lethargy, and bradycardia	…
Cilia R	…	600 mg/day	Serum LTM level was normal	…	After 1 month of the switch to low-dose aripiprazole (2.5 mg/day), her motor symptoms greatly improved and all borderline cognitive testing scores reversed to normal	A 9-months follow-up, SPECT scan showed an increase in binding values within the normal range. Neurological examination revealed a further improvement in motor symptoms and her activities of daily living and quality of life reversed to normal.	Used LTM + SSRI + benzodiazepines. Patient had a 4-year history of bilateral hand tremor and gait disturbance with freezing and unbalance leading to frequent falling, worsened further over the last 6 months. She was not taking any anti-PD medication; levodopa therapy for 12 months was unsuccessful. The switch to low-dose aripiprazole (2.5 mg/day) adequately compensated her psychiatric symptoms without influencing central dopaminegic transmission. After 1 month, her motor symptoms greatly improved (UPDRS-III 17/108) and all borderline cognitive testing scores reversed to normal	Neurological examination showed hypomimia, hypophonia and dysarthria, bilateral postural and rest tremor in the upper limbs, moderate-severe bilateral bradykinesia and muscle rigidity, normal DTRs, shuffling gait with freezing and absent arm swings, flexed posture with impaired postural stability.	Brain MRI showed mild cortico-subcortical atrophy. FP-CIT SPECT showed significant decrease of DAT uptake. A 18F-Dopa PET was performed and revealed normal nigrostriatal terminal density

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Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
						A 24-month follow-up scan showed a further increase in DAT density and no remarkable clinical sign of PKN		UPDRS-III 42/108, Hoehn and Yahr stage 3/5. Global cognition was normal (MMSE 28.2/30) but frontal lobe executive functions were mildly impaired	
Irons R	...	...	...	...	...	...	...	No specific detail was described. Indication for DaT was no benefit from levodopa. However, the DaT scan was negative	DaT scan was normal
Vandewalle W	...	...	...	...	...	...	...	Study that assessed modern mood stabilizers and the occurrence of movement disorders. In 2 individuals, the probable cause of PKN was LTM	...
Glass OM	...	...	...	...	...	...	PKN decreased as the LTM level was reduced to a range between 0.62 and 0.73 mEq/L. Specifically, the patient no longer had freezing of gait, her gait was less stooped, her tremors and posture improved. The patient's mood also remained stable on the lower serum LTM level. MOCA score improved to 19. UPDRS decreased to 24	Her physical examination showed masked facies, postural tremors, resting and kinetic tremors in both upper and lower extremities neck rigidity, and moderate upper limb rigidity with cogwheeling. She had bradykinesia with freezing of gait. UPDRS was initially 52. Baseline MOCA was 10	DaTscan was positive to drug-induced PKN

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Hermida AP	Parkinson disease	1200 mg/day	...	...	...	...	Despite a 40-year history of BD, the patient had remained stable on LTM with occasional irritability. Previous trials of mood stabilizers and augmentation agents (aripiprazole, lamotrigine, VPA, isocarboxazid, tranylcypromine, and fluphenazine) failed due to adverse effects. Her last manic episode occurred 2 years earlier, and her last inpatient psychiatric hospitalization was 14 years before our evaluation. Medications included carbidopa-levodopa 125/500 mg/day, LTM 1200 mg/day, donepezil 10 mg/day, and memantine 20/day. Her previous provider stopped risperidone 11 months before our evaluation due to worsening PD-like features. However, the discontinuation did not improve her symptomatology. Family history was negative for PD and any other movement disorders	She was experiencing worsening gait, weakness, confusion, and forgetfulness. Examination demonstrated masked face, mild-to-moderate postural/kinetic tremor in the upper extremity (left > right), slight resting tremors in both legs and arms, and moderate neck and limb rigidity. She also had moderate-to-severe bradykinesia (left > right), slow gait with freezing, and a stooped posture with decreased arm swing	…
Noyce AJ	...	...	...	...	...	...	...	Assessment of a group of people at increased risk of Parkinson's disease. One individual was excluded because he was diagnosed with drug-induced PKN	...
Kumar N	...	1500 mg/day	1.1 mmol/L	...	3 months	...	...	2-year history of progressive left lateral truncal flexion DTN disappearing on lying supine known as Pisa syndrome, along with anterocollis and PKN	...

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Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
Aikoye SA	Hypertension	1200 mg/day	2.9 mMol/L	2 months (symptoms had worsened in the last 2 months before presentation)	1 month (with the removal of LTM and glomerular filtration improved and the patient's cognition and neurological symptoms decreased within 3-4 weeks in the hospita)	...	She was initially seen in a neurology clinic few weeks before her inpatient hospitalization, diagnosed as idiopathic Parkinson's disease. She was also on lisinopril, diclofenac, levothyroxine, atorvastatin, topiramate, and trazodone. The treatment with LTM was stopped, and replaced by L-dopa and other drugs in conjunction with the physical therapy intervention	Rigidity, tremors, cognitive impairment, masked facies, positive cogwheel rigidity, bradykinesia, and festinating gait	...
Chandana G	History of varicose veins treated with a surgery	900 mg/day	…	About 6 years	…	…	Admitted with chief complaint of giddiness for the past 1 month. History of tremors and weakness of lower limbs for 2 months. Further, fever, muscle stiffness, and generalized body pain for 2 months were observed. He has the sign of cogwheel rigidity. It indicates the presence of tremors and the muscle rigidity	Giddiness, tremor, weakness of lower limbs, cogwheel sign	…
Cruz CC	Hypertension and diabetes mellitus	…	3.9 mEq/L	…	…	…	The patient is currently under treatment with levomepromazine, VPA, and LTM. He came to the emergency department due to tremor and rigidity in extremities of 2 months of evolution. Hemodialysis has been performed. It was necessary to transfer him to the ICU, where he remained in a coma for several days. On awakening from coma, he presented a defective appearance with regressive behavior and unintelligible language, which could be due to cognitive impairment because a possible cortical involvement	Rigidity in limb mobilization, sign of positive cogwheel in wrists, dysarthria, and tremor. Fluctuating level of consciousness alterations, disconnection of the medium and disorientation. Coma	Brain MRI showed diffuse cortico-subcortical atrophy
Florescu A	...	...	...	1 week	No recovery	4 months after the neuroleptic withdrawal, with persistence of the severe parkinsonism (UPDRS: 63)	The individuals had been treated for many years with LTM and olanzapine. His neuroleptics were stopped suddenly	1 week after the neuroleptics stopped, he presented with generalized weakness, shuffling gait, severe bradykinesia, bilateral resting tremor, and altered mental status	DaT scan was normal

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Yomtoob J	...	...	...	...	...	...	...	Study about DaT-SPECT imaging in cases of drug-induced PKN. No specific details are described about LTM. However, they concluded that DaT-SPECT results lead to changes in management and the outcomes of these changes are consistent with scan results	...
Shingavi S	...	1200 mg/day	...	10 years	5 weeks of removal of the LTM and physiotherapeutic intervention	...	She was on LTM 1200 mg/day for over 10 years and without any history of serum LTM check. After consultation with psychiatrist, his LTM carbonate medication was stopped and medical management for PKN with L-dopa and other medications were started along with physiotherapy intervention. Physiotherapy treatment was given for 5 times a week for 5 days	Difficulty in bed mobility, bradykinesia, weakness in bilateral upper and lower extremities, trunk instability, intentional tremors, and hypokinetic voice	...
						DKN			
Peters HA	...	Intoxication	...	...	...	Recovered	...	...	...
Crews EL	...	1200 mg/day, then 3×/day, then 2×/day	2.02 mEq/L (9th day). 12th day: 2.18 mEq/L. 15th day: 1.72 mEq/L. 20th day: 1.11 mEq/L	11 days	5 days	...	She had been taking trifluoperazine and benztropine mesylate, which were stopped 1 week before her admission. LTM was started on the 2nd hospital day. Other medications were trifluoperazine and benztropine mesyate	Had motor symptoms before taking LTM (TD). Presented choreoathetosis, "fly-catcher" tongue. At admission, repetitive purposeless turning of the head, continuous athetoid movement of fingers on both hands, difficulty speaking and swallowing, hyperactivity, irritability, and rapid speech	...

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Beitman BD	...	900 mg/day	0.9 mEq/L	2 years	...	...	She had facial contortions when in use of thioridazine in the past, similar to the one caused by LTM. Self-discontinued LTM at some point restarted with onset of depression 1 week latter. The DKN ceased immediately during a short trial with trihexyphenidyl. After being stabilized on 2 mg of trihexyphenidyl 3×/day for 3 months, she experienced a mild recurrence of symptoms. The interruption of the anticholinergic worsened the symptoms, and also stopping LTM, worsened it further. Both medications were resumed, and DKN was reduced but still present	Grimacing and spontaneous facial movement wich increased when specific tasks involving the extremities where requested. Orofacial DKN	...
Stancer HC	Chronic back pain	900 mg/day	1.1 mEq/L	...	...	These symptoms did not cease when the tranylcypromine was stopped for 12 months and LTM carbonate was given alone	Concomitantly with the use of LTM, she used tranylcypromine, 40 mg/day	Involuntary chewing movements associated with the sensation of a phantom mass lodged against the upper palate just behind the maxillary central incisors. TD not associated with neuroleptics	...
	...	1200 mg/day	1.0 mEq/L	18 months	...	During the reduction of the tranylcypromine dosage, he began to complain of persistent involuntary chewing movements that had not ceased when the antidepressant was discontinued	Concomitantly with the use of LTM, he used 30 mg/day of tranylcypromine	Persistent involuntary chewing started when reducing tranylcypromine. TD not associated with neuroleptics	
Thomas CJ	...	...	...	2 days after starting haloperidol while already in use of LTM for 7 years	3 months, still having evidence of organic brain damage, considerable disorientation and impairment of memory	She got evidence of severe organic brain damage with considerable disorientation and impairment of memory	Both drugs were stopped when the symptoms occurred	Marked rigidity, which made walking unaided impossible, and continual orofacial DKN. Associated with this was a severe confusional state with total disorientation	EEG during the episode revealed diffuse slow waves

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Himmelhoch JM	...	...	0.45-0.65 mEq/L	...	...	...	...	Of 81 subjects, 17 patients had hard neurological illness (12 had extrapyramidal syndromes, and 5 chronic dementia). Extrapyramidal syndromes (PKN and/or facial DKN)	...
Sachdeva JR	...	...	...	...	...	...	...	...	...
Heim J	...	...	...	...	...	...	A case of permanent neurological sequelae by LTM intoxication during a thyrotoxicosis	...	...
Weiner WJ	...	...	...	...	...	...	Appearance of the movement disorder was associated with neuroleptic withdrawal	Meige-like symptoms were attributed to chronic neuroleptic use. The symptoms occurring as part of a TD suggest that dopaminergic mechanisms play a role in idiopathic Meige syndrome	...
	...	...	...	...	...	...	The movement disorder began while neuroleptic therapy continued	Meige-like symptoms were attributed to chronic neuroleptic use. The symptoms occurring as part of a TD suggest that dopaminergic mechanisms play a role in idiopathic Meige syndrome	...
Lieberman A	Parkinson disease and on-off phenomena. DPS	975 mg/day (mean)	0.6-1.5 mEq/L (unclear)	...	...	...	In 12 individuals with Parkinson's disease, LTM was assessed to evaluate the on-off phenomena. All 12 patients had been treated with levodopa/carbidopa (Sinemet) for a mean duration of 10.0 years.	Increased dyskinesia in 1 patient	...

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Supplemental Table 2: Contd...

Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
							The original improvement on Sinemet had disappeared and 8 patients were worse than they had been before starting the drug. Attempts to increase levodopa aggravated on-off phenomena or increased dyskinesias, and efforts to rearrange the timing of the levodopa doses or the ratio of levodopa to carbidopa were unsuccessful. Attempts to decrease levodopa resulted in worsening of disease. The mean dose of levodopa (in Sinemet) was 813 mg (range, 200-1400 mg) and the mean ratio of levodopa to carbidopa was 7:1 (range, 4:1-10:1). Eleven of the patients had been treated with bromocriptine and 8 had at one time improved. Bromocriptine had been discontinued in 4 because of adverse effects and in 6 because of declining efficacy. 7 patients had been treated with pergolide, all with improvement. Pergolide had been discontinued in 2 patients because of adverse effects and in another 2 because of declining efficacy. 8 patients had been treated with lisuride, and all had improved. Lisuride had been discontinued in 3 patients because of declining response. LTM carbonate was begun at a dose of 300-600 mg and was increased by 300 mg/day until therapeutic blood levels (0.6-1.5 mEq/L) were attained, within 15-30 days. Mean daily dose of LTM was 975 mg (range, 600-1200 mg). All other medications remained constant throughout the study. LTM was discontinued in 8 patients because of lack of efficacy and in 1 because of falling. LTM was continued in the other 3 patients until their improvement declined, usually after 4 months		

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Supplemental Table 2: Contd...

Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
Lewis DA	...	600 mg/day	0.7-0.9 mEq/L; 0.6-0.8 mEq/L	2 years or 24 years (unclear)	6 months (10 days after stopping LTM)	At 8-month follow-up, he remained free of any neurological symptoms except for the preexistent mild oromandibular DKN	His persistent ATX and dysarthria were thought to be due to a midline cerebellar infarction. Before discontinuing LTM: Impaired coordination, ataxic, and dysarthric. Borderline-defective level on a battery of intelligence tests and memory tests, which was well below expectations based on his educational and occupational background. 10 days after discontinuing LTM: Psychometric evaluation revealed substantial improvement in intellectual (WAIS IQ, 91) and memory function (Weschler memory quotient, 87). Other medications: Desipramine hydrochloride, 75 mg, diazepam, 15 mg at bedtime, and cimetidine, 300 mg four times daily, which had been prescribed for the treatment of insomnia and reflux esophagitis; borderline-defective level. The patient also had a 3-year history of mild, involuntary buccal-lingual movements that were attributed to previous neuroleptic therapy	ATX, dysarthria, dysdiadochokinesia	2 years before, CT scan revealed mild cortical atrophy and an EEG revealed bilaterally diffuse delta slow waves and slight slowing of the background activity
Mann SC	…	...	1.07 mEq/L	2 weeks	...	His DKN diminished during the period of neuroleptic treatment but then fully reemerged and has now been present for 18 months. Severe DKN developed after 7 days of combined therapy with haloperidol. He used haloperidol 5 mg 3×/day, benztropine 2 mg 1×/day	...	Eye blinking, shoulder shrugging, buccolingual masticatory movements, facial tics, head nodding, shoulder shrugging, truncal torsion movement, and choreoathetoid movements of the fingers, wrists, and toes. Further, it was observed cogwheel rigidity and AKT	Cranial CT scan and EEG were normal
Manor E	...	...	3.9 mEq/L	...	...	2 years later, she was still ataxic and had sporadic choreoathetoid movements	She had alternating paroxysmal atrial fibrillation and sinus-node abnormalities with prolonged pauses of sinus arrest. During these pauses, nodal escape beats and nodal rhythm appeared. After peritoneal dialysis, the cardiac rhythm reverted to normal	Impaired consciousness, twitching, and fasciculation characterized by the author as DKNs	...

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Supplemental Table 2: Contd...

Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
Rao AV	...	750-1000 mg/day divided in 3 doses	0.6-1.2 mEq/L	The duration of therapy ranged from 3 months to 6 years. Symptoms appeared between 3 months and 1 year	In 7 patients, the tremors were controlled with 40 mg propranolol per day which was discontinued after 2-3 months and tremors did not recur. In others, the magnitude of the tremors diminished over time and settled without any measure to counter	...	...	Tremors (26.6%), polyuria (20%), salivation, nausea and abdominal discomfort; weight gain, memory defects, hypothyroidism, TD, acne and hair fall, gait. Fine tremor, DKN, ATX	...
Standish-Barry HMAS	...	...	0.79-1.24 mEq/L	...	4 weeks	...	In association with a urinary tract infection, her plasma LTM level rose briefly to 1.64 mEq/L. Treatment with procyclidine 10 mg 3×/day was started and her symptoms subsided after 6 days. Further, thioridazine 50 mg 2×/day	2 days after urinary tract infection, she had severe choreoathetoid movements, AKT, orofacial DKN (bruxism), and posturing	Cranial CT scan and EEG were normal
Zorumski CF	...	1200 mg/day	1.2 mEq/L	9 days	3 months	Her depressive symptoms recurred after her discharge and were treated with trazodone 150 mg/day. She then became euthymic and had significant improvement by 6 weeks; choreiform movements disappeared by 3 months of follow-up	Because of poor affective disorder, she was given a trial of carbamazepine 200 mg. History of ATX and confusion, in 2 previous trials with LTM, which cleared over several days after discontinuation of LTM. Other medications: Amitriptyline 75 mg/day, haloperidol 2 mg/day	Confusion, dysarthria, confusion, and marked choreoathetoid movements of her extremities, vomiting. Neurologic consultation revealed mild PKN features	Cranial CT scan and EEG were normal
Coffey CE	Parkinson disease and on-off phenomena	...	0.78 mEq/L	Discontinued after 3 weeks	...	...	...	Choreoathetosis, hemiballismus, DKN	...

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	Parkinson disease and on-off phenomena	...	0.85 mEq/L	4 weeks	...	...	On initiation of LTM carbonate, he showed a 75% reduction in akinesia. Other med levodopa/carbidopa 10/100 mg 7×/day, bromocriptine 2.5 mg 8×/day. Reduction of levodopa/carbidopa (10/100 mg q.i.d.) and bromocriptine (25 mg q.i.d.) improved DKN. LTM was continued at the same dosage	Choreoathetosis of all extremities, hemiballismus, orofacial DKN, shoulder/neck DTN. The involuntary movements were associated with psychomotor agitation, but no confusion, dysarthria, or cerebellar signs	...
	Parkinson disease and on-off phenomena	...	0.8 mEq/L	17 weeks	...	After 3 years, the patient was well	LTM therapy resulted in 62% reduction in akinesia. Other medications: Levodopa/carbidopa 25/250 mg 5×/day, bromocriptine 2.5 mg 10×/day. Reduction of levodopa/carbidopa 25/250 mg q.i.d. and bromocriptine 2.5 mg 8×/day managed the choreoatetosis and hemiballismus; LTM was continued	Choreoathetosis, hemiballismus	...
	Parkinson disease and on-off phenomena	...	0.79 mEq/L	22 weeks	...	...	LTM therapy resulted in 50% reduction in akinesia. LTM was discontinued and the dosage of levodopa/carbidopa tapered (25/100 mg q.i.d.), and the hallucinations and dyskinesia were resolved	Insomnia, visual hallucinations, upper-extremity choreoathetosis, dystonic posturing of the shoulders	...
	Parkinson disease and on-off phenomena	...	0.8 mEq/L	28 weeks	...	...	LTM therapy resulted in 80% reduction in akinesia. LTM was tapered and eventually discontinued, levodopa/carbidopa dosage reduced to 25/250 mg q.i.d., with resolution of dyskinesias and hallucinations	Motor restlesness, insomnia, visual hallucination, orofacial dyskinesias	...
Perényi A	…	…	…	…	...	...	TD in patients receiving LTM maintenance therapy	…	…
Campbell WG	Episodic alcohol abuse during manic phases of his illness. Haloperidol. Mild hypertension, which was treated ith propranolol, 100 mg/day	1200 mg/day	3.0 mEq/L	10 years	...	After his death, a small focal area of neuronal loss and gliosis was noted in the depth of the horizontal sulcus of the cerebellum.			

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Supplemental Table 2: Contd...

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						In addition, neuronal loss and gliosis were noted bilaterally in the Hi segment of the hippocampus, and multifocal gliosis was noted in the thalamus.			
						These lesions were compatible with remote ischemic-hypoxic episodes	Suicide attempt with LTM and haloperidol. Benztropine mesylate, 4 mg	Orofacial DKN	…
Walevski A	Rheumatic arthritis (indomethacin 150 mg/day)	900 mg/day	0.9-2.5 mEq/L	14 days	72 h	...	2 previous psychiatric admissions, first postpartum psychosis and second a manic-like psychotic state caused by steroid administration due to severe rheumatic arthritis. During 10 years, she was treated with indomethacin 150 mg/day	Choreoathetosis movements, dysarthria, random jerky movements, and writhing movements on the upper part of the body. Pressure of speech, flight of ideas with euphoric affect	...
	Partial thyroidectomies for goiter at the age of 35 and 40	1200 mg/day	1.4 mEq/L	3 days (9 of treatment)	10 days	...	Haloperidol 15 mg/day was first used and then stopped because it caused severe TD after 6 days. LTM was then introduced	Flight of ideas, dyskinesia, choreoathetosis movements (slow purposeless movements), looseness of associations, and grandiose ideas with manic effect	EEG was normal and showed symmetrical irregular waves in the 8-11 Hz range
Haggerty JJ Jr.	Neuroleptic malignant syndrome	900 mg/day	0.6 mEq/L	Patient had TD for 3 years. About 1 month before admission, LTM was introduced	…	DKN continued at the same level of severity as had been seen on admission and was unaffected by a trial of lecithin and later increases in the bromocriptine 27.5 mg/day. 3 months after the onset, he was successfully weaned from bromocriptine and was discharged home	He had taken neuroleptic medication, including thioridazine, oral and depot fluphenazine, and trifluoperazine continuously for 7 years. He was treated with diazepam 30 mg/day together with LTM. Reserpine was begun at 0.25 mg/day and was slowly increased over a 2-week interval to 1.25 mg/day.	TD, choreoathetoid movement, involving all four extremities, spasms of his neck and back muscles, twisting movements of his neck and trunk, grimacing, and occasional grunting.	EEG, CT scan, and ceruloplasm were normal

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							Initially, he appeared to benefit, exhibiting a relative decrease in truncal movements and having improved sleep. However, at doses of 1-1.25 mg of reserpine, his movements became more pronounced, and he developed transient blood pressure elevations to 170/110 mmHg, intermittent diaphoresis, tachycardia, and pallor. LTM and reserpine were discontinued; thioridazine 100 mg and haloperidol over 5 mg were given. Following each dose, he fell asleep and became free of movements for several hours. Within 4 h after receiving haloperidol, he became extremely rigid. Unexplained temperature fluctuation, diaphoresis, and leukocytosis persisted intermittently for 7 weeks and seemed to worsen whenever bromocriptine doses were withheld. DKN movements continued at the same level of severity had been seen on admission and were unaffected by a trial of lecithin and later increases in the bromocriptine dose to 27.5 mg/day. The subsequent course was complicated by the development of acute renal failure secondary to rhabdomyolysis (CPK >99 999 U), which required renal hemodialysis	The patient developed intermittent stridor, dysphagia, and auditory hallucinations 5 days after the discontinuation of reserpine and 3 days after discontinuation of LTM	
Nagaraja D	…	600-2100 mg/day	1.1 mEq/L	36 months	...	...	Precipitating factor, probably were fever and chlorpromazine. Sequelae: cerebellar, pyramidal, DKN, and neuropathy	Ataxia, confusion, tremor, cerebellar, pyramidal, DKN, and neuropathy	Cranial CT scan showed cerebellar atrophy
	...	600-2100 mg/day	3.0 mEq/L	6 months	...	...	Precipitating factors: Fever, chlorpromazine, dehydration; Sequelae: cerebellar, pyramidal, DKN	Coma, cerebellar, pyramidal, DKN	...
	...	1200 mg/day	0.7 mEq/L	175 months	...	...	Precipitating factors: Chlorpromazine, butyrophenone. Sequelae: Cerebellar, pyramidal, neuropathy, DKN	Cerebellar ATX, pyramidal, neuropathy, DKN	...

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Nasrallah HA	...	590 mg/day (mean)	...	...	...	...	...	Of 46 maniac patients using LTM and other neuroleptics such as haloperidol, fluphenazine, trifluoperazine, 12 developed a DTN reaction	...
Dinan TG	...	...	...	...	...	...	...	Of 40 psychiatric individuals, 9 developed DKN. The researchers observed that patients with and without TD did not differ in terms of duration of affective illness or exposure to neuroleptics, but those patients with tardive dyskinesia had significantly more psychiatric admissions and were on LTM for significantly greater lengths of time	...
Helmuth D	...	600 mg/day - 19 days after they changed to 900 mg 3 times a day	1.07-1.10 mEq/L	4 days after verapamil was added	3-4 days after discontinued verapamil	...	Verapamil (120 mg 3 times/day) was added together with LTM to treat mania	Choreoathetosis. He had mild voluntary tongue and mandibular movements which were similar to TD by haloperidol	...
Matsis PP	...	500 mg/ day - later add more 250 mg	2.0 mEq/L	2 days	3 days (not clear)	...	Hypercalcemia and hyperamylasemia. For years, her maintenance therapy had been phenelzine 30 mg 3×/day and LTM 500 mg 1×/day. Several days before hospital admission, she had developed anorexia and become withdrawn. Believing that these symptoms were the prodroma of an impending DPS, her family practitioner increased the LTM to 250 mg in the morning and 500 mg at bedtime. In 2 days before her admission, she became increasingly confused and disorientated, complained of thirst, and eventually became bedbound with “muscle twitches”	On admission, she was restless, markedly confused, and disorientated in time, place, and person. She was able to obey simple commands but was dysarthric.	...

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								On examination, she had an unsteady ataxic gait and could not cooperate in other tests of coordination. DTRs were symmetrically brisk with bilateral equivocal extensor plantar responses. There was no neck stiffness. In addition to restlessness, she had small purposeless movements in all four limbs. Spontaneous irrepressible choreiform movements of arms, legs, and trunk became marked	
Reed SM	…	…	0.85 mEq/L	8 days	1 week	...	To “calm himself down,” the patient took increasing amounts of LTM and triazolam. About 5 days before evaluation, a nonpruritic rash appeared on his forearms, lower abdomen, thighs, and dorsum of his hands. Three days later, he became confused and disoriented, and a tremor began, which gradually increased in intensity. He then developed purposeless movements of his arms, legs, and head; these became so severe that he was unable to eat, drink, or dress himself. The patient had been treated with LTM for the past 12 years, and, before LTM, ECT, and antipsychotics. His history was remarkable for an episode of LTM toxicity when he took excessive amounts of medication during a manic phase. His LTM level at that time was 1.92 mEq/L. LTM was discontinued and then restarted 1 year later. Since that time, the patient had done well on LTM, except for manic episodes usually associated with noncompliance. The patient reported a distant history of episodic alcohol abuse	Constant choreoathetoid movements of his arms, hands, and neck. Choreoathetoid movements of his legs were present but less pronounced. He occasionally rolled his eyes. A glabellar reflex was present. His speech was pressured and dysarthric	EEG was normal

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	…	…	2.18 mEq/L	48 h	1 week	…	Thioridazine and chlorpromazine were his only known medications at the time of admission. Additional information obtained from another hospital shortly after admission indicated that the patient had been taking LTM and had a 20-year history of BD	At admission, physical examination was significant for garbled speech, hyperreflexia, MCL, asterixis, perseveration, poor stereognosis, and graphesthesia. Choreoathetosis	Head CT showed diffuse atrophy, and EEC showed diffuse and paroxysmal slowing
Sternbach H	…	1200 mg/day	0.9-1.0 mEq/L	...	...	1 month later, she reported a recurrence of chewing movements	LTM prophylaxis since 1971. In addition to LTM, the patient was taken l-thyroxin 0.1 mg/day for 7 years (due to LTM-induced hypothyroidism) and conjugated estrogens 0.3 mg/day for 15 years	She went to consultation due complaints of 2-year history of involuntary chewing movements. Vermiform movement of tongue, chewing movements including lips, jaw, and tongue, slight acting tremor	...
Scappa S	…	1200 mg/day	…	…	…	He developed a manic episode within the next 2 months and both the TD and PKN vanished completely. From the 4-6 episodes that occurred annually, it was noted that his TD disappeared during mania and worsened a week before the onset of DPS	He had been taking methotrimeprazine 300 mg and LTM 1200 mg/day. Profound DPS was noted during the examination. Trimipramine 200 mg was started. In addition, he displayed shuffling gait, drooling, rigidity, and choreoathetotic bucco-oral, truncal, and extremity movements accompanied by jerky respiration. He developed a manic episode within the next 2 months, and both the TD and PKN vanished completely. From the 4-6 episodes that occurred annually, it was noted that his TD disappeared during mania and worsened a week before the onset of DPS	Shuffling gait, drooling, rigidity, and choreoathetotic bucco-oral DKN, truncal, and extremity movements accompanied by jerky respiration	...

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	...	900-1500 mg/day	…	…	…	In November 1991, she developed a manic episode during which all these movements disappeared	During the first decade of her illness, she intermittently took LTM (900-1500 mg/day) and haloperidol (10-40 mg/day). Mania almost always followed an episode of DPS. After the onset of her rapid cycling, she developed severe choreoathetotic and DTN movements which waxed and waned depending on whether she had suffered a manic or a DPS episode. 2 weeks later (February 20, 1989), she went to the emergency room of the hospital to be treated for a manic episode. No abnormal involuntary movements occurred once she was placed on haloperidol (2-5 mg/day). On January 10, 1990, she reported stiffness all over her body, shuffling gait, involuntary movements of the neck and shoulder, and inability to sit still. The examination revealed DPS, typical buccolingual movements, truncal DKN, neck and shoulder DTN, and occasional grunting and jerky breathing. 2 weeks later, the DPS and involuntary movements simultaneously worsened. Clonazepam, propranolol, Vitamin E, and pyridoxine, taken in sequence, did not produce any response. However, in November 1991, she developed a manic episode during which all these movements disappeared	Choreoathetotic and dystonic involuntary movements. Typical buccolingual movements, truncal DKN, neck and shoulder DTN, and occasional grunting and jerky breathing	...
Lazarus A	Epilepsy	900 mg/day	0.5-0.7 mEq/L	5 years	...	...	The patient was treated with phenytoin (1981-1983) and thereafter with carbamazepine 400 mg/day. Both LTM and carbamazepine were stopped in 1992 after persistent movement disorder	Striking dystonic movements, truncal DTN, opisthotonic posturing, myoclonic jerks, blepharospasm, and irregular respirations	Normal

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Trugman JM	…	1500 mg/day	…	…	…	…	Examination in June 1986, while taking fluphenazine (80 mg/day) showed evidence of AKT. The patient was treated with fluphenazine (55 mg/day), benztropine (1 mg/day), LTM (1500 mg/day), and lorazepam (6 mg/day) for the next 6 months, during which time a severe movement disorder became apparent. Fluphenazine was tapered and replaced with thioridazine (500 mg/day). Drug-induced PKN, including bradykinesia, cogwheel rigidity, and intermittent left arm tremor, was noted at this time. Thioridazine was tapered (50 mg/day), but this was not tolerated due to worsening psychosis. Trihexyphenidyl (30 mg/day), in combination with reserpine (0.25 mg/day), was poorly tolerated and ineffective	Examination in November 1986 showed a gait disorder characterized by high steps, pelvic thrusting, and extension of the arms. Mild lip pursing and tongue movements and foot tapping were also noted. Tardive DTN	…
Podskalny GD	Hypertension	600 mg/day	2.2 mEq/L, then 1.7 mEq/L	10 years	…	2 weeks after discharge, there was no sign of chorea or ATX	The patient had a history of BD and had been treated by a psychiatrist for 30 years. Her affective disorder was well controlled for 10 years with LTM 600 mg/day. A few weeks before her admission, the patient was seen by her primary care physician, who prescribed furosemide (40 mg/day) and potassium chloride (20 mEq) due to hypertension. She had not taken neuroleptics for >10 years. She had a slight metabolic acidosis with respiratory compensation	The patient was lethargic and somewhat confused but would follow simple commands. Her speech was extremely dysarthric. The patient's muscle tone was normal with generalized weakness but no focal weakness. Slight hyperreflexia in the right upper extremity. Plantar responses were flexor bilaterally.	Normal cranial CT scan. Brain MRI revealed an old 1.5-mm left caudate head lacunar infarct. EEG was remarkable for slowing of the posterior dominant rhythm (6-7 Hz) and theta and delta slowing of the background activity, which supports a diagnosis of metabolic encephalopathy. There were abundant spike and sharp transient waves originating independently from both posterior quadrants. Trains of pseudoperiodic sharp transients briefly occurred in both parietal regions with a frequency of 0.5 cycles/s. A repeated EEG during the later part of the hospitalization was improved

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								Involuntary movements developed. Her head, neck, trunk, and extremities were in almost constant motion. These movements had the appearance of being spontaneous, irregular, purposeless, writhing, twisting, flowing, and rocking in nature. Voluntary movement or sustained posture increased the severity of these movements, which were judged to be choreoathetosis. In addition, the patient had marked dysarthria and limb, trunk, and gait ATX	
Meyer-Lindenberg A	...	...	1.1 mEq/L	...	...	…	In 1991, she developed a transient orofacial DKN for the first time during a depressive episode. In September 1994, she was readmitted because of ATX gait, slurred speech, and disorientation. LTM intoxication due to insufficient fluid intake was diagnosed, and the LTM was discontinued. The ATX and intention tremor rapidly subsided, but the chorea of the digits and the pronounced orofacial and abdominal DKN persisted	Occasional blepharospasm and abdominal dyskinesia compromising speech and respiration. She also had chorea of the toes and fingers, slight intention tremor, and ATX gait with pronounced impairment of righting reflexes	EEG was normal
Higes-Pascual F	Hypertension	1000 mg/day (400-200-400)	2.07 mEq/L	28 days	48 h	…	In 1982, hypertension diagnosis and was in use of captopril 100 mg/day	Choreoathetosis of limbs and head	…

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Normann C	...	1125 mg/day	0.92 mEq/L	6 days. History of about 20 years of chronic LTM therapy. She had PKN 6 days after admission, before LTM was reintroduced	6 days	Involuntary irregular choreoathetoid movements of the muscles of the upper limbs and the trunk together with perioral and finger movements were noted which were found to be persistent after 6 months	At the time of admission, she was receiving LTM (900 mg/day) with plasma levels between 0.6-0.8 mEq/L and amitriptyline (30 mg/day). The psychopathology was relevant for an elevated and expansive mood, psychomotor agitation, and aggressive outbursts. Her formal thinking was characterized by loosened associations, neologisms and rhyming. She expressed paranoid delusions and stated that she had not slept for several days. A diagnosis of a manic episode with psychotic symptoms was established and therapy with valproate (1200 mg/day) and haloperidol (24 mg/day) was started. During hospitalization she also used biperiden, perazine, and clonazepam. On day 56th, all drugs were stopped. The patient showed a rapid and dramatic recovery. Within 6 days, she was completely orientated with no further thought disturbance	Neuroleptic-induced muscular rigidity and akinesia. In a progressive manner, she became disoriented in time, place, and person and was no longer able to perform the activities of daily living. Severe delirium characterized by disorientation, restlessness, fear and optical hallucination. Mild pallhypesthesia of both feet. Rigor of all extremities. Involuntary irregular choreoathetoid movements of the muscles of the upper limbs and the trunk together with perioral and finger movements	Normal cranial CT scan and brain MRI. The baseline EEG on the 8th day was normal except for a mild diffuse slowing. The EEG on the 30th day showed a slowing of the occipital background activity and a marked diffuse slowing. On day 56th, the occipital background activity was 6 Hz while the diffuse slowing was almost continuously present. On day 63th, the EEG improved gradually until a normal recording was achieved on day 100th
Gerding LB	…	900 mg/day	…	24 years (maybe 24 years. Symptoms started 6 years before report, considering that he was the 30 previous years in LTM therapy. Not clear)	After 2 weeks on clonazepam, the patient displayed only mild residual TD in his face and fingers. He continued to have mild TD for 4 months. He then missed a routine follow-up appointment and stopped taking clonazepam.	…	Consistent use of various neuroleptics including thioridazine (50-500 mg/day), chlorpromazine (200-600 mg/day), haloperidol (2-10 mg/day), and benztropine (1-2 mg/day). At age 75 years, he developed mild TD. At the onset of TD, the haloperidol dose was reduced from 5 to 1 mg/day and then discontinued, with initial worsening of TD and then mild residual TD that the patient tolerated. Other medications used: LTM, risperidone, buspirone, quetiapine, and clonazepam	Athetoid movements of the lips, tongue, and fingers. He had marked tongue movements causing difficulty speaking, and he became anxious about being in public. His AIMS score was in the severe range, with severe DKN and DTN oral and facial movements and moderate finger athetoid movements	...

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Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
					Over 2 weeks, his TD worsened and hypomania returned. His AIMS score returned to the severe range. He was restarted on clonazepam, 0.5 mg bid, with a rapid improvement of TD and reduction of hypomania. The athetoid movements resolved nearly completely over 1 week, and he has continued to be well for 4 months		Clonazepam led to a profound improvement of his TD. After 2 weeks on clonazepam, the patient displayed only mild residual TD in his face and fingers		
McGavin CL	Borderline personality disorder	300 mg/day	...	...	3 weeks after resuming levetiracetam 1000 mg/day	...	5 months earlier, adjunctive antidepressant treatment with LTM (300 mg/day) was discontinued after 10 years because of improvement in DPS. DKN began 4 weeks later and progressed to subjective maximum within 1 month. A 1-month trial of haloperidol (5 mg per day) 4 years earlier produced identical movements that resolved completely upon discontinuation of haloperidol. Current medications were fluoxetine (20 mg/day) and sustained release bupropion (300 mg/day)A diagnosis of TD was made and treatment with clonidine (0.3 mg per day) produced a decrease in symptoms. Levetiracetam (500 mg per day) was started. Examination 3 weeks later demonstrated only rare orobuccal movements. AIMS score was 3.	Abnormal movements of the tongue, mouth, and hands. Frequent orobuccolingual dyskinesias, which produced a mild dysarthria, were present on examination. Intermittent choreic movements of the trunk and choreoathetoid movements of the forearms and hands were seen.	...

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Supplemental Table 2: Contd...

Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
							Because of the marked improvement, the patient discontinued levetiracetam and clonidine. Dyskinesias returned to their pretreatment level within 4 weeks. Levetiracetam was restarted and increased to 1000 mg per day. 3 weeks later, no dyskinesias were present on examination	Tremor, rigidity, and bradykinesia were absent. Gait was of normal base and station. Stress gait maneuver exacerbated all of the dyskinesias and produced dystonic posturing of the right hand. Signs of psychosis and cognitive impairment were absent. AIMS score was 35	
Stemper B	…	...	2.43 mEq/L	1.5 years	5 days	…	Referring physician suspected transient ischemic attack. The patient was being treated for hypertension with beta-blocker, an acetyl cholinesterase inhibitor, and a thiazide diuretic. About 1 h after admission, the patient's symptoms had worsened. Considering the patient's advanced age and the apparently impaired kidney function, she underwent hemodialysis. After hemodialysis, the LTM level decreased to 0.2 mEq/L, the patient became more alert and the choreoathetotic movements subsided	Dysarthric speech, seemed somewhat confused. She had difficulties answering questions regarding the date, time, location, her date of birth, and her symptoms. She was not able to walk. There were no involuntary movements at the time of admission. After 1 h, unable to communicate and was not following even simple commands. In addition, she started to show spontaneous twisting, choreoathetotic movements of both hands and arms. Severe gait ataxia	Normal cranial CT scan

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Wada K	Hypertension, chronic hepatitis type C, and diabetes mellitus	1200 mg/day	3.52 mEq/L	...	23 days	...	...	Consciousness disturbance and choreoathetosis were observed in her face and upper and lower extremities	EEG showed bilateral symmetrical slow-wave activity
Bender S	...	...	...	...	...	...	...	Study that assessed the safety and efficacy of combined clozapine-LTM pharmacotherapy. Of 44 patients, 3 developed orofacial DKN	...
Mendhekar DN	...	900 mg/day	...	1 year after stopping LTM and dothiepine	He showed good improvement within 2 weeks of trial, and at the end of 4 weeks, his score went down to 1 on AIMS	He was followed up for 4 months, and there was no recurrence of DKN movements of the mouth	His past history revealed that he had a first episode of severe major DPS about 4 years back, which was treated with LTM (900 mg/day), dothiepin (75 mg/day), and 6 ECT without any complications (including movement disorders). The patient continued this regimen for 4 months, and later on stopped it, as he was symptom-free. 1 year after the stoppage of these drugs, he started exhibiting stereotyped abnormal movements of the mouth in the form of puckering of lips, which increased in intensity during emotional situations and disappeared completely while sleeping. Separate trials of tetrabenazine (100 mg/day), propranolol (80 mg/day), trihexyphenidyl (6 mg/day), and clonazepam (6 mg/day) for approximately 4-6 weeks did not show any improvement on the rating scale. In view of the possibility of the idiopathic nature of DKN, risperidone (1 mg/day) was started. He showed good improvement within 2 weeks of trial, and at the end of 4 weeks, his score went down to 1 on AIMS	Stereotyped abnormal movements of the mouth in the form of puckering of lips. Further assessment revealed continuous repetitive, stereotyped puckering movements of the lips. He would control his movements but only for 1-2 min. He scored 7 on the AIMS, which was moderate to severe in intensity	...

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Supplemental Table 2: Contd...

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Mendhekar DN	...	800 mg/day	0.7 mEq/L	1 month (2 weeks +2 weeks +3 days). However, it is not clear if the patient was using LTM when admitted	All her DKN movements disappeared within 5 min of IV administration of 50 mg promethazine	…	Mania precipitating factor being malarial fever that was treated with tablet chloroquine for 4 days. 2 previous episodes. For the current episode, she was given LTM (800 mg/day); 2 weeks later, risperidone (2 mg/day) was added. The risperidone was subsequently increased (5 mg/day) over 2 weeks Her case was diagnosed as rabbit syndrome, and both the drugs were stopped. She scored 9 on the AIMS. All her DKN movements disappeared within 5 min of IV administration of promethazine (50 mg). Subsequently, she was given olanzapine (10 mg/day) and trihexyphenidyl (2 mg/day), along with the same dosage of LTM, without any recurrence of DKN movements	Abnormal perioral movements characterized by rapid, fine, rhythmic involuntary movement of her lips and jaw on a vertical axis, associated with AKT and occasional synchronous lingual movement. Diagnosed as rabbit syndrome	…
Ozsoy S	Pneumonia	1200 mg/day	0.9 mEq/L	4 months (unclear)	...	…	He had been taking LTM 1200 mg/day, lamotrigine 300 mg/day, and escitalopram 10 mg/day for 4 months, and he was in remission for 3 months. There was pneumonic infiltration in X-ray. Pneumonia was diagnosed. He was hospitalized to infectious diseases clinic and cured with antibiotics (levofloxacin 500 mg/day, sulbactam-ampicillin 6 g/day). His psychiatric medication was stopped	In the psychiatric examination, he had dysarthria, normal orientation, and anxious affect. When neurologically examined, he had ataxia and dyskinesia. He was unable to stand, or walk at all, or to sit without support, had bilateral dysmetria and severe tremor in finger-to-nose and finger-to-finger tests, severe dysarthria, and bilateral horizontal nystagmus. The patient was diagnosed as cerebellar syndrome by the neurology department	Brain MRI and SPECT were normal. EEG showed epileptic activity in the areas of both temporal and left parietal although there was no epilepsy clinically

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Hunter CB	...	...	...	...	...	...	...	...	...
Lloyd RB	...	400 mg/day	2.5 mEq/L	1 week	5 days	No	Treated over the past 6 years with aripiprazole (20 mg/day), VPA (1000 mg/day), clonazepam (1.5 mg/day), trazodone (100 mg), and LTM (300 mg/day). 1 week before her admission, her LTM dose had been increased (400 mg/day). Shortly after the increase, she became increasingly lethargic, disoriented, and withdrawn. This change was attributed to oversedation, so the clonazepam and trazodone were withheld. All psychotropic medications were withheld, and she was aggressively rehydrated. The nephrology service was consulted and determined that hemodialysis was not warranted at that time. 72 h later, her LTM level decreased (0.9 mEq/L); the hypernatremia resolved; and she was more alert; however, she developed involuntary choreoathetoid movements. Her psychotropic medications were restarted, with the exception of LTM, which was discontinued. On discharge, she had residual, intermittent tongue protrusions that interrupted her speech, with slight ocular rolling movements; her mental status had returned to baseline	The neurologic examination was significant for pinpoint pupils and a downward Babinski reflex. Choreoathetosis	Cranial CT scan showed confluent periventricular hypodensities compatible with moderate-to-severe nonspecific white matter disease
Chung AK	Obesity, diabetes mellitus, hyperlipidemia	…	0.6-0.9 mEq/L	…	…	…	He had failed mood-stabilizer monotherapy including LTM, carbamazepine, and VPA before. Between 2002 and 2006, he was in remission with oral haloperidol used as adjunct to carbamazepine as maintenance treatment. Later, he developed TD involving the oropharyngeal region despite receiving prior stable dosages of haloperidol and carbamazepine for 18 months. TD resolved after switching to quetiapine (400 mg/day) and Vitamin E (800 IU/day) with carbamazepine continued over the next 7 months. He remained in remission during that period. He was admitted to the psychiatric hospital for stabilization and later discharged with the regimen of LTM, VPA and 2-weekly risperidone (25 mg). He had no extrapyramidal side effects	He complained of involuntary, lateral oscillatory movements over the middle part of his neck	…

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Arambewela MH	Type 2 diabetes mellitus, hypertension	500 mg/day	2.57 mEq/L	1 week	5 days of commencement of steroids	No	LTM (1500 mg/day) was commenced along with a small dose of prednisolone. 1 week afterward, he presented with unsteadiness of gait, slurring of speech, agitation, altered level of consciousness, and reduced urine output. Before these symptoms, he had experienced vomiting and diarrhea. An initial working diagnosis was LTM toxicity with possible meningoencephalitis in the back ground of thyrotoxicosis. LTM was omitted, and the patient was hydrated and dialyzed. IV ceftriaxone and acyclovir for a possible meningoencephalitis was commenced. Carbimazole was continued. There was no neurological improvement following hemodialysis and normalization of LTM levels and renal functions. This prompted consideration of any alternative diagnosis such as Hashimoto's encephalopathy and oral prednisolone 60 mg/day was initiated. Thyroid autoantibodies inclusive of thyroglobulin antibodies and thyroid peroxidase antibodies were twice negative. He made a remarkable neurological improvement within 5 days of commencement of steroids and was discharged following 2 weeks of hospital stay. It was planned to tail off the steroids and titrate antithyroid drugs	Neurological examination revealed increased tone in all four limbs with exaggerated reflexes and bilateral extensor plantar responses. Choreiform movements involving face and upper limbs were noted. There was no neck stiffness, and he was moderately dehydrated	EEG showed nonspecific generalized delta activity
Cobb A	...	...	2.2 mEq/L	The patient came to the emergency room, after a 3-day history of word-finding difficulty, confusion, dysarthria, tremor, impaired short-term memory, and ATX	On discharge (hospital day 10th), the choreoathetosis had completely resolved, and she was back to her baseline level of cognitive and physical functioning	...	Relevant medical history included bipolar type I disorder treated with lithium for 34 years. On hospital day 2, the patient developed dramatic choreoathetosis - involuntary, irregular, nonrhythmic, high amplitude, dance-like writhing. Her movements were unremitting, requiring one-on-one nursing care to ensure her safety. Voluntary muscle control was limited. The patient did not report any discomfort with these movements. Despite normalization of her renal function and lithium level, her choreoathetosis continued. On discharge (hospital day 10), the choreoathetosis had completely resolved	Tremor of the upper limbs and facial muscles and choreoathetosis. Physical examination showed a fine rapid tremor of the upper limbs and facial muscles. The neurological examination was notable for a positive Romberg sign, perseveration, and bradykinesia	Head CT, ECG, and CXR performed in the ED were normal

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Vandewalle W	...	...	...	...	...	...	Study that assessed the movement disorders caused by different antidepressants. They reported 2 individuals with DKN and more 2 individuals with TD	...	...
Amamou B	…	1500 (mg/day)	…	…	5 weeks after starting clozapine	Since April 2015, the patient showed no relapse neither in mood nor in TD	In 2001, the patient was initially treated with carbamazepine (600 mg/day) and haloperidol (40 mg/day) treating a manic episode; he developed an induced TD involving muscles spasm in the neck and nape, which completely resolved after stopping haloperidol for 3 weeks. The reintroduction of haloperidol (10 mg/day) was well tolerated in combination with LTM carbonate treating the second manic relapse. In 2007, during the 3rd maniac relapse, he was treated with olanzapine (30 mg/day) in combination with LTM with recurrence of the TD. The neurological examination and brain scan were in favor of iatrogenic origin. From 2008 to 2014, several antipsychotics (to treat tardive DTN) in combination with LTM were tried. The patient did not show any improvement and DKN became very troublesome, with TD assessment score of 70. In 2015, clozapine was started, with improvement of TD after 5 weeks	TD	…
Huang SS	...	900 mg/day	3.18 mEq/L	...	6 months later, she had total recovery of the involuntary movements of the face, mouth, extremities, and trunk. However, she still experienced the neurological sequelae of general weakness and dysarthria	No	Had been taking the medications such as LTM (900 mg/day) and quetiapine (600 mg/day) for 6 months	The patient developed involuntary movements such as biting and mouth chewing, and rapid, purposeless, irregular, and spontaneous choreic movements of her arms, wrists, and hands.	Brain MRI showed a symmetrical high signal intense lesion in the splenium of the corpus callosum on the three-directional diffusion image, which was consistent with axonal injury

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								Foot squirming and twisting of neck and shoulder were also noted. The involuntary movements subsided when sleeping. We restored quetiapine monotherapy for her BD. 1 month later, the delirium resolved, and she could reply with simple words. However, the patient still had ATX, dysarthria, and involuntary movement. Owing to severe involuntary movements, we added amantadine (100 mg/day), clonazepam (1 mg/day), and haloperidol (0.75 mg/day). 4 weeks after prescribing medications (the baseline time point), the patient was able to try an oral diet. 6 weeks after the baseline time point, the patient could sit on the bed for a few minutes	

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Rachamallu V	Diabetes mellitus type 1, history of occasional cocaine use	900 mg/day	…	77 days (unclear, but maybe it was 77 days after starting clozapine)	…	…	The patient's psychiatric medication history included aripiprazole, risperidone, olanzapine, haloperidol, VPA, benztropine, clonazepam, fluoxetine, and citalopram. Due to the lack of improvement with other antipsychotics, the patient was started on clozapine. The patient's other medications at the time included LTM, citalopram, clonazepam, and atenolol. In subsequent clinic visits, due to the worsening symptoms of stuttering, the patient and the parents decided to proceed with the tapering-off of LTM and the start of VPA. After 4 weeks of VPA (1000 mg/day), the patient and the family reported improvement in perioral twitching and stuttering	Rare infrequent orofacial DKN with perioral twitching, persistent stuttering	Brain MRI was normal. Abnormal waking and sleep EEG. Several episodes of generalized spike and wave activity of 3 Hz that lasted 2-3 s during photic stimulation and hyperventilation suggested epileptiform activity. Due to the intermittent form of this activity, we will hereafter refer to it as a "microseizure"
Fountoulakis KN	...	600 mg/day	0.6 mEq/L	15 years (The article does not report the exact time of the onset of symptoms, it only states that it started a few months ago. Despite the fact that the patient used LTM 15 years ago)	...	...	Before using LTM, she was treated with neuroleptics and other forms of humor stabilizers	...	...
Silva DG	...	...	3.17 mEq/L	...	5 days	Complete recovery	Chorea and encephalopathy. Retrospective study of acute chorea in the emergency room	...	Brain MRI was normal
						AKT			
Loudon JB	...	...	1.2 mEq/L	5 days. The symptoms started after adding haloperidol 12 mg/day	4 weeks	...	8-year history of manic-depressive illness. Symptoms caused by combination of drugs (LTM + haloperidol), also used procyclidine	ATX, rigidity	...

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Channabasavanna, SM	…	900-1500 mg/day	1.2 mEq/L	2 years (3 days after increasing dosage of LTM to 1500 mg/day)	3 weeks	…	A local doctor suspected manic excitement and gave chlorpromazine 200 mg. This worsened his restlessness further. The patient was given promethazine IV 50 mg stat and again after an hour. Trihexyphenidyl 4 mg/day was added to LTM 1500 mg/day. AKT, dysarthria, and gait disturbances completely resolved within 36 h after starting anticholinergics. However, mild cogwheel rigidity and hand tremors persisted for >3 weeks	Restlessness, inability to sit still even for a brief time, and an irresistible urge to pace the floor. Higher mental functions, fundi and superficial and deep reflexes were normal Short, shuffling gait, without associated movements, rapid hand tremors, generalized cogwheel rigidity and dysarthric speech	EEG was normal
Price WA	…	…	…	10 days	36 h	…	Her problems were cleared within 36 h with the addition of trihexyphenidyl 4 mg/day. LTM was not stopped	…	…
Zubenko GS	…	…	0.8 mEq/L	1 year	10 days after discontinuation of trazodone	…	He was taking LTM + trazodone for over 1 year with no symptoms. However, just before the onset of his decompensation, his daily dosage of trazodone was increased from 200 to 300 mg/day. Trazodone was discontinued, and by the 10th day, the symptoms of motor restlessness and anxiety had entirely remitted	Inability to sit for more than a few moments at a time. Inability to fall asleep because could not find comfortable position. Motor restlessness	…
Patterson JF	…	900 mg/day	…	1 week	24 h	Fully recovery. He was discharged to outpatient follow-up	He responded to haloperidol 20 mg/day. LTM 900 mg/day was started. Shortly after, he felt intense restless in his legs. Haloperidol was discontinued. However, AKT persisted. 1 week after discontinuation of haloperidol, LTM was discontinued, and the symptoms stopped within 24 h. 1 month after discharge, he started LTM 900 mg/day and he developed AKT in 24 h. The therapy was discontinued and frequent follow-up was substituted for prophylactic therapy	Intense restless on his legs and a compulsive need to move about the ward	EEG and cranial CT scan were normal
Yassa R	LTM-induced hypothyroidism	1200 mg/day	0.75 mEq/L	4 years	48 h (after lorazepam 1 mg)	After 1 year indicates no further recurrences	Symptoms started 7 days before. The patient has been taking LTM for 4 years. For hypothyroidism, he took thyroid tablets 0.2 mg/day. He had not received neuroleptics for 8 years before admission	Feeling jumpy, anxious, restless, and unable to sit still	…

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Poyurowsky M	Drug abuse	900-1500 mg/day	0.58-0.94 mEq/L	4 weeks and 3 days after restarting LTM, 3 days after raising the dose from 900 to 1500 mg/day	1 week	No recurrence of AKT during 3 weeks of follow-up	Present admission was due to unsuccessful attempt to discontinue LTM and levomepromazine. After AKT started, biperiden 4 mg/day was given; after 1 week, only partial improvement was noted. Biperiden was interrupted, and after 2 days washout, mianserin 15 mg per os was started. 7 days later, he had complete amelioration. AKT returned after mianserin discontinuation. Mianserin was rechallanged and led again to disappearance of symptoms	Restlessness, tension, irresistible urge to move. Unable to sit still for >2 min, had to constantly change body position. Diagnosed as acute AKT	…
Muthane UB	Diabetic peripheral neuropathy	900 mg/day	1.5 mEq/L	10 days (unclear)	…	At follow-up 10 months later, her PKN features persisted despite being on amantadine 200 mg/day. Orofacial DKN also persisted but was less severe	She was started on LTM 900 mg/day by her family physician. Her psychiatric symptoms improved dramatically 10 days later. Subsequently, following mild fever for a day, she developed severe AKT. She worsened and developed disabling PKN in the form of tremors and slowness. Within 4 days of stopping LTM, her PKN had improved with associated reduction of serum LTM level to 0.2 mEq/L. She was less AKT. However, at the end of a week, she developed orofacial DKN	AKT, PKN in the form of tremors and slowness, mutism, orofacial DKN	…
Scorr L	...	...	...	...	...	...	...	No previous exposure to neuroleptics. He presented with the sensation of beads and wire on his teeth, which he said led to constant restless movements of his tongue and mouth	...
Vandewalle W	...	...	...	...	...	...	Study that assessed the movement disorders caused by different antidepressants. AKT was associated with LTM in 1 individual	...	...
Demir B	...	600 mg/day	...	...	...	...	LTM replaced with VPA. The AKT did not respond to reducing the dose of risperidone and addition of propranolol and lorazepam	...	...

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						RLS			
Heiman EM	...	1800 mg/day	0.9 mEq/L	...	48-72 h	...	LTM therapy was discontinued, and the patient was started on treatment with clonazepam 2 mg at bedtime	Nocturnal MCL aggravation - persistent and increasing jerking sensation on legs when tried to sleep. She described an "electric" sensation going slowly down her legs	...
Terao T	...	1000 mg/day	0.8-0.9 mEq/L	9 days (approximate)	1 day after reduce dosage	CR	He started with lithium 800 mg/day and later added levomepromazine to insomnia (first 5 mg/night and later 15 mg/night). The patient reported an unpleasant creeping sensation in his lower legs at night and levomepromazine was discontinued. Because compulsive symptoms remained, we increased LTM to 1000 mg/day. On the night of the 13th, he complained of a severe creeping sensation in his lower legs and an urge to move or rub them. As we suspected that LTM (0.8-0.9 mEq/L)-induced RLS, the dosage was reduced to 400 mg/day (0.3-0.4 mEq/L). The following day, RLS was alleviated and serum-free MHPG was decreased to 3.5 ng/ml on the 20th. Thereafter, he was put on LTM 400 mg/day without RLS and discharged	Creeping sensation in lower limbs at night, slight paresthesia and insomnia	...
Kauta S	Anxiety and DPS	...	...	6 weeks before she sought help, right after starting LTM	...	...	Her nocturnal urge to move her toes began when she was a teenager and progressively worsened over the years; however, she did not seek medical evaluation. She recalls that the urge worsened when she was treated with antidepressants (fluoxetine and sertraline), and as a result, she stopped taking these medications. At age 49, she was started on gabapentin for back pain, thought to be related to degenerative disk disease in her lumbar spine, and noticed that her toe-related symptoms completely resolved	Abnormal sensation in her toes described as a strong urge to squeeze her toes together while attempting to fall asleep at night. The symptoms were bilateral and would go away briefly when she pressed her toes together.	...

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								Symmetric reflexes in her lower extremities with no gross evidence of abnormalities in pain sensation or proprioception	
Demirci K	...	600 mg/day	...	...	2 weeks	CR	She developed these symptoms when she had received LTM 300 mg with quetiapine 300 mg at the same time at nights. The woman was recommended to take LTM 300 mg in the morning and in the afternoon with subsequent doses of lithium 300 mg and quetiapine 300 mg in the evening with 2 h intervals. Her symptoms started to disappear from the 1st day of this regimen, and 2 weeks later, her symptoms completely resolved, and she did not show any subsequent symptoms	Restlessness, urge to move legs, numbness, and tingle sensations	...
Chen PH	...	600 mg/day	...	...	...	CR	He tried suicide with 40 years, and psychopharmacotherapy with sertraline was provided at that time in the psychiatric ward to treat his acute DPS. After admission, escitalopram 20 mg/day and LTM 600 mg/day were administered. After 3 weeks on this drug regimen, his depressive symptoms had not remitted. Consequently, quetiapine 100 mg/day was added to the treatment regimen. 1 week later, when the 100 mg/day dosage proved to be ineffective, the dosage of quetiapine was increased to 150 mg/day. Within 24 h, he began to experience paresthesias and an urge to move his uncomfortable legs during the night. He had a remission of depressive symptoms while he was receiving combination treatment with escitalopram 20 mg/day, LTM 600 mg/day, and lamotrigine 50 mg/day. After quetiapine withdrawal, the symptoms of RLS were completely resolved	Paresthesias and an urge to move his uncomfortable legs during the night	...
Öhlund L	...	...	...	...	...	...	...	...	...

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						Stutter			
Netski AL	...	1200 mg/day	0.7 mEq/L	1 month	...	...	Persistent developmental stutter since childhood. He had a history of DPS for the past 4-5 years and was receiving fluoxetine 20 mg/day. During this recent manic episode, the patient was hospitalized, and LTM was added to fluoxetine for treatment of BD. The patient's mood was stabilized on LTM at a dose of 1200 mg/day. 1 month following treatment initiation, the patient experienced lightheadedness, hand tremor, and worsening of stutter. LTM was tapered off in this patient; due to these changes, treatment with VPA was started, which was successful in continued stabilization of his mood at a dose of 2750 mg/day and a blood concentration of 87 µg/mL. His stutter returned to baseline within a few weeks of discontinuing LTM therapy	1 month following treatment initiation, the patient experienced lightheadedness, hand tremor, and worsening of stutter	...
Gulack BC	Attention-deficit/hyperactivity disorder, conduct disorder, developmental stuttering	1800 mg/day	0.62-1.24 mEq/L	...	2 days	...	LTM was started at 150/day during the 3rd week of the patient's hospitalization to target symptoms of mania. The patient had been on oral risperidone since admission, and the dose was increased to 4 mg at bedtime 1 week before starting LTM. He was prescribed oral clonidine on admission and the dose was increased to 0.1 mg 3 times daily 2 weeks before starting LTM. When the LTM dose was increased to 1800 mg/day to better control the BD, his developmental stutter worsened. When the LTM dose was reduced to 600 mg in the morning and 900 mg at night, the stutter returned to baseline	The stutter consisted of syllable repetitions, occurred only at the beginning of sentences, and did not bother the patient. He began having trouble expressing himself, had to engage in circumlocutions, and became distressed about his stutter. He showed no specific signs of LTM toxicity such as confusion, lethargy, tremor, ataxia, myoclonic jerks, polyuria, or gastrointestinal upset	...

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Supplemental Table 2: Contd...

Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
Sabillo S	Dementia, epilepsy	…	2.0 mEq/L	…	2 weeks	…	Chronic medications included donepezil, primidone, risperidone, and LTM. 1 day, she complained to her nurse that she had been stuttering, finding it difficult to complete a sentence, as well as sing. She grew increasingly bothered by her faltering speech as the days wore on and also pointed out that her grip on objects was becoming weak. Her attending physician was subsequently informed of these new symptoms. Physical and neurological examinations were unremarkable aside from her obvious stutter. She was able to talk straight for a few words, and then would begin to repeat syllables and words until she became obviously frustrated and abruptly terminated her sentence. Her stuttering persisted for 3 more months until a LTM level was checked and came back elevated at 2.0 mEq/L (0.6-1.2 mEq/L). LTM was promptly stopped, and after about 2 weeks, her level was back to normal, and her stuttering had completely resolved	Stuttering, finding it difficult to complete a sentence. Her grip on objects was becoming weak. Physical and neurological examinations were unremarkable aside from her obvious stutter	Cranial CT scan was normal
						CJLS			
Helmchen H	...	...	...	...	...	...	...	...	Abnormal EEG
Kemperman CJ	…	…	2.3 mEq/L	...	...	...	These EEG abnormalities decreased the weeks thereafter	…	EEG showed periodic sharp waves, triphasic waves, and diffuse slowing

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Smith SJ	...	250 mg/day	1.2 mEq/L	2 months later after she was treated with benzhexol hydrochloride and Madopar (levodopa/ benserazide)	3 weeks after stop all medication	...	Patient used LTM for 32 years, no symptoms. Mild PKN was diagnosed, and she was treated with benzhexol hydrochloride and levodopa/ benserazide. 2 months later, she developed the sequelae. She became confused and withdrawn. She deteriorated over the ensuing few weeks, becoming bed-bound, mute, and incontinent with coarse tremor in both arms. All treatment (LTM, promethazine, chlorpheniramine, indomethacin, and Madopar) was stopped. Over the next 3 weeks, her mental state improved, and she could walk unaided	There was generalized hyperreflexia, bilaterally extensor plantar response, and bilateral grasp reflexes	EEG showed a slow dominant rhythm of 4-6 Hz, with fast rhythms (12-16 Hz) and runs of periodic sharp waves, some with a triphasic outline, at 1.5-2 Hz. There were occasional episodes of high amplitude delta waves
	...	800 mg/day	3.2 mEq/L	1 month	15 days. The myoclonic jerks disappeared after 3 days, and after a phase of perseveration and emotional liability, the mental state had returned to normal by 10 days	Three further EEGs recorded at 3, 7, and 15 days after admission showed steady improvement with return of normal rhythms	She had been treated for 10 years with LTM 800 mg/day, blood levels being monitored regularly. 1 month before developing neurological symptoms, she had an operation for knee replacement. In the next few days, she vomited several times but had no diarrhea. She became confused and deteriorated during the 2 weeks before admission	On examination, she was uncooperative, confused, and only occasionally responding to simple commands. There were irregular twitching movements of the face and lips and MCL movements of the limbs at rest, more obvious when the limbs were passively moved, but not affected by sudden noise. Tone in the limbs was slightly increased, power and reflexes were normal, plantars were absent	EEG showed widespread slow activity and runs of periodic sharp waves (1-2.5 Hz)

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Broussolle E	Parkinson's disease	12,000 mg/day (intoxication)	...	6 days	5 days after LTM withdrawal	...	Since the patient presented with an atypical PKN with DPS, levodopa plus LTM therapy was started. On the 10th day after admission, levodopa (without dopa decarboxylase inhibitor) was introduced progressively, reaching a daily dose of 2 g within 6 days. LTM gluconate at a daily dose of 12 g was added 13 days after admission. On the 19th day, the patient became confused and agitated, and treatment was stopped. Nonetheless, she worsened during the next 48 h, presenting with a precomatose state, mutism, rigidity, sporadic jerks that were prominent in the lower limbs, and urinary incontinency	Rigidity, sporadic MCL that was prominent in the lower limbs, and urinary incontinency. Akinesia, tremor prominent in the left lower limb, bradyphrenia	EEG with increased theta activity of 5 Hz and delta activity, predominantly in the frontal fields; triphasic waves and sharp waves particularly in the frontal fields, that were not synchronized with the concomitant jerks of the upper limbs
Primavera A	...	450 mg/day	...	...	...	...	...	...	...
	...	...	2.6 mEq/L	...	...	...	...	Organic brain syndrome with choreoathetoid movements and action MCL was associated with elevated serum levels (2-6 mEq/L)	...
Waldman AJ	Congestive heart failure, gout, COPD, coronary artery disease	...	...	...	1 week after discontinuation of all medication	...	She was seeing more than 1 psychiatrist and besides LTM she was taking trazodone, benztropine, methylphenidate, warfarin, trifluoperazine, theophylline, allopurinol, diltiazem, alprazolam, estrogen, albuterol inhaler, and cimetidine	Tremor on all upper limbs	...
Fineli PF	...	...	...	...	12 days	1 month after discharge, the patient was cognitively intact and a repeat EEG was normal	He was taking LTM and nortriptyline	Myoclonic jerks, fasciculation, and a postural tremor were noted along with a positive stare and unsteady gait with retropulsion	EEG showed slowing delta range. Brain MRI showed mild atrophy

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Supplemental Table 2: Contd...

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Casanova B	…	1200 mg/day	1.03 mEq/L	4 months	3 weeks after admission	...	He has been successfully treated with LTM and lorazepam 1 mg/day for 2 years	Generalized hyperreflexia, bilaterally extensor plantar response, cogwheel rigidity, and archaic reflexes. MCL, PKN, akinesia, inability to walk, sphincter incontinence	First EEG showed widespread background slowing and disorganization with mixed frequencies in the theta range and scarce alpha activity accompanied by generalized sharp waves of variable frequency, maximal posteriorly and occasionally repetitive at 1-2 Hz
Masmoudi K	…	…	…	…	…	…	Long-term LTM use	…	…
Laasonen-Balk T	…	Intoxication	…	…	…	…	…	…	…
Takahashi M	…	…	Intoxication	7 years	3 weeks	…	She subsequently developed dysphagia, dysarthria, unsteady gait, and progressive deterioration of the higher cortical function over 1.5 months. The plasma concentration of LTM was found to be over the therapeutic range. Reduction of LTM dose almost completely resolved her symptoms within 3 weeks	Mild tremulousness of both hands. Dysarthria, unsteady gait, and progressive deterioration of the higher cortical function. Her tremulousness deteriorated until it resembled MCL	EEG showed periodic sharp wave complexes appearing predominantly over the bilateral parieto-occipital areas
Kikyo H	…	600 mg/day	0.82 mEq/L (CSF)	…	Full recovery 21 days after admission. MCL was gone 3 days after starting (2 days after admission)	…	Admitted with coma and MCL. She had a history of manic and depressive disease for 8 years and had been treated with 200 mg LTM carbonate, 25 mg chlorpromazine, and 10 mg levomepromazine daily. Her first symptom was forgetfulness, then appetite loss, diarrhea, MCL, and gait disturbance. At the same time, she complained of visual disturbance. Gradually, her conscious level declined. When she was admitted, she had convulsions. At that time, she was injected with 200 mg phenobarbitone intramuscularly, and this was continued for 2 more days at the same dose. Her MCL disappeared and her conscious level gradually improved. She was discharged on June 25 fully recovered. The cause of her high LTM concentration was clear with the discovery that she took three times as much as prescribed when she could not sleep well	Forgetfulness, MCL, gait disturbance, visual disturbance, convulsions, coma. Neurologically, there were general hypotonus and hyporeflexia without Babinski's sign	EEG showed slow basic activity and periodic synchronous discharges. Cranial CT scan and brain MRI were normal

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Slama M	Dementia, Parkinson's disease	...	1.3 mEq/L	13 years (approximately)	32 days	78 days after admission, clinical examination was mainly normal apart from memory disorders concerning recent events, temporospatial disorientation, and a slight speech disorder	The onset of deep coma and respiratory distress secondary to bronchopulmonary congestion required intubation and mechanical ventilation	Neurological examination revealed temporospatial disorientation, resting tremor of the upper limbs, diffuse MCL, and generalized hyperreflexia	EEG revealed a slowed background activity and a generalized periodic activity suggestive of Creutzfeldt-Jakob encephalopathy
Mouldi S	…	…	…	9 years	…	…	Progressive dementia with MCL and cerebellar syndrome suggesting a diagnosis of Creutzfeldt-Jakob encephalopathy. The results of the different investigations and the favorable course after discontinuation of LTM were in favor of diagnosis of drug-induced CJLS	MCL and cerebellar syndrome suggesting a diagnosis of Creutzfeldt-Jakob encephalopathy	…
Isikay CT	…	…	1.88 mEq/L	...	Death	…	Her first symptoms were anorexia, nausea, vomiting, diarrhea, and fever that started 1 month before admission	Declined consciousness, fever, and generalized seizures. Systemic symptoms of LTM toxicity such as anorexia, nausea, vomiting, diarrhea, and insomnia for 1 month. Neurological examination disclosed declined consciousness, generalized hypotonia, and hyporeflexia	EEG showed widespread slow-wave activity and runs of periodic sharp waves, some with a triphasic pattern
Kim SW	…	…	…	…	…	…	Patient who was treated with LTM and developed subacute MCL and cognitive dysfunction	...	Changes in perfusion pattern identified using brain SPECT

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Fernández-Torre JL	Diabetes mellitus type 2, Parkinson's disease	600 mg/day	4.2 mEq/L	...	12 days. She had a normal mental state and the fourth EEG showed a normal background activity with occasional FIRDA. The serum LTM level was undetectable	...	Admitted for slowly progressive psychomotor agitation, mutism, and nocturnal MCL for the last 10 days. She was using levodopa (250 mg/day), LTM (600 mg/day), and aripiprazole (5 mg/day). She was treated with IV hydration and hemodialysis	There were occasional jerks affecting the lower limbs with cogwheel rigidity, but tremor was absent	Cranial CT scan showed cerebral atrophy. EEG revealed a slowing of the background activity with frequent runs of generalized PSWC of triphasic morphology occurring at a rate of 2.0 Hz. PSWC consisted of three phases: A surface positive high-amplitude wave preceded and followed by negative components with smaller amplitude. These waves had frontopolar or frontocentral predominance, and spread with an anterior-posterior time lag on bipolar derivations. PSWCs showed a dipolar distribution of the electrical field, observing maximal electropositivity on the frontal areas and electronegativity on the parieto-temporo-occipital regions. PSWC was not affected by eye opening or stimuli. During the recording, the patient experienced myoclonic jerks of both legs, not associated with PSWC or epileptiform discharges. To help distinguish between toxic encephalopathy and NCSE, they administrated 5 mg of IV diazepam, after which PSWC amplitude attenuated slightly, occurred more frequently along with abundant superimposed fast activity. A third EEG revealed frequent generalized bursts of intermittent delta activity with frontal maximum (FIRDA) that occasionally assumed a triphasic appearance with sharp components. On day 12, the patient had a normal mental state and the fourth EEG showed a normal background activity with occasional FIRDA

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Madhusudhan BK	…	…	4.7 mEq/L	25 years	…	…	Laboratory tests revealed leukocytosis (13,450 cells/mm^3), hyponatremia (128), and elevated serum creatinine (2.3 mg/dL). Considering the toxicity of lithium, we started hemodialysis. However, in spite of 3 cycles of dialysis, decreased lithium levels (1.2) and other normal parameters, the patient remained unconscious. Considering the clinical possibility of NCSE, she got an EEG. She was treated with IV lorazepam. She showed gradual improvement in her sensorium that correlated with the decline in blood LTM levels and the return of a normal background alpha rhythm on EEG. At the time of discharge, she had recovered completely, with no apparent neurological deficit or cognitive impairment	Neurologically, the patient was comatose, her pupils were small and reactive, and her extraocular movements were restricted, with generalized hypotonia, hyporeflexia, and no other focal deficits	The EEG demonstrated bihemispheric slowing (4-5 Hz theta range) with bilateral periodic triphasic waves of 1-2 Hz frequency, similar to the EEG changes seen in Creutzfeldt-Jakob disease
						DTN			
Aronson TA	…	…	…	…	…	…	He was initially treated successfully with LTM, but this had to be discontinued because of troublesome side effects. Symptoms started after use of haloperidol. Other medications: Tranylcypromine, desipramine, haloperidol, diphenhydramine	DTN reaction with protruding tongue and dysarthria, generalized rigidity, bradykinesia, mask-like facies, pill rolling tremor, dysarthria, and a shuffling gait	…
Goetting MG	…	300 mg/1×	1.0 mEq/L	9 h	3 h	During the following 3 h, her DTN and hyperreflexia disappeared and her speech became clear. 5 h after the 1st LTM level, she had a new level of 0.78 mEq/L. This gradually declined during the next 2 days. She remained asymptomatic. 2 years after the ingestion, she is a bright, coordinated child without apparent defect	Syrup of ipecac was administered, promptly resulting in a large emesis. She was treated with IV saline infusion	DTN and hyperreflexia. Slurred speech and she repetitively puckered and licked her lips. The cranial nerve examination findings were normal. There was no nystagmus.	…

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								While sitting, her posture was wavering. Purposeful arm movements were uncoordinated. Intermittently, her lips puckered and she displayed writhing tongue movements and lip smacking. There were episodes lasting several minutes in which her hands assumed an extended posture with wrist flexion and her legs were extended with scissoring. Her tone was increased throughout with brisk DTRs, but Babinski signs and clonus were absent. Gait was not tested	
Yazici O	…	…	1.0 mEq/L	…	…	…	A combined treatment of LTM and thioridazine (400 mg/day) was initiated. Neuroleptic treatment was gradually decreased over 3 weeks and discontinued, while the LTM level was maintained at approximately 1 mEq/L. By the end of the 4 weeks, the patient almost resumed her premorbid mood and was discharged to be followed up, maintaining a serum LTM level of 0.8 mEq/L. After discharge, torticollis was observed.	Torticollis was observed, appearing initially as a slight rotation of the neck to the left which aggravated in time to result in a DTN posture persisting for 4-5 s. DTN in the neck, tendency to posturing, an internal rotation of the left arm starting from the shoulder, and pain in the left arm and wrist	…

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							In the past, she had been prescribed a negligible amount of neuroleptics (haloperidol 5 mg/day; thioridazine 50 mg/day) and biperiden (2 mg/day) for prophylaxis from 1978 to 1982, after which neuroleptics were prescribed solely to treat attacks. DTN first emerging in 1984, while the patient was without medication and in a euthymic state, as a slight torsion of the head toward the left which was followed by persistent rotations. The attacks recurred, however, with increasing frequency in the following years. We noticed that with each manic attack, DTN disappeared completely or almost completely, only to recur in remission when the mood was restored to normal. DTN sometimes preceded the normalization of mood by a few days		
	…	…	0.9 mEq/L	…	…	After her discharge, although she gave up her treatment and missed her follow-up, we were able to obtain information about the recurrence of attacks and the continuance of the same pattern of tardive DTN. In our opinion, this case also has a tendency to become a rapid cycler	Nonpsychotic and psychotic depressive attack (with hypo manic phase) treated with low doses of antidepressants combined with various neuroleptics for 1-2 months. After an attack, she complied poorly to the proposed neuroleptic prophylaxis (haloperidol 5-10 mg/day) in the 8 months to follow. Many therapeutic attempts with amitriptyline (150 mg/day), haloperidol (10 mg/day), biperiden(4 mg/day), thioridazine (100-400 mg/day), carbamazepine (400-600 mg/day), tetrabenazine (100 mg/day), L-dopa (600 mg/day), and benserazide (150 mg/day). LTM prophylaxis was reinstated, although it could not be ensured that she complied sufficiently. DTN reappeared 1 month after the remission of the manic attack in 1988 in euthymic phase. No secondary causes of DTN were found. 2 weeks after the discontinuation of LTM, a manic attack emerged during which the DTN remitted, to recur during the anxious dysthymic period following the manic phase and to resume its former severity. The patient was discharged from the clinic in normal mood state, and her DTN improved slightly	....	...

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Manji H		...	...	...	...	No	At the time of admission, she was experiencing frequent and painful spasms which consisted of flexion of both arms, DTN posturing, and tremor of the right foot and leg. These required the administration of IV midazolam. Trials of tetrabenazine, pimozide, clonazepam, L-dopa + benserazide, carbamazepine, and LTM were unsuccessful. On stopping the LTM, the spasms worsened requiring larger and more frequent doses of midazolam. In view of her increasing exhaustion and severe discomfort, she was electively paralyzed with atracurium and ventilated. She was sedated with infusions of midazolam, propofol, and morphine for 10 days. By day 8, she was self-ventilating on midazolam. She was gradually weaned off midazolam, and during this period, she started on a combination of pimozide (gradually increasing to 12 mg/day), tetrabenazine 75 mg/day, and benztropine. The latter was subsequently stopped because of urinary retention. She was discharged on tetrabenazine, pimozide, and intermittent oral clonazepam to be taken in the event of recurring spasms	Posttraumatic DTN, painful spasms which consisted of flexion of both arms, dystonic posturing, and tremor of the right foot and leg	...
Durrenberger S	...	...	...	...	...	...	...	Acute dystonic reaction to LTM and risperidone	...
Chakrabarti S	...	800 mg/day	...	3 years	...	On follow-up 12 months later, he was on 150-200 mg of clozapine daily (VPA had been stopped) and showed remarkable improvement. He was euthymic, AIMS rating was down to 2, and disability was minimal. He was back at work and lead a more or less normal life	He had been stable on a combination of LTM 800 mg/day, carbamazepine 100 mg/day, and chlordiazepoxide 10 mg/day for 3 years, when he first started experiencing twisting of head and neck to the left side and arching of his back. The movements were worse when he was tense but disappeared during sleep. All drugs were stopped on his first visit to the outpatient department.	Twisting of head and neck to the left side and arching of his back. Torticollis, retrocollis, and opisthotonus, without any cranial nerve or sensorimotor deficits. AIMS score at this point was 11	EEG and cranial CT scan were normal

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							He had significant depressive symptoms, which remitted with fluoxetine 20 mg/day for 8 weeks. He subsequently developed a manic episode during which the DTN movements actually got better. Clozapine was started and adjusted at 250 mg/day, the maximum he could tolerate. Clonazepam was tapered off and VPA reduced to 400 mg/day. At discharge, 3 weeks later, he had no manic symptoms (MRS-1). DTN movements, pain, and discomfort had also reduced (AIMS-10)		
Rosebush PI	…	...	…	10 years	…	…	About 10 years after illness onset, he developed DTN (torticollis). DTN would disappear during the manic phase, only to reappear when the manic symptoms abated, with or without antipsychotic dose reduction. He has been given botulinum toxin (injectable), tetrabenazine, and trihexyphenidyl to control the DTN, without success. For the last 3 years, he has been treated with atypical antipsychotics. He is now receiving olanzapine and VPA	DTN (torticollis) affecting the left sternocleidomastoid and platysma muscles	...
Silva MC	…	450 mg/day	…	1 day after decrease in LTM dose	24 h after restitution of LTM dose	…	5-year history of insidious onset of forgetfulness and personality change and 2-year history of an acute right-sided hemiparesis. At presentation, the patient had regressed behavior and double incontinence. A provisional diagnosis of dementia was made. Symptomatic treatment was started with haloperidol 7.5 mg/day. It had to be stopped as the patient developed PKN. The EPSs remitted with a week of therapy with anticholinergics. LTM was started and showed modest improvement in arousal. After 4 weeks, an attempt was made to decrease LTM to a minimum effective dose, by decreasing it to 300 mg/day.	Left-sided truncal DTN	...

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							Within a day of decrease, the patient developed left-sided truncal DTN. The DTN did not remit for 3 days despite injectable promethazine 50 mg/day and later oral promethazine 75 mg/day. LTM was restituted to 450 mg/day. Patient's DTN remitted within 24 h of these changes		
Oommen E	...	450 mg/day	...	8 months of LTM start. 2 months after aripiprazole exposure, there was worsening in dystonic symptoms	...	...	The patient has a previous history of 2 psychotic episodes and 3 episodes of mania. LTM was reduced	Tardive DTN	...
Kwan Y	...	...	...	...	His tardive DTN gradually improved and resolved completely after 21 months of treatment with clozapine	CR	He had the diagnosis of BD in 1996. He was initially treated with LTM and haloperidol. He had multiple relapses of mania, resulting in an increase in haloperidol up to 8 mg/day, after switched to risperidone 6 mg/day, after switched to quetiapine. The diagnosis of tardive DTN was made in May 2002. A trial of a lower potency antipsychotic thioridazine at 50 mg/day was started in May 2002, but it worsened his movement disorder. He was then switched to tetrabenazine with doses up to 75 mg/day for 6 months with minimal improvement. Then, he underwent 12 sessions of ECT during a manic episode in 2002. Clozapine was started in September 2002 in view of his multiple relapses of mania when treated with LTM or VPA alone. His mental state stabilized after 10 months, with clozapine up to 300 mg daily. His tardive DTN gradually improved and resolved completely after 21 months of treatment with clozapine. He remained symptom-free despite subsequent reduction of the clozapine to the current dose of 200 mg daily	Tardive DTN	...

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Mclaren JL	...	600 mg/day	...	33 h after stopping methylphenidate	30 min after diphenhydramine 50 mg	No	On admission, the patient was taking aripiprazole at 30 mg/day, extended-release OROS methylphenidate 108 mg/day, LTM 900 mg/day, clonidine 0.4 mg/day. The patient had been treated with aripiprazole for 2 years and methylphenidate for 4 years; neither medication had been increased in the previous 6 months. On admission, we were concerned about the patient's high doses of multiple medications and wanted to simplify his medication regimen. The methylphenidate was discontinued; 33 h after the last dose of this medication, the patient developed an acute dystonic reaction. The patient complained of spasmodic muscular contractions of his jaw that was witnessed by nursing staff and the child psychiatrist. The patient was observed to have forceful jaw closure, contraction, and tension with difficulty opening his mouth. The patient disclosed that this adverse effect had occurred on one occasion previously when he had forgotten to take his extended-release OROS methylphenidate. IM diphenhydramine 50 mg was administered promptly, and within 30 min, the patient had complete resolution of the DTN with complete relaxation of the jaw and the ability to easily open his mouth, with no recurrence of DTN. Benztropine 2 mg/day was continued for the next 48 h to prevent another dystonic reaction	Acute DTN reaction associated with methylphenidate	...
Vandewalle W	...	...	...	...	...	...	Study that assessed the movement disorders caused by different antidepressants. They reported one individual with DTN	...	...

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Chandar P	In the ICU he was also noted to have central sleep apnea and clinical characteristics suspicious of acromegaly (tall stature, thick tongue and extremities) that was confirmed by endocrinological testing	…	…	…	…	…	Came to the ER with complaints of progressive dyspnea, hoarseness of voice, increased salivation, and swelling of his lips progressing over 2 weeks. Laryngoscopy revealed mild edema of the vocal cords but no signs of airway compromise. He was admitted to the ICU for close monitoring and started on a regimen of IV steroids, antihistamines and diphenhydramine. A detailed interview revealed the patient taking risperidone and LTM for DPS. After consultation with neurology and psychiatry, and extensive literature review, his angioedema was attributed to LTM and it was stopped. His symptoms gradually improved over few days despite continued use of risperidone and his dystonic movements improved after starting amantadine	On examination, he was noted to have facial dystonic movements, swollen tongue and lips, profound dysarthria, and stable vital signs	…
Engel A	…	900 mg/day	…	3 days	…	Recurrence of dysarthria on day 54th after LTM was restarted	Long history of schizoaffective disorder, who was treated for many years with ziprasidone and VPA and was admitted with SAD exacerbation. Due to increased QT interval, the medication was switched to lurasidone. After 2 weeks, due to increased ammonia level, VPA was switched to LTM 900 mg/day	Intermittent episodes of acute DTN, manifested as mutism, dysarthria, upper and lower extremity muscle rigidity, dysphagia, and tremor	…
Huang SY	…	900 mg/day	0.61 mEq/L	The symptoms started appear after 2 weeks switching from quetiapine to clotiapine	On returning to quetiapine and stopping clotiapine, the symptoms of DTN ceased within 10 days	…	She was admitted due to manic symptoms after discontinuation of all medications (VPA 1500 mg/day, long-term quetiapine 600 mg/day). To improve the Pisa syndrome, clotiapine was reverted to quetiapine 600 mg/day	Lateral truncal DTN	Cranial CT scan was normal

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Aggarwal R	Hypothyroidism	800 mg	...	25 years	The patient had some improvement with withdrawal of LTM and the addition of the anticholinergic agent trihexyphenidyl	...	The patient has been treated with LTM for 25 years and has developed hypothyroidism for 10 years and uses levothyroxine ever since	Lingual DTN. His neurological examination disclosed repetitive involuntary movements of the tongue which exacerbated on speaking and on eating. There were no associated involuntary movements of the masticatory or oral muscles. Mini-mental state examination and detailed lobar assessment were normal. Motor and sensory examination was within normal limits. There were no features of PKN. Other neurological and systemic physical examination was also normal	Brain MRI showed multiple lacunar infarcts in subcortical white matter in bilateral frontoparietal regions
Yildiz MÇ	...	1200 mg/day	...	...	...	...	His psychiatric treatment includes VPA 1250 mg/day LTM 1200 mg/day biperidene 4 mg/day propranolol 60 mg/day and quetiapine 600 mg/day. VPA, biperiden, propranolol, quetiapine was reduced and stopped. Clozapine 25 mg/day ordered and titrated up to 400 mg/day. When the patient used LTM 1200 mg/day and clozapine 400 mg/day, he had urinary tract infections. Because of this ciprofloxacin 1000 mg/day was ordered. 3 days later he presented with DTN and because of drug interaction ciprofloxacin was stopped and DTN healed	EPS symptoms	...

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Supplemental Table 2: Contd...

Main author	Comorbidities besides LTM indication	LTM dose (mg)	LTM levels	Time from LTM start to symptoms	Time from management to recovery	Follow-up	Important CH and CM	Neurological symptoms and clinical examination	Neuroimaging - CT scan, brain MRI, and EEG
Pikard JL	...	900 mg/day	…	Symptoms started before LTM was introduced, and recurred 41 days after LTM was rechallenged	…	…	The present case is characterized by BD compounded by an anoxic brain injury (after suicide attempt) and sensitivity to antipsychotics and LTM. Approximately 64 days after receiving IM aripiprazole and 41 days after starting LTM, the patient developed another acute dystonic reaction, and all medications were discontinued. Other medications: Sertraline, aripiprazole 400 mg IM, benztropine, vortioxetine, quetiapine, clonazepam, oxazepam, temazepam, nozinan, zopiclone, and lorazepam	After suicide attempt, he was admitted to the ICU with a Glascow coma score of 3. Once discharged, he was noted to be dystonic on transfer with several movement concerns. He described muscle contracture in his arms which kept them angled at 90° and a consistent need to walk around the unit due to restlessness. He displayed repetitive movements of the arms and hands and reported stiffness in his neck and back. At times, the movements of his hands would display a tremor	EEG showed an abnormality possibly associated with anoxic brain injury. Brain MRI was unremarkable
Chaudhari P	...	800 mg/day	1.7 mEq/L	8 days	8 days	Complete recovery	LTM was discontinued. LTM changed to VPA	She developed complaints of grinding of the teeth, throughout the day which would stop only when she would be asleep	...
Hsieh H	Alzheimer disease	600 mg/day	...	1 week after LTM dose increase. 6 years of LTM use	5 days	Complete recovery	LTM dose was increased, and the truncal DTN worsened. After LTM dose reduction, the symptoms ameliorate	Truncal DTN on the left side with a 20° deviation from the midline while standing or sitting	...
Kumar A	...	750 mg/day	0.49 mEq/L	3 weeks after dose increase. 7 years of LTM use	4 weeks	Complete recovery	LTM changed to VPA with symptoms recovery. The DTN improved with the LTM dose decrease	Spasmodic opening and closing movements of the eyes	Brain MRI was normal

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					Tics				
Kerbeshian J	Attention-deficit/ hyperactivity disorder	...	1.0 mEq/L	...	...	...	The 5 LTM nonresponders exhibited either no change in tics or a slight worsening in tics	...	...
Potter PO	Attention-deficit/ hyperactivity disorder, mood symptoms	300 mg/day	0.10 mEq/L	2 months	...	...	The spasm attacks occurred with guanfacine + LTM. When guanfacine was stopped and LTM was increased with risperidone and lisdexamfetamine was started, the patient recovered	Worsening of attention-deficit hyperactivity disorder symptoms	...
					Cerebellar syndrome				
Nagaraja D	...	1350 mg/ day	0.9 mEq/L	8 months	...	...	Precipitating factors: Fever, dehydration. Sequelae: Cerebellar, pyramidal	Ataxia, dysarthria, confusion	Cranial CT scan showed cerebellar atrophy
	...	1650 mg/ day	0.4 mEq/L	3-175 months	...	...	Precipitating factors: Fever, chlorpromazine. Sequelae: Cerebellar, pyramidal	Ataxia, confusion	Cranial CT scan was normal
	...	900 mg/day	0.7 mEq/L	3 months	...	...	Sequelae: Ataxia	Ataxia, dysarthria	Cranial CT scan showed cerebral and cerebellar atrophy
Tesio L	...	24 g/1×	3.7 mEq/L	24 h	8 months	2 years after poisoning the clinical picture was unchanged	He ingested with 24 g of lithium 5 L of beer and 20 mg of benzodiazepine in a suicide attempt	Cerebellar atrophy, coma, hyperthermia, neck stiffness, tetraplegia, incontinence, massive hematuria, and respiratory failure. There were generalized weakness incoordination, horizontal bilateral nystagmus, double vision on upward gaze, dysarthria with slurred and scanning speech, but neither sensory deficits nor abnormal plantar responses	Cranial CT scan showed enlargement of the 4th ventricle, indicating cerebellar atrophy, after 45 days of LTM poisoning

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Yoshimoto Y	...	1.800 mg/day	...	7 days	3 months	On August 16, the symptoms were almost completely stabilized, although irreversible neurological symptoms such as truncal ataxia and vertical downbeat nystagmus remained as sequelae. On August 18, he visited the ENT outpatient clinic for consultation	On June 18, twisting of muscle fiber bundles, muscular rigidity, and fever were observed. At this point, the case was diagnosed as LTM intoxication, and the medication was discontinued. From June 19, IV drip infusion (5% glucose containing Vitamin B) was initiated. On June 22, the symptoms became severe and the patient lapsed into a coma. MCL-like involuntary movement and muscular rigidity were observed. On June 23 and 24, hemodialysis was performed with a favorable response in terms of restoring consciousness, and improvement in involuntary movement and muscular rigidity. During this period, vertical nystagmus and cerebellar syndrome were noted. On July 16, the patient was able to walk	Truncal ATX on standing or walking and ATX of the arms were observed. Marked downbeat vertical nystagmus. There were no pyramidal or EPS, superficial sensory disturbance, or cranial nerve signs. Psychotic symptoms were stabilized and there was no recurrence of manic manifestations	...
Others not clearly defined - EPSs without clearly stating other of the above, or unclear relation to lithium									
Shopsin B	...	1500 mg/day	0.48 mEq/L	...	...	...	...	Motor stereotypies, confusion, perplexity, memory deficits, disorientation, irrelevant speech, incessant rambling. Urinary incontinence	...
	...	1500 mg/day	0.9 mEq/L	3 days	14 days	...	LTM was terminated on the 7th day, and chlorpromazine was started and in 14 days returned to near predrug condition	Grimacing, posturing, motor stereotypies. Yoga and womb-like positions were noted on several occasions along with body stiffening	EEG with bilateral synchronized bursts of 3-4 cps, atypical spiking, and slow-wave discharges with a suggestive left-sided origin. 3 days after LTM discharge another EEG failed to show paroxysmal activity, abnormal tracing and excess of slower frequencies persisted. Skull X-ray, brain scan, and lumbar puncture examinations showed no abnormalities

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McCaul JA	Reduce dyskinesias caused by Parkinson's disease	250 mg/day	...	...	...	...	...	LTM in modifying the manifestations of Parkinson's disease and diminishing levodopa-induced DKN. Single-blind pilot trial. The results showed that LTM could alleviate painful muscle spasms and cramps, but does not is helpful in the management of PKN disabilities	...
Gabriel E	...	...	...	...	...	...	...	...	...
Johnels B	...	...	2.0 mEq/L	9 years	2 weeks	Subsequently, she has remained well and completely free from EPSs on a maintenance dosage of LTM lower than the previous one	...	Rigidity, stiffness of the neck musculature, dysarthria, cogwheel rigidity, hypokinesia with slight tremor. Dysphagia, anxiety, insomnia	...
	2 weeks	...	1.9 mEq/L	7 years	2 weeks	...	Admitted with diarrhea and lassitude. Haloperidol 2-3 mg daily and LTM were discontinued on the day of admission. Other medications: Neuroleptics and trycyclic for periods	Rigidity of cogwheel type in the neck and arms, forward-leaning gait, short steps without related movement. Impairment of alertness, slurred speech, and unsteady gait, diarrhea	...
Kane J	...	900-2700 mg/day (mean 1300)	0.5-1.3 mEq/L (mean 0.79)	Patients used LTM from 3 months to 5 years before evaluation. Mean duration of LTM treatment=15.6 months	...	...	2 patients had cogwheel rigidity, 17 had dine and rapid tremor, of moderate severity. 1 patient had several abnormal ratings - gaits +1; arm dropping, +3; elbow rigidity, +2; wrist rigidity; tremor, +3; and AKT, + 1, this patient had normal pressure hydrocephalus 6 other patients received ratings of 1 on the following items - AKT (*n*=2), spontaneity of speech (*n*=1), wrist rigidity (*n*=1), arm dropping (*n*=1), and gait (*n*=1)	Gait, arm dropping, elbow rigidity, wrist rigidity	...

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Bone S	…	...	0.5-1.5 mEq/L	...	...	...	Of the 90 euthymic patients, 18% of those on LTM alone and 41% of those on LTM and other psychotropic medications complained of having at least 1 side effect that was moderately severe or worse. Of the 37 dysphoric patients, 38% on LTM alone and 46% on lithium and other psychotropic medications complained of having at least I side effect that was moderately severe or worse. Other medications: Of the 44 patients who were also receiving psychotropic medications, 33 were taking tricyclic antidepressants. Of the 11 remaining patients, 9 were taking antipsychotic medications and 3 were taking minor tranquilizers	Hand tremor, incoordination, muscle weakness. Dry mouth and constipation, the effect of psychotropic medication was significant for patients who were euthymic. For dysphoric patients, the effect of psychotropic medications in increasing perception of side effects was significant only for dry mouth. The effect of mood for patients on lithium alone was significant for lightheadedness, dazed feeling, constipation, abdominal pain, and drowsiness	...
Miller F	...	900 mg/day	0.98 mEq/L	...	10 days	...	...	Delirium, disorientation, episodically incoherent, disturbed sleep-wakefulness cycles, and fluctuating levels of consciousness	...
	...	1500 mg/day	1.84 mEq/L	...	10 days	...	...	Delirium, disorientation, episodically incoherent, disturbed sleep-wakefulness cycles, and fluctuating levels of consciousness	...
	...	900 mg/day	1.08 mEq/L	...	10 days	...	...	Delirium, disorientation, episodically incoherent, disturbed sleep-wakefulness cycles, and fluctuating levels of consciousness	...

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Sachdev PS		750 mg/day	1.0 mEq/L	6 days	5 days	Stoppage of benztropine after 1 week produced immediate recurrence of mild rigidity and tremor, necessitating resumption of the drug. Benztropine was successfully tapered 8 weeks later	Patient already in use of fluphenazine decanoate 25 mg/week and benztropine mesylate 4 mg/day. Sintoms started after LTM was introduced. The extrapyramidal side effects responded to benztropine, 2 mg IV and not to normal saline in a blind trial administration. LTM was stopped and treatment with oral benztropine 6 mg/day was started. Other medications: Fluphenazine decanoate, 25 mg/week, and benztropine mesylate, 4 mg/day	Mild rigidity, cogwheel rigidity, akinesia, and coarse tremor of her upper limbs. A score of 3.8 on the Simpson and Angus Scale, and almost complete immobility	EEG was normal
Miller F	…	1047 mg (SD=567) (mean)	1.23 mEq/L (SD=0.27) (mean)	…	…	…	…	Delirium, disorientation, incoherence, disturbed sleep-wakefulness cycle, fluctuating levels of consciousness. EPSs were present in all cases with 5 (83%) manifesting tremor, 5 (83%) rigidity, 3 (50%) AKT, and 2 (33%) ataxia	…
Morgenstern H	…	…	…	…	…	…	…	A cross-sectional study was conducted to identify predictors of TD in a group of 180 psychiatric outpatients, 12 were in use of LTM. They observed no other interaction effects between pairs of predictor variables, nor did they find significant independent effects of LTM use	…

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Addonisio G		…	0.65-1.27 mEq/L	Evaluation at day 3, 6, 9, and 12	…	…	…	Gait, shoulder shaking, elbow rigidity, and tremor increased significantly. Wrist rigidity, glabellar tap, cogwheel rigidity, masked facies, and subjective perception of stiffness increased in nonsignificant degree	
Nasrallah HA	...	...	...	...	...	...	...	...	...
Waddington JL	...	...	...	...	...	...	...	The prognostic factors found in the study to develop an abnormal movement were poorer cognitive function, had fewer major depressive episodes, and had received briefer exposure to LTM	...
Axelsson R	...	...	...	...	...	...	...	...	...
Moskowitz AS	Stroke	1200 mg/day	...	Unclear (several instances of LTM introduction and cessation, with a background sequelae from stroke	...	...	After 6 years of treatment with LTM, he had a stroke and after that the symptoms started	Dysarthria, left upper and lower extremity hemiparesis, pseudobulbular palsy (after stroke)	Infarction of the posterior limb of the right interior capsule, evidenced by CT
Kohler J	…	…	…	…	…	…	Neurological complications associated with Q-fever - A synergetic neurotoxic effect of *Cociella burneti* infection and LTM is discussed as a possible cause of the severe cerebellar pattern of symptoms	…	…

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Holroyd S	...	...	...	...	...	...	...	...	...
Arya DK	Pneumonia	500 mg/day	0.9 mEq/L	1 year	4 days after discontinuation	...	Started on LTM in 1977, which was continued until 1987 when she developed fine tremors. Considered to be LTM-induced. LTM was discontinued. However, after 6 months, she had another manic episode and LTM 500 mg/day was restarted. Over the past 7 years, she remained on LTM 500 mg/day (serum lithium levels 0.5-0.6 mmol/l), trifluoperazine 4 mg/day, procyclidine 5 mg/day, and temazepam 20 mg/day. Except in 1990 when for 6 months, amoxapine was added to this treatment regimen for the treatment of a depressive episode	Tremors, rigidity in jaw and all limbs, slurring of speech, and flexed posture. On another trial - marked confusion, ataxia, postural instability, flexed posture, incoordination and EPSs (tremors, jaw stiffness and slurred speech)	...
Ghardirian AM	…	…	…	…	…	…	…	The prevalence of tremor was 20.8%; hypokinetic PKN, 7.7%; AKT, 4.6%; DTN, 3.8%; and TD, 9.2%. Tremor was associated with LTM and neuroleptic intake; hypokinesia was associated with neuroleptic treatment and age; and TD was associated with neuroleptic, LTM, and tricyclic intake and age. Seven of 51 patients taking lithium but without a history of neuroleptic treatment during the previous 6 months presented symptoms of TD	…

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Tuglu C	…	900 mg/day	3 mm/L	7 years	5 days (except perioral dyskinesia)	Examination 3 months later revealed that her mood was euthymic with appropriate affect. There was no evidence of hallucinations or delusions, but perioral dyskinesia	At admission, she was receiving 900 mg/day LTM and 5 mg/day olanzapine. All of the drugs she used were discontinued. Deterioration in her mental status last year after addition of a typical antipsychotic to her therapy to lessen her abrupt insomnia. She presented signs and symptoms of lethargy, confusion, and hyperprexia 10 days after initiation of chlorpromazine 200 mg/day. The discontinuation of all drugs resulted in complete remission within 72 h. Later, LTM therapy was re-initiated without recurrence of any mentioned clinical symptoms. After she did not receive any other concomitant drugs till 3 weeks before admission, when a physician prescribed olanzapine 5 mg/day due to her increased suspiciousness toward her neighbors and possible appearance of auditory hallucinations. At the current admission, carbamazepine was started to prevent the recurrence of bipolar disorder. The patient showed a rapid and dramatic recovery. At discharge, she was completely orientated with no further thought disturbances	Alteration in mental status, psychomotor slowness, difficulty in walking, and tremor in limbs. In her mental status examination, the patient's response to simple verbal commands was well, but disorientation to place and time was prominent. She also had loosened associations and rhyming. The neurological examination showed clear upward gaze palsy without a supranuclear component, severe bradykinesia, severe rigidity of the forelimbs with positive cogwheel, and rest and postural tremor with mild amplitude and frequency of 4-5 Hz in all limbs, predominantly on the right side	Cranial computed tomography did not reveal any pathology, except age-related cortical atrophy. The cranial MRI of our patient revealed multiple microlacunar infarcts which were not congruent with the level of the clinical picture
Brandt-Christensen M	…	…	…	…	…	…	…	…	…
Galpern WR	...	...	...	...	...	...	...	Study that assessed the use of LTM in corticobasal degeneration and supranuclear gaze palsy. The results were that LTM can aggravate these two disorders. The adverse events reported were tremor (59%), gait disturbance (35%), and hypokinesia (24%)	...

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Lyell VR	...	...	...	...	...	...	...	Study that assessed the individuals diagnosed with drug-induced PKN in a clinic and their taking medications. 328 individuals were assessed, 3 were taking LTM. They concluded that only a minority of new referrals from primary care to specialist are being prescribed drugs implicated in drug-induced PKN	...
Guillan M									
Vandewalle W	...	...	...	...	...	...	...	...	...
Marras C	...	...	...	...	...	...	...	Assessment of that there is an increased incidence of anti-Parkinson drug prescribing following LTM treatment. The results showed that LTM monotherapy was associated with an increased incidence of dopaminergic drug use (adjusted HR: 1.87, 95% CI: 1.06-3.30) and an increased incidence of anti-Parkinson drug	...

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Rey et al.	…	…	…	…	…	…	…	…	…
Thi Truong BE	…	…	…	…	…	…	…	Population-based cohort study, in which 7 individuals using LTM had RLS symptoms. LTM increased the incidence of RLS to near 75.0 per 10,000 person-year	...

AIMS: Abnormal Involuntary Movement Scale, ECT: Eletroconvulsive therapy, PKN: Parkinsonism, DTRs: Deep tendon reflexes, NCV: Nerve conduction velocity, CT: Computerized tomography, MNCV: Motor nerve conduction velocities, CMAP: Compound muscle action potentials, SNAP: Sensory nerve action potential, EMG: Electromyography, MUPs: Motor unit potentials, PSW: Positive sharp waves, PRES: Posterior reversible encephalopathy syndrome, IV: Intravenous, DKN: Dyskinesia, BARS: Barnes Akathisia Rating Scale, SAS: Simpson-Angus Scale, ALS: Amyotrophic lateral sclerosis, UPDRS: Unified Parkinson's Disease Rating Scale, RLS: Restless legs syndrome, CJLS: Creutzfeldt-Jakob like syndrome, PSWC: Periodic sharp wave complexes, NSCE: Nonconvulsive status epilepticus, DTN: Dystonia, MCL: Myoclonus, LTM: Lithium, EEG: Electroencephalographic, MD: Movement disorder, WBC: White blood cells, BD: Bipolar disorder, MRI: Magnetic resonance imaging, SEP: Somatosensory evoked potentials, ICU: Intensive care unit, ATX: Ataxia, AKT: Akathisia, EPS: Extrapyramidal symptom, SPECT: Single-photon emission computed tomography, DaT: Dopamine transporter, PD: Parkinson's disease, AKT: Akathisia, CI: Confidence interval, COPD: Chronic obstructive pulmonary disease, ACE: Angiotensin-converting enzyme, MMSE: Mini-Mental State Examination, PET: Positron emission tomography, CSF: Cerebrospinal fluid, ENT: Ear, nose, and throat, HR: Hazard ratio, PSP: Progressive supranucelar palsy, CH: Clinical history, CM: Clinical management VPA: Valproic acid, IM: Intramuscular, DTRs: Deep tendon reflex, DPS: Depression, ICU: Intensive care unit, MAP: Mean arterial pressure, SNCV: Sural nerve conduction velocity, FLAIR: Fluid-attenuated inversion recovery, ER: Emergency room, LLR: long-latency reflexes, NAA: N-acetylaspartate, TD: Tardive Dyskinesia, TDP: Transactive DNA-binding protein, MSA: Multiple system atrophy, PRN: Pro re nata, FP-CIT: iodine I 123–radiolabeled 2β-carbomethoxy-3β-(4-iodophenyl)-N-(3-fluoropropyl) nortropane, MOCA: Montreal cognitive assessment, WAIS: Wechsler adult intelligence scale, CR: Complete recovery, MHPG: 3-Methoxy-4-hydroxyphenylglycol, NCSE: Nonconvulsive status epilepticus, FIRDA: Frontal intermittent rhythmic delta activity, OROS: Osmotic release oral system, SAD: Schizoaffective disorder, RLS: Restless leg syndrome, MRS: Mania rating scale