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| **Study** | **HD**  **Agea** | **Disease Duration (yrs) or HD stage** | **Drug** | **Study Design** | **Outcome Measure(s)** | **Summary of Primary Findings** |
| Agid et al., 1983 [1] | 38 (2) | 6 (1) | FK 33-824 | crossover, placebo controlled | study specific (involuntary movements per minute) | involuntary movements did not improve after administration of drug |
| Albanese et al., 1995 [2] | range (21-61) | 4.4 | Apomorphine | randomized, placebo controlled | Study specific (motor performance, eye movements, chorea, gait, & posture) | subcutaneous injection improved motor performance |
| Aminoff & Marshall, 1974 [3] | range (35-64) | range (5-20) | Lithium Carbonate (Priadel) | placebo controlled | WAIS FSIQ, Study specific (mood, behavior, mobility, dressing, bathing, feeding) | no improvements over placebo |
| Asher & Aminoff, 1981 [4] | range (26-65) | --- | Tetrabenazine | crossover placebo | study specific (movement severity ratings) | Of 26 patients, 15 improved, 10 were unchanged, and 1 worsened |
| Bamford et al., 1995 [5] | 40 (10.3)  39.2 (10.4) | ---- | Baclofen | placebo controlled | TFC, Stroop, Trailmaking Test, PPVT, WAIS Digit Symbol, WAIS Block Design, Verbal Fluency | some improvements in chorea; less improvement for dystonic/athetoctic states |
| Bassi et al., 1986 [6] | 44.1 (14.2) | 5 | Transdihydrolisuride (TDHL) | placebo controlled | Raven’s Progressive Matrices Test, Kohs Cubes Syndrom Kurz test, Study specific—manual dexterity, gait, speech, chorea severity | improvements in disease severity (as determined by a composite score) in 7 of 10 patients |
| Beglinger et al., 2009 [7] | F&S Stage 1,2 | ---- | Atomoxetine | randomized, placebo controlled | Trailmaking Test, WAIS Digit Symbol, WAIS Letter Number, Stroop, Verbal Fluency, CAARS, UHDRS-m, SCL-90-R | no improvements over placebo |
| Beister et al., 2004 [8] | 39.7 | 2.5 | Memantine | open label | UHDRSb, AIMS, CGI, HD-ADL | no significant increases in chorea (i.e., neuroprotective effect) |
| Bender et al., 2005 [9] | 46 (7.3) | 4 (2.1) | Creatine | ---- | UHDRS-m, TFC, MMSE, H-MRS as metabolite level marker | no effect on clinical ratings |
| Blackwell et al., 2008 [10] | 57 (4) | ----- | Modafinal | randomized, placebo-controlled crossover | CANTAB, physiology | single dose improved altertness; no significant improvements in cognitive function or mood |
| Bonelli et al., 2004 [11] | 40 (10.3) | 4.5 (2.2) | Minocycline | open label | UHDRS, MMSE | improvement in motor and cognition at 6 months; stabilization in motor and cognition at 3 years |
| Bonelli et al., 2003 [12] | 41.4 (9.1);  33.2 (3.4) | 4.8 (2.6)  5 (2.9) | Minocycline | age/gender matched controls | UHDRS, MMSE | improvements in motor function and cognition after 6 months |
| Bonelli et al., 2002 [13] | 39.2 (10.1) | 6.3 (2.6) | Olanzapine | open label | UHDRS | significant improvements on most subscales of the UHDRS |
| Bonelli et al., 2002 [14] | 30 | 6 | high-dose Olanzapine | case study | UHDRS | improvement in grave choreatic attacks |
| Bonuccelli et al., 1994 [15] | 51.8 (8.6) | 7.2 (3.5) | Clozapine | open label | AIMS, M&Q scale, HAM, BPRS | improvements in motor functioning; no side effects during long-term treatment |
| Braun et al., 1989 [16] | range (24-77) | range (2-20) | SKF39393 | placebo controlled | AIMSb | no significant motor improvements |
| Brusa et al., 2009 [17] | 56.3 (12.4) | ---- | Aripiprazole (AP) & tetrabenazine (TBZ) | crossover | UHDRS (motor exam), CGI, HAM, ESS, MMSE | both AP & TBZ improved chorea & motor performance; TBZ associated with increased sleepiness |
| Caine et al., 1979 [18] | 51.3 | ---- | Clozapine | crossover, placebo controlled | study specific (abnormal movements) | 2 of 3 patients had improvements in abnormal movements |
| Caine et al., 1978 [19] | 51.9 | range (1-8) | Chlorpromazine, Carbidopa followed by Levodopa, Bromocriptine | randomized, placebo | plasma prolactin (PRL) levels | all treatments showed diminished PRL response (i.e., support for dopamine mediated HPA function) |
| Cankurtaran et al., 2006 [20] | 32 | 8 | Risperidone | ---- | AIMS, BPRS, MMSE | psychotic symptoms disappeared and improvements in motor symptoms |
| Caraceni et al., 1980 [21] | 42.6 | 5.9 | Apomorphine, Bromocryptine, Lysuride, Diazepam,  Cyproheptadine | ---- | study specific (abnormal involuntary movements, physiology) | Apomorphine, diazepam, and cypro improved movements; bromocryptine and lysuride had no effect or worsened movements |
| Caraceni et al., 1978 [22] | 49 | 4.9 | Deanol | crossover, randomized | Wechsler Memory Scale, study specific (hyperkinesia) | no improvements in chorea |
| Como et al., 1997 [23] | 43.7a (11.4) | 6.6 (4.5) | Fluoxetine | randomized, placebo controlled | TFC, HAM, MMSE, CBRS, Buschke Selective Reminding Test, Benton Visual Retention Test, Verbal Fluency, Ruff Figural Fuency Test, Trailmaking Test, Stroop, Digit Symbol Modalities Test | no improvements |
| Consroe et al., 1991 [24] | 47.8 (15.3) | 5 (2.8) | Cannabidiol (CBD) | randomized, crossover, placebo controlled | M&Q scale, TFC, Cannabis side effect inventory, plasma CBD levels | no group differences between placebo and CBD on chorea severity |
| Consroe et al., 1991 [25] | median 52.2, range (17-66) | ---- | oral cannabidiol | randomized, placebo controlled crossover | Plasma CBD levels | elimination half-life of CBD estimated at 2-5 days |
| Constantinescu et al., 2011 [26] | 47 (14) | 7 (4.0) | OPC-14117 (free-radical scavenger) | randomized, placebo controlled | UHDRS, CGI, BDI, Trailmaking Test, Hopkins Verbal Learning Test, WAIS Digit Span, Digit Ordering Task, Brief test of Attention, Luria Nebraska Mental Rotation Item, CSF [tau] | CSF total tau may be reliable biomarker but is not appropriate for use in isolation for diagnosis or clinical assessment |
| Corsini et al., 1978 [27] | 47.5 | 4.3 | Apomorphine HCl | placebo controlled | EEG, polygraph (for abnormal movements) | improvements in abnormal movements |
| Cubo et al., 2006 [28] | 46.2 (9.2) | 4.6 (3.4) | Donepezil | randomized, placebo controlled | UHDRS, MMSE, ADAS-c, SIPb | no improvements (chorea, cognition, nor quality of life) |
| Cudkowicz, 2004 [29] | 46.7 (8.9)  47.4 (9.3) | 5.3 (3.5)  6.9 (3.9) | Minocycline | randomized, placebo controlled | UHDRS, tolerability | drug well tolerated |
| Cudkowicz, 2010 [30] | 47.1 (10.3) | 6.4 (5.4) | Minocycline | randomized, controlled | TFC, UHDRS-m, UHDRS-f, UHDRS-I | Safe and tolerable; |
| Curtis et al., 2009 [31] | 50.6 (9.5)  54.3 (9.4) | ----- | Nabilone | crossover, placebo controlled | UHDRS-m, UHDRS-c, UHDRS-b, NPI | no improvement in motor or cognitive functioning. |
| Dallocchio et al., 1999 [32] | 51 (7) | 6 (3) | Risperidone | ---- | M&Q scale | improvement in motor disability; no side effects |
| Danivas et al., 2013 [33] | 58  51  48 | 23  4  3 | Lithium | Case studies | Study specific (patient reported abnormal movements) | abnormal movements did not worsen |
| Davis & Berger, 1978 [34] | Range (47-59) | ≥10 | Physotigmine, choline chloride | ---- | study specific (abnormal movements) | improvement in involuntary movements in 3 of 6 patients |
| Davis et al., 1978 [35] | ---- | -- | Physotigmine | placebo controlled | study specific (abnormal movements) | improvements in abnormal movements for 50% of patients |
| De Tommaso et al., 2004 [36] | 53.0 (8.7) | 8.9 (4) | Rivastigmine | randomized, controlled | TFC, M&Q scale, MMSE, AIMS | trend for improvements in cognition and movements |
| De Tommaso et al., 2005 [37] | 53.2 (7.8) | 7.4 (3.2) | Levetiracetam (LEV) | age/gender matched controls | UHDRS-m, UHDRS-b, TFC, MMSE | small improvement in involuntary movements and functional ability |
| De Tommaso et al., 2007 [38] | 55.7 (13) | 8.9 | Rivastigmine | HD controls | UHDRS-m, UHDRS-f, TFC, M&Q scale, AIMS, MMSE | improvements in motor functioning; trend for improvements in cognition and function |
| De Yebenes et al., 2011 [39] | 50.6 (10.5) | 4.8 (3.5) | Pridopidine | randomized, placebo controlled | UHDRS-mb(modified) | no improvements in motor functioning |
| Deroover et al., 1984 [40] | ---- | -- | Tiapride | randomized, placebo controlled crossover | Study specific (choreatic movements, motor skills) | improvements in choreatic movements and motor skills |
| Destee et al., 1984 [41] | 52 | 5.8 | Piracetam | placebo controlled | Study specific (involuntary movements) | increased choreic movements |
| Dorsey, 2008 [42] | 52.3 (9.8) | 6.8 | ethyl-EPA (omega3 fatty acid) | randomized, placebo controlled | UHDRS-m, UHDRS-c, MMSE, TFC | no improvements |
| Dorsey et al., 2011 [43] | ---- | ----- | Tetrabenazine | Randomized substudy, active drug group only | depressed mood item from UHDRS | no improvement in depressed mood |
| “randomized, double-blind, placebo-controlled…” JAMA Neurol, 2013 [44] | 53.3 (9.7) | 4.4 (3.6) | Latrepirdine | randomized, placebo controlled | UHDRS-m, MMSE, NPI, CIBIC-plus, AD-ADL | no improvements |
| Dubinsky & Gray, 2006 [45] | 49.2 | 6.6 | Cysteamine (cystagon) | open label | UHDRS-m, UHDRS-b,  UHDRS-I, TFC, max tolerated dose | no improvements; tolerated at 20 mg/kg per day with several limiting side effects |
| Dupont et al., 1978 [46] | 66 | 12 | Somatostatin | crossover, saline controlled case study | Study specific (neurological scores, involuntary movements, motor function) | no improvements |
| Esmaeilzadeh et al., 2011 [47] | range (39-75) | ----- | Pridopidine | ----- | PET, MRI | increased metabolic activity in several brain regions after treatment |
| Fahn, 1972 [48] | 51.3 | ---- | Perphenazine | placebo controlled crossover | study specific (chorea severity) | improvements in chorea for 70% of patients |
| Fekete et al., 2012 [49] | 58 (11) | 8.4 (3.5) | Tetrabenazine | ----- | UHDRS-m, study specific (computerized dynamic posturography system) | moderately improvement in balance |
| Fernandez et al., 2000 [50] | 58 | 7.5 | Donepezil HCL | open label | UHDRS, MMSE, supplemental neuropysch battery | improvements in motor function; no improvement in other domains |
| Foster et al., 1983 [51] | range (25-59) | ---- | THIP | placebo controlled | AIMS, BPRS, Columbia Rating scaleb | no improvement in motor or behavioral functioning |
| Frank, 2009 [52] | 50.9 (11.5) | 8.5 (4.5) | Tetrabenazine | placebo controlled | UHDRS | improvements in chorea for up to 80 weeks |
| Frank et al., 2008 [53] | 56.1 (9.7)  55.9 (8.5)  59.8 (14.2) | 10.1 (4.5)  8.9 (5.6)  11.4 (4.8) | Tetrabenazine withdrawal | randomized, placebo controlled | UHDRS, CGI | trend for reemergence of chorea in patients who were withdrawn from study drug |
| Frattola et al., 1977 [54] | 49 (3.1) | 7 | Bromocriptine | crossover, placebo controlled | study specific (chorea severity, finger dexterity, gait, speech) | improvements in involuntary movements |
| Frattola et al., 1983 [55] | 48.4 (3.3) | range (3-15) | Lisuride | placebo controlled | study specific (abnormal involuntary movements, chorea) | temporary improvement of abnormal involuntary movements |
| Gessa et al., 1991 [56] | 62 | ----- | Sch 23390 | placebo controlled case study | BPRS, study specific (involuntary movements) | 1mg dose improved involuntary movements |
| Gilligan et al., 1972 [57] | 38 (15.2) | ----- | Tetrabenazine | placebo controlled | study specific (motor tasks) | slight to moderate improvement in involuntary movements |
| Gimenez-Roldan & Mateo, 1989 [58] | 43.5 | 5.5 (3.6) | Tetrabenazine; Haloperidol | crossover | Kartzinel scale for involuntary movements | TBZ and haloperidol both improved chorea significant |
| Giuffra et al., 1992 [59] | Range (26-52) | 6 | Milacemide | randomized, placebo controlled | AIMSb, Buschke Selective Reminding Test, Verbal Fluency, ADAS-c | 1200 mg/day did not improve chorea or cognition |
| Goety et al., 1990 [60] | 51.6 (16.7) | 6.3 (3.6) | L-Acetyl-Carnitine | crossover, placebo controlled | TFC, AIMS, HAM, MMSE, Verbal fluency | drug had neither efficacy nor toxicity |
| Growdon, 1978 [61] | ---- | -- | Choline | healthy controls | biomarkers, study specific (speech, balance, gait) | transient improvement in balance and gait |
| Haslam, 1967 [62] | 27  35 (n=2) | 7  9 | Penicillamine | age/gender matched controls | biomarkers, study specific (dexterity, conversation, gait) | mild improvement in one patient and no improvement in the other |
| Hersch et al., 2006 [63] | 44.7 | 7.9 (3.5) | Creatine | randomized, placebo controlled | UHDRS, tolerability | study drug well tolerated; no improvements on clinical measures |
| Holl et al., 2010 [64] | 48.6 (10.5) | 5.9 (4.3) | Venlafaxine XR | ---- | HAM, BDI | significant improvement of depression |
| Hyson et al., 2010 [65] | 50.4 (8.4) | ---- | high dosage Coenzyme Q10 | healthy controls | Tolerability, AE frequency, blood levels | well tolerated; 82% achieved target dosage |
| Jankovic, 1982 [66] | 34 | ---- | Tetrabenazine | crossover, placebo controlled case study | study specific (hyperkinesia) | improvement of chorea |
| Jankovic & Beach, 1997 [67] | 54.8 | 7.27 (3.9) | Tetrabenazine | ---- | study specific (abnormal movements) | improvement in abnormal movements in 83% of patients |
| Kartzinel et al., 1976 [68] | range (41-54) | ---- | Bromocriptine | crossover, placebo controlled | study specific (motor disability) | high doses increased involuntary movements |
| Kenney et al., 2007 [69] | 56.3 (11.6) | 10.4 (5.8) | Tetrabenazine | ---- | UHDRS-m, BDI | single dose improves chorea for an average of 5 hours |
| Kieburtz, 2001 [70] | 47.5 (10.1)  47.4 (11)  48.2 (10.7) | 3.3 (2.3)  2.6 (2.2)  2.3 (2.0) | CoQ10, Remacemide | randomized, placebo controlled | UHDRS | no improvements with either drug |
| Kieburtz et al., 1996 [71] | 44.3 (14.8)  48.8 (11.6) | 9.5  8.1 | Remacemide | randomized, placebo controlled | TFC, HDMRS, MMSE, Trailmaking Test, Symbol Digit Modalities Test, Stroop, HVLT, BDI, tolerability | no differences between treatment arms; drug generally well tolerated |
| Kieburtz et al., 2010 [72] | 53.7 (10.9) | 4.4 | Latrepirdine | randomized, placebo controlled | UHDRS, MMSE,  ADAS-cog, tolerability | improved cognition (MMSE), but no improvements on other measures |
| “randomized, double-blind, placebo-controlled…” Mov Disord, 2013 [73] | 54.3 (11)  50.5 (10.5)  50.9 (9.7) | 4.6 (3.5)  4.4 (3.6)  4.1 (2.8) | Pridopidine | randomized, placebo controlled | UHDRS, CGI, HADS, Trailmaking A, Tolerability, lab tests | drug generally well tolerated; no improvements |
| Kotzailias et al., 2003 [74] | 60 (4) | ---- | Tiapride | age/gender matched controls | platelet counts | increased platelet counts |
| Kremer et al., 1999 [75] | 46.1 | 2.9 | Lamotrigine | placebo controlled | TFC | no improvements |
| Laks et al., 2004 [76] | 49  (n=1) | ---- | Olanzapine | Case reports | UHDRS | long term tolerability; improvement in motor and behavioral functioning |
| Lal et al., 1973 [77] | 54  46 (n=2) | 12  6 | Apomorphine, Pimozide, L-dopa | placebo crossover | Probenecid test, CSF levels | HVA and 5HIAA levels increased (i.e., unimpaired turnover of DA and 5HT) |
| Landwehrmeyer et al., 2007 [78] | 44.9a (9.6) | 5.0 (3.6) | Riluzole | randomized, placebo controlled | UHDRS, BDI, CGI | no improvements |
| Leonard et al., 1975 [79] | ---- | ---- | Lithium Carbonate, Haloperidol | randomized, crossover, placebo controlled | study specific (ultrasonic measurement, psychological variables) | no improvements |
| Lieberman et al., 1975 [80] | ---- | ---- | Piribedil | case study (n=2) | study specific (abnormal involuntary movements) | increase in abnormal involuntary movements |
| Lucetti et al., 2002 [81] | 60.4 (8.4) | 5.0 (1.9) | oral Amantadine | Open label | UHDRS-m, AIMS | improvement in dyskinesias |
| Lucetti et al., 2003 [82] | 60.7 (7.9) | 5.1 (1.8) | IV and oral amantadine | randomized, crossover, placebo controlled | AIMS, UHDRS-m, HAM, BDI, BPRS | improvements in choreic dyskinesias; no adverse effect on cognition |
| Lundin et al., 2010 [83] | 50.2 (7.0)a | 6.8 (5.0)a | Pridopidine (ACR16) | randomized, placebo controlled | UHDRS-m, HADS, CGI, Symbol Digit Modalities Test, Verbal Fluency, Stroop, Trailmaking Test A | no improvements in cognition |
| Manyam et al., 1990 [84] | 46 (15)a | Range (3-10)  --- | Isoniazid (plus pyridoxine) | randomized, crossover, placebo controlled | CSF levels of Choline and AChE | reduced level of choline in CSF on patients |
| Manyam et al., 1981 [85] | 41 | Range (3-20) | Isoniazid (plus pyridoxine) | randomized, crossover, placebo controlled | biomarkers, study specific (abnormal involuntary movements) | no significant improvements; serious side effects |
| Manyam et al., 1987 [86] | 46 (15) | ---- | Isoniazid (plus pyridoxine) | crossover, placebo controlled | amino acid levels in CSF and plasma | significant elevation in average CSF levels of several amino acids |
| Manyam et al., 1980 [87] | 35 (10) | ---- | Isoniazid (plus pyridoxine) | placebo controlled | GABA levels in CSF and plasma | elevation of brain GABA |
| Marshall, 2006 [88] | ---- | ---- | Tertrabenazine | randomized, placebo controlled | CGI, UHDRS | improvements in chorea and disease severity |
| Marshall, 1998 [89] | 47.7 (14.8)  47.1 (13.7)  45.3 (13.1) | 7.8 (5.6)  6.6 (3.6)  6.6 (4.6) | OPC-14117 (lipophilic  free-radical scavenger) | randomized, placebo controlled | CGI, UHDRS, tolerability, free radical levels in CSF and plasma | no significant differences between treatment arms; drug well tolerated |
| Marshall, 2003 [90] | 46.6 (9.1)  47.9 (8.7) | 5.0 (3.7)  6.3 (3.8) | Riluzole | randomized, placebo controlled | UHDRS | improvements in chorea, but not in other domains |
| Mateo & Gimenez-Roldan, 1996 [91] | ---- | ---- | Piracetam | placebo controlled | study specific (involuntary movements) | increased chorea |
| McLean, 1982 [92] | range (35-59) | ---- | Isoniazid | randomized, placebo controlled, crossover | study specific (movement frequency) | no improvements in chorea |
| McLellan et al., 1974 [93] | 51 | ---- | Tetrabenazine, thiopropazate | placebo controlled | study specific (chorea) | both study drugs improved chorea |
| Metman et al., 2002 [94] | Median 52 | Median 6 | Amantadine | randomized, placebo controlled crossover | UHDRS-m, UHDRS-c, RBANS, blood samples | chorea improved in all but one patient |
| Muller-Vahl et al., 1999 [95] | 58 | ---- | Nabilone | case study | Folstein chorea and motor impairment scale, WAIS Digit Span, CVLT, Benton Visual Retention Test, Raven’s Progressive Matrices Test | increased chorea |
| Murman et al., 1997 [96] | 48.4 (12.8) | 4.7 (3.9) | NMDA-receptor antagonist ketamine | randomized crossover (placebo administered as part of crossover) | UHDRS-m, BPRS, SRS, Buschke Selective Reminding Test, Washington Square Picture Memory Test, Verbal Fluency, WAIS Digit Span | declines in cognitive functioning |
| Newman et al., 1985 [97] | Range (30-50) | ---- | EMD 23,448 | crossover, placebo controlled | AIMS, hormone levels in blood | increased involuntary movements; plasma prolactin levels fell |
| Nutt et al., 1978 [98] | 47 | ---- | Arecoline | ---- | physiology, study specific (involuntary movements) | increased chorea; significant alterations in vital signs |
| Nutt et al., 1978 [99] | 47.3 | ---- | Naltrexone | crossover, placebo controlled | study specific (involuntary movements) | no improvements |
| Ondo et al., 2007 [100] | 53.5 (20.8) | ---- | Memantine | open label | UHDRS | improved motor symptoms, but not other domains |
| Ondo et al., 2002 [101] | 56.3 (12.4) | 8.1 (5.3) | Tetrabenazine | ---- | AIMS | improved motor symptoms |
| O'Suilleabhain & Dewey, 2003 [102] | 51 (13.0) | ---- | Amantadine | randomized, placebo controlled crossover | study specific (chorea, self-report improvement survey) | no objective improvements, although patients “felt better” |
| Paleacu et al., 2002 [103] | 47.6 (11.4) | 11.2 (3.3) | Olanzapine | ---- | UHDRS-b, UHDRS-m, CGI | improvements in behavioral symptoms; no improvements in motor symptoms |
| Perry et al., 1980 [104] | 37.6 | 5.7 | Aminooxyacetic acid (AOAA) | placebo controlled, crossover | study specific (chorea, motor functioning) | Inconclusive |
| Perry et al., 1979 [105] | 43.8 | 6.3 | Isoniazid (INH) | open label | biomarkers, study specific (mental function, movement) | 3 of 6 patients had some improvement. |
| Perry et al., 1982 [106] | 42.4 | 4.6 | Isoniazid (INH) | crossover, placebo controlled | biomarkers, study specific (motor function, neurologic assessment, psychometric testing) | minority of patients had improvements following high dose therapy |
| Peyser et al., 1995 [107] | ---- | Mild-moderate severity | a-tocopherol | randomized, placebo controlled | QNE, MMSE, informant rated HD-ADLS, WAIS Digit Span, Verbal Fluency, Trailmaking Test, CERAD Verbal Learning, Wisconsin Card Sorting Test, Benton Visual Retention Test, Go/No Go Test, Stroop, Design Fluency Test | drug may slow rate of motor decline early in the course of HD |
| Piolti et al., 1995 [108] | 50.5 (15.5) | 6.4 (3.0) | Proglumide | placebo controlled | BPRS, Raven’s Progressive Matrices Test, Kohs Cubes, study specific (abnormal movements, motor function) | no improvements |
| Puri et al., 2005 [109] | 50 (9.3) | ----  ---- | Ethyl-EPA | randomized, placebo controlled | UHDRS | no group differences on motor functioning |
| Puri et al., 2002 [110] | 53.1 (11.1) | ----  ---- | Ethyl-EPA | randomized, placebo controlled, pilot | UHDRS-m, MRI | improvements in cerebral structure and function (relative to placebo) |
| Puri et al., 2008 [111] | 51.3 (2.5) | ----  ---- | Ethyl-EPA | randomized, placebo controlled | MRI | significant group-level reductions in brain atrophy |
| Quinn & Marsden, 1984 [112] | 53 | 6.7 | Sulpiride | randomized, crossover | study specific (movement, chorea, functional scale) | improvements in dyskinesia and movements; no functional improvements |
| Ranen et al., 1996 [113] | 43.9 (13.7) | 5.9 | Idebenone | randomized, placebo controlled | HD-ADL, QNE, MMSE, Buschke Selective Reminding Test, Benton Visual Retention Test, WAIS Arithmetic, Trailmaking Test, Stroop | no group differences |
| Rosas et al., 1999 [114] | 45 (10.2) | 6.1 (4.1) | Riluzole | Open label | UHDRS-chorea, dystonica, TFC, lactate levels | improvements in chorea; no effect on dystonia or functional capacity |
| Rubin et al., 1993 [115] | 42.2 (10.1) | 8.1 (3.4) | Baclofen | placebo controlled | study specific (saccade latency and velocity) | declines in saccade latency and mean velocity in controls |
| Saft et al., 2006 [116] | 10.25 | ---- | Valproic acid | ---- | UHDRS-m | improvements in motor score for 7 of 8participants |
| Satoh et al., 2009 [117] | 54.8 | 19.3 | Yi-Gan San, chaihu-Jia-Longgu-Muli Tan | crossover | UHDRS-m, MMSE, Barthel Index, Lab tests | both drugs improved chorea |
| Scigliano et al., 1984 [118] | 48.8 | 6.8 | y-vinyl GABA | placebo controlled, crossover | physiology, study specific (chorea, motor function) | no improvements |
| Scott, 2011 [119] | 49.2 | 8.3 | Tetrabenazine | placebo controlled | CGI, UHDRS | improvements in chorea |
| Seppi et al., 2001 [120] | 46.4 (9.3) | 8 (3.3) | Riluzole | open label | UHDRS | transient improvement in chorea; sustained improvements in psychomotor speed and behavior |
| Shoulson & Chase, 1975 [121] | 56 | 6.0 | Caffeine | crossover, placebo controlled | study specific (tremor, rigidity, akinesia) | no improvements |
| Shoulson et al., 1989 [122] | 38.0 (10.2) | 5.2 (3.7) | Baclofen | randomized, placebo controlled | TFC | no improvements |
| Shoulson, et al., 1977 [123] | ---- | --- | Muscimol | crossover, placebo controlled | lab tests, study specific (motor and cognitive performance, EEG) | no improvement in hyerkinesia; improved chorea in the most severely hyperkinetic patient |
| Shoulson et al., 1978 [124] | 43.9 | 7.1 | Muscimol | crossover, placebo controlled | Trailmaking Test, Wechsler Memory Scale, study specific (motor, chorea, dystonia, ADLs) | no improvements in motor or cognition |
| Shoulson et al., 1976 [125] | 47 | 5.0 | DPA & GABA | crossover | study specific (chorea, finger dexterity, gait, speech) | at maximum dose, combined drugs increased turnover of dopamine and serotonin |
| Shults et al., 1986 [126] | range (28-52) | ---- | Cysteamine | placebo controlled, crossover | Road Map test, Recurring figures test, Visual form discrimination, Dichotomous listening test, study specific (chorea, rigidity, akinesia) | no improvements on motor or cognitive functioning |
| Squitieri et al., 2009 [127] | 46.7 (12.0) | ----  ---- | Riluzole | placebo controlled | UHDRS-m, UHDRS-b, TFC, BDNF serum levels | placebo showed significantly greater volume loss of grey matter; no differences between groups on UHDRS scores |
| Squitieri et al., 2013 [128] | 50.6 (10.60 | ----- | Pridopidine | Placebo controlled | UHDRS-m, UHDRS-c, tolerability, lab tests | acceptable safety profile and generally well tolerated |
| Stocchi et al., 1989 [129] | 52.2 | 3.8 | Transdihydrolisuride (TDHL) | crossover, placebo controlled | M&Q scale, AIMS | no improvements on chorea |
| Symington et al., 1978 [130] | 45.7 | ---- | Sodium Valproate | open label | biomarkers, study specific (body movements) | no improvements on movements |
| Tabrizi et al., 2003 [131] | 42.2 (5.6) | ---- | Creatine | age matched controls | UHDRS, MRS | no change in motor functioning, functional capacity or cognition at 12-months; Creatine was significantly elevated in brain and muscle tissue |
| Tabrizi et al., 2005 [132] | 44.2 (5.7) | ---- | high dose Creatine | placebo controlled | UHDRS, MRS | no change in motor functioning, functional capacity or cognition at 24-months; Creatine was significantly elevated in brain and muscle tissue |
| Tan et al., 1976 [133] | 50 (n=1) | ---- | Sodium Valproate | placebo controlled | biomarkers, study specific (chorea) | tolerance to study drug |
| Tarsy & Bralower, 1977 [134] | 55.7 | 9.7 | Deanol Acetamidobenzoate | placebo controlled, crossover | study specific (involuntary movements, motor function) | no improvements in chorea |
| Tell et al., 1981 [135] | 48 | 6.5 | y -acetylenic GABA | placebo controlled | biomarkers, study specific (abnormal movements, motor function) | GABA concentration increased; no motor improvement |
| Terrence, 1976 [136] | 52.2 | 2.7 | Fluphenazine decanoate | placebo controlled | study specific (chorea) | improvements in chorea |
| Thomas et al., 2004 [137] | range (21-66) | 9 | Minocycline | pilot | UHDRS, AIMS, MMSE, lab tests | drug tolerated; no improvements on outcome measures |
| Tolosa, 1976 [138] | 41.5 | ---- | Levodopa, Haloperidol | open label | Study specific (chorea) | Levodopa did not improve chorea; Haloperidol improved chorea |
| Tourian, 1972 [139] | 50.8 | 7 | 5-hydroxy-L- tryptophan | crossover | WAIS Digit Span, WAIS Block Design, WAIS Arithmetic, WAIS Digit Symbol, WAIS FSIQ, study specific (physical and neurologic exam) | no improvements in cognitive, behavioral or motor functioning |
| Vaddadi et al., 2002 [140] | 49.8 | ---- | HUFA (highly unsaturated fatty acids) | randomized, placebo controlled | UHDRS, Rockland-Simpson Dyskinesia Scale (motor) | improvement in motor function; no significant cognitive improvements |
| Van Vugt et al., 1997 [141] | 43.6 (11.4)  50.5 (7.9) | 9.3 (7.5)  7.3 (3.8) | Clozapine | randomized, placebo controlled | UHDRS-chorea, AIMS | improvement in motor function (as per AIMS, not UHDRS) |
| Verbessem et al., 2003 [142] | 49.6 (1.9) | 8.6 (1.5) | Creatine | randomized, placebo controlled pilot | UHDRS, study specific (strength and coordination tasks) | no improvements |
| Verhagen Metman et al., 2002 [143] | median 52  range (32-68) | median 6  range (2-15) | Amantadine | crossover, placebo controlled | UHDRS-chorea, MMSE, RBANS, Verbal Fluency, Symbol Digit Modalities Test, Stroop | improvements in chorea |
| Vestergaard et al., 1977 [144] | 49 | 6.7 | Lithium | crossover, placebo controlled | study specific (motor, hyperkinesia, global health) | no improvements |
| Vitale et al., 2007 [145] | 45.9 | 6.3 | Apomorphine HCL | randomized, crossover trial | UHDRS-m, AIMS, HAM | improvements in chorea for some patients with continuous injection |
| Walker & Hunt, 1989 [146] | 44.4 | ---- | Dextromethorphan | Open label | TFC, QNE, Benton Visual Retention Test, Verbal Fluency | declines in functioning |
| Wesseling & Lakke, 1980 [147] | range (38-72) | range (8-20) | 4-aminopyridine | placebo controlled | study specific (involuntary movements) | no group differences |
| Zesiewicz et al., 2006 [148] | 51.9 (9.3) | ---- | Levetiracetam (LEV) | open label | UHDRS-m, CGI, ESS | slight improvements in motor functioning; significant improvements in chorea |
| "randomized, placebo controlled trial…" Neurology, 2001 [149] | 47.5c  (10.1)  47.4 (11.0)  48.2 (10.7) | 5.3 (2.7)c  4.9 (2.6)  4.6 (3.2) | Coenzyme Q10, Remacemide HCL | randomized | TFC | declines in functional capacity |
| "TBZ as anti chorea therapy…." Neurology, 2006 [150] | ---- | ---- | Tetrabenazine | randomized, placebo | UHDRS, CGI, ESS, HAM | improvements in chorea (relative to controls) |

a Reported as mean (standard deviation) unless otherwise specified.

b Scale was modified

c Numbers reported in text and table were discrepant for this publication, we report the number from the table in this appendix

ADAS-cog, Alzheimer Disease Assessment Scale (cognitive subsection); AIMS; Abnormal Involuntary Movement Scale; BDI; Beck Depression Inventory; BPRS, Brief Psychiatric Rating Scale; CAARS, Connors’ Adult ADHD Rating Scale; CBRS, Cognitive Behavior Rating Scale; CGI, Clinical Global Impression scale; ESS, Epworth Sleepiness Scale; HADS, Hospital Anxiety and Depression Scale; HAM, Hamilton Depression scale; HD-ADL, Huntington disease activities of daily living scale; HDMRS, HD motor rating scale; MMSE, Mini-Mental State Exam; M&Q scale, Marsden and Quinn chorea severity scale; NPI, Neuropsychiatric Inventory; QNE, quantitative neurologic examination; RSDRS, Rockland-Simpson Dyskinesia Rating Scale; SIP, sickness impact profile; SRS, National Institute of mental health's self-rating score; UHDRS, Unified Huntington’s Disease Rating Scale (-m: motor; -c: cognitive; -f: functional; -b: behavioral; -I: independence scale; -TFC: total functional capacity)

**References**

[1] Agid Y, Destee A, Lallemand A. Effect of a methionine-enkephalin analog in Huntington's disease. Adv Neurol. 1983;37:299-304.

[2] Albanese A, Cassetta E, Carretta D, Bentivoglio AR, Tonali P. Acute challenge with apomorphine in Huntington's disease: a double-blind study. Clin Neuropharmacol. 1995;18:427-434.

[3] Aminoff MJ, Marshall J. Treatment of Huntington's chorea with lithium carbonate. A double-blind trial. Lancet. 1974;1:107-109.

[4] Asher SW, Aminoff MJ. Tetrabenazine and movement disorders. Neurology. 1981;31:1051-1054.

[5] Bamford KA, Caine ED, Kido DK, Cox C, Shoulson I. A prospective evaluation of cognitive decline in early Huntington's disease: functional and radiographic correlates. Neurology. 1995;45:1867-1873.

[6] Bassi S, Albizzati MG, Corsini GU, Frattola L, Piolti R, Suchy I, Trabucchi M. Therapeutic experience with transdihydrolisuride in Huntington's disease. Neurology. 1986;36:984-986.

[7] Beglinger LJ, Adams WH, Paulson H, Fiedorowicz JG, Langbehn DR, Duff K, Leserman A, Paulsen JS. Randomized controlled trial of atomoxetine for cognitive dysfunction in early Huntington disease. J Clin Psychopharmacol. 2009;29:484-487.

[8] Beister A, Kraus P, Kuhn W, Dose M, Weindl A, Gerlach M. The N-methyl-D-aspartate antagonist memantine retards progression of Huntington's disease. J Neural Transm Suppl. 2004;(68):117-122.

[9] Bender A, Auer DP, Merl T, Reilmann R, Saemann P, Yassouridis A, Bender J, Weindl A, Dose M, Gasser T, Klopstock T. Creatine supplementation lowers brain glutamate levels in Huntington's disease. J Neurol. 2005;252:36-41.

[10] Blackwell AD, Paterson NS, Barker RA, Robbins TW, Sahakian BJ. The effects of modafinil on mood and cognition in Huntington's disease. Psychopharmacology (Berl). 2008;199:29-36.

[11] Bonelli RM, Hödl AK, Hofmann P, Kapfhammer HP. Neuroprotection in Huntington's disease: a 2-year study on minocycline. Int Clin Psychopharmacol. 2004;19:337-342.

[12] Bonelli RM, Heuberger C, Reisecker F. Minocycline for Huntington's disease: an open label study. Neurology. 2003;60:883-884.

[13] Bonelli RM, Mahnert FA, Niederwieser G. Olanzapine for Huntington's disease: an open label study. Clin Neuropharmacol. 2002;25:263-265.

[14] Bonelli RM, Niederwieser G, Tribl GG, Koltringer P. High-dose olanzapine in Huntington's disease. Int Clin Psychopharmacol. 2002;17:91-93.

[15] Bonuccelli U, Ceravolo R, Maremmani C, Nuti A, Rossi G, Muratorio A. Clozapine in Huntington's chorea. Neurology. 1994;44:821-823.

[16] Braun A, Mouradian MM, Mohr E, Fabbrini G, Chase TN. Selective D-1 dopamine receptor agonist effects in hyperkinetic extrapyramidal disorders. J Neurol Neurosurg Psychiatry. 1989;52:631-635.

[17] Brusa L, Orlacchio A, Moschella V, Iani C, Bernardi G, Mercuri NB. Treatment of the symptoms of Huntington's disease: preliminary results comparing aripiprazole and tetrabenazine. Mov Disord. 2009;24:126-129.

[18] Caine ED, Polinsky RJ, Kartzinel R, Ebert MH. The trial use of clozapine for abnormal involuntary movement disorders. Am J Psychiatry. 1979;136:317-320.

[19] Caine E, Kartzinel R, Ebert M, Carter AC. Neuroendocrine function in Huntington's disease: dopaminergic regulation of prolactin release. Life Sci. 1978;22(10):911-918.

[20] Cankurtaran ES, Ozalp E, Soygur H, Cakir A. Clinical experience with risperidone and memantine in the treatment of Huntington's disease. J Natl Med Assoc. 2006;98:1353-1355.

[21] Caraceni TA, Girotti F, Giovannini P, Pederzoli M, Parati EA. Effects of DA agonist in Huntington disease hyperkinesia. Ital J Neurol Sci. 1980;1:155-161.

[22] Caraceni TA, Girotti F, Celano I, Parati E, Balboni L. 2-dimethylaminoethanol (Deanol) in Huntington's chorea. J Neurol Neurosurg Psychiatry. 1978;41:1114-1118.

[23] Como PG, Rubin AJ, O'Brien CF, Lawler K, Hickey C, Rubin AE, Henderson R, McDermott MP, McDermott M, Steinberg K, Shoulson I. A controlled trial of fluoxetine in nondepressed patients with Huntington's disease. Mov Disord. 1997;12:397-401.

[24] Consroe P, Laguna J, Allender J, Snider S, Stern L, Sandyk R, Kennedy K, Schram K. Controlled clinical trial of cannabidiol in Huntington's disease. Pharmacol Biochem Behav. 1991;40:701-708.

[25] Consroe P, Kennedy K, Schram K. Assay of plasma cannabidiol by capillary gas chromatography/ion trap mass spectroscopy following high-dose repeated daily oral administration in humans. Pharmacol Biochem Behav. 1991;40:517-522.

[26] Constantinescu R, Romer M, Zetterberg H, Rosengren L, Kieburtz K. Increased levels of total tau protein in the cerebrospinal fluid in Huntington's disease. Parkinsonism Relat Disord. 2011;17:714-715.

[27] Corsini GU, Onali P, Masala C, Cianchetti C, Mangoni A, Gessa G. Apomorphine hydrochloride-induced improvement in Huntington's chorea: stimulation of dopamine receptor. Arch Neurol. 1978;35:27-30.

[28] Cubo E, Shannon KM, Tracy D, Jaglin JA, Bernard BA, Wuu J, Leurgans SE. Effect of donepezil on motor and cognitive function in Huntington disease. Neurology. 2006;67:1268-1271.

[29] Cudkowicz M. Minocycline safety and tolerability in Huntington disease. Neurology. 2004;63:547-549.

[30] Cudkowicz M. A futility study of minocycline in huntington's disease. Movement Disorders. 2010;25:2219-2224.

[31] Curtis A, Mitchell I, Patel S, Ives N, Rickards H. A pilot study using nabilone for symptomatic treatment in Huntington's disease. Mov Disord. 2009;24:2254-2259.

[32] Dallocchio C, Buffa C, Tinelli C, Mazzarello P. Effectiveness of risperidone in Huntington chorea patients. J Clin Psychopharmacol. 1999;19:101-103.

[33] Danivas V1, Moily NS, Thimmaiah R, Muralidharan K, Purushotham M, Muthane U, Jain S. Off label use of lithium in the treatment of Huntington's disease: A case series. Indian J Psychiatry. 2013;55:81-83.

[34] Davis KL, Berger PA. Pharmacological investigations of the cholinergic imbalance hypotheses of movement disorders and psychosis. Biol Psychiatry. 1978;13:23-49.

[35] Davis KL, Hollister LE, Berger PA, Vento AL. Studies on choline chloride in neuropsychiatric disease: human and animal data. Psychopharmacol Bull. 1978;14:56-58.

[36] de Tommaso M, Specchio N, Sciruicchio V, Difruscolo O, Specchio LM. Effects of rivastigmine on motor and cognitive impairment in Huntington's disease. Mov Disord. 2004;19:1516-1518.

[37] de Tommaso M, Di Fruscolo O, Sciruicchio V, Specchio N, Cormio C, De Caro MF, Livrea P. Efficacy of levetiracetam in Huntington disease. Clin Neuropharmacol. 2005;28:280-284.

[38] De Tommaso M, Difruscolo O, Sciruicchio V, Specchio N, Livrea P. Two years' follow-up of rivastigmine treatment in Huntington disease. Clin Neuropharmacol. 2007;30:43-46.

[39] de Yebenes JG, Landwehrmeyer B, Squitieri F, Reilmann R, Rosser A, Barker RA, Saft C, Magnet MK, Sword A, Rembratt A, Tedroff J; MermaiHD study investigators. Pridopidine for the treatment of motor function in patients with Huntington's disease (MermaiHD): a phase 3, randomised, double-blind, placebo-controlled trial. Lancet Neurol. 2011;10:1049-1057.

[40] Deroover J, Baro F, Bourguignon RP, Smets P. Tiapride versus placebo: a double-blind comparative study in the management of Huntington's chorea. Curr Med Res Opin. 1984;9:329-338.

[41] Destée A, Petit H, Warot P. Effect of piracetam in Huntington's chorea. Eur Neurol. 1984;23:89-91.

[42] Dorsey ER. Randomized controlled trial of ethyl-eicosapentaenoic acid in huntington disease the trend-hd study. Archives of Neurology. 2008;65:1582-1589.

[43] Dorsey R, Biglan K, Eberly S, Auinger P, Brocht A, Umeh CC, Oakes D, Clarence-Smith K, Marshall F, Shoulson I, Frank S. Use of Tetrabenazine in Huntington Disease Patients on Antidepressants or with Advanced Disease: Results from the TETRA-HD Study. PLoS Curr. 2011;3:RRN1283.

[44] HORIZON Investigators of the Huntington Study Group and European Huntington's Disease Network. A randomized, double-blind, placebo-controlled study of latrepirdine in patients with mild to moderate Huntington disease. JAMA Neurol. 2013;70:25-33.

[45] Dubinsky R, Gray C. CYTE-I-HD: phase I dose finding and tolerability study of cysteamine (Cystagon) in Huntington's disease. Mov Disord. 2006;21:530-533.

[46] Dupont E, Hansen AP, Juul-Jensen P, Lundbaek K, Magnussen I, de Fine Olivarius B. Somatostatin in the treatment of patients with extra-pyramidal disorders and patients with EEG abnormalities. Acta Neurol Scand. 1978;57:488-493.

[47] Esmaeilzadeh M, Kullingsjö J, Ullman H, Varrone A, Tedroff J. Regional cerebral glucose metabolism after pridopidine (ACR16) treatment in patients with Huntington disease. Clin Neuropharmacol. 2011;34:95-100.

[48] Fahn S. Treatment of choreic movements with perphenazine. Dis Nerv Syst. 1972;33:653-658.

[49] Fekete R, Davidson A, Ondo WG, Cohen HS. Effect of tetrabenazine on computerized dynamic posturography in Huntington disease patients. Parkinsonism Relat Disord. 2012;18:896-898.

[50] Fernandez HH, Friedman JH, Grace J, Beason-Hazen S. Donepezil for Huntington's disease. Mov Disord. 2000;15:173-176.

[51] Foster NL, Chase TN, Denaro A, Hare TA, Tamminga CA. THIP treatment of Huntington's disease. Neurology. 1983;33:637-639.

[52] Frank S. Tetrabenazine as anti-chorea therapy in Huntington disease: an open-label continuation study. Huntington Study Group/TETRA-HD Investigators. BMC Neurol. 2009;9:62. Erratum in: BMC Neurol. 2011;11:18.

[53] Frank S, Ondo W, Fahn S, Hunter C, Oakes D, Plumb S, Marshall F, Shoulson I, Eberly S, Walker F, Factor S, Hunt V, Shinaman A, Jankovic J. A study of chorea after tetrabenazine withdrawal in patients with Huntington disease. Clin Neuropharmacol. 2008;31:127-133.

[54] Frattola L, Albiazzati MG, Spano PF, Trabucchi M. Treatment of Huntington's chorea with bromocriptine. Acta Neurol Scand. 1977;56:37-45.

[55] Frattola L, Albizzati MG, Alemani A, Bassi S, Ferrarese C, Trabucchi M. Acute treatment of Huntington's chorea with lisuride. J Neurol Sci. 1983;59:247-253.

[56] Gessa GL, Canu A, Del Zompo M, Burrai C, Serra G. Lack of acute antipsychotic effect of Sch 23390, a selective dopamine D1 receptor antagonist. Lancet. 1991;337:854-855.

[57] Gilligan BS, Wodak J, Veale JL, Munro OR. Tetrabenazine in the treatment of extrapyramidal dyskinesias. Med J Aust. 1972;2:1054-1056.

[58] Giménez-Roldán S, Mateo D. [Huntington disease: tetrabenazine compared to haloperidol in the reduction of involuntary movements]. Neurologia. 1989;4:282-287. Spanish.

[59] Giuffra ME, Mouradian MM, Chase TN. Glutamatergic therapy of Huntington's chorea. Clin Neuropharmacol. 1992;15:148-151.

[60] Goety CG, Tanner CM, Cohen JA, Thelen JA, Carroll VS, Klawans HL, Fariello RG. L-acetyl-carnitine in Huntington's disease: double-blind placebo controlled crossover study of drug effects on movement disorder and dementia. Mov Disord. 1990;5:263-265.

[61] Growdon JH. Effects of choline on tardive dyskinesia and other movement disorders. Psychopharmacol Bull. 1978;14:55-56.

[62] Haslam MT. Cellular magnesium levels and the use of penicillamine in the treatment of Huntington's chorea. J Neurol Neurosurg Psychiatry. 1967;30:185-188.

[63] Hersch SM, Gevorkian S, Marder K, Moskowitz C, Feigin A, Cox M, Como P, Zimmerman C, Lin M, Zhang L, Ulug AM, Beal MF, Matson W, Bogdanov M, Ebbel E, Zaleta A, Kaneko Y, Jenkins B, Hevelone N, Zhang H, Yu H, Schoenfeld D, Ferrante R, Rosas HD. Creatine in Huntington disease is safe, tolerable, bioavailable in brain and reduces serum 8OH2'dG. Neurology. 2006;66:250-252.

[64] Holl AK, Wilkinson L, Painold A, Holl EM, Bonelli RM. Combating depression in Huntington's disease: effective antidepressive treatment with venlafaxine XR. Int Clin Psychopharmacol. 2010;25:46-50.

[65] Hyson HC, Kieburtz K, Shoulson I, McDermott M, Ravina B, De Blieck EA, Cudkowicz ME, Ferrante RJ. Safety and tolerability of high-dosage coenzyme Q10 in Huntington's disease and healthy subjects. Movement Disorders. 2010;25:1924-1928.

[66] Jankovic J. Treatment of hyperkinetic movement disorders with tetrabenazine: a double-blind crossover study. Ann Neurol. 1982;11:41-47.

[67] Jankovic J, Beach J. Long-term effects of tetrabenazine in hyperkinetic movement disorders. Neurology. 1997;48:358-362.

[68] Kartzinel R, Hunt RD, Calne DB. Bromocriptine in Huntington chorea. Arch Neurol. 1976;33:517-518.

[69] Kenney C, Hunter C, Davidson A, Jankovic J. Short-term effects of tetrabenazine on chorea associated with Huntington's disease. Mov Disord. 2007;22:10-3.

[70] Kieburtz K. A randomized, placebo-controlled trial of coenzyme Q10 and remacemide in Huntington's disease. Neurology. 2001;57:397-404.

[71] Kieburtz K, Feigin A, McDermott M, Como P, Abwender D, Zimmerman C, Hickey C, Orme C, Claude K, Sotack J, Greenamyre JT, Dunn C, Shoulson I. A controlled trial of remacemide hydrochloride in Huntington's disease. Mov Disord. 1996;11:273-277.

[72] Kieburtz K, McDermott MP, Voss TS, Corey-Bloom J, Deuel LM, Dorsey ER, Factor S, Geschwind MD, Hodgeman K, Kayson E, Noonberg S, Pourfar M, Rabinowitz K, Ravina B, Sanchez-Ramos J, Seely L, Walker F, Feigin A, Cudkowicz M, Seitz W. A randomized, placebo-controlled trial of latrepirdine in Huntington disease. Arch Neurol. 2010;67:154-160.

[73] Huntington Study Group HART Investigators. A randomized, double-blind, placebo-controlled trial of pridopidine in Huntington's disease. Mov Disord. 2013;28:1407-1415.

[74] Kotzailias N, Finsterer J, Aull S, Eichler HG, Pratscher B, Jilma B. Influence of tiapride on platelet counts in healthy volunteers and patients with movement disorders. Prog Neuropsychopharmacol Biol Psychiatry. 2003;27:595-599.

[75] Kremer B, Clark CM, Almqvist EW, Raymond LA, Graf P, Jacova C, Mezei M, Hardy MA, Snow B, Martin W, Hayden MR. Influence of lamotrigine on progression of early Huntington disease: A randomized clinical trial. Neurology. 1999;53:1000-1011.

[76] Laks J, Rocha M, Capitao C, Domingues RC, Ladeia G, Lima M, Engelhardt E. Functional and motor response to low dose olanzapine in Huntington's disease: case report. Arq Neuropsiquiatr 2004;62:1092-1094.

[77] Lal S, De la Vega C, Garelis E, Sourkes TL. Apomorphine, pimozide, L-Dopa and the probenecid test in Huntington's chorea. Psychiatr Neurol Neurochir. 1973;76:113-117.

[78] Landwehrmeyer GB, Dubois B, De Yebenes JG, Kremer B, Gaus W, Kraus PH, Przuntek H, Dib M, Doble A, Fischer W, Ludolph AC. Riluzole in Huntington's disease: A 3-year, randomized controlled study. Ann Neurol. 2007;62:262-272.

[79] Leonard DP, Kidson MA, Brown JG, Shannon PJ, Taryan S. A double blind trial of lithium carbonate and haloperidol in Huntington's chorea. Aust N Z J Psychiatry. 1975;9:115-118.

[80] Lieberman AN, Shopsin B, Brun YL, Boal D, Zolfaghari M. Studies on piribedil in Parkinsonism. Adv Neurol. 1975;9:399-407.

[81] Lucetti C, Gambaccini G, Bernardini S, Dell'Agnello G, Petrozzi L, Rossi G, Bonuccelli U. Amantadine in Huntington's disease: open-label video-blinded study. Neurol Sci. 2002;23 Suppl 2:S83-84.

[82] Lucetti C, Del Dotto P, Gambaccini G, Dell' Agnello G, Bernardini S, Rossi G, Murri L, Bonuccelli U. IV amantadine improves chorea in Huntington's disease: An acute randomized, controlled study. Neurology. 2003;60:1995-1997.

[83] Lundin A, Dietrichs E, Haghighi S, Goller ML, Heiberg A, Loutfi G, Widner H, Wiktorin K, Wiklund L, Svenningsson A, Sonesson C, Waters N, Waters S, Tedroff J. Efficacy and safety of the dopaminergic stabilizer pridopidine (ACR16) in patients with Huntington's disease. Clini Neuropharmacol. 2010;33:260-264.

[84] Manyam BV, Giacobini E, Colliver JA. Cerebrospinal fluid acetylcholinesterase and choline measurements in Huntington's disease. J Neurol. 1990;237:281-284.

[85] Manyam BV, Katz L, Hare TA. Isoniazid-induced elevation of CSF GABA levels and effects on chorea in Huntington's disease. Ann Neurol. 1981;10:35-37.

[86] Manyam BV, Ferraro TN, Hare TA. Isoniazid-induced alteration of CSF neurotransmitter amino acids in Huntington's disease. Brain Res. 1987;408:125-130.

[87] Manyam NVB, Hare TA, Katz L. Effect of isoniazid on cerebrospinal fluid and plasma GABA levels in Huntington's disease. Life Sci. 1980;26:1303-1308.

[88] Marshall FJ. Tetrabenazine as antichorea therapy in Huntington disease: A randomized controlled trial. Neurology. 2006;66:366-372.

[89] Marshall FJ. Safety and tolerability of the free-radical scavenger OPC-14117 in Huntington's disease. The Huntington Study Group. Neurology. 1998;50:1366-1373.

[90] Marshall FJ. Dosage effects of riluzole in Huntington's disease: A multicenter placebo-controlled study. Neurology. 2003;61:1551-1556.

[91] Mateo D, Gimenez-Roldan S. Effect of piracetam on involuntary movements in Huntington's disease. A double-blind placebo-controlled study. Neurologia. 1996;11:16-19.

[92] McLean DR. Failure of isoniazid therapy in Huntington disease. Neurology. 1982;32:1189-1191.

[93] McLellan DL, Chalmers RJ, Johnson RH. A double-blind trial of tetrabenazine, thiopropazate, and placebo in patients with chorea. Lancet. 1974;1:104-107.

[94] Metman LV, Morris MJ, Farmer C, Gillespie M, Mosby K, Wuu J, Chase TN. Huntington's disease: A randomized, controlled trial using the NMDA-antagonist amantadine. Neurology. 2002;59:694-699.

[95] Muller-Vahl KR, Schneider U, Emrich HM. Nabilone increases choreatic movements in Huntington's disease. Mov Disord. 1999;14:1038-1040.

[96] Murman DL, Giordani B, Mellow AM, Johanns JR, Little RJA, Hariharan M, Foster NL. Cognitive, behavioral, and motor effects of the NMDA antagonist ketamine in Huntington's disease. Neurology. 1997;49:153-161.

[97] Newman RP, Tamminga CA, Chase TN, LeWitt PA. EMD 23,448: effects of a putative dopamine autoreceptor agonist in chorea. J Neural Transm. 1985;61:125-129.

[98] Nutt JG, Rosin A, Chase TN. Treatment of Huntington disease with a cholinergic agonist. Neurology. 1978;28:1061-1064.

[99] Nutt JG, Rosin AJ, Eisler T, Calne DB, Chase TN. Effect of an opiate antagonist on movement disorders. Arch Neurol. 1978;35:810-811.

[100] Ondo WG, Mejia NI, Hunter CB. A pilot study of the clinical efficacy and safety of memantine for Huntington's disease. Parkinsonism Relat Disord. 2007;13:453-454.

[101] Ondo WG, Tintner R, Thomas M, Jankovic J. Tetrabenazine treatment for Huntington's disease-associated chorea. Clin Neuropharmacol. 2002;25:300-302.

[102] O'Suilleabhain P, Dewey Jr RB. A randomized trial of amantadine in Huntington disease. Arch Neurol. 2003;60:996-998.

[103] Paleacu D, Anca M, Giladi N. Olanzapine in Huntington's disease. Acta Neurol Scand. 2002;105:441-444.

[104] Perry TL, Wright JM, Hansen S, Allan BM, Baird PA, MacLeod PM. Failure of aminooxyacetic acid therapy in Huntington disease. Neurology. 1980;30:772-775.

[105] Perry TL, Wright JM, Hansen S, MacLeod PM. Isoniazid therapy of Huntington disease. Neurology. 1979;29:370-375.

[106] Perry TL, Wright JM, Hansen S. A double-blind clinical trial of isoniazid in Huntington disease. Neurology. 1982;32:354-358.

[107] Peyser CE, Folstein M, Chase GA, Starkstein S, Brandt J, Cockrell JR, Bylsma F, Coyle JT, McHugh PR, Folstein SE. Trial of d-(alpha)-tocopherol in Huntington's disease. Am J Psychiatry. 1995;152:1771-1775.

[108] Piolti R, Appollonio I, Perego M, Pozzi C, Rovati L, Ferrarese C, Frattola L. Proglumide, a cholecystokinin receptor antagonist, reduces neuroleptic action in Huntington's chorea. Eur Neurol. 1995;35:344-348.

[109] Puri BK, Leavitt BR, Hayden MR, Ross CA, Rosenblatt A, Greenamyre JT, Hersch S, Vaddadi KS, Sword A, Horrobin DF, Manku M, Murck H. Ethyl-EPA in Huntington disease: A double-blind, randomized, placebo-controlled trial. Neurology. 2005;65:286-292.

[110] Puri BK, Bydder GM, Counsell SJ, Corridan BJ, Richardson AJ, Hajnal JV, Appel C, McKee HM, Vaddadi KS, Horrobin DF. MRI and neuropsychological improvement in Huntington disease following ethyl-EPA treatment. Neuroreport. 2002;13:123-126.

[111] Puri BK, Bydder GM, Manku MS, Clarke A, Waldman AD, Beckmann CF. Reduction in cerebral atrophy associated with ethyl-eicosapentaenoic acid treatment in patients with Huntington's disease. J Int Med Res. 2008;36:896-905.

[112] Quinn N, Marsden CD. A double blind trial of sulpiride in Huntington's disease and tardive dyskinesia. J Neurol Neurosurg Psychiatry. 1984;47:844-847.

[113] Ranen NG, Peyser CE, Coyle JT, Bylsma FW, Sherr M, Day L, Folstein MF, Brandt J, Ross CA, Folstein SE. A controlled trial of idebenone in Huntington's disease. Mov Disord. 1996;11:549-554.

[114] Rosas HD, Koroshetz WJ, Jenkins BG, Chen YI, Hayden DL, Beal MF, Cudkowicz ME. Riluzole therapy in Huntington's disease (HD). Mov Disord. 1999;14:326-330.

[115] Rubin AJ, King WM, Reinbold KA, Shoulson I. Quantitative longitudinal assessment of saccades in Huntington's disease. J Clin Neuroophthalmol. 1993;13:59-66.

[116] Saft C, Lauter T, Kraus PH, Przuntek H, Andrich JE. Dose-dependent improvement of myoclonic hyperkinesia due to Valproic acid in eight Huntington's Disease patients: a case series. BMC Neurol. 2006;6:11.

[117] Satoh T, Takahashi T, Iwasaki K, Tago H, Seki T, Yaegashi N, Tobita M, Arai H. Traditional Chinese medicine on four patients with Huntington's disease. Mov Disord. 2009;24:453-455.

[118] Scigliano G, Giovannini P, Girotti F. Gamma-vinyl GABA treatment of Huntington's disease. Neurology. 1984;34:94-96.

[119] Scott LJ. Tetrabenazine: For chorea associated with huntingtons disease. CNS Drugs. 2011;25:1073-1085.

[120] Seppi K, Mueller J, Bodner T, Brandauer E, Benke T, Weirich-Schwaiger H, Poewe W, Wenning GK. Riluzole in Huntington's disease (HD): an open label study with one year follow up. J Neurol. 2001;248:866-869.

[121] Shoulson I, Chase T. Caffeine and the antiparkinsonian response to levodopa or piribedil. Neurology. 1975;25:722-724.

[122] Shoulson I, Odoroff C, Oakes D, Behr J, Goldblatt D, Caine E, Kennedy J, Miller C, Bamford K, Rubin A, et al. A controlled clinical trial of baclofen as protective therapy in early Huntington's disease. Ann Neurol. 1989;25:252-259.

[123] Shoulson I, Goldblatt D, Charlton M, Joynt RJ. Huntington's disease: treatment with muscimol, a GABA-mimetic drug. Trans Am Neurol Assoc. 1977;102:124-125.

[124] Shoulson I, Goldblatt D, Charlton M, Joynt RJ. Huntington's disease: treatment with muscimol, a GABA-mimetic drug. Ann Neurol. 1978;4:279-284.

[125] Shoulson I, Kartzinel R, Chase TN. Huntington's disease: treatment with dipropylacetic acid and gamma-aminobutyric acid. Neurology. 1976;26:61-63.

[126] Shults C, Steardo L, Barone P, Mohr E, Juncos J, Serrati C, Fedio P, Tamminga CA, Chase TN. Huntington's disease: effect of cysteamine, a somatostatin-depleting agent. Neurology. 1986;36:1099-1102.

[127] Squitieri F, Orobello S, Cannella M, Martino T, Romanelli P, Giovacchini G, Frati L, Mansi L, Ciarmiello A. Riluzole protects Huntington disease patients from brain glucose hypometabolism and grey matter volume loss and increases production of neurotrophins. Eur J Nucl Med Mol Imaging. 2009;36:1113-1120.

[128] Squitieri F, Landwehrmeyer B, Reilmann R, Rosser A, Garcia, Prang A, Ivkovic J, Bright J, Rembratt A. One-year safety and tolerability profile of pridopidine in patients with Huntington disease. Neurology. 2013;80:1086-1094.

[129] Stocchi F, Carta A, Berardelli A, Antonini A, Argenta M, Formica A, Agnoli A. Effects of terguride in patients with Huntington's disease. Clin Neuropharmacol. 1989;12:435-439.

[130] Symington GR, Leonard DP, Shannon PJ, Vajda FJ. Sodium valproate in Huntington's disease. Am J Psychiatry. 1978;135:352-354.

[131] Tabrizi SJ, Blamire AM, Manners DN, Rajagopalan B, Styles P, Schapira AH, Warner TT. Creatine therapy for Huntington's disease: clinical and MRS findings in a 1-year pilot study. Neurology. 2003;61:141-142.

[132] Tabrizi SJ, Blamire AM, Manners DN, Rajagopalan B, Styles P, Schapira AHV, Warner TT. High-dose creatine therapy for Huntington disease: A 2-year clinical and MRS study. Neurology. 2005;64:1655-1656.

[133] Tan BK, Leijnse-Ybema HJ, Zee MF. Sodium valproate in Huntington's chorea. Clin Neurol Neurosurg. 1976;79:62-65.

[134] Tarsy D, Bralower M. Deanol acetamidobenzoate treatment in choreiform movement disorders. Arch Neurol. 1977;34:756-758.

[135] Tell G, Bohlen P, Schechter PJ, Koch-Weser J, Agid Y, Bonnet AM, Coquillat G, Chazot G, Fischer C. Treatment of Huntington disease with gamma-acetylenic GABA an irreversible inhibitor of GABA-transaminase: increased CSF GABA and homocarnosine without clinical amelioration. Neurology. 1981;31:207-211.

[136] Terrence CF. Fluphenazine decanoate in the treatment of chorea: a double-blind study. Curr Ther Res Clin Exp. 1976;20:177-183.

[137] Thomas M, Ashizawa T, Jankovic J. Minocycline in Huntington's disease: a pilot study. Mov Disord. 2004;19:692-695.

[138] Tolosa ES. Studies on the anti-dyskinesia effect of apomorphine in man. Neurol Neurocir Psiquiatr. 1976;17:223-229.

[139] Tourian AY. Administration of 5-hydroxy-L-tryptophan to individuals with Huntington's chorea. Neurology. 1972;22:1201-1204.

[140] Vaddadi KS, Soosai E, Chiu E, Dingjan P. A randomised, placebo-controlled, double blind study of treatment of Huntington's disease with unsaturated fatty acids. NeuroReport. 2002;13:29-33.

[141] Van Vugt JPP, Siesling S, Vergeer M, Van Der Velde EA, Roos RAC. Clozapine versus placebo in Huntington's disease: A double blind randomised comparative study. J Neurol Neurosurg Psychiatry. 1997;63:35-39.

[142] Verbessem P, Lemiere J, Eijnde BO, Swinnen S, Vanhees L, Van Leemputte M, Hespel P, Dom R. Creatine supplementation in Huntington's disease: A placebo-controlled pilot trial. Neurology. 2003;61:925-930.

[143] Verhagen Metman LV, Morris MJ, Farmer C, Gillespie M, Mosby K, Wuu J, Chase TN. Huntington's disease: A randomized, controlled trial using the NMDA-antagonist amantadine. Neurology. 2002;59:694-699.

[144] Vestergaard P, Baastrup PC, Petersson H. Lithium treatment of Huntington's chorea. A placebo-controlled clinical trial. Acta Psychiatr Scand. 1977;56:183-188.

[145] Vitale C, Marconi S, Di Maio L, De Michele G, Longo K, Bonavita V, Barone P. Short-term continuous infusion of apomorphine hydrochloride for treatment of Huntington's chorea: A double blind, randomized cross-over trial. Mov Disord. 2007;22:2359-2364.

[146] Walker FO, Hunt VP. An open label trial of dextromethorphan in Huntington's disease. Clin Neuropharmacol. 1989;12:322-330.

[147] Wesseling H, Lakke JPWF. Observations with 4-aminopyridine in Huntington's chorea. IRCS Medical Science. 1980;8:332-333.

[148] Zesiewicz TA, Sullivan KL, Hauser RA, Sanchez-Ramos J. Open-label pilot study of levetiracetam (Keppra) for the treatment of chorea in Huntington's disease. Movement Disorders. 2006;21:1998-2001.

[149] Huntington Study Group. A randomized, placebo-controlled trial of coenzyme Q10 and remacemide in Huntington's disease. Neurology. 2001;57:397-404.

[150] Huntington Study Group. Tetrabenazine as antichorea therapy in Huntington disease: a randomized controlled trial. Neurology. 2006;66:366-372.