1. Neurol Clin. 2020 May;38(2):379-396. doi: 10.1016/j.ncl.2020.01.004. Epub 2020

Feb 28.

**Treatment of Tardive Dyskinesia.**

Tardive dyskinesia (TD) is an iatrogenic condition that encompasses a wide

phenomenological spectrum of movement disorders caused by exposure to dopamine

receptor blocking agents (DRBAs). TD may cause troublesome or disabling symptoms

that impair quality of life. Due to frequent, often inappropriate, use of DRBAs,

TD prevalence rates among patients exposed to DRBAs continue to be high. The

judicious use of DRBAs is key to the prevention of TD, reduction of disease

burden, and achieving lasting remission. Dopamine-depleting vesicular monoamine

transporter type 2 inhibitors are considered the treatment of choice of TD.

Copyright © 2020 Elsevier Inc. All rights reserved.

DOI: 10.1016/j.ncl.2020.01.004

PMID: 32279716 [Indexed for MEDLINE]

2. Curr Opin Neurol. 2010 Aug;23(4):420-5. doi: 10.1097/WCO.0b013e32833b7798.

**Deep brain stimulation for hyperkinetics disorders: dystonia, tardive**

**dyskinesia, and tics.**

PURPOSE OF REVIEW: This review focuses on new insights in deep brain stimulation

(DBS) for patients with hyperkinetic movement disorders: dystonia, tardive

dyskinesia and Gille de la Tourette's syndrome, during the last 18 months.

RECENT FINDINGS: The recent literature confirms the efficacy of high-frequency

stimulation of the globus pallidus internus (GPi) for primary dystonia,

generalized or not, with a stable effect over time. The benefit of DBS in other

forms of localized dystonia remains to be demonstrated in larger studies. Some

clinical and radiological predictive factors have been determined with a

predominant influence of the disease duration. Tardive dystonia and

myoclonus-dystonia are also improved by GPi stimulation. Encouraging results

obtained in cerebral palsy may pave the way for the application of DBS in other

secondary dystonia. In Gilles de la Tourette's syndrome, both stimulation of the

centre-median/parafascicular nucleus of the thalamus and GPi stimulation

(ventromedial) have demonstrated efficacy with stable long-term effect. Thalamic

stimulation failed to improve obsessions and compulsions in some patients.

Stimulation of the nucleus accumbens has been tested in few cases with

contradictory efficacy. In both diseases, complications are rare with no major

side effects.

SUMMARY: The few controlled studies showed that bilateral GPi stimulation is a

well tolerated and a long-term effective treatment for hyperkinetic disorders.

However, recent published data of DBS applied in different targets or patients

(especially secondary dystonia) are mainly uncontrolled case reports, precluding

the clear determination of the efficacy of this procedure and the choice of the

'good' target for the 'good' patient.

DOI: 10.1097/WCO.0b013e32833b7798

PMID: 20610993 [Indexed for MEDLINE]

3. J Neurol Sci. 2018 Jun 15;389:55-60. doi: 10.1016/j.jns.2018.02.013. Epub 2018

Feb 5.

**Deep brain stimulation for tardive syndromes: Systematic review and**

**meta-analysis.**

Among the broad entity of tardive syndromes, tardive dystonia and classical

tardive dyskinesia sometimes require advanced treatments like deep brain

stimulation of the globus pallidus internum (Gpi-DBS) or the subthalamic nucleus

(STN-DBS). This systematic review has analyzed the currently available

literature reporting cases with either tardive dystonia or dyskinesia treated

with DBS. The key words for the literature search included all tardive syndromes

and "deep brain stimulation." Thirty-four level VI studies and one level II

study with 117 patients were included. Level I studies were not identified. Only

four of the patients had tardive dyskinesia. All the others had tardive

dystonia. The majority had Gpi-DBS (n = 109). Patients had a mean age of 47.4 (±

SD 14.7) years. The duration of follow-up was 25.6 months ± 26.2. The Abnormal

Involuntary Movement Scale was reported in 51 patients with an improvement of

62 ± 15% and the Burke-Fahn-Marsden scale was reported in 67 cases with an

improvement of 76 ± 21%. Reported adverse events were surgery-related in 7

patients, stimulation-induced in 12, and psychiatric in 3 patients. These

reports thus suggest favorable effects of DBS and it seems to be relatively

safe. DBS can be considered for patients with severe, medication-resistant

symptoms. Controlled and randomized studies with blinded outcomes are needed.

Copyright © 2018 Elsevier B.V. All rights reserved.

DOI: 10.1016/j.jns.2018.02.013

PMID: 29433807 [Indexed for MEDLINE]

4. J Clin Psychiatry. 2012 Nov;73(11):1434-8. doi: 10.4088/JCP.12r07643.

**Efficacy and safety of deep brain stimulation in patients with**

**medication-induced tardive dyskinesia and/or dystonia: a systematic review.**

BACKGROUND: Tardive dyskinesia and dystonia (TDD) are severe side effects of

dopamine-blocking agents, particularly antipsychotics. While deep brain

stimulation (DBS) has proven effective in the treatment of TDD, little is known

about the possible psychiatric complications of DBS in psychiatric patients.

OBJECTIVE: To assess the efficacy and safety, specifically the psychiatric side

effects, of DBS in patients with medication-induced TDD.

DATA SOURCES: PubMed and EMBASE databases were searched systematically on May

25, 2011, for articles written in English, using the search terms deep brain

stimulation AND tardive.

STUDY SELECTION: Of the 88 original articles retrieved, 17 studies involving 50

patients with TDD who underwent DBS were included in the review.

DATA EXTRACTION: Data on the severity of the movement disorders before and after

DBS, as rated on the Burke-Fahn-Marsden Dystonia Rating Scale or similar scales,

were extracted. Data on psychiatric symptoms before and after DBS were used to

calculate the percent improvement per patient per rating scale. Overall

improvement and confidence intervals were calculated using a 1-sample, 2-sided

Student t test.

RESULTS: The mean improvement of TDD of the combined patients 3 to 76 months

after implantation was 77.5% (95% CI, 71.4%-83.3%; P < .000) on the

Burke-Fahn-Marsden Dystonia Rating Scale. Of the 50 patients, 1 experienced an

exacerbation of depression, and 1 experienced an exacerbation of psychosis.

CONCLUSIONS: DBS seems to be effective and relatively safe for patients with

treatment-resistant TDD; however, the results should be interpreted with

caution, as most of the data are from case reports and small trials.

© Copyright 2012 Physicians Postgraduate Press, Inc.

DOI: 10.4088/JCP.12r07643

PMID: 23218160 [Indexed for MEDLINE]

5. Aust N Z J Psychiatry. 2018 Jul;52(7):717. doi: 10.1177/0004867418760712. Epub

2018 Mar 5.

**Tardive dyskinesia responsive to deep brain stimulation.**

DOI: 10.1177/0004867418760712

PMID: 29506398 [Indexed for MEDLINE]

6. Parkinsonism Relat Disord. 2013 Feb;19(2):141-7. doi:

10.1016/j.parkreldis.2012.09.016. Epub 2012 Oct 23.

**Globus pallidus interna deep brain stimulation for tardive dyskinesia: case**

**report and review of the literature.**

Tardive dyskinesia (TD) can be a disabling condition and is frequently

refractory to medical therapy. Over the past decade there have been many reports

of TD patients experiencing significant benefit with deep brain stimulation

(DBS) of the globus pallidus interna (GPi). The growing literature on this

treatment option for TD consists predominantly of case reports and series. The

reported benefit ranges widely, but the majority of cases experienced at least a

50% improvement in symptoms. The anatomical distribution of dyskinesias has not

clearly influenced outcome, though fixed postures appear less likely to improve

than phasic movements. Onset of benefit can be immediate or take months, and

benefit is sustained in most cases, for at least 6 months and up to several

years. A wide variety of voltages, frequencies, and pulse widths have

demonstrated efficacy. A small number of reports which examined psychiatric

symptoms before and after surgery did not find any decline, and in some cases

revealed improvement in mood. However, these overall positive results should be

interpreted with caution, as the majority of reports lacked blinded assessments,

control groups, or standardized therapy parameters. Finally, we present an

illustrative case of refractory tardive dyskinesia treated with GPi-DBS with 5

years of follow-up and 4 accompanying video segments.

Published by Elsevier Ltd.

DOI: 10.1016/j.parkreldis.2012.09.016

PMID: 23099106 [Indexed for MEDLINE]

7. Neurol India. 2015 Jan-Feb;63(1):9-18. doi: 10.4103/0028-3886.152623.

**Deep brain stimulation: current status.**

In the last two decades, applications of deep brain stimulation (DBS) have

expanded rapidly in the field of neurosciences. The most common indications for

DBS are Parkinson's disease, medically refractory seizures, essential tremors,

and primary dystonia. This device has also been used as an investigational tool

in patients having Tourette's syndrome, tardive dyskinesia, and refractory

seizures. In the field of psychiatry, DBS has been used for the treatment of

refractory obsessive compulsive disorder and depression. The complications are

mainly related to surgery, the device, and its stimulation. This article

provides an overview of the current status and recent advances in the field of

DBS.

DOI: 10.4103/0028-3886.152623

PMID: 25751463 [Indexed for MEDLINE]

8. J Neurol Sci. 2018 Jun 15;389:67-75. doi: 10.1016/j.jns.2018.02.010. Epub 2018

Feb 5.

**Updating the recommendations for treatment of tardive syndromes: A systematic**

**review of new evidence and practical treatment algorithm.**

BACKGROUND: Management of tardive syndromes (TS) is challenging, with only a few

evidence-based therapeutic algorithms reported in the American Academy of

Neurology (AAN) guideline in 2013.

OBJECTIVE: To update the evidence-based recommendations and provide a practical

treatment algorithm for management of TS by addressing 5 questions: 1) Is

withdrawal of dopamine receptor blocking agents (DRBAs) an effective TS

treatment? 2) Does switching from typical to atypical DRBAs reduce TS symptoms?

3) What is the efficacy of pharmacologic agents in treating TS? 4) Do patients

with TS benefit from chemodenervation with botulinum toxin? 5) Do patients with

TS benefit from surgical therapy?

METHODS: Systematic reviews were conducted by searching PsycINFO, Ovid MEDLINE,

PubMed, EMBASE, Web of Science and Cochrane for articles published between 2012

and 2017 to identify new evidence published after the 2013 AAN guidelines.

Articles were classified according to an AAN 4-tiered evidence-rating scheme. To

the extent possible, for each study we attempted to categorize results based on

the description of the population enrolled (tardive dyskinesia [TD], tardive

dystonia, tardive tremor, etc.). Recommendations were based on the evidence.

RESULTS AND RECOMMENDATIONS: New evidence was combined with the existing

guideline evidence to inform our recommendations. Deutetrabenazine and

valbenazine are established as effective treatments of TD (Level A) and must be

recommended as treatment. Clonazepam and Ginkgo biloba probably improve TD

(Level B) and should be considered as treatment. Amantadine and tetrabenazine

might be considered as TD treatment (Level C). Pallidal deep brain stimulation

possibly improves TD and might be considered as a treatment for intractable TD

(Level C). There is insufficient evidence to support or refute TS treatment by

withdrawing causative agents or switching from typical to atypical DRBA (Level

U).

Copyright © 2018 Elsevier B.V. All rights reserved.

DOI: 10.1016/j.jns.2018.02.010

PMID: 29454493 [Indexed for MEDLINE]

9. Handb Clin Neurol. 2013;116:167-87. doi: 10.1016/B978-0-444-53497-2.00014-0.

**Deep brain stimulation for dystonia.**

The few reported controlled studies show that bilateral stimulation of the

globus pallidus interna (GPi) is a safe and effective long-term treatment for

hyperkinetic disorders. However, the recently published data on deep brain

stimulation (DBS) applied to different targets or patients (especially those

with secondary dystonia) are mainly uncontrolled case reports, precluding a

clear determination of its efficacy, and providing little guidance as to the

choice of a "good" target in a "good" patient. This chapter reviews the

literature on DBS in primary dystonia, paying particular attention to the

risk:benefit ratio in focal and segmental dystonias (cervical dystonia, cranial

dystonia) and to the predictive factors for a good outcome. The chapter also

highlights recent data on the marked benefits of the technique in myoclonus

dystonia (in which pallidal, as opposed to thalamic, stimulation is more

effective) and in tardive dystonia-dyskinesia. Although, the decision to treat

appears relatively straightforward in patients with primary dystonia,

myoclonus-dystonia, and tardive dystonia who have a normal findings on magnetic

resonance imaging and normal cognitive function, there are still no reliable

tools to help predict the timescale of postoperative benefit. This chapter

provides a comprehensive analysis of the use of the treatment in various types

of secondary dystonia, with little to moderate benefit in most cases, based on

single cases or small series. Beyond the reduction in the severity of dystonia,

the global motor and functional outcome is difficult to determine owing to the

paucity of adequate evaluation tools. Because of the large interpatient

variability, different targets may be effective depending on the symptoms in

each individual.

© 2013 Elsevier B.V. All rights reserved.

DOI: 10.1016/B978-0-444-53497-2.00014-0

PMID: 24112893 [Indexed for MEDLINE]

10. Expert Rev Neurother. 2016 Sep;16(9):1067-78. doi: 10.1080/14737175.2016.1196139. Epub 2016 Jun 10.

**Deep brain stimulation for the treatment of hyperkinetic movement disorders.**

INTRODUCTION: Deep brain stimulation effectiveness is well recognized for

different movement disorders including Parkinson's disease, dystonia and

essential tremor, however several other diseases in this field may benefit from

the technique although experience is sparse and evidences of benefit and risks

are not established.

AREAS COVERED: In this review, we explored available evidence for effectiveness

and safety of DBS in selected hyperkinetic movement disorders, including tardive

dyskinesia, Huntington's disease, neuroacanthocytosis, myoclonus-dystonia,

Tourette syndrome, orthostatic and Holmes' tremor. Expert commentary: The data

referenced and discussed showed potential effectiveness for DBS in these

disabling and refractory diseases. On the other hand, these disorders are quite

complex and multifaceted, often composed of different movement disorders, as

well as other motor and non-motor symptoms. Therefore, the possible contribution

of DBS in improving patients' quality of life should be weighted in a strictly

individual basis, keeping in mind the progressive nature of most of these

disorders, as well as risk/benefit ratio.

DOI: 10.1080/14737175.2016.1196139

PMID: 27254274 [Indexed for MEDLINE]

11. Neurotherapeutics. 2020 Oct;17(4):1681-1693. doi: 10.1007/s13311-020-00914-6.

**Current Management of Tics and Tourette Syndrome: Behavioral, Pharmacologic, and**

**Surgical Treatments.**

Tourette syndrome is a heterogeneous neurobehavioral disorder manifested by

childhood-onset motor and phonic tics, often accompanied by a variety of

behavioral comorbidities, including attention deficit and obsessive compulsive

disorder. Treatment must be tailored to the needs and goals of the individual

patients and their families. All patients should receive education on the

condition and, if possible, engage behavioral therapy targeted towards tics

and/or comorbidities. Pharmacological therapies, such as alpha agonists,

topiramate, and vesicular monoamine transport type 2 inhibitors, are generally

used as first-line therapies in patients with troublesome tics that are not

controlled by behavioral therapy or when the latter is not available or

accessible. Botulinum toxin injections can be used in patients with bothersome

focal tics. Second-line therapy includes antipsychotics, such as fluphenazine,

aripiprazole, risperidone, and ziprasidone. These medications are generally

efficacious but carry the risk of metabolic syndrome, tardive dyskinesia, and

other side effects. Much more research is needed before novel therapies such as

cannabis-derived products or transcranial magnetic stimulation can be

recommended. There is promise in ongoing clinical trials with D1 receptor

antagonist ecopipam and other experimental therapeutics. Patients with tics that

are refractory to conventional treatments may be candidates for deep brain

stimulation, but further studies are needed to determine the optimal target

selection.

DOI: 10.1007/s13311-020-00914-6

PMCID: PMC7851278

PMID: 32856174

12. Tremor Other Hyperkinet Mov (N Y). 2015 Feb 2;5:278. doi: 10.7916/D84X56HP.

eCollection 2015.

**Uncommon applications of deep brain stimulation in hyperkinetic movement**

**disorders.**

BACKGROUND: In addition to the established indications of tremor and dystonia,

deep brain stimulation (DBS) has been utilized less commonly for several

hyperkinetic movement disorders, including medication-refractory myoclonus,

ballism, chorea, and Gilles de la Tourette (GTS) and tardive syndromes. Given

the lack of adequate controlled trials, it is difficult to translate published

reports into clinical use. We summarize the literature, draw conclusions

regarding efficacy when possible, and highlight concerns and areas for future

study.

METHODS: A Pubmed search was performed for English-language articles between

January 1980 and June 2014. Studies were selected if they focused primarily on

DBS to treat the conditions of focus.

RESULTS: We identified 49 cases of DBS for myoclonus-dystonia, 21 for

Huntington's disease, 15 for choreacanthocytosis, 129 for GTS, and 73 for

tardive syndromes. Bilateral globus pallidus interna (GPi) DBS was the most

frequently utilized procedure for all conditions except GTS, in which medial

thalamic DBS was more common. While the majority of cases demonstrate some

improvement, there are also reports of no improvement or even worsening of

symptoms in each condition. The few studies including functional or quality of

life outcomes suggest benefit. A limited number of studies included blinded

on/off testing. There have been two double-blind controlled trials performed in

GTS and a single prospective double-blind, uncontrolled trial in tardive

syndromes. Patient characteristics, surgical target, stimulation parameters, and

duration of follow-up varied among studies.

DISCUSSION: Despite these extensive limitations, the literature overall supports

the efficacy of DBS in these conditions, in particular GTS and tardive

syndromes. For other conditions, the preliminary evidence from small studies is

promising and encourages further study.

DOI: 10.7916/D84X56HP

PMCID: PMC4314611

PMID: 25713746

13. Neurol Neurochir Pol. 2016;50(2):114-22. doi: 10.1016/j.pjnns.2016.01.004. Epub

2016 Jan 16.

**Deep brain stimulation for intractable tardive dystonia: Literature overview.**

BACKGROUND: Tardive dystonia (TD) represents a side effect of prolonged intake

of dopamine receptor blocking compounds. TD can be a disabling movement disorder

persisting despite available medical treatment. Deep brain stimulation (DBS) has

been reported successful in this condition although the number of treated

patients with TD is still limited to small clinical studies or case reports. The

aim of this study was to present the systematical overview of the existing

literature regarding DBS for intractable TD.

METHODS AND RESULTS: A literature search was carried out in PudMed. Clinical

case series or case reports describing the patients with TD after DBS treatment

were included in the present overview. Literature search revealed 19 articles

reporting 59 individuals operated for TD. GPi was the target in 55 patients,

while subthalamic nucleus (STN) was the target in the remaining 4. In most

studies the motor part of Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) was

improved by more than 80% when compared to preoperative BFMDRS scores.

CONCLUSIONS: The performed literature analysis indicates that bilateral GPi DBS

is an effective treatment for disabling TD. The response of TD to bilateral GPi

DBS may be very rapid and occurs within days/weeks after the procedure. The

efficacy of bilateral GPi DBS in TD patients is comparable to results achieved

in patients with primary generalized dystonia.

Copyright © 2016 Polish Neurological Society. Published by Elsevier Urban &

Partner Sp. z o.o. All rights reserved.

DOI: 10.1016/j.pjnns.2016.01.004

PMID: 26969568 [Indexed for MEDLINE]

14. J Psychosoc Nurs Ment Health Serv. 2014 Apr;52(4):23-6. doi:

10.3928/02793695-20140324-01.

**Update on deep brain stimulation.**

Deep brain stimulation (DBS) is a commonly used neurosurgical form of

therapeutic brain stimulation that has been demonstrated to be safe, well

tolerated, and effective for the treatment of essential tremor, Parkinson's

disease, and primary dystonia. These particular uses have been approved by the

U.S. Food and Drug Administration (FDA). Investigational studies using DBS have

been conducted for refractory epilepsy, obesity, chronic pain, tardive

dyskinesia, Tourette syndrome, and other movement disorders, but none of these

studies has led to FDA approval for these indications. Although the use of DBS

has been approved by the FDA under a Humanitarian Device Exemption for the

treatment of treatment-resistant obsessive-compulsive disorder, studies

systematically investigating the potential use of DBS for various severe chronic

psychiatric disorders are in their earliest stages, and further studies are

warranted.

Copyright 2014, SLACK Incorporated.

DOI: 10.3928/02793695-20140324-01

PMID: 24702284 [Indexed for MEDLINE]

15. Handb Clin Neurol. 2013;116:209-15. doi: 10.1016/B978-0-444-53497-2.00016-4.

**Deep brain stimulation for other tremors, myoclonus, and chorea.**

Deep brain stimulation (DBS) is a well established treatment for essential

tremor and for the tremor associated with Parkinson's disease. The efficacy of

DBS in these common tremors has led some investigators to apply the technique to

rarer tremors such as such as Holmes' tremor, posttraumatic tremor, orthostatic

tremor, and the tremor associated with multiple sclerosis. Likewise, DBS of the

thalamus and globus pallidus directly suppresses levodopa-induced dyskinesias in

Parkinson's disease, suggesting the application of DBS to other hyperkinetic

states such as Huntington's disease, tardive dyskinesia, and hemiballism.

Myoclonus has also been treated with DBS, especially in cases where it is

associated with dystonia. This chapter reviews the reported results of DBS for

these conditions. Due to the rarity of these indications, most of the literature

reviewed takes the form of case reports or small single-center case series.

© 2013 Elsevier B.V. All rights reserved.

DOI: 10.1016/B978-0-444-53497-2.00016-4

PMID: 24112895 [Indexed for MEDLINE]

16. CNS Drugs. 2018 Feb;32(2):135-147. doi: 10.1007/s40263-018-0494-8.

**Tardive Dyskinesia Associated with Atypical Antipsychotics: Prevalence,**

**Mechanisms and Management Strategies.**

All antipsychotics, including the atypical antipsychotics (AAPs), may cause

tardive dyskinesia (TD), a potentially irreversible movement disorder, the

pathophysiology of which is currently unknown. The prevention and treatment of

TD remain major challenges for clinicians. We conducted a PubMed search to

review the prevalence and etiology of and management strategies for TD

associated with AAPs. TD prevalence rates varied substantially between studies,

with an estimated prevalence of around 20% in patients using AAPs. The risk of

TD is lower with AAPs than with typical antipsychotics (TAPs) but remains a

problem because AAPs are increasingly being prescribed. Important risk factors

associated with TD include the duration of antipsychotic use, age, and ethnicity

other than Caucasian. Theories about the etiology of TD include supersensitivity

of the dopamine receptors and oxidative stress, but other neurotransmitters and

factors are probably involved. Studies concerning the management of TD have

considerable methodological limitations. Thus, recommendations for the

management of TD are based on a few trials and clinical experience, and no

general guidelines for the management of TD can be established. The best

management strategy remains prevention. Caution is required when prescribing

antipsychotics, and regular screening is needed for early detection of TD. Other

strategies may include reducing the AAP dosage, switching to clozapine, or

administering vesicular monoamine transporter (VMAT)-2 inhibitors. In severe

cases, local injections of botulinum toxin or deep brain stimulation may be

considered. More clinical trials in larger samples are needed to gather valid

information on the effect of interventions targeting TD.

DOI: 10.1007/s40263-018-0494-8

PMID: 29427000 [Indexed for MEDLINE]

17. Eur J Neurol. 2018 Mar;25(3):434-e30. doi: 10.1111/ene.13548. Epub 2018 Feb 1.

**Potential indications for deep brain stimulation in neurological disorders: an**

**evolving field.**

Deep brain stimulation (DBS) is an established therapy for appropriately

selected patients with movement disorders and neuropsychiatric conditions.

Although the exact mechanisms and biology of DBS are not fully understood, it is

a safe and well-tolerated therapy for many refractory cases of neuropsychiatric

disease. Increasingly, DBS has been explored in other conditions with

encouraging results. In this paper, available data is reviewed and new DBS

targets, challenges and future directions in neurological disorders are

explored. A detailed search of the medical literature discussing the potential

use of DBS for neurological disorders excluding accepted indications was

conducted. All reports were analyzed individually for content and redundant

articles were excluded by examining individual abstracts. The level of evidence

for each indication was summarized. Multiple studies report promising

preliminary data regarding the safety and efficacy of DBS for a variety of

neurological indications including chronic pain, tinnitus, epilepsy, Tourette

syndrome, Huntington's disease, tardive dyskinesia and Alzheimer's disease. The

initial results of DBS studies for diverse neurological disorders are

encouraging but larger, controlled, prospective, homogeneous clinical trials are

necessary to establish long-term safety and effectiveness. The field of

neuromodulation continues to evolve and advances in DBS technology, stereotactic

techniques, neuroimaging and DBS programming capabilities are shaping the

present and future of DBS research and use in practice.

© 2017 EAN.

DOI: 10.1111/ene.13548

PMID: 29266596 [Indexed for MEDLINE]

18. Int Rev Neurobiol. 2011;98:187-210. doi: 10.1016/B978-0-12-381328-2.00008-0.

**Tardive dyskinesia: clinical presentation and treatment.**

Tardive dyskinesia (TD) is a common and potentially irreversible side effect of

dopamine blocking agents, most often antipsychotics. It is often socially and

sometimes also physically disabling. The clinical picture can be divided into

orofacial, limb-truncal, and respiratory dyskinesia. The clinical options to

prevent or mitigate TD include psychoeducation, systematic screening, and

evaluation of the need for antipsychotics and/or dosages, managementof known

risk factors, and switching to an antipsychotic with a lower risk of TD. There

is no evidence-based approach for treating existing TD but several clinical

interventions can be effective including discontinuing the antipsychotics or

reducing the dosage, switching to clozapine, adding an antidyskinetic agent, or

applying deep brain stimulation.

Copyright © 2011 Elsevier Inc. All rights reserved.

DOI: 10.1016/B978-0-12-381328-2.00008-0

PMID: 21907088 [Indexed for MEDLINE]

19. Handb Clin Neurol. 2013;116:189-208. doi: 10.1016/B978-0-444-53497-2.00015-2.

**Role of deep brain stimulation in the treatment of secondary dystonia-dyskinesia**

**syndromes.**

Dystonia-dyskinesia syndromes (DDS) are severe disabling movement disorders,

characterized by twisting and repetitive movements or abnormal postures.

Movement disorders are differentiated as primary or secondary. Primary movement

disorders are of genetic or idiopathic origin, whereas secondary forms result

from exogenous injuries. A PubMed literature search identified 32 clinical

research studies reporting on a total of 153 patients with secondary dystonia

treated with deep brain stimulation. For 116 patients, the mean

Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) score improved by 49%. The

greatest mean BFMDRS improvement was achieved for tardive dyskinesia. The

majority of patients were implanted in the globus pallidus. Fewer patients

received thalamic or subthalamic nucleus stimulation. Electrical neuromodulation

of subcortical structures can be very useful for a small number of patients with

movement disorders due to a structural damage of the brain.

© 2013 Elsevier B.V. All rights reserved.

DOI: 10.1016/B978-0-444-53497-2.00015-2

PMID: 24112894 [Indexed for MEDLINE]

20. Surg Neurol Int. 2020 Dec 16;11:444. doi: 10.25259/SNI\_723\_2020. eCollection

2020.

**Resolution of tardive tremor after bilateral subthalamic nucleus deep brain**

**stimulation placement.**

BACKGROUND: Tardive tremor (TT) is an underrecognized manifestation of tardive

syndrome (TS). In our experience, TT is a rather common manifestation of TS,

especially in a setting of treatment with aripiprazole, and is a frequent cause

of referrals for the evaluation of idiopathic Parkinson disease. There are

reports of successful treatment of tardive orofacial dyskinesia and dystonia

with deep brain stimulation (DBS) using globus pallidus interna (GPi) as the

primary target, but the literature on subthalamic nucleus (STN) DBS for tardive

dyskinesia (TD) is lacking. To the best of our knowledge, there are no reports

on DBS treatment of TT.

CASE DESCRIPTION: A 75-year-old right-handed female with the medical history of

generalized anxiety disorder and major depressive disorder had been treated with

thioridazine and citalopram from 1980 till 2010. Around 2008, she developed

orolingual dyskinesia. She was started on tetrabenazine in June 2011. She

continued to have tremors and developed Parkinsonian gait, both of which

worsened overtime. She underwent DBS placement in the left STN in January 2017

with near-complete resolution of her tremors. She underwent right STN

implantation in September 2017 with similar improvement in symptoms.

CONCLUSION: While DBS-GPi is the preferred treatment in treating oral TD and

dystonia, DBS-STN could be considered a safe and effective target in patients

with predominating TT and/or tardive Parkinsonism. This patient saw a marked

improvement in her symptoms after implantation of DBS electrodes, without

significant relapse or recurrence in the years following implantation.

Copyright: © 2020 Surgical Neurology International.

DOI: 10.25259/SNI\_723\_2020

PMCID: PMC7771401

PMID: 33408929

21. Arch Gen Psychiatry. 2007 Feb;64(2):170-6. doi: 10.1001/archpsyc.64.2.170.

**Bilateral deep brain stimulation of the globus pallidus to treat tardive**

**dyskinesia.**

CONTEXT: Tardive dyskinesia (TD) is a common and potentially disabling disorder

induced by use of antipsychotic drugs for which medical treatment often gives

disappointing results.

OBJECTIVE: To assess the efficacy of bilateral deep brain stimulation of the

internal part of the globus pallidus to treat severe TD.

DESIGN: Prospective phase 2 multicenter study.

SETTING: Six French university hospitals. Patients Patients with severe TD

refractory to medical treatment were studied to evaluate the severity of

abnormal involuntary movements before and after 6 months of bilateral globus

pallidus deep brain stimulation. A 2-step open Fleming procedure was used to

avoid unnecessary accrual of patients. A successful outcome was defined as a

decrease of more than 40% in the main outcome measure at 6 months. The early

stopping rule was invoked if the number of successful outcomes in 10 patients

was fewer than 2, or 5 or more. A double-blind evaluation in the presence and

absence of stimulation was performed at 6 months after surgery. Main Outcome

Measure Change in score on the Extrapyramidal Symptoms Rating Scale.

RESULTS: At 6 months after surgery, the Extrapyramidal Symptoms Rating Scale

score had decreased compared with baseline by more than 40% (mean improvement,

61%; range, 44%-75%) in the first 10 patients included. In accord with the

2-step open Fleming procedure, we ended the trial at the first step and

concluded that pallidal stimulation is an effective treatment for TD. The

efficacy of the treatment was confirmed by a double-blind evaluation, with a

mean decrease of 50% (range, 30%-66%) (P = .002) in the Extrapyramidal Symptoms

Rating Scale score when stimulation was applied compared with the absence of

stimulation. There were no marked changes in the patients' psychiatric status.

CONCLUSION: Although these results need to be confirmed in a larger group of

patients with a longer follow-up, bilateral globus pallidus deep brain

stimulation seems to offer a much-needed new treatment option for disabling TD.

DOI: 10.1001/archpsyc.64.2.170

PMID: 17283284 [Indexed for MEDLINE]

22. Brain Stimul. 2018 Nov-Dec;11(6):1368-1377. doi: 10.1016/j.brs.2018.08.006. Epub

2018 Sep 11.

\*\*Duplicate from other search\*\*

**Neurostimulation in tardive dystonia/dyskinesia: A delayed start, sham**

**stimulation-controlled randomized trial.**

INTRODUCTION: Growing evidence suggests that pallidal deep brain stimulation

represents a potential new therapeutic avenue in tardive dystonia/dyskinesia,

but controlled and blinded randomized studies (RCT) are missing. The present RCT

compares dystonia/dyskinesia severity of pallidal neurostimulation in patients

with tardive dystonia using a delayed-start design paradigm.

METHODS: Dystonia/dyskinesia severity was assessed via blinded videos following

pallidal neurostimulation at 3 (blinded phase) and 6 months (open extension

phase). Primary endpoint was the percentage change of dystonia severity

(Burke-Fahn-Marsden-Dystonia-Rating-Scale, BFMDRS) at 3 months between active

vs. sham neurostimulation using blinded-video assessment. Secondary endpoints

comprised clinical rating scores for movement disorders. Clinicaltrials.gov

NCT00331669.

RESULTS: Twenty-five patients were randomized (1:1) to active (n = 12) or sham

neurostimulation (n = 13). In the intention-to-treat analyses the between group

difference of dystonia severity (BFMDRS) between active vs. sham stimulation was

not significant at 3 months. Three months post-randomisation dystonia severity

improved significantly within the neurostimulation by 22.8% and

non-significantly within the sham group (12.0%) compared to their respective

baseline severity. During the open-label extension with both groups being

actively treated, significant and pronounced improvements of 41.5% were observed

via blinded evaluation. Adverse events (n = 10) occurred in 10/25 of patients

during the 6 months, mostly related to surgical implantation of the device; all

resolved without sequelae.

CONCLUSION: The primary endpoint of this randomized trial was not significant,

most likely due to incomplete recruitment. However, pronounced improvements of

most secondary endpoints at 3 and 6 months provide evidence for efficacy and

safety of pallidal neurostimulation in tardive dystonia.

Copyright © 2018 Elsevier Inc. All rights reserved.

DOI: 10.1016/j.brs.2018.08.006

PMID: 30249417 [Indexed for MEDLINE]

23. Neurology. 2016 Feb 16;86(7):651-9. doi: 10.1212/WNL.0000000000002370. Epub 2016

Jan 20.

\*\*Duplicate\*\*

**Long-term efficacy and tolerability of bilateral pallidal stimulation to treat**

**tardive dyskinesia.**

OBJECTIVE: To confirm the efficacy and safety of deep brain stimulation (DBS) of

the internal part of the globus pallidus in improving severe tardive dyskinesia

(TD).

METHODS: Nineteen patients with severe pharmacoresistant TD were included. All

were assessed at baseline and at 3, 6 (main outcome measure), and 12 months, and

in the long term (6-11 years) for 14 patients, after bilateral pallidal DBS,

using motor scales (Extrapyramidal Symptoms Rating Scale [ESRS], Abnormal

Involuntary Movement Scale [AIMS]), cognitive scales, and a psychiatric

assessment. At 6 months, a double-blind ESRS evaluation was performed in the

stimulation "on" and stimulation "off" conditions.

RESULTS: At 6 months, all patients had a decrease of more than 40% on the ESRS.

The efficacy of the procedure was confirmed by a double-blind evaluation. This

improvement was maintained at 12 months (ESRS: decrease of 58% [21%-81%];

AIMS: decrease of 50% [7%-77%]) and in the long term (ESRS: decrease of 60%

[22%-90%];

AIMS: decrease of 63% [14%-94%], n = 14). All the subscores of the ESRS

(parkinsonism, dystonia, and chorea) and of the AIMS (facial, oral, extremities,

and trunk movements) improved. Despite psychiatric comorbidities at baseline,

cognitive and psychiatric tolerability of the procedure was excellent. No

cognitive decline was observed and mood was improved in most of the patients.

CONCLUSIONS: Pallidal DBS procedure should be considered as a therapeutic option

in disabling TD refractory to medical treatment.

CLASSIFICATION OF EVIDENCE: This study provides Class II evidence that in

patients with severe pharmacoresistant TD with implanted pallidal leads, the

stimulation "on" condition significantly improved ESRS scores compared to the

stimulation "off" condition.

© 2016 American Academy of Neurology.

DOI: 10.1212/WNL.0000000000002370

PMID: 26791148 [Indexed for MEDLINE]

24. Front Psychiatry. 2016 Dec 26;7:207. doi: 10.3389/fpsyt.2016.00207. eCollection

2016.

**Therapeutic Perspective on Tardive Syndrome with Special Reference to Deep Brain**

**Stimulation.**

Tardive syndrome (TDS) is a potentially permanent and irreversible hyperkinetic

movement disorder caused by exposure to dopamine receptor blocking agents.

Guidelines published by the American Academy of Neurology recommend

pharmacological first-line treatment for TDS with clonazepam (level B), ginkgo

biloba (level B), amantadine (level C), and tetrabenazine (level C). Recently, a

class II study provided level C evidence for use of deep brain stimulation (DBS)

of the globus pallidus internus (GPi) in patients with TDS. Although the precise

pathogenesis of TDS remains to be elucidated, the beneficial effects of GPi-DBS

in patients with TDS suggest that the disease may be a basal ganglia disorder.

In addition to recent advances in understanding the pathophysiology of TDS, this

article introduces the current use of DBS in the treatment of medically

intractable TDS.

DOI: 10.3389/fpsyt.2016.00207

PMCID: PMC5183634

PMID: 28082923

25. Parkinsonism Relat Disord. 2017 Aug;41:58-65. doi:

10.1016/j.parkreldis.2017.05.010. Epub 2017 May 19.

\*\*Duplicate from other search\*\*

**Long-term follow-up of bilateral subthalamic deep brain stimulation for**

**refractory tardive dystonia.**

BACKGROUND: No effective treatment for tardive dystonia (TD) has been well

established. Deep brain stimulation (DBS) can ameliorate motor manifestations in

primary dystonia, and may also be an effective approach for TD.

OBJECTIVES: This study aimed to illuminate the long-term efficacy and safety of

subthalamic nucleus (STN)-DBS in treating TD.

METHODS: Ten patients with refractory TD underwent STN-DBS therapy and were

assessed by the Burke-Fahn-Marsden dystonia rating scale (BFMDRS), Abnormal

Involuntary Movement Scale (AIMS), Hamilton Depression Scale (HAMD), Hamilton

Anxiety Scale (HAMA), and the Short Form (36) Health Survey (SF-36) at four time

points: pre-operation, 1 week post-operation, 6 months post-operation, and at a

final long-term postsurgical follow-up time point.

RESULTS: The mean follow-up time was 65.6 ± 30.4 months (range, 12-105 months).

At the first follow-up, BFMDRS motor and disability scores had improved by

55.9± 28.3% and 62.6± 32.0%, respectively, while AIMS scores improved by

53.3± 26.7%. At the second follow-up, BFMDRS motor and disability scores

improved further, by 87.3± 17.0% and 84.3% ± 22.9%, respectively, while AIMS

scores improved by 88.4 ± 16.1%. At the last follow-up, this benefit was

sustained and had plateaued. Quality of life was improved significantly at the

long-term follow-up, and the HAMA and HAMD scores displayed a significant

reduction that persisted after the first follow-up.

CONCLUSION: STN-DBS may be an effective and acceptable procedure for TD, leading

to persistent and significant improvement in both movement and psychiatric

symptoms.

Copyright © 2017 Elsevier Ltd. All rights reserved.

DOI: 10.1016/j.parkreldis.2017.05.010

PMID: 28552340 [Indexed for MEDLINE]

26. Neuromodulation. 2006 Oct;9(4):253-61. doi: 10.1111/j.1525-1403.2006.00067.x.

**Deep brain stimulation for dystonia: a meta-analysis.**

Objective.  To use a meta-analysis on all reported cases of deep brain

stimulation (DBS) for dystonia to determine which factors significantly

influence outcome. The Burke-Fahn-Marsden (BFM) movement scale, the most

reported measure, was chosen as the primary outcome measure for this analysis.

Methods.  A MEDLINE search identified 137 patients who underwent DBS for

dystonia in 24 studies that had individual BFM scores. Individual patient data,

including age at onset of dystonia, age at surgery, gender, distribution of

dystonia, etiology of dystonia, presence of associated features, abnormality of

preoperative imaging, prior stereotactic surgeries, nucleus stimulated, type of

anesthesia used, use of physiologic monitoring, type of imaging used for

localization, stimulation parameters used, time of response to stimulation, and

timing of outcome assessment were entered into an SPSS database for statistical

analysis. Results.  The mean BFM percentage change (improvement in postoperative

score from baseline) was 51.8% (range -34% to 100%). Significantly better

outcomes were achieved with stimulation of the globus pallidus internus (GPi)

than with stimulation of the posterior portion of the ventral lateral (VLp)

nucleus of the thalamus (p = 0.0001). The etiology of the dystonia also had a

significant effect on outcomes. Statistically significant improvements in

outcomes were seen for all etiologic categories, except encephalitis. Dystonia

due to birth injury and encephalitis had significantly worse outcomes when

compared to other etiologies. However, there were no significant differences in

the outcomes of patients who were DYT1 (DYT1 is the gene associated with the

disorder Dystonia Musculorum Deformans) gene positive, DYT1 gene negative, or

had pantothenate kinase-associated neurodegeneration (PKAN), tardive dyskinesia,

and idiopathic and posttraumatic dystonias. Longer duration of dystonia symptoms

correlated negatively with surgical outcome. A regression model using the three

variables-stimulation site, etiology of dystonia, and duration of dystonia

symptoms-explained 51% of the variance in outcomes. Conclusion.  Deep brain

stimulation of the GPi provides significant improvement in BFM scores in a

variety of dystonic conditions.

DOI: 10.1111/j.1525-1403.2006.00067.x

PMID: 22151759

27. J Neurol Neurosurg Psychiatry. 2018 Jul;89(7):777-787. doi:

10.1136/jnnp-2017-316946. Epub 2017 Dec 14.

**Approaches to neuromodulation for schizophrenia.**

Based on the success of deep brain stimulation (DBS) for treating movement

disorders, there is growing interest in using DBS to treat schizophrenia (SZ).

We review the unmet needs of patients with SZ and the scientific rationale

behind the DBS targets proposed in the literature in order to guide future

development of DBS to treat this vulnerable patient population. SZ remains a

devastating disorder despite treatment. Relapse, untreated psychosis,

intolerable side effects and the lack of effective treatment for negative and

cognitive symptoms contribute to poor outcome. Novel therapeutic interventions

are needed to treat SZ and DBS is emerging as a potential intervention.

Convergent genetic, pharmacological and neuroimaging evidence implicating

neuropathology associated with psychosis is consistent with SZ being a circuit

disorder amenable to striatal modulation with DBS. Many of the DBS targets

proposed in the literature may modulate striatal dysregulation. Additional

targets are considered for treating tardive dyskinesia and negative and

cognitive symptoms. A need is identified for the concurrent development of

neurophysiological biomarkers relevant to SZ pathology in order to inform DBS

targeting. Finally, we discuss the current clinical trials of DBS for SZ, and

their ethical considerations. We conclude that patients with severe symptoms

despite treatment must have the capacity to consent for a DBS clinical trial in

which risks can be estimated, but benefit is not known. In addition, psychiatric

populations should have access to the potential benefits of neurosurgical

advances.

DOI: 10.1136/jnnp-2017-316946

PMID: 29242310 [Indexed for MEDLINE]

28. Drugs. 2016 May;76(7):779-87. doi: 10.1007/s40265-016-0568-1.

**Drug-Induced Dyskinesia, Part 2: Treatment of Tardive Dyskinesia.**

Dyskinesias encompass a variety of different hyperkinetic phenomenologies,

particularly chorea, dystonia, stereotypies, and akathisia. The main types of

drug-induced dyskinesias include levodopa-induced dyskinesia (LID) in patients

with Parkinson's disease and tardive syndrome (TS), typically present in

patients with psychiatric or gastrointenstinal disorders treated with dopamine

receptor blocking drugs, also referred to as neuroleptics. Besides preventive

measures (i.e., avoiding the use of the offending drugs), general treatment

strategies include slow taper of the offending agent and use of

dopamine-depleting agents like tetrabenazine. Botulinum toxin may be helpful for

wearing off focal dystonia and some forms of tardive dystonia. Deep brain

stimulation is usually reserved for patients with disabling motor fluctuations,

LID, and for severe TS that cannot be managed medically.

DOI: 10.1007/s40265-016-0568-1

PMID: 27091214 [Indexed for MEDLINE]

29. Curr Opin Neurol. 2009 Aug;22(4):394-9. doi: 10.1097/WCO.0b013e32832d9dc4.

**Drug-induced dyskinesias.**

PURPOSE OF REVIEW: Recent studies have improved our knowledge of the factors

responsible for the development of dyskinesias in Parkinson's disease and the

associated pathophysiology. Deep brain stimulation has been shown to be

effective to treat severe tardive dyskinesias. This review highlights some

recent findings related to levodopa-induced and antipsychotic-induced

dyskinesias.

RECENT FINDINGS: The reported advantage of using a dopamine agonist as an

initial treatment to prevent the development of dyskinesias in Parkinson's

disease appears to be less evident after a long-term follow-up. Other factors,

related to the etiopathogenesis of Parkinson's disease or to patients'

endophenotypes, are beginning to be identified. Several brain changes have been

found to be associated with levodopa-induced dyskinesias. PET studies have

evidenced an increased level of synaptic dopamine in the striatum.

Neurophysiological studies have suggested that dyskinesias might reflect

abnormal skill memorization processes within the cortico-subcortical loops. A

dysfunction of the mechanisms trying to compensate for dopamine deficiency and

its brain consequences could be responsible for these changes induced by the

dopaminergic treatment. Bilateral pallidal stimulation has been shown to be an

effective and safe treatment for severe tardive dyskinesias.

SUMMARY: These findings will improve future strategies to prevent and treat

Parkinson's disease dyskinesias and offer a much needed treatment for severe

tardive dyskinesias.

DOI: 10.1097/WCO.0b013e32832d9dc4

PMID: 19491677 [Indexed for MEDLINE]

30. Int Rev Neurobiol. 2011;98:289-96. doi: 10.1016/B978-0-12-381328-2.00012-2.

**Surgery for tardive dyskinesia.**

Tardive dyskinesia (TD) is an often bothersome side effect of antipsychotic

treatment. Medical treatment options are usually disappointing. A few single

case reports have suggested some efficacy of lesionning surgery (i.e.

pallidotomy or thalamotomy). A much greater number of series (including one

controlled-study) have assessed the effects of deep brain stimulation applied to

the internal globus pallidus. All of them have shown a marked improvement of

motor symptoms without any major psychiatric side effects.

Copyright © 2011 Elsevier Inc. All rights reserved.

DOI: 10.1016/B978-0-12-381328-2.00012-2

PMID: 21907092 [Indexed for MEDLINE]

31. J Psychiatr Res. 2007 Nov;41(9):801-3. doi: 10.1016/j.jpsychires.2006.07.010.

Epub 2006 Sep 8.

**Mood improvement after deep brain stimulation of the internal globus pallidus**

**for tardive dyskinesia in a patient suffering from major depression.**

Deep brain stimulation (DBS) has the unique characteristic to very precisely

target brain structures being part of functional brain circuits in order to

reversibly modulate their function. It is an established adjunctive treatment of

advanced Parkinson's disease and has virtually replaced ablative techniques in

this indication. Several cases have been published relating effectiveness in

neuroleptics-induced tardive dyskinesia. It is also investigated as a potential

treatment of mood disorders. We report on the case of a 62 years old female

suffering from a treatment refractory major depressive episode with comorbid

neuroleptic-induced tardive dyskinesia. She was implanted a deep brain

stimulation treatment system bilaterally in the globus pallidus internus and

stimulated for 18 months. As well the dyskinesia as also the symptoms of

depression improved substantially as measured by the Hamilton Rating Scale of

Depression (HRSD) score and the Burke-Fahn-Marsden-Dystonia-Rating-Scale

(BFMDRS) score. Scores dropped for HRSD from 26 at baseline preoperatively to 13

after 18 months; and for BFMDRS from 27 to 17.5. This case illustrates the

potential of deep brain stimulation as a technique to be investigated in the

treatment of severe and disabling psychiatric and movement disorders. DBS at

different intracerebral targets being actually investigated for major depression

might have similar antidepressant properties because they interact with the same

cortico-basal ganglia-thalamocortical network found to be dysfunctional in major

depression.

DOI: 10.1016/j.jpsychires.2006.07.010

PMID: 16962613 [Indexed for MEDLINE]

32. J Neurosci. 2012 Jul 11;32(28):9574-81. doi: 10.1523/JNEUROSCI.1196-12.2012.

**Contribution of decreased serotonin release to the antidyskinetic effects of**

**deep brain stimulation in a rodent model of tardive dyskinesia: comparison of**

**the subthalamic and entopeduncular nuclei.**

Mechanisms whereby deep brain stimulation (DBS) of the subthalamic nucleus (STN)

or internal globus pallidus (GPi) reduces dyskinesias remain largely unknown.

Using vacuous chewing movements (VCMs) induced by chronic haloperidol as a model

of tardive dyskinesia (TD) in rats, we confirmed the antidyskinetic effects of

DBS applied to the STN or entopeduncular nucleus (EPN, the rodent homolog of the

GPi). We conducted a series of experiments to investigate the role of serotonin

(5-HT) in these effects. We found that neurotoxic lesions of the dorsal raphe

nuclei (DRN) significantly decreased HAL-induced VCMs. Acute 8-OH-DPAT

administration, under conditions known to suppress raphe neuronal firing, also

reduced VCMs. Immediate early gene mapping using zif268 in situ hybridization

revealed that STN-DBS inhibited activity of DRN and MRN neurons. Microdialysis

experiments indicated that STN-DBS decreased 5-HT release in the dorsolateral

caudate-putamen, an area implicated in the etiology of HAL-induced VCMs. DBS

applied to the EPN also suppressed VCMs but did not alter 5-HT release or raphe

neuron activation. While these findings suggested a role for decreased 5-HT

release in the mechanisms of STN DBS, further microdialysis experiments showed

that when the 5-HT lowering effects of STN DBS were prevented by pretreatment

with fluoxetine or fenfluramine, the ability of DBS to suppress VCMs remained

unaltered. These results suggest that EPN- and STN-DBS have different effects on

the 5-HT system. While decreasing 5-HT function is sufficient to suppress

HAL-induced VCMs, 5-HT decrease is not necessary for the beneficial motor

effects of DBS in this model.

DOI: 10.1523/JNEUROSCI.1196-12.2012

PMCID: PMC6622267

PMID: 22787043 [Indexed for MEDLINE]

33. Mov Disord. 2004 May;19(5):583-5. doi: 10.1002/mds.10705.

**Unilateral deep brain stimulation of the internal globus pallidus alleviates**

**tardive dyskinesia.**

We describe a patient with fluspirilene-induced tardive dyskinesia of the

choreiform oro-facial-laryngeal type resistant to various conservative

approaches for 7 years who underwent deep brain stimulation of the internal

pallidal globe. We found immediate and marked suppression of her perioral

involuntary movements with unilateral stimulation at 60 Hz.

Copyright 2003 Movement Disorder Society

DOI: 10.1002/mds.10705

PMID: 15133825 [Indexed for MEDLINE]

34. Eur Neuropsychopharmacol. 2011 May;21(5):393-400. doi:

10.1016/j.euroneuro.2010.06.012. Epub 2010 Jul 10.

**Deep brain stimulation of the subthalamic or entopeduncular nucleus attenuates**

**vacuous chewing movements in a rodent model of tardive dyskinesia.**

Deep brain stimulation (DBS) has recently emerged as a potential intervention

for treatment-resistant tardive dyskinesia (TD). Despite promising case reports,

no consensus exists as yet regarding optimal stimulation parameters or

neuroanatomical target for DBS in TD. Here we report the use of DBS in an animal

model of TD. We applied DBS (100 μA) acutely to the entopeduncular nucleus (EPN)

or subthalamic nucleus (STN) in rats with well established vacuous chewing

movements (VCMs) induced by 12 weeks of haloperidol (HAL) treatment. Stimulation

of the STN or EPN resulted in significant reductions in VCM counts at

frequencies of 30, 60 or 130 Hz. In the STN DBS groups, effects were

significantly more pronounced at 130 Hz than at lower frequencies, whereas at

the EPN the three frequencies were equipotent. Unilateral stimulation at 130 Hz

was also effective when applied to either nucleus. These results suggest that

stimulation of either the EPN or STN significantly alleviates oral dyskinesias

induced by chronic HAL. The chronic HAL VCM model preparation may be useful to

explore mechanisms underlying DBS effects in drug-induced dyskinesias.

Copyright © 2010 Elsevier B.V. All rights reserved.

DOI: 10.1016/j.euroneuro.2010.06.012

PMID: 20624675 [Indexed for MEDLINE]

35. Parkinsonism Relat Disord. 2014 Jan;20 Suppl 1:S113-7. doi:

10.1016/S1353-8020(13)70028-2.

**Tardive dyskinesia syndromes: current concepts.**

Tardive syndromes (TS) encompass a broad spectrum of abnormal movements due to

chronic exposure to dopamine receptor blocking agents. This review provides a

compiled update on TS, including phenomenology, epidemiology, pathophysiology,

genetic correlations and therapeutics, highlighting the emerging experience with

atypical antipsychotics. The advent of atypical antipsychotics, which have lower

affinity for dopamine receptors and act on 5-HT2A and 5-HT2C serotonin

receptors, was expected to dramatically reduce the prevalence and incidence of

this iatrogenic problem. Recent studies have shown that the reduction has been

more modest than expected and TS remains an important challenge. Recent insights

on pathophysiology, risk factors and genetic correlations have raised the hope

for further individualized treatment for schizophrenic patients, and more strict

use of antipsychotics. Up to now, there is no definite treatment for TS, but

options range from relatively innocuous low doses of propranolol to more

invasive procedures such as deep brain stimulation.

Copyright © 2013 Elsevier Ltd. All rights reserved.

DOI: 10.1016/S1353-8020(13)70028-2

PMID: 24262160 [Indexed for MEDLINE]

36. Expert Rev Neurother. 2017 Sep;17(9):883-894. doi:

10.1080/14737175.2017.1361322. Epub 2017 Aug 3.

**Antipsychotic-induced Tardive dyskinesia: from biological basis to clinical**

**management.**

Tardive dyskinesia (TD) is a chronic and disabling movement disorder with a

complex pathophysiological basis. A significant percentage of patients does not

receive correct diagnosis, resulting in delayed or inaccurate treatment and poor

outcome. Therefore, there is a critical need for prompt recognition,

implementation of efficacious treatment regimens and long-term follow up of

patients with TD. Areas covered: The current paper provides an overview of

emerging data concerning proposed pathophysiology theories, epidemiology, risk

factors, and therapeutic strategies for TD. Expert commentary: Despite

considerable research efforts, TD remains a challenge in the treatment of

psychosis as the available strategies remain sub-optimal. The best scenario will

always be the prophylaxis or prevention of TD, which entails limiting the use of

antipsychotics.

DOI: 10.1080/14737175.2017.1361322

PMID: 28750568 [Indexed for MEDLINE]

37. Rev Neurosci. 2013;24(2):153-66. doi: 10.1515/revneuro-2012-0083.

**The role of serotonin in the antidyskinetic effects of deep brain stimulation:**

**focus on antipsychotic-induced motor symptoms.**

Treatment with the classic antipsychotic drugs (APDs), such as haloperidol

(HAL), is associated with both acute and chronic motor side effects. Acutely,

these drugs may induce extrapyramidal symptoms, whereas a prolonged treatment

may result in tardive dyskinesia (TD). Atypical antipsychotics have a lower

incidence of motor side effects, which have been partially ascribed to the

antagonism of serotonin (5-HT) receptors. Although there is currently no

satisfactory pharmacotherapy for TD, deep brain stimulation (DBS) has emerged as

a promising therapy. However, the mechanisms underlying its effects remain

largely unknown. DBS has been shown to affect several neurotransmitter systems,

including 5-HT. In this review, we outline the involvement of 5-HT in the

development of HAL-induced catalepsy and TD. We also discuss the evidence for

DBS-induced alterations in 5-HT function and the relevance of serotonergic

alterations to the antidyskinetic effects of DBS. The evidence suggests that the

serotonergic mechanisms may be involved in the acute and chronic motor side

effects of APDs as well as in adverse psychiatric effects that have been

reported following DBS. However, the current evidence suggests that 5-HT

alterations do not play an important role in the effectiveness of DBS in models

of dyskinesias induced by chronic APDs.

DOI: 10.1515/revneuro-2012-0083

PMID: 23399586 [Indexed for MEDLINE]

38. Postgrad Med J. 2011 Feb;87(1024):132-41. doi: 10.1136/pgmj.2010.103234. Epub

2010 Dec 3.

**Spectrum of tardive syndromes: clinical recognition and management.**

Tardive syndrome (TS) refers to a group of delayed onset disorders characterised

by abnormal movements and caused by dopamine receptor blocking agents (DRBAs).

Classical tardive dyskinesia is a specific type of oro-buccal-lingual

dyskinesia. However, TS may exist in other forms--for example, stereotypy,

dystonia, and akathisia--and frequently occur in combination. The onset

typically is insidious and after reaching its maximum severity it often

stabilises. Frequently reported risk factors are age, dose and duration of

neuroleptic exposure, the use of conventional DRBAs, and co-existing mood

disorders. This review highlights the broad spectrum of TS, not limited to

classical tardive dyskinesia, as well as the clues for its recognition. Despite

challenges in the treatment of TS, dictated by the different phenomenology,

severity of TS and the need for ongoing neuroleptic treatment, the authors

provide evidence based recommendations for patient management, which is not

restricted to only withdrawal of the offending neuroleptics or the selection of

an alternative medication, such as clozapine. In a minority of cases with

significant functional disability, symptomatic or suppressive treatments should

be considered. Recently, there has been a resurgence of stereotactic pallidal

surgery for the treatment of TS. Although the efficacy of both pallidotomy and

pallidal deep brain stimulation in dystonia has been encouraging, the evidence

is still limited.

DOI: 10.1136/pgmj.2010.103234

PMID: 21131613 [Indexed for MEDLINE]

39. Acta Neurol Scand. 2009 Apr;119(4):269-73. doi:

10.1111/j.1600-0404.2008.01115.x. Epub 2008 Oct 25.

**A double-blind study on a patient with tardive dyskinesia treated with pallidal**

**deep brain stimulation.**

BACKGROUND: Tardive dyskinesia (TD) is a neurological disorder typically induced

by long-term exposure to neuroleptics. Deep brain stimulation (DBS) of the

globus pallidus internus (GPi) may represent a therapeutic alternative for TD,

which is often resistant to conservative treatment.

AIMS OF THE STUDY: This report's objective is to present a case of TD

successfully treated with DBS, as well as to indicate a putative role of brain

perfusion scintigraphy as a helpful tool correlating functional imaging findings

with clinical responsiveness to DBS.

METHODS/RESULTS: A 42-year-old male patient suffering from refractory TD

underwent bilateral GPi DBS surgery. Post-operative Burke-Fahn-Mardsen Dystonia

Rating Scale (BFMDRS) and Abnormal Involuntary Movement Scale (AIMS) total

scores have been reduced by 90.7% and 76.7% respectively on the 6-month

follow-up assessment. Brain perfusion scintigraphy, performed post-operatively

in the two stimulation states, revealed a decrease in cerebral blood flow,

during the 'on-DBS', compared with the 'off-DBS' state.

CONCLUSIONS: Clinical improvement of this patient, correspondent to previous

studies, suggests that continuous bilateral GPi DBS may provide a promising

treatment option for TD. Furthermore, this report could imply, as no previous

such comparison study exists, a possible correlation between brain functional

imaging findings and the movement disorder's response to DBS.

DOI: 10.1111/j.1600-0404.2008.01115.x

PMID: 18976318 [Indexed for MEDLINE]

40. Neurol Neurochir Pol. 2016 Jul-Aug;50(4):258-61. doi:

10.1016/j.pjnns.2016.04.006. Epub 2016 Apr 26.

\*\*Duplicate of other search\*\*

**Deep brain stimulation of the internal globus pallidus for disabling**

**haloperidol-induced tardive dystonia. Report of two cases.**

AIM: Tardive dystonia (TD) represents a side effect of prolonged intake of

neuroleptic drugs. TD can be a disabling movement disorder persisting despite

available medical treatment. Deep brain stimulation (DBS) has been reported

successful in this condition although the number of treated patients with TD is

still limited to small clinical studies or case reports. In this study, we

present 2 additional cases of patients after bilateral globus pallidus internus

(GPi) stimulation.

METHODS: The formal assessment included the Burke-Fahn-Dystonia Rating Scale

(BFMDRS). The preoperative and postoperative functional and motor parts of this

scale were compared in each patient. The postoperative assessments were done

every 6 months.

RESULTS: Both patients underwent successful bilateral GPi DBS for TD. The

postoperative motor score improved by 78% at 24 months in patient 1 and 69% at

12 months in patient 2. There were no surgical or hardware-related complications

over follow-up period.

CONCLUSION: Our experience indicates that bilateral GPi DBS can be an effective

treatment for disabling TD. The response of TD to bilateral GPi DBS is very

rapid and occurs within days after the procedure.

Copyright © 2016 Polish Neurological Society. Published by Elsevier Urban &

Partner Sp. z o.o. All rights reserved.

DOI: 10.1016/j.pjnns.2016.04.006

PMID: 27375139 [Indexed for MEDLINE]

41. Neurol Sci. 2021 Jul;42(7):2987-2989. doi: 10.1007/s10072-021-05112-6. Epub 2021

Feb 12.

**Deep brain stimulation in Fragile X syndrome with tardive dystonia.**

DOI: 10.1007/s10072-021-05112-6

PMID: 33576914 [Indexed for MEDLINE]

42. Drugs. 2018 Apr;78(5):525-541. doi: 10.1007/s40265-018-0874-x.

**Treatment of Tardive Dyskinesia: A General Overview with Focus on the Vesicular**

**Monoamine Transporter 2 Inhibitors.**

Tardive dyskinesia (TD) encompasses the spectrum of iatrogenic hyperkinetic

movement disorders following exposure to dopamine receptor-blocking agents

(DRBAs). Despite the advent of atypical or second- and third-generation

antipsychotics with a presumably lower risk of complications, TD remains a

persistent and challenging problem. Prevention is the first step in mitigating

the risk of TD, but early recognition, gradual withdrawal of offending

medications, and appropriate treatment are also critical. As TD is often a

persistent and troublesome disorder, specific antidyskinetic therapies are often

needed for symptomatic relief. The vesicular monoamine transporter 2 (VMAT2)

inhibitors, which include tetrabenazine, deutetrabenazine, and valbenazine, are

considered the treatment of choice for most patients with TD. Deutetrabenazine-a

deuterated version of tetrabenazine-and valbenazine, the purified parent product

of one of the main tetrabenazine metabolites, are novel VMAT2 inhibitors and the

only drugs to receive approval from the US FDA for the treatment of TD. VMAT2

inhibitors deplete presynaptic dopamine and reduce involuntary movements in many

hyperkinetic movement disorders, particularly TD, Huntington disease, and

Tourette syndrome. The active metabolites of the VMAT2 inhibitors have high

affinity for VMAT2 and minimal off-target binding. Compared with tetrabenazine,

deutetrabenazine and valbenazine have pharmacokinetic advantages that translate

into less frequent dosing and better tolerability. However, no head-to-head

studies have compared the various VMAT2 inhibitors. One of the major advantages

of VMAT2 inhibitors over DRBAs, which are still being used by some clinicians in

the treatment of some hyperkinetic disorders, including TD, is that they are not

associated with the development of TD. We also briefly discuss other treatment

options for TD, including amantadine, clonazepam, Gingko biloba, zolpidem,

botulinum toxin, and deep brain stimulation. Treatment of TD and other

drug-induced movement disorders must be individualized and based on the

severity, phenomenology, potential side effects, and other factors discussed in

this review.

DOI: 10.1007/s40265-018-0874-x

PMID: 29484607 [Indexed for MEDLINE]

43. Eur Neuropsychopharmacol. 2012 Jul;22(7):506-17. doi:

10.1016/j.euroneuro.2011.11.004. Epub 2011 Dec 7.

**Early gene mapping after deep brain stimulation in a rat model of tardive**

**dyskinesia: comparison with transient local inactivation.**

Deep brain stimulation (DBS) has been extensively used in Parkinson's disease

and is also currently being investigated in tardive dyskinesia (TD), a movement

disorder induced by chronic treatment with antipsychotic drugs such as

haloperidol (HAL). In rodents, vacuous chewing movements (VCMs) following

chronic HAL administration are suggested to model orofacial dyskinesias in TD.

We show that 60 min of DBS (100 μA, 90 μs, 130 Hz) applied to the entopeduncular

(EPN) or subthalamic (STN) nuclei significantly decreases HAL-induced VCMs.

Using zif268 as a neural activity marker, we found that in HAL-treated animals

EPN stimulation increased zif268 mRNA levels in the globus pallidus (+65%) and

substantia nigra compacta (+62%) and reticulata (+76%), while decreasing levels

in the motor cortex and throughout the thalamus. In contrast, after STN DBS

zif268 levels in HAL-treated animals decreased in all basal ganglia structures,

thalamus and motor cortex (range: 29% in the ventrolateral caudate-putamen to

100% in the EPN). Local tissue inactivation by muscimol injections into the STN

or EPN also reduced VCMs, but to a lesser degree than DBS. When applied to the

EPN muscimol decreased zif268 levels in substantia nigra (-29%), whereas STN

infusions did not result in significant zif268 changes in any brain area. These

results confirm the effectiveness of DBS in reducing VCMs and suggest that

tissue inactivation does not fully account for DBS effects in this preparation.

The divergent effects of STN vs. EPN manipulations on HAL-induced zif268 changes

suggest that similar behavioral outcomes of DBS in these two areas may involve

different neuroanatomical mechanisms.

Copyright © 2011 Elsevier B.V. and ECNP. All rights reserved.

DOI: 10.1016/j.euroneuro.2011.11.004

PMID: 22153973 [Indexed for MEDLINE]

44. Chin Med J (Engl). 2016 May 20;129(10):1257-8. doi: 10.4103/0366-6999.181977.

**Long-term Effects of Subthalamic Nucleus Deep Brain Stimulation in Tardive**

**Dystonia.**

DOI: 10.4103/0366-6999.181977

PMCID: PMC4878179

PMID: 27174342 [Indexed for MEDLINE]

45. Stereotact Funct Neurosurg. 2010;88(5):304-10. doi: 10.1159/000316763. Epub 2010

Jun 24.

\*\*Duplicate\*\*

**Long-term benefit sustained after bilateral pallidal deep brain stimulation in**

**patients with refractory tardive dystonia.**

BACKGROUND/AIMS: Tardive dystonia (TD) can be a highly disabling, permanent

condition related to the use of dopamine-receptor-blocking medications. Our aim

was to evaluate the long-term effect of bilateral pallidal deep brain

stimulation (DBS) for TD.

METHODS: Five consecutive patients with disabling TD who underwent stereotactic

placement of bilateral globus pallidus internus DBS leads were included. All

patients had a history of mood disorder or schizophrenia previously treated with

neuroleptic medication, with a mean duration of motor symptoms of 10.2 years.

Dystonia severity was measured using the Burke-Fahn-Marsden Dystonia Rating

Scale (BFMDRS) movement score by a blinded neurologist reviewing pre- and

postoperative videotaped examinations.

RESULTS: The mean baseline movement BFMDRS score was 49.7 (range 20-88).

Overall, we observed a mean reduction of 62% in the BFMDRS movement score within

the first year after surgery. Persistent improvement in dystonia (71%) was seen

at the last follow-up ranging from 2 to 8 years after surgery.

CONCLUSION: Our experience suggests that pallidal DBS can be an effective

therapy with long-term benefits for patients with TD.

2010 S. Karger AG, Basel.

DOI: 10.1159/000316763

PMID: 20588082 [Indexed for MEDLINE]

46. Neurotherapeutics. 2014 Jan;11(1):166-76. doi: 10.1007/s13311-013-0222-5.

**Tardive dyskinesia: therapeutic options for an increasingly common disorder.**

Tardive dyskinesia (TD) is a serious, often disabling, movement disorder that is

caused by medications that block dopamine receptors (i.e., neuroleptics,

anti-emetics). There is currently no standard treatment approach for physicians

confronted with such patients. This may be the result of notions that TD is

disappearing because of the switch to second-generation antipsychotic agents and

that it is largely reversible. In this article we demonstrate that

second-generation antipsychotics do, indeed, cause TD and, in fact, the

frequency is likely higher than expected because of growing off-label uses and a

tripling of prescriptions written in the last 10 years. In addition, studies

demonstrate that TD actually remits in only a minority of patients when these

drugs are withdrawn. Furthermore, neuroleptic agents are often utilized to treat

TD, despite prolonged exposure being a risk factor for irreversibility. The

outcome of these trends is a growing population afflicted with TD. We review

non-neuroleptic agents that have shown positive results in small, early-phase,

blinded trials, including tetrabenazine, amantadine, levetiracetam, piracetam,

clonazepam, propranolol, vitamin B6, and Ginkgo biloba. Other options, such as

botulinum toxin and deep brain stimulation, will also be discussed, and a

suggested treatment algorithm is provided. While these agents are reasonable

treatment options at this time there is a need, with a concerted effort between

neurology and psychiatry, for full-scale drug development, including

multicenter, randomized, blinded trials to confirm the effectiveness of the

agents that were positive in phase 2 trials and the development of newer ones.

DOI: 10.1007/s13311-013-0222-5

PMCID: PMC3899488

PMID: 24310603 [Indexed for MEDLINE]

47. Mov Disord. 2004 Aug;19(8):969-72. doi: 10.1002/mds.20092.

**Bilateral globus pallidus internus deep brain stimulation in tardive dyskinesia:**

**a case report.**

The clinical response of a 53-year-old woman with tardive dyskinesia treated

with bilateral globus pallidus interna deep brain stimulation is described. At

18 months follow-up, her Burke-Fahn-Marsden Dystonia Rating Scale score fell

from 52 (preoperative) to 21 (60% improvement).

Copyright 2004 Movement Disorder Society

DOI: 10.1002/mds.20092

PMID: 15300668 [Indexed for MEDLINE]

48. Focus (Am Psychiatr Publ). 2021 Jan;19(1):14-23. doi:

10.1176/appi.focus.20200038. Epub 2021 Jan 25.

**Tardive Dyskinesia: Spotlight on Current Approaches to Treatment.**

Tardive dyskinesia (TD) is a debilitating, iatrogenic, and potentially severe

movement disorder characterized by involuntary, repetitive, purposeless

movements that are present throughout the body. The authors present a review of

studies of past, current, and possible future treatment approaches to the

management of TD; consider the phenomenology, assessment, and putative

pathophysiological mechanisms of TD, early pharmacological trials, a focus on

the newer vesicular monoamine transporter 2 inhibitors, and other evidence-based

approaches, such as clozapine; and present preliminary evidence for newer

approaches, such as deep brain stimulation and repetitive transcranial magnetic

stimulation. On the basis of the evidence presented here, the authors highlight

the importance of early recognition and assessment of TD, as well as how to best

approach management of these often incapacitating symptoms.

Copyright © 2021 by the American Psychiatric Association.

DOI: 10.1176/appi.focus.20200038

PMCID: PMC8412148

PMID: 34483762

49. Expert Rev Neurother. 2021 Jan;21(1):9-20. doi: 10.1080/14737175.2021.1848548.

Epub 2020 Nov 23.

**Deutetrabenazine for treatment of involuntary movements in patients with tardive**

**dyskinesia.**

Introduction: Tardive dyskinesia (TD) is a hyperkinetic movement disorder that

arises as a complication of exposure to dopamine receptor blocking agents.

Vesicular monoamine transporter type 2 (VMAT2) inhibitors reduce dyskinesia by

decreasing transport of monoamines, including dopamine, into presynaptic

vesicles, leaving unpackaged dopamine to be metabolized by monoamine oxidase.

Deutetrabenazine was adapted from an earlier VMAT2 inhibitor, tetrabenazine, by

substituting three deuterium isotopes in place of three hydrogen isotopes at the

site of metabolic degradation to improve upon the pharmacokinetics of the parent

compound. Areas covered: The authors reviewed the pivotal trials examining the

safety and efficacy of deutetrabenazine, as well as long-term data from an

open-label extension. Also reviewed were posters and oral presentations, as well

as information from the product label and the United States Food and Drug

Administration. Expert opinion: Deutetrabenazine is effective at decreasing

dyskinesia in TD, but drug selection and cost-effectiveness between existing

VMAT2 inhibitors are evolving areas of study. Other areas of investigation

include novel anti-dyskinetic agents and use of deep brain stimulation.

DOI: 10.1080/14737175.2021.1848548

PMID: 33174440

50. J Neurol Sci. 2017 Feb 15;373:342-343. doi: 10.1016/j.jns.2017.01.034. Epub 2017

Jan 10.

**Excoriation disorder as a risk factor for deep brain stimulation hardware**

**removal.**

DOI: 10.1016/j.jns.2017.01.034

PMID: 28131218 [Indexed for MEDLINE]

51. Can J Neurol Sci. 2021 May 24:1-2. doi: 10.1017/cjn.2021.117. Online ahead of

print.

**Delayed Stroke in Globus Pallidus Internus Deep Brain Stimulation.**

DOI: 10.1017/cjn.2021.117

PMID: 34024308

52. Neurol Clin Pract. 2017 Apr;7(2):163-169. doi: 10.1212/CPJ.0000000000000344.

**Movement disorders and chronic psychosis: Five new things.**

PURPOSE OF REVIEW: To discuss selected peer-reviewed research articles published

between 2014 and 2016 and highlight 5 clinically relevant messages related to

hyperkinetic and hypokinetic movement disorders in patients with chronic

psychosis.

RECENT FINDINGS: A recent population-based study complemented data from clinical

trials in showing increased risk of developing extrapyramidal symptoms with

antipsychotic use. A community service-based longitudinal study showed that

dopamine transporter imaging could help identify subgroups of patients with

parkinsonism associated with antipsychotics with a progressive course,

potentially manageable with l-dopa. Data from recent noteworthy clinical trials

showed that a new VMAT-2 inhibitor and, for pharmacologically refractory tardive

dyskinesia, deep brain stimulation of the globus pallidus internus are promising

interventions. Finally, a population-based study has confirmed that

hyperkinesias (encompassing chorea, dystonia, and stereotypies) may be early

predictors of psychosis even in childhood and adolescence.

SUMMARY: Movement disorders associated with new-generation antipsychotics,

including widely used agents (e.g., aripiprazole), are not rare occurrences.

Better monitoring is needed to assess their true effect on patients' quality of

life and functioning and to prevent underascertainment.

DOI: 10.1212/CPJ.0000000000000344

PMCID: PMC5669418

PMID: 29185545

53. Acta Neurochir (Wien). 2011 Dec;153(12):2319-27; discussion 2328. doi:

10.1007/s00701-011-1147-6. Epub 2011 Sep 11.

**Treatment of secondary dystonia with a combined stereotactic procedure:**

**long-term surgical outcomes.**

OBJECTIVE: There is some debate about the effects of pallidal deep brain

stimulation (DBS) or lesioning on secondary dystonia. We applied a multimodal

method to maximize the treatment effects of deep brain stimulation in patients

with secondary dystonia.

METHODS: Between March 2003 and January 2009, four patients underwent bilateral

globus pallidus internus (GPi) DBS and six patients underwent bilateral GPi DBS

plus unilateral thalamotomy for treatment of cerebral palsy (CP). Among the

patients with secondary dystonia without CP, five were also treated by DBS. We

classified patients with generalized secondary dystonia with cerebral palsy into

group I and patients with focal dystonia without CP into group II. Clinical

outcome assessments were based on Burke-Fahn-Marsden Dystonia Rating Scale

movement and disability scores. Heath-related quality of life was assessed with

a 36-item short-form general health survey questionnaire preoperatively and at

the last follow-up.

RESULTS: The movement and disability scores of group I-A had improved by 32.0%

(P = 0.285) and 14.3% (P = 0.593), respectively, at the last follow-up compared

with baseline. The movement and disability scores of group I-B had improved by

31.5% and 0.18% at the last follow-up compared with baseline, respectively. In

comparison with patients in group I-A, patients in group I-B showed a

significant improvement in movement scores for the contralateral arm

(P = 0.042). Group II patients showed a marked improvement in movement and

disability scores of 77.7% (P = 0.039) and 80.0% (P = 0.041), respectively.

CONCLUSIONS: We demonstrated that DBS plus unilateral ventralis oralis

thalamotomy for CP patients with fixed states in the upper extremities is useful

not only to treat secondary dystonic movement but also to improve quality of

life. In group II patients with post-traumatic dystonia and tardive dyskinesia,

we achieved excellent clinical outcomes using a stereotactic procedure.

DOI: 10.1007/s00701-011-1147-6

PMID: 21909834 [Indexed for MEDLINE]

54. J Neurol Sci. 2016 Jul 15;366:68-73. doi: 10.1016/j.jns.2016.04.033. Epub 2016

Apr 19.

**Local field potential oscillations of the globus pallidus in cervical and**

**tardive dystonia.**

BACKGROUND: Reports about neural oscillatory activity in the globus pallidus

internus (GPi) have targeted general (GD) and cervical dystonia (CD), however to

our knowledge they are nonexistent for tardive dystonia (TD).

METHODS: Local field potentials (LFPs) from seven CD and five TD patients were

recorded intraoperatively. We compared LFP power in thetadelta, alpha and beta

band during rest and sensory palmar stimulation (SPS) in patients with general

anesthesia and local/analgo sedation.

RESULTS: We found prominent LFP power activity in thetadelta for both CD and TD.

Unlike TD, a significant difference between rest and SPS was revealed for CD.

CONCLUSIONS: Our data support the presence of LFP oscillatory activity in CD and

TD. Thetadelta power modulation in the GPi is suggested as a signature for

sensory processing in CD.

Copyright © 2016 Elsevier B.V. All rights reserved.

DOI: 10.1016/j.jns.2016.04.033

PMID: 27288779 [Indexed for MEDLINE]

55. J Acupunct Meridian Stud. 2017 Jan;10(1):55-61. doi: 10.1016/j.jams.2016.12.005.

Epub 2016 Dec 18.

**A Single Case of Tourette's Syndrome Treated with Traditional Chinese Medicine.**

The objective of this case study was to investigate the effectiveness of Chinese

medicine in treating Tourette's syndrome. Tourette's syndrome is a childhood-

onset disorder that is characterized by sudden, involuntary movements or tics.

The participant in this study was a 33-year-old male who had been diagnosed with

Tourette's syndrome at the age of 9 years. His major complaints included facial

tics, shoulder shrugging, and clearing the throat. Using a combination of

acupuncture, herbs, Gua-Sha, and lifestyle changes once a week for 35

treatments, all the symptoms were reduced by 70%, as reported by the patient. In

this case, the results indicated that Chinese medicine was able to minimize the

symptoms of Tourette's syndrome. Further investigation is needed to support this

argument. Tourette's syndrome, which was first described in 1885 by a French

physician named Gilles de la Tourette, is characterized by facial tics,

involuntary body movements from the head to the extremities, or vocal tics, and

it usually has its onset in childhood. It is a neuropsychiatric disorder. The

treatment for Tourette's syndrome is based on pharmacological treatment,

behavior treatment, and deep brain stimulation. Unfortunately, none of these

could completely control the symptoms; furthermore, antipsychiatric drugs might

cause additional side effects, such as Parkinson symptoms, tardive dyskinesia,

and metabolic disturbances. Finding acupuncture and oriental medicine literature

on treatment of Tourette's syndrome was difficult, especially that written in

English. Some research papers that have been translated into English indicated

that Chinese herbs and acupuncture could reduce the tics significantly. For

example, a study by Dr Pao-Hua Lin reported the significant effects of using

acupuncture and oriental medicine in treating 1000 Tourette's syndrome cases.

This case was treated to further investigate the principles of Dr Lin's study.

Copyright © 2017 Medical Association of Pharmacopuncture Institute. Published by

Elsevier B.V. All rights reserved.

DOI: 10.1016/j.jams.2016.12.005

PMID: 28254105 [Indexed for MEDLINE]

56. J Neurol. 2002 May;249(5):622-5. doi: 10.1007/s004150200073.

**Full remission of tardive dyskinesia following general anaesthesia.**

A 44 year old woman with a severe drug induced tardive dyskinesia had previously

been treated with a left thalamotomy and right deep brain stimulation.

Thalamotomy abolished the right hemiballismus. Deep brain stimulation caused a

moderate reduction of the remaining involuntary movements on the left side.

After a minor orthopaedic operation under general anaesthesia, the dyskinesia

disappeared completely, even with the deep brain stimulation turned off. The

remission has now lasted for 41 months.

DOI: 10.1007/s004150200073

PMID: 12021954 [Indexed for MEDLINE]

57. Neurology. 2006 Sep 26;67(6):940-3. doi: 10.1212/01.wnl.0000237446.06971.72.

**Severe tongue protrusion dystonia: clinical syndromes and possible treatment.**

We describe intermittent or sustained severe involuntary tongue protrusion in

patients with a dystonic syndrome. Speech, swallowing, and breathing

difficulties can be severe enough to be life threatening. Causes include

neuroacanthocytosis, pantothenate kinase-associated neurodegeneration,

Lesch-Nyhan syndrome, and postanoxic and tardive dystonia. The pathophysiology

of intermittent severe tongue protrusion remains unknown. Tongue protrusion

dystonia is often unresponsive to oral drugs but may benefit from botulinum

toxin injections into the genioglossus muscle. Bilateral deep brain pallidal

stimulation was beneficial in two cases.

DOI: 10.1212/01.wnl.0000237446.06971.72

PMID: 17000958 [Indexed for MEDLINE]

58. J Neurosurg. 2010 Dec;113(6):1246-50. doi: 10.3171/2010.3.JNS09981. Epub 2010

Apr 9.

**Restoration of erect posture in idiopathic camptocormia by electrical**

**stimulation of the globus pallidus internus.**

The authors report on 2 young patients who developed drug-resistant idiopathic

dystonic camptocormia (bent spine) and were treated successfully by deep brain

stimulation (DBS) of the globus pallidus internus (GPi). The first patient, a

26-year-old woman, suffered for 3 years from such severe camptocormia that she

became unable to walk and was confined to bed or a wheelchair. The second

patient, a 21-year-old man, suffered for 6 months from less severe camptocormia;

he was able to walk but only for short distances with a very bent spine, the

arms in a parallel position to the legs, and the hands almost approaching the

floor to potentially support him in case of a forward fall. Within a few days

following DBS, both patients experienced marked clinical improvement. At most

recent follow-up (44 months in one case and 42 in the other), the patients'

ability to walk upright remained normal. Similar findings have only been

reported recently in a few cases of camptocormia secondary to Parkinson disease

or tardive dyskinesia. On the basis of the experience of these 2 idiopathic

cases and the previously reported cases of secondary camptocormia with a

favorable response to GPi DBS, the authors postulate that specific patterns of

oscillatory activity in the GPi are vital for the maintenance of erect posture

and the adoption of bipedal walking by humans.

DOI: 10.3171/2010.3.JNS09981

PMID: 20380528 [Indexed for MEDLINE]