BEST in Mental Health
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Best Evidence Summaries of Topics in Mental Healthcare

BEST *in* MH *clinical question-answering service*

Question

For adults with (and adults without) learning disabilities who have tardive dyskinesia/ tardive dystonia/ chorea or other movement disorders, how effective are pharmacological interventions at managing or improving their movement disorder?

Clarification of question using *PICO* structure

Patients: Adults with (and without) learning disabilities, and tardive dyskinesia/ tardive dystonia/ chorea or other movement disorders
Intervention: Pharmacological intervention
Comparator: Any intervention
Outcome: Management or improvement of tardive dyskinesia/ tardive dystonia/ chorea or other movement disorders

Plain language summary

There is very little research in this area; only one, well conducted, but small, study was identified, which found that clomipramine reduces repetitive movements. Further, larger studies are required which look at other pharmacological interventions with individuals both with and without learning disabilities.

Clinical and research implications

One small crossover trial in 10 participants with severe or profound mental retardation found that treatment with clomipramine reduced the frequency of repetitive behaviours in body and object movements compared with placebo. It also reduced the number of days requiring behavioural intervention by staff but had no impact on the frequency of compulsions or self-injurious behaviour, or teachers' assessments of hyperactivity, irritability or lethargy. Although this was a well-conducted study, due to its small size no definite conclusions about the effectiveness of clomipramine can be made. Further, larger-scale, controlled trials assessing clomipramine and other pharmacological interventions in adults with or without learning disabilities are needed.

What does the evidence say?

Number of included studies/reviews (number of participants)

One randomised crossover trial in 10 participants living in a state facility for adults with mental retardation in the US, was included. All participants had severe or profound mental retardation and some form of body or object movements or self-injurious behaviour.

Main findings

All participants received up to 3 mg/kg of clomipramine and a matching placebo, in a random order, over a 19 week treatment period. Clomipramine significantly reduced the frequency of repetitive behaviours in body and object movements both in the classroom and the living unit, and also reduced movement intensity in the classroom. There was a significant reduction in movement measured by the teachers using the Aberrant Behaviour Checklist with clomipramine but it had no effect on hyperactivity, irritability or lethargy. The number of days requiring behavioural intervention by staff was also significantly lower with clomipramine compared to placebo.

No significant differences were observed between clomipramine and placebo in the frequency of compulsions, or the frequency or intensity of self-injurious behaviour. Three participants had to have their clomipramine dose changed due to side effects but they all remained in the study.

Author's conclusions

The authors concluded that clomipramine is effective in the treatment of stereotyped behaviours and the related repetitive behaviour disorders of self-injury and compulsions in adults with mental retardation.

Reliability of conclusions/Strength of evidence

Although this was a well-conducted study with a low risk of bias, due to its small size (10 participants in one centre) and the fact that some outcomes were only measured on 4 or 5 participants, the strength of evidence is very low. The conclusions of this study may be reliable but they need to be confirmed by a larger, multi-centre trial.

What do guidelines say?

There were no relevant NICE or SIGN guidelines that comment on pharmacological interventions in the treatment of movement disorders in adults with and without learning disabilities.

However on NICE Guideline does discuss Efficacy and Safety of “Deep brain stimulation therapy” as a non-pharmacological treatment for tremors and dystonia.

“2.3 Efficacy
2.3.1 A case–control series found that, in up to 27 months' follow-up, total tremor score improved in 17 patients treated with deep brain stimulation, but there was no significant improvement in most other efficacy outcomes…”

Date question received: 21/10/15
Date searches conducted: 26/10/15
Date answer completed: 06/11/15

References

Randomised controlled trials

1. Lewis, M. H., Bodfish, J. W., Powell, S. B., & Golden, R. N. (1995). Clomipramine treatment for stereotypy and related repetitive movement disorders associated with mental retardation. *American Journal on Mental Retardation*, 100(3) 299-312.

Guidelines

The National Institute for Health and Care Excellence (2006) Deep brain stimulation for tremor and dystonia (excluding Parkinson's disease) NICE Interventional procedure guidance [IPG 188] http://www.nice.org.uk/guidance/ipg188

Results

Randomised controlled trials

Author (year)	Inclusion criteria	Number of participants	Summary of results	Risk of bias
Lewis (1995)	***Participants*:** 10 adults (2 females, 8 males) between the age of 18 – 42 with mental retardation and repetitive movement disorder who lived in a state facility for people with mental retardation in the US. They had to have excessive stereotyped behaviour judged to significantly interfere with training and socialisation. ***Intervention*:** Clomipramine (titrated up to a maximum dose of 3 mg/kg over 3 weeks, then a maintenance phase of 4 weeks, then titrated down by 50 mg/day over 1 week) ***Comparator*:** Placebo (following the same titration pattern). The total treatment period over both treatments was 19 weeks. ***Outcomes*:** - Frequency of repetitive behaviour	10 (3 had clomipramine dose modifications due to side effects but continued in the study)	Four participants had severe mental retardation and six were profound, all were ambulatory. Before the start of the study all participants showed body movements such as rocking; six showed object movements such as toy-shaking; five had repetitive self-injurious behaviour such as head-hitting and three had repetitive compulsive behaviours such as checking or hoarding. Two participants had a history of seizures and were taking carbamazepine but both had been seizure-free in the six months prior to the study. Two other participants were taking low doses of antipsychotic medication (thioridazine and chlorpromazine). In the classroom there was a statistically significant decrease in repetitive behaviours in body movements with clomipramine compared to placebo (mean 44.9 vs. 58.9, $p < 0.01$) and object movements (mean 29.6 vs. 48.6, $p < 0.05$). There was also a significantly greater reduction in movement intensity with clomipramine (mean 2.5 vs. 2.8, $p < 0.01$). Similar results were seen in the living unit, with a significantly greater increase in the percentage interval between repetitive behaviours in body movements with	Low This was a placebo-controlled trial with randomisation performed by the pharmacist. The participants, research team, professional and direct care staff were blind to treatment group. All outcomes appear to have been reported. The only limitation was

	(Direct observation) - Adaptive Engagement (Direct observation) - Intensity of repetitive behaviour (5 point Likert scale) - Mental Retardation (Aberrant Behaviour Checklist) - Medication Related side-effects (Treatment Emergent Side Effects Scale) Participants were observed in both their classrooms and living unit. ***Study design:*** Double-blind, placebo-controlled crossover trial with each participant receiving both treatments in a random order.		clomipramine compared to placebo (mean 39.3 vs. 48.8, $p < 0.05$) and object movements (mean 34.9 vs. 46.2, $p < 0.05$). There were no significant differences between clomipramine and placebo in either setting for the frequency of compulsions, or the frequency or intensity of self-injurious behaviour. For teacher ratings using the Aberrant Behaviour Checklist, there was a significant decrease in movement severity score with clomipramine (mean 1.2 vs. 1.6, $p < 0.05$) but no effect on hyperactivity, irritability or lethargy factor scores. Behavioural intervention by staff was significantly lower with clomipramine compared to placebo (17% vs. 70% of days during the treatment maintenance phase, $p < 0.01$).	that this was a very small study and not all the outcomes were measured on all 10 participants.

Risk of bias

Randomised controlled trials

Study	RISK OF BIAS					
	Random allocation	**Allocation concealment**	**Blinding of participants and personnel**	**Blinding of outcome assessment**	**Incomplete outcome data**	**Selective Reporting**
Study 1	☺	☺	☺	☺	☹	☺

☺Low risk ☹High risk ? Unclear risk

Search details

Source	Search Strategy	Number of hits	Relevant evidence identified
Guidelines			
NICE	Movement disorder	82	1
SIGN	Movement disorder	25	0
Systematic Reviews			
MEDLINE			
EMBASE	1 exp Dyskinesia, Drug-Induced/ (14647) 2 exp Movement Disorders/ (579318) 3 exp Chorea/ or exp Parkinson Disease/ or exp Huntington Disease/ (138595) 4 (tardive adj3 (dystine* or diskine*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (19) 5 (abnormal adj3 movement*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (5529) 6 (involuntar* adj3 movement).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (4939) 7 1 or 2 or 3 or 4 or 5 or 6 (652532) 8 exp Learning Disorders/ (28556) 9 exp Intellectual Disability/ (388925) 10 (learning adj3 difficult$).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (4136) 11 (mental$ adj3 (handicap$ or retard$)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (47264) 12 (learning adj3 (disable$ or disabilit$)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (10141) 13 (intellect$ adj3 (disable$ or disabilit$)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (13255) 14 (mental adj3 (deficien$ or incapacit$)).mp. [mp=title, abstract, heading word, drug trade name, original title, device	143	1

	manufacturer, drug manufacturer, device trade name, keyword] (62657) 15 (intellect$ adj3 impair$).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (14661) 16 (learning adj3 difficult$).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (4136) 17 down$ syndrome.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (32034) 18 (fragile adj3 syndrome).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (7425) 19 (cognitiv$ adj3 impair$).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (70672) 20 cognitiv$ impair$.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (62795) 21 (subnormal$ adj3 intel$).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (130) 22 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 (472419) 23 7 and 22 (82445) 24 exp therapeutics/ or exp drug therapy/ (7064914) 25 exp botulinum toxins/ or exp botulinum toxins, type a/ (26015) 26 exp Tetrabenazine/ (2814) 27 (pharma* adj2 (intervent* or therap*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (42820) 28 (tetrabenazine or nitoman or xenazine).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (2987) 29 (miraplex or pramiperole or dihydrocholride).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (1) 30 ((botulinum adj2 toxin) or botox).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (27825) 31 24 or 25 or 26 or 27 or 28 or 29 or 30 (7098649) 32 23 and 31 (27050) 33 (systematic$ review$ or systematic$ literature review$ or meta-analytic$ or meta?analysis or metanalysis or meta analysis or meta?synthesis or meta synthesis or meta?regression or meta regression).ab,ti. (162605)		

	34 ((synthes$ adj3 literature) or (synthes$ adj3 evidence) or (synthes$ adj2 qualitative) or integrative review or data synthesis or research synthesis or narrative synthesis or systematic study or systematic studies or systematic comparison$ or systematic overview$).ab,ti. (31338) 35 ((systematic adj2 search$) or systematic$ literature research$ or (review adj3 scientific literature) or (literature review adj2 side effect$) or (literature review adj2 adverse effect$) or (literature review adj2 adverse event$) or (evidence-based adj2 review) or (evidence-based adj2 review)).ab,ti. (18215) 36 (comprehensive review or critical review or critical analysis or quantitative review or structured review or realist review or realist synthesis or (pooled adj2 analysis) or (pooled data adj6 (studies or trials)) or (medline and (inclusion adj3 criteria)) or (search adj (strateg$ or term$))).ab,ti. (75173) 37 exp "systematic review"/ (97089) 38 meta analysis/ (100712) 39 (Medline or pubmed or Cochrane or embase or cinahl or psyc?lit or psyc?info or lilacs or (literature adj3 search$) or (database$ adj3 search$) or (bibliographic adj3 search$) or (electronic adj3 search$) or (electronic adj3 database$) or (computeri?ed adj3 search$) or (internet adj3 search$)).ab. (187254) 40 ((inclusion adj3 studies) or inclusion criteria or selection criteria or predefined criteria or predetermined criteria or (assess$ adj3 (quality or validity)) or (select$ adj3 (study or studies)) or (data adj3 extract$) or extracted data or (data adj2 abstracted)).ab. (226937) 41 ((data adj3 abstraction) or published intervention$ or ((study or studies) adj2 evaluat$) or (intervention$ adj2 evaluat$) or confidence interval$ or heterogeneity or pooled or pooling or odds ratio$ or (Jadad or coding) or evidence-based).ab. (942111) 42 33 or 34 or 35 or 36 or 37 or 38 (290965) 43 39 or 40 or 41 (1218803) 44 review.pt. (2110177) 45 43 and 44 (150429) 46 review.ti. (351095) 47 43 and 46 (76348) 48 (review$ adj10 (papers or trials or trial data or studies or evidence or intervention$ or evaluation$ or outcome$ or findings)).ab,ti. (345203) 49 (retriev$ adj10 (papers or trials or studies or evidence or intervention$ or evaluation$ or outcome$ or findings)).ab,ti. (17162) 50 42 or 45 or 47 or 48 or 49 (622930) 51 (letter or editorial).pt. (1407914)		

	52 50 not 51 (614825) 53 exp animal/ (20921796) 54 nonhuman/ (4635611) 55 53 or 54 (22185312) 56 human/ (16332606) 57 55 not 56 (5852706) 58 52 not 57 (587419) 59 ("cochrane database of systematic reviews$" or "the cochrane database of systematic reviews").jn. (12835) 60 58 not 59 (575711) 61 conference abstract.pt. (2006413) 62 60 not 61 (505148) 63 limit 62 to yr="2010" (31277) 64 32 and 63 (143)		
PsycINFO/CINAHL	1 exp Movement Disorders/ (22591) 2 exp Chorea/ or exp Parkinson Disease/ or exp Huntington Disease/ (2564) 3 (tardive adj3 (dystine* or diskine*)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (6) 4 (abnormal adj3 movement*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (2405) 5 (involuntar* adj3 movement).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (1636) 6 exp Learning Disorders/ (22005) 7 (learning adj3 difficult$).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (4772) 8 (mental$ adj3 (handicap$ or retard$)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (23840) 9 (learning adj3 (disable$ or disabilit$)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (18479) 10 (intellect$ adj3 (disable$ or disabilit$)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (11424) 11 (mental adj3 (deficien$ or incapacit$)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (544)		0

	12 (intellect$ adj3 impair$).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (990) 13 (learning adj3 difficult$).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (4772) 14 down$ syndrome.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (5528) 15 (fragile adj3 syndrome).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (1752) 16 (cognitiv$ adj3 impair$).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (41439) 17 cognitiv$ impair$.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (38258) 18 (subnormal$ adj3 intel$).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (33) 19 exp therapeutics/ or exp drug therapy/ (106824) 20 (pharma* adj2 (intervent* or therap*)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (5487) 21 (tetrabenazine or nitoman or xenazine).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (139) 22 (miraplex or pramiperole or dihydrocholride).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (5) 23 ((botulinum adj2 toxin) or botox).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (1164) 24 exp Dyskinesia/ (3402) 25 exp Developmental Disabilities/ or exp Cognitive Impairment/ (37856) 26 1 or 2 or 3 or 4 or 5 or 24 (24192) 27 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 25 (107292) 28 19 or 20 or 21 or 22 or 23 (110804) 29 26 and 27 and 28 (191) 30 (Cochrane$ or review or overview or (review adj2 literature) or (synthes$ adj3 (literature$ or research or studies or data))).ti. (107209) 31 (meta analysis or literature review or systematic review).md. (111385)		

	32 (pooled analys$ or ((data adj2 pool$) and studies) or ((hand or manual$ or database$ or computer$ or electronic$) adj2 search$) or ((electronic$ or bibliographic$) adj2 (database$ or data base$))).ab,ti. (9102) 33 exp Meta Analysis/ (3481) 34 30 or 31 or 32 or 33 (192344) 35 (comment reply or editorial or letter or review book or review media).dt. (225541) 36 (electronic collection or dissertation abstract or encyclopedia).pt. (299575) 37 (rat or rats or mouse or mice or hamster or hamsters or animal or animals or dog or dogs or cat or cats or bovine or sheep).ab,sh,ti. (204223) 38 35 or 36 or 37 (689929) 39 34 not 38 (120499) 40 limit 39 to yr="2010" (7179) 41 29 and 40 (1)		
Primary Studies			
MEDLINE	1 exp Dyskinesia, Drug-Induced/ (6482) 2 exp Movement Disorders/ (114518) 3 exp Chorea/ or exp Parkinson Disease/ or exp Huntington Disease/ (65206) 4 (tardive adj3 (dystine* or diskine*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (9) 5 (abnormal adj3 movement*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (3786) 6 (involuntar* adj3 movement).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1304) 7 1 or 2 or 3 or 4 or 5 or 6 (116965) 8 exp Learning Disorders/ (19935) 9 exp Intellectual Disability/ (85626) 10 (learning adj3 difficult$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (2811) 11 (mental$ adj3 (handicap$ or retard$)).mp. [mp=title, abstract, original title, name of substance word, subject	34	0

	heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (36970) 12 (learning adj3 (disable$ or disabilit$)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (7713) 13 (intellect$ adj3 (disable$ or disabilit$)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (57002) 14 (mental adj3 (deficien$ or incapacit$)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (4937) 15 (intellect$ adj3 impair$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1732) 16 (learning adj3 difficult$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (2811) 17 down$ syndrome.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (26636) 18 (fragile adj3 syndrome).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (5541) 19 (cognitiv$ adj3 impair$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (46248) 20 cognitiv$ impair$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (40556) 21 (subnormal$ adj3 intel$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (96)		

	22 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 (178120) 23 7 and 22 (5264) 24 exp therapeutics/ or exp drug therapy/ (3595935) 25 exp botulinum toxins/ or exp botulinum toxins, type a/ (13101) 26 exp Tetrabenazine/ (1066) 27 (pharma* adj2 (intervent* or therap*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (28766) 28 (tetrabenazine or nitoman or xenazine).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1392) 29 (miraplex or pramiperole or dihydrocholride).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1) 30 ((botulinum adj2 toxin) or botox).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (11517) 31 24 or 25 or 26 or 27 or 28 or 29 or 30 (3626989) 32 23 and 31 (554) 33 "randomized controlled trial".pt. (414741) 34 (random$ or placebo$ or single blind$ or double blind$ or triple blind$).ti,ab. (892478) 35 (retraction of publication or retracted publication).pt. (8316) 36 33 or 34 or 35 (988045) 37 (animals not humans).sh. (4040452) 38 ((comment or editorial or meta-analysis or practice-guideline or review or letter or journal correspondence) not "randomized controlled trial").pt. (3590216) 39 (random sampl$ or random digit$ or random effect$ or random survey or random regression).ti,ab. not "randomized controlled trial".pt. (56072) 40 36 not (37 or 38 or 39) (735398) 41 32 and 40 (34)		
EMBASE	1 exp Dyskinesia, Drug-Induced/ (14647) 2 exp Movement Disorders/ (579318)	1204	1

	3 exp Chorea/ or exp Parkinson Disease/ or exp Huntington Disease/ (138595) 4 (tardive adj3 (dystine* or diskine*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (19) 5 (abnormal adj3 movement*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (5529) 6 (involuntar* adj3 movement).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (4939) 7 1 or 2 or 3 or 4 or 5 or 6 (652532) 8 exp Learning Disorders/ (28556) 9 exp Intellectual Disability/ (388925) 10 (learning adj3 difficult$).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (4136) 11 (mental$ adj3 (handicap$ or retard$)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (47264) 12 (learning adj3 (disable$ or disabilit$)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (10141) 13 (intellect$ adj3 (disable$ or disabilit$)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (13255) 14 (mental adj3 (deficien$ or incapacit$)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (62657) 15 (intellect$ adj3 impair$).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (14661) 16 (learning adj3 difficult$).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (4136) 17 down$ syndrome.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (32034) 18 (fragile adj3 syndrome).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (7425) 19 (cognitiv$ adj3 impair$).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (70672) 20 cognitiv$ impair$.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (62795)		

	21 (subnormal$ adj3 intel$).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (130) 22 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 (472419) 23 7 and 22 (82445) 24 exp therapeutics/ or exp drug therapy/ (7064914) 25 exp botulinum toxins/ or exp botulinum toxins, type a/ (26015) 26 exp Tetrabenazine/ (2814) 27 (pharma* adj2 (intervent* or therap*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (42820) 28 (tetrabenazine or nitoman or xenazine).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (2987) 29 (miraplex or pramiperole or dihydrocholride).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (1) 30 ((botulinum adj2 toxin) or botox).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (27825) 31 24 or 25 or 26 or 27 or 28 or 29 or 30 (7098649) 32 23 and 31 (27050) 33 (random$ or placebo$ or single blind$ or double blind$ or triple blind$).ti,ab. (1143190) 34 RETRACTED ARTICLE/ (7800) 35 33 or 34 (1150806) 36 (animal$ not human$).sh,hw. (3960454) 37 (book or conference paper or editorial or letter or review).pt. not exp randomized controlled trial/ (4276992) 38 (random sampl$ or random digit$ or random effect$ or random survey or random regression).ti,ab. not exp randomized controlled trial/ (67466) 39 35 not (36 or 37 or 38) (884914) 40 32 and 39 (1204)		
PsycINFO/CINAHL	1 exp Movement Disorders/ (22591) 2 exp Chorea/ or exp Parkinson Disease/ or exp Huntington Disease/ (2564) 3 (tardive adj3 (dystine* or diskine*)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (6) 4 (abnormal adj3 movement*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (2405)	28	0

	5 (involuntar* adj3 movement).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (1636) 6 exp Learning Disorders/ (22005) 7 (learning adj3 difficult$).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (4772) 8 (mental$ adj3 (handicap$ or retard$)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (23840) 9 (learning adj3 (disable$ or disabilit$)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (18479) 10 (intellect$ adj3 (disable$ or disabilit$)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (11424) 11 (mental adj3 (deficien$ or incapacit$)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (544) 12 (intellect$ adj3 impair$).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (990) 13 (learning adj3 difficult$).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (4772) 14 down$ syndrome.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (5528) 15 (fragile adj3 syndrome).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (1752) 16 (cognitiv$ adj3 impair$).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (41439) 17 cognitiv$ impair$.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (38258) 18 (subnormal$ adj3 intel$).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (33) 19 exp therapeutics/ or exp drug therapy/ (106824) 20 (pharma* adj2 (intervent* or therap*)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (5487) 21 (tetrabenazine or nitoman or xenazine).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (139)		

	22 (miraplex or pramiperole or dihydrocholride).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (5) 23 ((botulinum adj2 toxin) or botox).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (1164) 24 exp Dyskinesia/ (3402) 25 exp Developmental Disabilities/ or exp Cognitive Impairment/ (37856) 26 1 or 2 or 3 or 4 or 5 or 24 (24192) 27 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 25 (107292) 28 19 or 20 or 21 or 22 or 23 (110804) 29 26 and 27 and 28 (191) 30 (random$ or placebo$ or single blind$ or double blind$ or triple blind$).ti,ab. (147019) 31 (animals not humans).sh. (3303) 32 exp Clinical Trials/ (9083) 33 random*.mp. (131073) 34 32 not 33 (3908) 35 30 not (31 or 34) (146457) 36 29 and 35 (28)		

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