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PROCHLORERAZOINE INDUCED PARKINSONISM: A CASE REPORT

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INTRODUCTION
The first study of the extrapyramidal side effects (EPS) of the antipsychotic chlorpromazine found that about 40% of these patients exhibited parkinsonism,[7] and several subsequent epidemiological studies found that DIP is the second most common etiology of parkinsonism. Drug-induced movement disorders include drug-induced parkinsonism (DIP), tardive dyskinesia (TD), tardive dystonia, akathisia, myoclonus, and tremor. Among these, DIP is the most common movement disorder induced by drugs that affect dopamine receptors.[1,3] Since the clinical manifestations of DIP are very similar to those of Parkinson's disease (PD), patients with DIP are frequently misdiagnosed as having PD.[1,4] These patients are often prescribed antiparkinsonian drugs unnecessarily for long periods of time, despite recovery being possible simply by discontinuing the offending drugs. Dopamine transporter (DAT) imaging may be used in the differential diagnosis of various etiologies of parkinsonism, including DIP.[5,6] The aim of this review was to provide clinicians with updated information about the clinical characteristics and DAT imaging findings of patients with DIP, and about the correct treatment for DIP.

CASE REORT

A 69 years old male patient was admitted with Aalleged h/o sustained hit over occipital region and right side ain hip following skip and fall in bathroom.She had medical history of diabetes mellitus,systemic hypertension and dyslipidemia and medication history wereT.Atorva (Atorvastatin)10mg,Tab.Okamet(Metformin)500mg, Tab. Amlopres (Amlodipine)5mg, Tab. Nausetil (Prochlorperazine)5mg. Hematological investigations showed elevated ESR(105), RBS(286), CRP(22.5) and decresed parameters are Hb(7.2), sodium(130). Renal and lipid profile were normal. USG Abdomen shows fatty liver and right adnexal cyst. Magnetic resonance imaging shows diffused cerebral atrophy,bilateral lateral ventricles show mild disproportionate dilatation with mild periventricular T2WI FLAIR hyperintensitis, mild dilatation of bilateral sylvian cisterns noted with narrowing in the high arietal convexit likely due to normal pressure hydrocephalus .CT brain shows age related brain atrophy with small vessel ischemic changes. Based on his clinical features and review of the laboratory evaluations, he was diagnosed to have prochlorperazine induced parkinsonism. The drug induced parkinsonism is treated by cessation of the prochlorperazine. On the hospital sta the ast medications were continued. Tab Clopilet (Cloidogrel) for preventing clot formation ,Inj.Viatran (Cefoerazone+sulbactam) for treating bacterial infection. T.Selgin (Selegiline), T.Pramiex (Pramipexole) for treating parkinsonism. . Over the next few days, the patient became afebrile. The patient was discharged after 12 days with ongoing medicines.

PATHOPHYSIOLOGY OF ROCHLORERAZOINE

Dopamine receptors in the brain consist of those of the D_1 family, comprising D_1 and D_5 receptors, and the D_2 family, comprising D_2, D_3, and D_4 receptors.[55] The central dopaminergic system consists of the mesolimbic, mesocortical, tuberoinfundibular, and nigrostriatal pathways. All antipsychotic drugs have potent D_2 receptor blocking capacity and the therapeutic effects of these drugs on psychosis are related to their action on the limbic system, where they reduce dopamine transmission. The blockage of D_2 receptors by antipsychotic drugs in the striatum leads to disinhibition of GABA- and encephalin-containing striatal neurons at the origin of the indirect pathway without alteration of the direct pathway, followed by disinhibition of the subthalamic nucleus. This leads to increased GABAergic inhibition of the thalamocortical projection by facilitation of the inhibitory projection from the globus pallidus/substantia nigra pars reticulata (Fig. 1A). This pathway resembles the model of disturbance of the basal ganglia-motor loop in PD. More than 80% of D_2 receptors were found to be occupied in patients with EPS who were taking neuroleptics,[56] in agreement with results showing that clinical symptoms of PD began when over 80% of nigral neurons had degenerated.

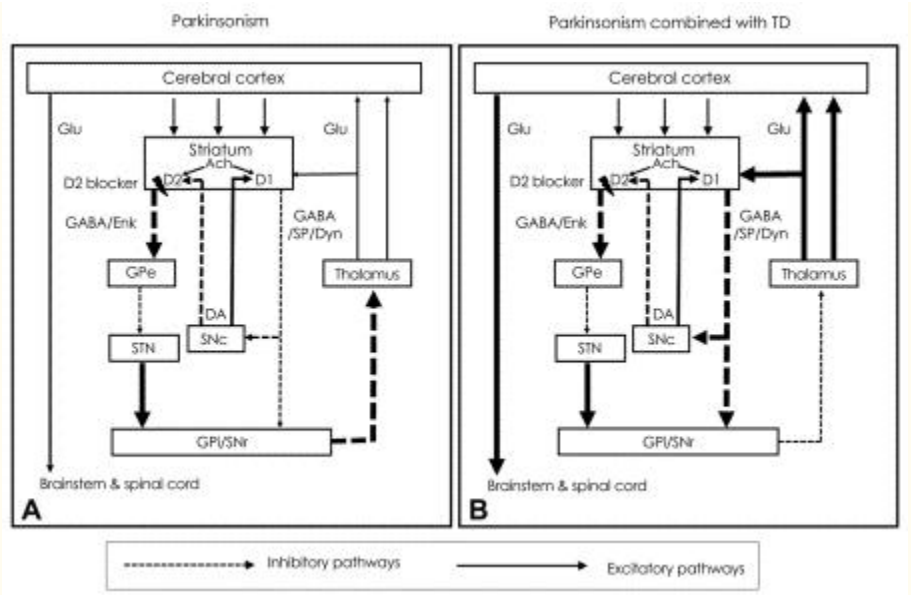

Fig. 1: Open in a separate window

Changes in basal ganglia-thalamocortical motor loop due to blockade of D_2 receptors by DRBAs. The blockage of D_2 receptors by DRBAs in the striatum leads to disinhibition of GABA- and encephalin-containing striatal neurons at the origin of the indirect pathway, followed by a disinhibition of the subthalamic nucleus. This leads to increased GABAergic inhibition of the thalamocortical projection by facilitation of the inhibitory projection from the GPi/SNr (A). Chronic D_2 receptor blockade also induces changes in the direct pathways of the basal ganglia-motor loop to cause orolingual dyskinesia (B). DA: dopamine, DRBAs: dopamine receptor blocking agents, GABA: gamma-aminobutyrik acid, GPe: globus pallidus pars externa, GPi: globus pallidus pars internal, SNc: substantia nigra pars compacta, SNr: substantia nigra pars reticulata, STN: subthalamic nucleus, TD: tardive dyskinesia.

TD, defined as hyperkinetic movement in the orolingual or oromandibular area, is caused by long-term use of dopaminergic blocking agents, and frequently accompanies DIP. The co-occurrence of TD with parkinsonism may be due to dopaminergic receptor supersensitivity resulting from long-term D_2 receptor blocking. Chronic administration of these drugs increases dopamine D_2 receptor density in the striatum. Moreover, withdrawal from neuroleptics was found to aggravate dyskinetic symptoms, whereas increased doses of neuroleptics transiently suppressed dyskinesia. D1 receptors may also be involved in the development of orolingual dyskinesia when D_2 receptors are chronically blocked. Chronic administration of D_2 receptor blockers also induces changes in the direct pathway of the basal ganglia-motor loop to activate the striatonigral pathway and increase the inhibition of the striatopallidal pathway (Fig. 1B).[25,57] This imbalance between direct (D_1) and indirect (D_2) motor pathways and the resulting alterations in the globus pallidus/substantia nigra pars reticulata complex may lead to hyperkinetic orolingual movements, thus explaining the coexistent and sequential development of parkinsonism and dyskinesia.

CONCLUTION

DIP is important because it is a common etiology of parkinsonism and is frequently either unrecognized or misdiagnosed as PD. In addition, parkinsonism in DIP patients is sufficiently severe to affect daily activities and may persist for long periods of time even after cessation of the offending drug. DAT imaging may be useful for accurately diagnosing patients with DIP and may help to identify the clinical characteristics and exact prognosis of this disorder.

About 50% of patients with DIP and other movement disorders are treated with DRBAs for conditions unrelated to psychosis, including depression, GI disturbance, anxiety, and insomnia.[1] Physicians should avoid prescribing DRBAs and CCBs for inappropriate reasons such as anxiety, insomnia, dizziness or dyspepsia in elderly patients and should monitor these patients' neurological signs, especially parkinsonism and other movement disorders, when prescribing these drugs.

REFERENCE

1. Miller LG, Jankovic J. Neurologic approach to drug-induced movement disorders: a study of 125 patients. *South Med J.*, 1990; 83: 525–532. [PubMed] [Google Scholar]
2. Montastruc JL, Llau ME, Rascol O, Senard JM. Drug-induced parkinsonism: a review. *Fundam Clin Pharmacol.*, 1994; 8: 293–306. [PubMed] [Google Scholar]
3. Sethi KD. Movement disorders induced by dopamine blocking agents. *Semin Neurol.*, 2001; 21: 59–68. [PubMed] [Google Scholar]
4. Esper CD, Factor SA. Failure of recognition of drug-induced parkinsonism in the elderly. *Mov*

Disord., 2008; 23: 401–404. [PubMed] [Google Scholar]
5. Hall RA, Jackson RB, Swain JM. Neurotoxic reactions resulting from chlorpromazine administration. *J Am Med Assoc.*, 1956; 161: 214–218. [PubMed] [Google Scholar]
6. Benito-León J, Bermejo-Pareja F, Rodríguez J, Molina JA, Gabriel R, Morales JM Neurological Disorders in Central Spain (NEDICES) Study Group. Prevalence of PD and other types of parkinsonism in three elderly populations of central Spain. *Mov Disord.*, 2003; 18: 267–274. [PubMed] [Google Scholar]
7. Wenning GK, Kiechl S, Seppi K, Müller J, Högl B, Saletu M, et al. Prevalence of movement disorders in men and women aged 50-89 years (Bruneck Study cohort): a population-based study. *Lancet Neurol.*, 2005; 4: 815–820. [PubMed] [Google Scholar]
8. Barbosa MT, Caramelli P, Maia DP, Cunningham MC, Guerra HL, Lima-Costa MF, et al. Parkinsonism and Parkinson's disease in the elderly: a community-based survey in Brazil (the Bambuí study) *MovDisord.*, 2006;21:800–808. [PubMed] [Google Scholar].
9. Wenning GK, Kiechl S, Seppi K, Müller J, Högl B, Saletu M, et al. Prevalence of movement disorders in men and women aged 50-89 years (Bruneck Study cohort): a population-based study. *Lancet Neurol.*, 2005; 4: 815–820. [PubMed] [Google Scholar]
10. Barbosa MT, Caramelli P, Maia DP, Cunningham MC, Guerra HL, Lima-Costa MF, et al. Parkinsonism and Parkinson's disease in the elderly: a community-based survey in Brazil (the Bambuí study) *Mov Disord.*, 2006; 21: 800–808. [PubMed] [Google Scholar]
11. Avorn J, Bohn RL, Mogun H, Gurwitz JH, Monane M, Everitt D, et al. Neuroleptic drug exposure and treatment of parkinsonism in the elderly: a case-control study. *Am J Med.*, 1995; 99: 48–54. [PubMed] [Google Scholar]
12. Susatia F, Fernandez HH. Drug-induced parkinsonism. *Curr Treat Options Neurol.*, 2009; 11: 162–169. [PubMed] [Google Scholar]
13. Thanvi B, Treadwell S. Drug induced parkinsonism: a common cause of parkinsonism in older people. *Postgrad Med J.*, 2009; 85: 322–326. [PubMed] [Google Scholar]
14. Volkow ND, Ding YS, Fowler JS, Wang GJ, Logan J, Gatley SJ, et al. Dopamine transporters decrease with age. *J Nucl Med.*, 1996; 37: 554–559. [PubMed] [Google Scholar]
15. Stephen PJ, Williamson J. Drug-induced parkinsonism in the elderly. *Lancet.*, 1984; 2: 1082–1083. [PubMed] [Google Scholar]
16. Hardie RJ, Lees AJ. Neuroleptic-induced Parkinson's syndrome: clinical features and results of treatment with levodopa. *J Neurol Neurosurg Psychiatry*, 1988; 51: 850–854. [PMC free article] [PubMed] [Google Scholar]
17. Miller LG, Jankovic J. Metoclopramide-induced movement disorders. Clinical findings with a review of the literature. *Arch Intern Med.*, 1989; 149: 2486–2492. [PubMed] [Google Scholar]
18. Bedard P, Langelier P, Villeneuve A. Oestrogens and extrapyramidal system. *Lancet.*, 1977; 2: 1367–1368. [PubMed] [Google Scholar]
19. Metzer WS, Newton JE, Steele RW, Claybrook M, Paige SR, McMillan DE, et al. HLA antigens in drug-inducedparkinsonism. *Mov disord.*, 1989; 4: 121–128. [PubMed] [Google Scholar]
20. Liou YJ, Wang YC, Chen JY, Bai YM, Lin CC, Liao DL, et al. Association analysis of polymorphisms in the N-methyl-D-aspartate (NMDA) receptor subunit 2B (GRIN2B) gene and tardive dyskinesia in schizophrenia. *Psychiatry Res.*, 2007; 153: 271–275. [PubMed] [Google Scholar]
21. Inada T, Koga M, Ishiguro H, Horiuchi Y, Syu A, Yoshio T, et al. Pathway-based association analysis of genome-wide screening data suggest that genes associated with the gamma-aminobutyric acid receptor signaling pathway are involved in neuroleptic-induced, treatment-resistant tardive dyskinesia. *Pharmacogenet Genomics.*, 2008; 18: 317–323. [PubMed] [Google Scholar]
22. Shanon J, Kaplan SM, Pierce CM, Ross WD. An interesting reaction to a tranquilizer: tonic seizures with perphenazine (trilafon) *Am J Psychiatry*, 1957; 114: 556. [PubMed] [Google Scholar]
23. Christian CD, Paulson G. Severe motility disturbance after small doses of prochlorperazine. *N Engl J Med.*, 1958; 259: 828–830. [PubMed] [Google Scholar]
24. Janno S, Holi M, Tuisku K, Wahlbeck K. Prevalence of neuroleptic-induced movement disorders in chronic schizophrenia inpatients. *Am J Psychiatry*, 2004; 161: 160–163. [PubMed] [Google Scholar]
25. Ossowska K. Neuronal basis of neuroleptic-induced extrapyramidal side effects. *Pol J Pharmacol*, 2002; 54: 299–312. [PubMed] [Google Scholar]
26. Tarsy D, Baldessarini RJ, Tarazi FI. Effects of newer antipsychotics on extrapyramidal function. *CNS Drugs*, 2002; 16: 23–45. [PubMed] [Google Scholar]
27. Kuroki T, Nagao N, Nakahara T. Neuropharmacology of second-generation antipsychotic drugs: a validity of the serotonin-dopamine hypothesis. *Prog Brain Res.*, 2008; 172: 199–212. [PubMed] [Google Scholar]
28. Kapur S, Seeman P. Does fast dissociation from the dopamine d(2) receptor explain the action of atypical antipsychotics?: a new hypothesis. *Am J Psychiatry*, 2001; 158: 360–369. [PubMed] [Google Scholar]
29. Stahl SM. "Hit-and-Run" actions at dopamine receptors, part 2: illustrating fast dissociation from

dopamine receptors that typifies atypical antipsychotics. *J Clin Psychiatry*, 2001; 62: 747–748. [PubMed] [Google Scholar]
30. The Parkinson Study Group. Low-dose clozapine for the treatment of drug-induced psychosis in Parkinson's disease. *N Engl J Med.*, 1999; 340: 757–763. [PubMed] [Google Scholar]
31. Schotte A, Janssen PF, Gommeren W, Luyten WH, Van Gompel P, Lesage AS, et al. Risperidone compared with new and reference antipsychotic drugs: in vitro and in vivo receptor binding. *Psychopharmacology (Berl).*, 1996; 124: 57–73. [PubMed] [Google Scholar]
32. Gómez JC, Sacristán JA, Hernández J, Breier A, Ruiz Carrasco P, Antón Saiz C, et al. The safety of olanzapine compared with other antipsychotic drugs: results of an observational prospective study in patients with schizophrenia (EFESO Study). Pharmacoepidemiologic Study of Olanzapine in Schizophrenia. *J Clin Psychiatry*, 2000; 61: 335–343. [PubMed] [Google Scholar]
33. Rabey JM, Prokhorov T, Miniovitz A, Dobronevsky E, Klein C. Effect of quetiapine in psychotic Parkinson's disease patients: a double-blind labeled study of 3 months' duration. *Mov Disord.*, 2007; 22: 313–318. [PubMed] [Google Scholar]
34. Juncos JL, Roberts VJ, Evatt ML, Jewart RD, Wood CD, Potter LS, et al. Quetiapine improves psychotic symptoms and cognition in Parkinson's disease. *Mov Disord.*, 2004; 19: 29–35. [PubMed] [Google Scholar]
35. Wickremaratchi M, Morris HR, Ali IM. Aripiprazole associated with severe exacerbation of Parkinson's disease. *Mov Disord.*, 2006; 21: 1538–1539. [PubMed] [Google Scholar]
36. Sharma A, Sorrell JH. Aripiprazole-induced parkinsonism. *Int Clin Psychopharmacol.*, 2006; 21: 127–129. [PubMed] [Google Scholar]
37. Tonini M, Cipollina L, Poluzzi E, Crema F, Corazza GR, De Ponti F. Review article: clinical implications of enteric and central D2 receptor blockade by antidopaminergic gastrointestinal prokinetics. *Aliment Pharmacol Ther.*, 2004; 19: 379–390. [PubMed] [Google Scholar]
38. Kenney C, Hunter C, Davidson A, Jankovic J. Metoclopramide, an increasingly recognized cause of tardive dyskinesia. *J Clin Pharmacol.*, 2008; 48: 379–384. [PubMed] [Google Scholar]
39. Parkinsonism: an under-recognised complication of metoclopramide use. *Ceylon Med J.*, 1996; 41: 125. [PubMed] [Google Scholar]
40. Sethi KD, Patel B, Meador KJ. Metoclopramide-induced parkinsonism. *South Med J.*, 1989; 82: 1581–1582. [PubMed] [Google Scholar]
41. Shin HW, Kim MJ, Kim JS, Lee MC, Chung SJ. Levosulpiride-induced movement disorders. *Mov Disord.*, 2009; 24: 2249–2253. [PubMed] [Google Scholar]
42. Madej TH. Domperidone--an acute dystonic reaction. *Anaesthesia.*, 1985; 40: 202. [PubMed] [Google Scholar]
43. Sørensen PS, Hansen K, Olesen J. A placebo-controlled, double-blind, cross-over trial of flunarizine in common migraine. *Cephalalgia.*, 1986; 6 :7–14. [PubMed] [Google Scholar]
44. García-Ruiz PJ, Javier Jiménez-Jiménez F, García de Yébenes J. Calcium channel blocker-induced parkinsonism: clinical features and comparisons with Parkinson's disease. *Parkinsonism Relat Disord.*, 1998; 4: 211–214. [PubMed] [Google Scholar]
45. Martí-Massó JF, Poza JJ. Cinnarizine-induced parkinsonism: ten years later. *Mov Disord.*, 1998; 13: 453–456. [PubMed] [Google Scholar]
46. Negrotti A, Calzetti S. A long-term follow-up study of cinnarizine- and flunarizine-induced parkinsonism. *Mov Disord.*, 1997; 12: 107–110. [PubMed] [Google Scholar]
47. Takada M, Kono T, Kitai ST. Flunarizine induces a transient loss of tyrosine hydroxylase immunoreactivity in nigrostriatal neurons. *Brain Res.*, 1992; 590: 311–315. [PubMed] [Google Scholar]
48. Onofrj M, Thomas A, Paci C. Reversible parkinsonism induced by prolonged treatment with valproate. *J Neurol.*, 1998; 245: 794–796. [PubMed] [Google Scholar]
49. Easterford K, Clough P, Kellett M, Fallon K, Duncan S. Reversible parkinsonism with normal beta-CIT-SPECT in patients exposed to sodium valproate. *Neurology*, 2004; 62: 1435–1437. [PubMed] [Google Scholar]
50. Jamora D, Lim SH, Pan A, Tan L, Tan EK. Valproate-induced Parkinsonism in epilepsy patients. *Mov Disord.*, 2007; 22: 130–133. [PubMed] [Google Scholar]
51. Reches A, Tietler J, Lavy S. Parkinsonism due to lithium carbonate poisoning. *Arch Neurol.*, 1981; 38: 471. [PubMed] [Google Scholar]
52. Holroyd S, Smith D. Disabling parkinsonism due to lithium: a case report. *J Geriatr Psychiatry Neurol.*, 1995; 8: 118–119. [PubMed] [Google Scholar]
53. Tinazzi M, Antonini A, Bovi T, Pasquin I, Steinmayr M, Moretto G, et al. Clinical and [123I]FP-CIT SPET imaging follow-up in patients with drug-induced parkinsonism. *J Neurol.*, 2009; 256: 910–915. [PubMed] [Google Scholar]
54. Hassin-Baer S, Sirota P, Korczyn AD, Treves TA, Epstein B, Shabtai H, et al. Clinical characteristics of neuroleptic-induced parkinsonism. *J Neural Transm.*, 2001; 108: 1299–1308. [PubMed] [Google Scholar]
55. Jaber M, Robinson SW, Missale C, Caron MG. Dopamine receptors and brain function. *Neuropharmacology*, 1996; 35: 1503–1519. [PubMed] [Google Scholar]

56. Farde L, Nordström AL, Wiesel FA, Pauli S, Halldin C, Sedvall G. Positron emission tomographic analysis of central D1 and D2 dopamine receptor occupancy in patients treated with classical neuroleptics and clozapine. Relation to extrapyramidal side effects. *Arch Gen Psychiatry*, 1992; 49: 538–544. [PubMed] [Google Scholar]
57. Gunne LM, Andrén PE. An animal model for coexisting tardive dyskinesia and tardive parkinsonism: a glutamate hypothesis for tardive dyskinesia. *Clin Neuropharmacol.*, 1993; 16: 90–95. [PubMed] [Google Scholar]
58. Gershanik OS. Drug-induced parkinsonism in the aged. Recognition and prevention. *Drugs Aging*, 1994; 5: 127–132. [PubMed] [Google Scholar]
59. 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: 145–149. [PubMed] [Google Scholar]
60. Davis MR, Votaw JR, Bremner JD, Byas-Smith MG, Faber TL, Voll RJ, et al. Initial human PET imaging studies with the dopamine transporter ligand 18F-FECNT. *J Nucl Med.*, 2003; 44: 855–861. [PubMed] [Google Scholar]
61. Varrone A, Halldin C. Molecular imaging of the dopamine transporter. *J Nucl Med.*, 2010; 51: 1331–1334. [PubMed] [Google Scholar]
62. Diaz-Corrales FJ, Sanz-Viedma S, Garcia-Solis D, Escobar-Delgado T, Mir P. Clinical features and 123I-FP-CIT SPECT imaging in drug-induced parkinsonism and Parkinson's disease. *Eur J Nucl Med Mol Imaging*, 2010; 37: 556–564. [PubMed] [Google Scholar]
63. Lorberboym M, Treves TA, Melamed E, Lampl Y, Hellmann M, Djaldetti R. [123I]-FP/CIT SPECT imaging for distinguishing drug-induced parkinsonism from Parkinson's disease. *Mov Disord.*, 2006; 21: 510–514. [PubMed] [Google Scholar]
64. Tinazzi M, Ottaviani S, Isaias IU, Pasquin I, Steinmayr M, Vampini C, et al. [123I]FP-CIT SPET imaging in drug-induced Parkinsonism. *Mov Disord.*, 2008; 23: 1825–1829. [PubMed] [Google Scholar]
65. Poewe W, Scherfler C. Role of dopamine transporter imaging in investigation of parkinsonian syndromes in routine clinical practice. *Mov Disord.*, 2003; 18(Suppl 7): S16–S21. [PubMed] [Google Scholar]
66. Lavalaye J, Linszen DH, Booij J, Dingemans PM, Reneman L, Habraken JB, et al. Dopamine transporter density in young patients with schizophrenia assessed with [123]FP-CIT SPECT. *Schizophr Res.*, 2001; 47: 59–67. [PubMed] [Google Scholar]
67. Tolosa E, Coelho M, Gallardo M. DAT imaging in drug-induced and psychogenic parkinsonism. *Mov Disord.*, 2003; 18(Suppl 7): S28–S33. [PubMed] [Google Scholar]
68. Fann WE, Lake CR. Amantadine versus trihexyphenidyl in the treatment of neuroleptic-induced parkinsonism. *Am J Psychiatry*, 1976; 133: 940–943. [PubMed] [Google Scholar]
69. Jankovic J. Tardive syndromes and other drug-induced movement disorders. *Clin Neuropharmacol.*, 1995; 18: 197–214. [PubMed] [Google Scholar]
70. Rajput AH, Rozdilsky B, Hornykiewicz O, Shannak K, Lee T, Seeman P. Reversible drug-induced parkinsonism. Clinicopathologic study of two cases. *Arch Neurol.*, 1982; 39: 644–646. [PubMed] [Google Scholar]
71. Bishnoi M, Chopra K, Kulkarni SK. Protective effect of adenosine reuptake inhibitors in haloperidol-induced orofacial dyskinesia and associated behavioural, biochemical and neurochemical panges. *Pharmacology*, 2007; 79: 171–183. [PubMed] [Google Scholar]
72. Tsai G, Goff DC, Chang RW, Flood J, Baer L, Coyle JT. Markers of glutamatergic neurotransmission and oxidative stress associated with tardive dyskinesia. *Am J Psychiatry*, 1998; 155: 1207–1213. [PubMed] [Google Scholar]