Below are 14 golf-specific studies of the “yips” and 89 neuroscience studies of focal dystonia, which includes golf “yips”. Many of the links (those marked “Full Text”) have the complete research articles available for free online. The remaining articles are available for access by subscription or purchase.

1. The Functional Neuroanatomy of Dystonia (Full Text)

   Neurobiol Dis. Author manuscript; available in PMC 2012 October 23.

   Published in final edited form as:
   Published online 2011 February 12. doi: 10.1016/j.nbd.2011.01.026

   Vladimir K. Neychev,1 Robert Gross,2 Stephane Lehéricy,3 Ellen J. Hess,4 and H. A. Jinnah5

   Abstract
   Dystonia is a neurological disorder characterized by involuntary twisting movements and postures. There are many different clinical manifestations, and many different causes. The neuroanatomical substrates for dystonia are only partly understood. Although the traditional view localizes dystonia to basal ganglia circuits, there is increasing recognition that this view is inadequate for accommodating a substantial portion of available clinical and experimental evidence. A model in which several brain regions play a role in a network better accommodates the evidence. This network model accommodates neuropathological and neuroimaging evidence that dystonia may be associated with abnormalities in multiple different brain regions. It also accommodates animal studies showing that dystonic movements arise with manipulations of different brain regions. It is consistent with neurophysiological evidence suggesting defects in neural inhibitory processes, sensorimotor integration, and maladaptive plasticity. Finally, it may explain neurosurgical experience showing that targeting the basal ganglia is effective only for certain subpopulations of dystonia. Most importantly, the network model provides many new and testable hypotheses with direct relevance for new treatment strategies that go beyond the basal ganglia.

2. The "yips": a focal dystonia of golfers.


   The "yips": a focal dystonia of golfers.
McDaniel KD, Cummings JL, Shain S.
Source
Neurobehavior Unit, West Los Angeles VAMC, CA 90073.

Abstract
The "yips" is an involuntary motor disturbance affecting golfers. A 69-item questionnaire was constructed and distributed to 1,050 professional and amateur golfers in an effort to define and characterize this syndrome. Of the male golfers there was a 42% response rate and 28% reported suffering from the yips. The disorder was described most frequently as jerks, tremors, and spasms affecting the preferred arm distally and primarily during putting. When compared with unaffected golfers, afflicted golfers were significantly older and had more cumulative years of golfing. In 24%, activities other than golfing were affected and 25% reported involvement of body regions beyond the arms. These data support the hypothesis that the yips represents a focal dystonia and shares many features with other occupational dystonias.

3. A multidisciplinary study of the 'yips' phenomenon in golf: An exploratory analysis.


A multidisciplinary study of the 'yips' phenomenon in golf: An exploratory analysis.
Source
Department of Laboratory Medicine, Mayo Clinic, Rochester, Minnesota 55905, USA. smith.aynsley@mayo.edu

Abstract
BACKGROUND:
The 'yips' is a psychoneuromuscular impediment affecting execution of the putting stroke in golf. Yips symptoms of jerks, tremors and freezing often occur during tournament golf and may cause performance problems. Yips-affected golfers add approximately 4.7 strokes to their scores for 18 holes of golf, and have more forearm electromyogram activity and higher competitive anxiety than nonaffected golfers in both high and low anxiety putting conditions. The aetiology of the yips is not clear.

OBJECTIVE:
To determine whether the yips is a neurological problem exacerbated by anxiety, or whether the behaviour is initiated by anxiety and results in a permanent neuromuscular impediment.

METHODS:
In phase I, golf professionals assisted investigators in developing a yips questionnaire that was sent to tournament players (<12 handicap) to establish the prevalence and characteristics of the yips. Phase II measured putting behaviour in scenarios that contribute to the yips response. Four self-reported yips and 3 nonaffected golfers putted 3 scenarios using an uncorrected grip and a standard length putter. Heart rate was
superimposed on the videotape and the putter grip was instrumented with strain
gauges to measure grip force. Electromyograms and relative putting performance were
also measured.

RESULTS:
The questionnaire was sent to 2,630 tournament players, of whom 1,031 (39%)
responded (986 men and 45 women). Of these, 541 (52%) perceived they experienced
the yips compared with 490 (48%) who did not. Yips-affected golfers reported that the
most troublesome putts were 3, 4 and 2 feet (0.9, 1.2 and 0.6 metres) from the hole.
Fast, downhill, left-to-right breaking putts and tournament play also elicited the yips
response. Golfers affected by the yips had a faster mean heart rate, increased
electromyogram activity patterns and exerted more grip force than nonaffected golfers
and had a poorer putting performance.

CONCLUSIONS:
For <10 handicap male golfers and <12 handicap female golfers, the prevalence of the
yips is between 32.5% and 47.7%, a high proportion of serious golfers. This high
prevalence suggests that medical practitioners need to understand the aetiology of the
yips phenomenon so that interventions can be identified and tested for effectiveness in
alleviating symptoms. Although previous investigators concluded that the yips is a
neuromuscular impediment aggravated but not caused by anxiety, we believe the yips
represents a continuum on which 'choking' (anxiety-related) and dystonia symptoms
anchor the extremes. The aetiology may well be an interaction of
psychoneuromuscular influences. Future research to test the effect of medications such
as beta-blockers should assist in better identifying the contributions these factors make
to the yips phenomenon.

4. Geoff Mangum - Neurophysiology of Golf Putting: The Mayo Clinic Takes a "Stab" at the
Yips (Full Text)

ABSTRACT: The Mayo Clinic is undertaking a study of the "yips" in golf--the mysterious
affliction in putting manifested by freezing over the putt, shaky hands, and a stabbing
stroke. Previous researchers have classified yips as an occupational focal hand
dystonia, a type of movement disorder apparently caused by degeneration of neural
circuitry following decades of the same hand movement. The Mayo Clinic team departs
from earlier researchers by assigning a prominent role in the etiology of the yips to
psychological rather than neurological factors. They have also opted for a behavioral
definition of yips that does not distinguish between the contributions of anxiety and
dystonia. The team may therefore have difficulty identifying effective therapy. (Nov.
2002).

5. The 'yips' in golf: a continuum between a focal dystonia and choking.


The 'yips' in golf: a continuum between a focal dystonia and choking.
Abstract
The definition of the 'yips' has evolved over time. It is defined as a motor phenomenon of involuntary movements affecting golfers. In this paper, we have extended the definition to encompass a continuum from the neurologic disorder of dystonia to the psychologic disorder of choking. In many golfers, the pathophysiology of the 'yips' is believed to be an acquired deterioration in the function of motor pathways (e.g. those involving the basal ganglia) which are exacerbated when a threshold of high stress and physiologic arousal is exceeded. In other golfers, the 'yips' seems to result from severe performance anxiety. Physically, the 'yips' is manifested by symptoms of jerks, tremors or freezing in the hands and forearms. These symptoms can result in: (i) a poor quality of golf performance (adds 4.9 strokes per 18 holes); (ii) prompt use of alcohol and beta-blockers; and (iii) contribute to attrition in golf. Golfers with the 'yips' average 75 rounds per year, although many 'yips'-affected golfers decrease their playing time or quit to avoid exposure to this embarrassing problem. While more investigation is needed to determine the cause of the 'yips', this review article summarises and organises the available research. A small study included in this paper describes the 'yips' phenomenon from the subjective experience of 'yips'-affected golfers. The subjective experience (n = 72) provides preliminary support for the hypothesis suggesting that the 'yips' is on a continuum. Based on the subjective definitions of 72 'yips'-affected golfers, the 'yips' was differentiated into type I (dystonia) and type II (choking). A theoretical model provides a guide for future research on golfers with either type I or type II 'yips'.


The yips in golf: multimodal evidence for two subtypes.
Stinear CM, Coxon JP, Fleming MK, Lim VK, Prapavessis H, Byblow WD.
Source
Human Motor Control Laboratory, Department of Sport & Exercise Science, University of Auckland, Auckland, New Zealand. c.stinear@auckland.ac.nz

Abstract
PURPOSE:
To determine whether a model of two subtypes of yips is supported by evidence from a range of physiological, behavioral, and psychological measures.

METHODS:
Fifteen golfers who experience yips symptoms while putting (mean age 58.1 yr, SD 13.6 yr), and nine golfers with no yips symptoms (mean age 39.6 yr, SD 19.3 yr) were
recruited. Participants completed a golf history questionnaire to determine their playing experience and the nature of any yips symptoms experienced. In experiment 1, participants performed a putting task while electromyographic data were recorded from the forearm flexors and extensors and biceps brachii, bilaterally. The task was performed in two sessions, under low-pressure and high-pressure experimental conditions. The high-pressure condition was intended to increase anxiety through the use of a monetary incentive, video-taping of performance, and the presence of a confederate who provided negative feedback. Participants' state of anxiety was assessed using a questionnaire before each of the experimental sessions. In experiment 2, participants completed a task that required the inhibition of an anticipated response. Their accuracy and ability to inhibit their response was determined.

RESULTS:
The golfers who experienced yips could be categorized according to whether they reported mainly movement-related symptoms (Type I) or anxiety-related symptoms (Type II). The Type I group exhibited greater muscle activity during putting and greater errors and less inhibition of the anticipated response task. The Type II group exhibited greater changes in cognitive anxiety and normal performance of the anticipated response task.

CONCLUSION:
This study provides evidence in support of two yips subtypes. Type I is related to impaired movement initiation and execution, whereas Type II is related to performance anxiety.

7. Are the yips a task-specific dystonia or 'golfer's cramp'?

Adler CH, Crews D, Kahol K, Santello M, Noble B, Hentz JG, Caviness JN.

Abstract
This study compared golfers with and without the yips using joint movement and surface electromyographic detectors. Fifty golfers (25 with and 25 without complaints of the yips) were studied while putting. All putts were videotaped. Surface electromyography assessed arm cocontraction. A CyberGlove II (Immersion Technologies, Palo Alto, CA) assessed right-arm angular movements. Primary analysis was done by subjective complaint of the yips, whereas secondary analysis was done by video evidence of an involuntary movement. When grouped by subjective complaints, there were no differences in any movement parameter. When grouped by video evidence of an involuntary movement, yips cases had more (P < 0.001) angular movement in wrist pronation/supination and a trend (P = 0.08) for wrist flexor/extensor cocontraction (yips: 7 of 17, 41.2%; no yips: 6 of 33, 18.2%). Golfers with video evidence of an involuntary movement while putting have excessive rotation of the right
wrist in a pronation/supination motion and, as previously reported, a trend for wrist flexor/extensor cocontraction.

8. Mayo Clinic study on yips presented at World Scientific Congress of Golf | Mayo Clinic News

Mayo Clinic study on yips presented at World Scientific Congress of Golf

Posted on March 13, 2012 by susanashephard

A recent Mayo Clinic study on yips, a condition that has baffled golfers and scientists for decades, will be a featured presentation on March 16, 9:45 a.m., at the upcoming World Scientific Congress of Golf. The Congress tees off March 12-16 at the Embassy Suites and Stonecreek Golf Club, 4415 East Paradise Village Parkway, Phoenix.

The yips, affecting a significant number of already anxious golfers during putting or chipping, may be a physical movement disorder and not only the result of undue pressure to perform at the crucial moment of a stroke. In fact, in some cases the affliction can be likened to writers’ or musicians’ cramps, according to Charles H. Adler, M.D., Ph.D., neurologist and researcher at Mayo Clinic. His latest research on the yips was recently published in the journal Movement Disorders.

Dr. Adler and his colleagues at Mayo Clinic and Arizona State University suggest that in a subset of golfers, involuntary muscle contractions are to blame, resulting in “golfer’s cramp.” The annoying condition (sometimes described as “twitches” or “jerks”) that can ruin an otherwise successful round of golf was often thought to be psychological. Dr. Adler said that the overall effect of this study is to try to identify golfers who have a neurologic rather than a psychological cause to their yips.

Held every four years, the World Scientific Congress of Golf began in 1990 at St. Andrews, Scotland. For more information on the Congress visit golfscience.org.

Below is a link to a YouTube video with Dr. Adler where he describes the study findings.

http://yt.cl.nr/ooln7e-DM2A

9. Are the yips a task-specific dystonia or "golfer's cramp"? - Arizona State University - SciVal Experts 4.2

Are the yips a task-specific dystonia or "golfer's cramp"?

Charles H. Adler; Debra Crews; Kanav Kahol; Marco Santello; Brie Noble; Joseph G. Hentz; John N. Caviness (Profiled Authors: Marco Santello; Kanav Kahol)

This study compared golfers with and without the yips using joint movement and surface electromyographic detectors. Fifty golfers (25 with and 25 without complaints of the yips) were studied while putting. All putts were videotaped. Surface electromyography assessed arm cocontraction. A CyberGlove II (Immersion Technologies, Palo Alto, CA) assessed right-arm angular movements. Primary analysis was done by subjective complaint of the yips, whereas secondary analysis was done by video evidence of an involuntary movement. When grouped by subjective complaints, there were no differences in any movement parameter. When grouped by video evidence of an involuntary movement, yips cases had more (P < 0.001) angular movement in wrist pronation/supination and a trend (P = 0.08) for wrist flexor/extensor cocontraction (yips: 7 of 17, 41.2%; no yips: 6 of 33, 18.2%). Golfers with video evidence of an involuntary movement while putting have excessive rotation of the right wrist in a pronation/supination motion and, as previously reported, a trend for wrist flexor/extensor cocontraction. © 2011 Movement Disorder Society.  


Acupuncture for treatment of the yips?--a case report.

Rosted P
Source
Sheffield University. Prosted@aol.com

Abstract
A 65 year old golfer with the yips was treated with acupuncture at GV20, EX-HN-1 (Si Shen Cong) and TE5. The symptoms disappeared after one treatment and no relapse has occurred in the 24 months' follow up. Although it cannot be determined whether the effect in this case occurred from neurological stimulation or was the result of expectation, acupuncture may be worth trying in patients with the yips since this condition is otherwise difficult to treat.

PMID: 16430127 [PubMed - indexed for MEDLINE]

11. Golf and Music (What Arnold Jacobs taught me about Golf): THE YIPS (and Focal Dystonia)

Tuesday, July 27, 2010

THE YIPS (and Focal Dystonia)

THE YIPS:

One lesson I did not learn from Mr. Jacobs was how to avoid the yips. Unfortunately it was a lesson I learned for myself, the hard way. Golfers call it the “Yips”. Musicians
call it Focal Dystonia. I know people who have ‘gone back to square one’ and ‘rebuilt’ their embouchures. The problem as I see it is not ‘the embouchure’. It is some habits that have become improperly ingrained, perhaps from over-use, perhaps from over-analysis. To play a brass instrument we spend years taking fine motor muscle movements of the face and training them to behave like automatic responses to demands for a musical result. (I bristle when I hear someone say “Breath from your diaphragm.” That is like saying “Pump blood with your heart. One, two, ready, go.” That was the point of the breathing tube Mr. Jacobs used. It focused our attention on the air, not on our anatomy.) When the embouchure behaves at a subconscious level, as the vocal chords do in speech, fixing a problem by bringing the action to the conscious level only compounds the problem.

Put in terms of the ‘Self Two’ computer, I would say the process has been totally turned over to Self Two but one of the files has become damaged or has been moved. Have you ever put so many programs, so many files, so many pictures on your hard drive that it bogged down? Have you ever deleted files to clean up space? Have you ever inadvertently deleted a file that was necessary for a program?

Mr. Jacobs taught “Play by sound; not by feel.” But he taught us to breathe by feel. We learned the ‘feel’ of a full breath and we ordered the body to achieve that feeling of fullness when we took a breath. One of the best golf lessons I had was about feel. My instructor got my club in position at the top of my backswing and admonished me to memorize the feel, not the mechanics of how I got it there. This freed my mind to focus on the task of swinging the club through the ball. For my level of golf, ‘See the ball; be the ball’ is too advanced. The required muscle memory has not been grooved. I didn’t take up golf until the age of 45. ‘See the club head; be the clubhead’ is a more attainable goal for me. If I can make a good move on the ball, if I can pass the clubhead squarely through the ball, I can then turn over the results to the elements. The wind, the ground conditions will do what they may. I did my part. The musician must make his notes fit into the larger ensemble but he cannot be responsible for an out of tune or badly balanced cord, only his note in it.

Anyway, my two cents worth about ‘focal dystonia’ is to practice less with the instrument on your face and spend more time training the tuba in your head. This flies in the face of our training that says to practice more. More lip slurs; more arpeggios; more scales etc. I certainly did that and I’m here to tell you one thing for sure. That doesn’t work to fix Dystonia. You must do drills, but once learned, there is only damage to be done by beating them to death.

If you think you are developing Focal Dystonia, your focus is in the wrong place. Play in spite of your embouchure, not because of it. Practice on the tuba in your head more than the one in your hand. It was this approach that allowed Lee Trevino to play a wedge shot with a two iron.

Jake often said, “Don’t ask a question. Make a statement.” Golfers say it another way. “Don’t ‘pull the trigger’ until you are committed to the shot.” In concert, musicians do
not have that luxury. When the conductor gives the downbeat, they must respond. What they can do is be ready with a statement instead of a question.

Applying the lessons I learned about Dystonia, I do not spend hours putting. If I had the time to devote to golf that I used to spend on the tuba, I would study greens, I would watch others putt. I would roll golf balls on greens by hand. That's not to say I do not go to the driving range. I have a long way to go to get my swing with the driver, fairway woods and irons automatic and repeatable. And I spent far too many formative years becoming a musician to consider myself any kind of athlete. What I do look for on the range is to memorize the feel and develop repeatability.

Golf legend Harry Vardon said “One should guard against playing too much golf. Thirty six holes a day is enough.”

Of course I can’t go back in time and prove it, but I feel that had I taken a year off to play golf when I first developed ‘Focal Task Specific Dystonia’, I would still be able to play tuba today. I think the fix for my chops could have been better learned on a golf course. At the time of writing this I saw a golf channel interview with David Duval. Duval was the number one ranked golfer in the World in 1999. He is one of only three golfers to have ever shot a 59 in tournament play. He dropped to number 260 by 2005. He said to the interviewer that he should have taken a year off when he started his downward spiral. My wife and I turned to each other with a look of surprise because it so echoed what I have so often said about my chops.

At the time I developed FD I had never held a golf club. I was 33 when I developed Focal Dystonia. It wasn’t until I was 45 that I found golf filled that void previously filled with hours of tuba practice. If I could go back in time with the intention of being a better tuba player I would work on being a better musician and less on being a tuba player. I would study more scores and attend more concerts. And I would have taken up golf earlier. As I said once before, the most important lesson I learned from Dystonia was that playing tuba was something I did; not who I was. It was my job; not my identity. Keep the other aspects of your life in perspective.

See you on the links?

Richard Barth, June 2010

12. What Is Yips (Focal Dystonia)? What Are The Causes Of Yips?

The yips refer to a very real physical condition called focal dystonia. Dystonia is a neurologic disorder characterized by involuntary movements or spasms of small muscles. In focal hand dystonia, the fingers either curl into the palm or extend outward without control.

According to Medilexicon's medical dictionary:
Dystonia is a general term describing a variety of musculoskeletal problems resulting from overuse or repetitive stress, particularly applied to the fine muscle problems encountered by professional musicians.

In golf, putting requires precision and fine motor control of the small muscles that control these movements. In this case the yips may be related to overuse and fatigue of these small muscles.

Generally, dystonia is an uncommon condition. However, it is one of the most common neurological conditions. Dystonia can affect people of all ages, including children. However, symptoms most commonly begin when a person is between 40 and 60 years old.

**What are the symptoms of Focal Dystonia?**
A symptom is something the patient senses and describes, while a sign is something other people, such as the doctor notice. For example, drowsiness may be a symptom while dilated pupils may be a sign.

Symptoms vary according to the kind of dystonia involved. Focal dystonia early symptoms may include loss of precision muscle coordination (sometimes first manifested in declining penmanship, frequent small injuries to the hands, and dropped items), cramping pain with sustained use and trembling. Significant muscle pain and cramping may result from very minor exertions like holding a book and turning pages.

Direct symptoms may be accompanied by secondary effects of the continuous muscle and brain activity, including disturbed sleep patterns, exhaustion, mood swings, mental stress, difficulty concentrating, blurred vision, digestive problems and short temper. People with dystonia may also become depressed and find great difficulty adapting their activities and livelihood to a progressing disability.

In some cases, symptoms may progress and then plateau for years, or stop progressing entirely. The progression may be delayed by treatment or adaptive lifestyle changes, while forced continued use may make symptoms progress more rapidly.

**What are the causes of Focal Dystonia?**
Environmental and task-related factors are suspected to trigger the development of focal dystonia because it appears disproportionately in individuals who perform high precision hand movements such as musicians, engineers, architects and artists. It is generally "task specific," meaning that it is only problematic during certain activities.

Other key causes include nerves, anxiety or "choking" that many athletes experience during high-stress competition and overuse of the muscles involved in fine-motor control and precise movements.

In cases of primary dystonia, it is thought that the basal ganglia does not produce enough neurotransmitters, or it produces the wrong type of neurotransmitters, resulting in problems with muscle function. The basal ganglia is a collection of brain cells at the
front of the brain. They are responsible for sending messages from the brain to various muscles in order to move them.

Secondary focal dystonia can have causes stemming from more serious conditions such as Parkinson's disease (a neurological (brain-related) condition that is caused by a lack of a neurotransmitter called dopamine), Huntington's disease (an inherited condition that is caused by a lack of cholesterol in the brain) and Wilson's disease which is a genetic condition that leads to a build-up of copper in the tissues of the body. Multiple sclerosis, and cerebral palsy also may cause levels of the yips as they are nervous system function related.

Diagnosing Focal Dystonia
It is important to confirm whether your dystonia is primary or secondary. Confirming the type of dystonia is important because the treatment of secondary dystonia can vary from that of primary dystonia, depending on the underlying cause. Treating the underlying cause can in turn help to control symptoms of secondary dystonia.

Electrical sensors (EMG) inserted into affected muscle groups, while painful, can provide a definitive diagnosis by showing pulsating nerve signals being transmitted to the muscles even when they are at rest. When called upon to perform an intentional activity, the muscles fatigue very quickly and some portions of the muscle groups do not respond (causing weakness) while other portions over-respond or become rigid. This can be an effective diagnosis technique of more severe focal dystonia.

What are the treatment options for Focal Dystonia?
Reducing the types of movements that trigger or worsen dystonic symptoms provides some relief, as does reducing stress, getting plenty of rest, moderate exercise, and relaxation techniques.

This condition is also often treated with injections of botox, a commercially prepared form of botulinum toxin. Botox, however, merely targets the symptoms of the disorder and is not a cure for dystonia. Botulinum toxin stops the neurotransmitters that are responsible for muscle spasms from reaching the affected muscles. It is given by injection directly into the affected muscles.

Botox treatments are a temporary fix as the effects of the injection usually last for three months after which time one will need a further injection.

Clonazepam, an anti-seizure medicine, is also sometimes prescribed. However, for most their effects are limited and side effects like mental confusion, sedation, mood swings and short-term memory loss occur.

Anticholinergics are a type of medication that treat some types of focal dystonia. However, they are not effective for everyone. Anticholinergics work by blocking the release of a neurotransmitter called acetylcholine, which is known to cause muscle spasms in some cases of dystonia.
Finally, cannabidiol, one of the non-psychoactive cannabinoids found in cannabis sativa, was shown in independent studies to have reduced dystonic symptoms in all participants by up to 20-50%.

Preventing Focal Dystonia
There is no known way of preventing focal dystonia. To help reduce chances of getting this condition, it is important to take steps to reduce your risk of infection, stroke, trauma, and carbon monoxide poisoning or heavy metal poisoning.

Written by Sy Kraft (B.A.)

13. Five Questions: The yips - Los Angeles Times

Five Questions: Neurologist Charles H. Adler on the yips

April 07, 2012 | By Jessica Pauline Ogilvie, Special to the Los Angeles Times

The golf course is in pristine condition, there's nary a breeze, and you're about to sink a birdie on the 18th green. But just as the putter is about to meet the ball, your wrist jerks involuntarily — sending your round white nemesis 3 inches too far to the left.

Known as "the yips," this infuriating twitch has caused many a golfer to increase what would otherwise have been a perfectly respectable handicap. To the untrained eye, it looks like a clear-cut case of nerves kicking in at a crucial moment. But the way Mayo Clinic neurologist Charles H. Adler sees it, the yips might not be psychological at all; in fact, they may have their roots in the nervous system.

Among the afflicted are golf legends Ben Hogan and Sam Snead, as well as Tom Watson and Bernhard Langer, who are competing this week in the 2012 Masters Tournament at Augusta National. Adler, who works at Mayo's Parkinson's Disease and Movement Disorders Center in Scottsdale, Ariz., explained why he thinks researchers are getting closer to finding a cure.

How do you define the yips?

The yips is a term used by golfers to describe an involuntary movement — a twist, a jerk or a shake — that usually happens when putting, although some people will describe it when doing other activities like chipping.

What makes you think there's more to this than golfers choking at a crucial moment?

There are a number of people who have a neurological illness called dystonia, which can cause cramps or pulling in the fingers or wrist while doing a specific task. It's known to occur in writers and musicians — in many cases the only time that they have
a problem is when they are trying to perform a task related to their writing or music. In between they are completely normal.

We're trying to determine if there are some golfers who have a golfer's cramp that would be equitable to writer's or musician's cramps. With dystonia there is no diagnostic test, so what we're doing is pattern recognition. We found that there are some individuals who complain of the yips and have a twitch or a movement at the time of making the putt. We're trying to narrow down the pool of golfers that may have a neurological disorder so we can do further studies.

Is it worse for the pros, who play on TV and have serious prize money at stake?

Stress and anxiety make all movement disorders worse, so when somebody with a tremor of the hand, for instance, gets stressed or anxious, the tremor gets worse. A lot of people say the yips come out during tournaments, but that doesn't mean it's all psychological; it means that with stress, the movement disorder gets worse.

Could there be a cure someday?

If someone has a psychological cause to their yip, different treatments may be beneficial versus if someone has a neurological disorder.

There are a number of interventions we could look at. One would be just changing how a golfer holds the golf club. Changing the type of club may change how movement occurs too. There is a potential that some sort of pill might be beneficial since this might be neurological, or for botulinum injections to be helpful — in writer's or musician's cramp, it weakens the muscles that are cramping.

Some people use playing a round of golf as an excuse to have a few beers. Do the yips get better or worse with alcohol?

Alcohol is a relaxant, and it's very clear that some people with movement disorders can get some relief that way. The problem with alcohol is that over the years, tremor can get worse if people use alcohol to treat it. Because of its ill effects, it certainly would not be a recommended treatment.

health@latimes.com


Golf is a precision game that requires a perfect balance between mobility and stability. Other than coordinated and complex body movements to generate power
for the golf swing one also needs to have excellent control of fine movements of the hands, especially during chipping and putting. Therefore, any form of movement disorder in golfers can have a significant impact on their game. In addition to golfer’s cramps or the ‘yips’, other movement disorders, such as tremors and dystonia, can also interfere with the game. The aim of this report is to systematically review the literature and our own experience with movement disorders in golfers. We describe four patients, all avid golfers, in whom the “yips” and various other movement disorders interfered with their ability to play golf, but the hyperkinesias did not significantly affect other motor activities. The “yips” and other forms of task-specific dystonia and tremor may be an important cause of disability among athletes, including golfers.

Discussion

The common theme to all these cases is that if they were not golfers they would not be troubled by their movement disorders. The first case, a professional golfer, who initially attributed his deterioration in putting to the ‘yips’, clearly has left hand focal dystonia which is also accompanied by cervical dystonia. Thus the yip in this case may actually represent a forme fruste of focal dystonia. This notion of the yips representing a focal dystonia is also supported by the third case who had “yips” involving the right arm for 25 years before he developed cervical dystonia. The second case represents another task-specific disorder, namely cervical dystonia, which occurs only while playing golf. Finally, the fourth case is an example of a patient with very mild essential tremor that is markedly exacerbated during putting. In all these patients the movement disorder jeopardized their golf career, despite rehabilitation with physical therapy and various muscle relaxants and other medications, until their movement disorder was satisfactorily treated with botulinum toxin injections targeting the abnormally contracting muscles.

The overall frequency and burden of movement disorders in golfers is not known, although the yips (or golfer’s cramps) are thought to be relatively common but often under-recognized condition among amateur and professional golfers. Based on questionnaire surveys of professional and amateur golfers, prevalence of the yips has been estimated to be 28% in one study and 52% in another.

Diagnosis of these task-specific movement disorders is mostly based on symptoms described by affected individuals. A review by a movement disorder expert of a
proper video recording of the abnormality will facilitate the diagnosis. Therefore, affected golfers should be encouraged to describe their symptoms and to have someone observe and videotape them (focusing on the hands and the forearms) during the particular activity as this will enable a better understanding of the phenomenology which, in turn, will also help in planning the most appropriate treatment strategy.

Although muscle relaxant (e.g. benzodiazepines, baclofen) and anticholinergic drugs have been used in the treatment of dystonia, focal hand dystonia, including task-specific dystonia, is best treated with botulinum toxin injection\textsuperscript{6,7}. We suggest that botulinum toxin injection be considered in the yips-affected individuals with dystonic type of symptoms that is significant enough to affect their game. The selection of the appropriate dosage and site of injection is obviously critical for a successful outcome. Only the overacting muscles must be targeted, minimizing spread of the biologic activity into those muscles required for playing whose strength must be preserved. Unfortunately, there is no published data yet to guide such therapy and it is not yet known whether such therapy is sufficiently successful to allow golfers to continue maintaining the standards of their game.

Conclusion

Table. Summary of the clinical features and treatment outcome of the four cases of movement disorders in golfers seen in our movement disorder clinic

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Clinical manifestation of symptoms</th>
<th>Duration of symptoms</th>
<th>Exam findings</th>
<th>Diagnosis</th>
<th>Treatment and Outcome</th>
</tr>
</thead>
</table>
Case 1

62 M Left hand would “turn inward” while holding a golf club and putting. Also, occasionally jerked his head to the left.

5 years Pronation of the left hand when holding a golf club along with tightness of biceps and forearm flexors. Mild left torticollis with head tilt to the right.

Task specific focal hand dystonia Treated with botulinum toxin injections to pronator teres and pronator quadratus muscles with excellent response that allowed him to return to playing golf.

Case 2

80 M Involuntary pulling of the head backwards, more pronounced when looking down, for example when putting.

12 years Retrocollis and laterocollis to the left along with torticollis to the right.

Cervical dystonia Excellent response to botulinum toxin injections to both splenius, left scalenus and sternocleidomastoid.
Case 3

52 M

Right arm spasm and jerking while putting which evolved over 25 years to also cause involuntary head turning to the right when putting or making a swing.

Moderate right torticollis with mild right laterocolli s dystonia evolved over 25 years to also cause involuntary head turning to the right when putting or making a swing.

Task specific focal hand dystonia and cervical dystonia evolved over 25 years to also cause involuntary head turning to the right when putting or making a swing.

Treated with botulinum toxin injections to left sternocleidomastoid, right splenius and right scalenus with near complete control of his cervical dystonia except for jerky movement of the head to the right when trying to putt or make a swing.

Case 4

72 M

Mild hand tremors that was markedly exacerbated when holding a golf club and putting.

Mild postural hand tremor that markedly worsened when he picked up a putter.

Essential tremor.

Marked improvement of the tremor with botulinum toxin injections into the biceps, flexor carpi radialis and ulnaris muscles.

Conclusion

Any form of movement disorder can be devastating to the professional career of a golfer. Golfers cramps or the yips may represent a form of task specific focal dystonia, at least on some players. Botulinum toxin should be considered in the yips-affected golfers with predominantly dystonic type of symptoms.

References


Robert J. Bell, School of Physical Education, Sport, and Exercise Science. Ball State University, and Charles L. Thompson, Dept of Educational Psychology & Counseling The University of Tennessee, Solution-Focused Guided Imagery for a Golfer Experiencing the Yips: A Case Study, Athletic Insight: The Online Journal of Sport Psychology, March, 2007 Volume 9, Issue 1

ABSTRACT

A single-subject across situations design with repeated measures was used to test the efficacy of solution focused guided imagery with a 40 year old golfer suffering from a three year case of the “yips”. Yips are defined as jerks, tremors, or a freezing of the putting stroke which at the very least can add several strokes per round of golf. The current participant was experiencing an average of 9.2 yips per round during the baseline phase of the study and was able to decrease his number of yips to virtually zero, with an average rate of 0.2 yips per round during treatment.

15. Imaging Reveals Abnormalities In Pathways Connecting Brain Areas In Those With Writer's Cramp

Abnormalities in the fibers connecting different brain areas may contribute to muscle disorders such as writer's cramp, according to a report in the April issue of Archives of Neurology, one of the JAMA/Archives journals. Previous studies of individuals with writer's cramp have identified changes in the gray matter of several brain areas, according to background information in the article. These include the basal ganglia (structures that help control and start movement), sensorimotor cortex (controls sensory and motor functions), thalamus (coordinates multiple impulses including some related to the senses) and cerebellum (controls voluntary movements, posture and balance).

In the new study, Christine Delmaire, M.D., of Centre Hospitalier Régional Universitaire Roger Salengro, Lille, France, and Institut National de la Santé et de la Récherche Médicale, Paris, studied 26 right-handed patients with writer's cramp and 26 right-handed control participants who were the same sex and age but did not have writer's cramp. All participants underwent diffusion-tensor magnetic resonance imaging (DTI), which has been shown to assess the status of white matter (coated nerve fibers that allow impulses to travel through the brain).

The DTI scans of patients with writer's cramp revealed areas of abnormalities in the white matter of nerve pathways connecting the main sensorimotor cortex to brain areas below the cortex, such as the thalamus. The same abnormalities were not observed in healthy controls.

"In conclusion, this study suggests that writer's cramp is associated with microstructural changes involving fibers that carry afferents [information from senses to the brain] and efferents [motor information from the brain to the muscles] to the primary sensorimotor cortex," the authors write. "However, it is unknown how these changes relate to the physiopathology of the disease."

This study was supported by grants from the Clinical Investigation Center of the Salpêtrière Hospital, the Action Concertée Incitative 2001, the IFR49, the INSERM French Dystonia Network 19 and GIS maladies rares and the Action de Recherche Cooperative DMRI 2007.

16. Stimulating Muscles May Improve Musician's Dystonia


ScienceDaily (Jan. 3, 2008) — Therapy that stimulates the hand muscles may help treat the condition called musician's dystonia, a movement disorder that causes muscles spasms in musicians, according to a new study.

Musician's dystonia occurs in musicians who have practiced particular complicated movements for years. The muscle spasms are usually painless and generally occur only
when playing the instrument.

For the study, researchers applied low-amplitude vibration to the hand muscles in 24 people: six who had musician's dystonia, six professional musicians with no dystonia, six healthy non-musicians, and six people with writer's cramp, which is another type of dystonia that occurs in people while they write.

Using transcranial magnetic stimulation, the researchers evaluated the reaction in the sensorimotor area of the brain back to the muscle during vibration of a single hand muscle. In healthy people, the vibration of a muscle increases the amount of brain messages back to the muscle and at the same time reduces the amount of messages to muscles that did not receive vibration. In people with musician's dystonia, vibration in any one hand muscle increases the amount of messages to all hand muscles. In writer's cramp, vibration to one muscle has no effect on any muscle.

Now, in an intervention that lasts only 15 minutes, muscle vibration was applied to a thumb muscle, and the participant's attention was either directed on that muscle itself or away from it. The reaction of the brain's sensorimotor areas to the muscles was then tested again using transcranial magnetic stimulation.

"Our hope is that stimulation can retrain how the brain responds," said study author Karin Rosenkranz, MD, with UCL Institute of Neurology in London, United Kingdom. The study found that the vibration intervention in which subjects had to attend to their thumb muscle tended to restore a more normal pattern in the sensorimotor area of the brain in people with musician's dystonia. This effect was less pronounced in the people with writer's cramp.

"More research is needed to see if prolonged use of stimulation can improve hand motor function," Rosenkranz said. "These results also suggest that the underlying mechanism of the disorder may be different in musician's dystonia and writer's cramp."

The full research article is published in the December 26, 2007, online issue of Neurology®, the medical journal of the American Academy of Neurology.

17. Decreased Activity Of Basal Ganglia Is Main Cause Of Abnormal Muscle Constrictions In Dystonia


ScienceDaily (Jan. 7, 2009) — Dystonia is a neurological disorder characterized by involuntary abnormal muscle constrictions. More than 300,000 people in North America are affected, but the mechanism of abnormal muscle constrictions has not been well understood.
Now, a Japanese research team led by Prof Atsushi Nambu and Dr Satomi Chiken of National Institute for Physiological Sciences (NIPS) in Japan, with Dr. Pullanipally Shashidharan of Mt Sinai School of Medicine in USA, has found that the decreased activity of the basal ganglia, a part of the brain structure, is the main cause of abnormal muscle constrictions of dystonia using a mouse model.

They report their findings in Journal of Neuroscience, on Dec. 17, 2008.

They investigated neuronal activity in the basal ganglia of a dystonia mouse model, which was generated by transferring human dystonia genes, in awake state. Basal ganglia send inhibitory signals to the motor cortex and tune optimal movement in normal state. However, in the dystonia mouse model, the neuronal activity is decreased so that basal ganglia cannot inhibit motor cortical activity related to unnecessary movements. The research team has concluded that this is the main cause of involuntary abnormal muscle constrictions in dystonia patients.

"Now we understand the mechanism of abnormal muscle constrictions in dystonia. If we can artificially increase basal ganglia activity, abnormal muscle constrictions in dystonia patients could be well controlled," said Prof Nambu and Dr Chiken.

18. Abnormal neural activity recorded from the deep brain of Parkinson's disease and dystonia patients


ScienceDaily (Mar. 10, 2011) — Movement disorders such as Parkinson's disease and dystonia are caused by abnormal neural activity of the basal ganglia located deep in the brain. The basal ganglia are connected to the cerebral cortex in the brain surface through complex neural circuits. Their basic structure and connections, as well as the dysfunctions in movement disorders, have been examined extensively by using experimental animals. On the other hand, little is known about the human brain that is much more complex in either normal or diseased states.

An international joint research team led by Professor Toru Itakura and Assistant Professor Hiroki Nishibayashi from Wakayama Medical University, Japan, Professor Atsushi Nambu from the National Institute for Physiological Sciences, Japan, and Professor Hitoshi Kita from The University of Tennessee Health Science Center, TN, succeeded, for the first time, in recording cortically induced neural activity of the basal ganglia in patients with Parkinson's disease and dystonia during stereotaxic neurosurgery for the deep brain stimulation (DBS).

This research has been reported in the journal Movement Disorders.
With the consent of patients and based on the ethical guidelines of Wakayama Medical University, the team recorded the neural activity of the globus pallidus, one of the nuclei in the basal ganglia, and examined their activity changes in response to the stimulation of the primary motor cortex. Typical triphasic responses were observed in patients with Parkinson's disease, and enhanced inhibitory responses were observed in a dystonia patient. The results confirmed previous data observed in experimental animals. These results suggest: 1) Cortically evoked neural responses in the basal ganglia can be useful for determining the target location of the DBS electrodes, and 2) Enhanced inhibitory neural responses in the globus pallidus may cause abnormal movements observed in dystonia.

This research was supported by Grants-in-Aid for Scientific Research, from the MEXT, Japan.

19. **Key brain regions, basal ganglia and cerebellum, talk directly with each other**


ScienceDaily (Apr. 19, 2010) — Researchers at the University of Pittsburgh have found new evidence that the basal ganglia and the cerebellum, two important areas in the central nervous system, are linked together to form an integrated functional network. The findings are available online this week in the Proceedings of the National Academy of Sciences.

"The basal ganglia and the cerebellum are two major subcortical structures that receive input from and send output to the cerebral cortex to influence movement and cognition," explained senior author Peter L. Strick, Ph.D., professor of neurobiology and co-director of the Center for the Neural Basis of Cognition, Pitt School of Medicine.

Each subcortical structure houses a unique learning mechanism. Basal ganglia circuits are thought to be involved in reward-driven learning and the gradual formation of habits. In contrast, cerebellar circuits are thought to contribute to more rapid and plastic learning in response to errors in performance.

"In the past, these two learning mechanisms were viewed as entirely separate, and we wondered how signals from the two were integrated," Dr. Strick said. "Using a unique method for revealing chains of synaptically linked neurons, we have demonstrated that the cerebellum and basal ganglia are actually interconnected and communicate with each other."

This result not only has important implications for the normal control of movement and cognition, but it also helps to explain some puzzling findings from patients with basal
ganglia disorders.

For example, Parkinson's disease is known to be caused by the degeneration of a specific set of neurons and their synapses in the basal ganglia. However, one of the treatments for the characteristic "resting" tremor of Parkinson's disease is to interrupt signals from the cerebellum to the cerebral cortex. Imaging studies of patients with Parkinson's disease and patients with dystonia, another disorder thought to be of basal ganglia origin, show abnormal increases in activity in the cerebellum.

"Our findings provide a neural basis for these findings," Dr. Strick said. "In essence, the pathways that we have discovered may enable abnormal signals from the basal ganglia to disrupt cerebellar function. The alterations in cerebellar function are likely to contribute to the disabling symptoms of basal ganglia disorders. Thus, a new approach for treating these symptoms might be to attempt to normalize cerebellar activity."

Andreea C. Bostan, a doctoral student in the Center for Neuroscience at the University of Pittsburgh, and Richard P. Dum, Ph.D., Center for the Neural Basis of Cognition, co-authored the paper. The study was funded by the Department of Veterans Affairs and the National Institutes of Health.


Pathology of idiopathic dystonia: findings from genetic animal models.

Richter A, Löscher W.

Source

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Abstract

Dystonia is a common movement disorder which is thought to represent a disease of the basal ganglia. However, the pathogenesis of the idiopathic dystonias, i.e. the neuroanatomic and neurochemical basis, is still a mystery. Research in dystonia is complicated by the existence of various phenotypic and genotypic subtypes of idiopathic dystonia, probably related to heterogeneous dysfunctions. In neurological diseases in which no obvious neuronal degeneration can be found, such as in idiopathic dystonia, the identification of a primary defect is difficult, because of the large number of chemically distinct, but functionally interrelated, neurotransmitter systems in the brain. The variable response to pharmacological agents in patients with idiopathic dystonia supports the notion that the underlying biochemical dysfunctions vary in the subtypes of idiopathic dystonia. Hence, in basic research it is important to clearly define the involved type of dystonia. Animal models of dystonias were described as limited. However, over the last years, there has been considerable
progress in the evaluation of animal models for different types of dystonia. Apart from animal models of symptomatic dystonia, genetic animal models with inherited dystonia which occurs in the absence of pathomorphological alterations in brain and spinal cord are describe. This review will focus mainly on genetic animal models of different idiopathic dystonias and pathophysiological findings. In particular, in the case of the mutant dystonic (dt) rat, a model of generalized dystonia, and in the case of the genetically dystonic hamster (dt(sz)), a model of paroxysmal dystonic choreoathetosis has been used, as these show great promise in contributing to the identification of underlying mechanisms in idiopathic dystonias, although even a proper animal model will probably never be equivalent to a human disease. Several pathophysiological findings from animal models are in line with clinical observations in dystonic patients, indicating abnormalities not only in the basal ganglia and thalamic nuclei, but also in the cerebellum and brainstem. Through clinical studies and neurochemical data several similarities were found in the genetic animal models, although the current data indicates different defects in dystonic animals which is consistent with the notion that dystonia is a heterogenous disorder. Different supraspinal dysfunctions appear to lead to manifestation of dystonic movements and postures. In addition to increasing our understanding of the pathophysiology of idiopathic dystonia, animal models may help to improve therapeutic strategies for this movement disorder.


The pathophysiological basis of dystonias.

Breakefield XO, Blood AJ, Li Y, Hallett M, Hanson PI, Standaert DG.

Source
Department of Neurology and Radiology, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts 02114, USA. breakefield@hms.harvard.edu

Abstract
Dystonias comprise a group of movement disorders that are characterized by involuntary movements and postures. Insight into the nature of neuronal dysfunction has been provided by the identification of genes responsible for primary dystonias, the characterization of animal models and functional evaluations and in vivo brain imaging of patients with dystonia. The data suggest that alterations in neuronal development and communication within the brain create a susceptible substratum for dystonia. Although there is no overt neurodegeneration in most forms of dystonia, there are functional and microstructural brain alterations. Dystonia offers a window into the mechanisms whereby subtle changes in neuronal function, particularly in sensorimotor circuits that are associated with motor learning and memory, can corrupt normal coordination and lead to a disabling motor disorder.


Bull Acad Natl Med. 2011 Apr-May;195(4-5):921-34; discussion 934.
Dystonia is defined by the occurrence of abnormal twisting movements and posture, and may be generalized or focal. Many subtypes of dystonias have been described, including monogenic forms (eg. DYT1 and DYT6), secondary dystonias related to metabolic disorders, forms due to brain lesions (including post-anoxic brain injury), and tardive dystonia. Dystonia may also be associated with myoclonus (myoclonus-dystonia, DYT11) or parkinsonism (rapid-onset dystonia parkinsonism DYT1). Paroxystic dystonias are a subgroup of paroxysmal dyskinesias. Diagnosis is based mainly on clinical features, age at onset, outcome, associated neurological signs, and brain MRI. Until recently, basal ganglia dysfunction and alterations of the sensory-motor network with maladaptive cortical plasticity were the core pathophysiological features of dystonia. Cerebellar and cerebello-thalamic anatomic-functional abnormalities may also play a role. The main objectives of this review are to highlight the principal characteristics of dystonias and to provide an overview of known culprit genes and environmental factors. Current pathophysiological knowledge, including anatomic-functional abnormalities, is summarized.


The monogenic primary dystonias.

Müller U.

Source

Institut für Humangenetik, Justus-Liebig-Universität, Schlangenzahl 14, 35392 Giessen, Germany. ulrich.mueller@humangenetik.med.uni-giessen.de

Abstract

Presently, 17 distinct monogenic primary dystonias referred to as dystonias 1- 4, 5a,b, 6-8, 10-13 and 15-18 (loci DYT 1-4, 5a,b, 6-8, 10-13, 15-18) have been recognized. Twelve forms are inherited as autosomal dominant, four as autosomal recessive and one as an X-linked recessive trait. Three additional autosomal dominant forms (DYT9, DYT19 and DYT20) might exist based on linkage mapping to regions apparently different from, yet in close proximity to or overlapping with the known loci DYT18, DYT10 and DYT8. Clinically, this group of movement disorders includes pure dystonias and dystonia plus syndromes. In addition, dyskinesias (paroxysmal dystonias), although phenotypically distinct from classical dystonias, are discussed within this group. In pure dystonias, dystonia is occasionally accompanied by tremor. In dystonia plus
syndromes, dystonia as the prominent sign concurs with other movement abnormalities such as myoclonus and parkinsonism. In the dyskinesias, dystonia occurs as a paroxysmal sign in association with other movement anomalies and sometimes seizures. While gross neuropathological changes are absent in most primary dystonias, including the paroxysmal forms, striking morphological alterations are found in some, such as in the X-linked dystonia-parkinsonism syndrome (DYT3). Neuropathological findings at the microscopic level have also been reported in several cases of dystonia 1 and 5, both of which were previously thought to be morphologically normal. One locus, DYT14 had been erroneously assigned, by linkage mapping, in a family with dystonia 5. There are two forms of dystonia 5, one autosomal dominant and one autosomal recessive. These forms are designated here as dystonia 5a and dystonia 5b (DYT5a, DYT5b), respectively. The disease gene has been identified in 10 primary dystonias, seven autosomal dominant (TOR1A/DYT1, GCH1/DYT5a, THAP1/DYT6, PNKD1/MR-1/DYT8, SGCE/DYT11, ATP1A3/DYT12 and SLC2A1/DYT18), two autosomal recessive (TH/DYT5b and PRKRA/DYT16) and one X-chromosomal recessive (TAF1/DYT3). This article summarizes all known aspects on each of the monogenic primary dystonias, including phenotype, neuropathology, imaging, inheritance, mapping, molecular genetics, molecular pathology, animal models and treatment. Suggestions for the diagnostic procedure in primary dystonias are given. Although much is now known about the molecular basis of primary dystonias, treatment of patients is still mainly symptomatic. The only exceptions are dystonias 5a and 5b with their excellent long-term response to L-dopa substitution.


Brain. 2002 Apr;125(Pt 4):695-721.
The genetics of primary dystonias and related disorders.

Németh AH.
Source
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Abstract
Dystonias are a heterogeneous group of disorders which are known to have a strong inherited basis. This review details recent advances in our understanding of the genetic basis of dystonias, including the primary dystonias, the ‘dystonia-plus’ syndromes and heredodegenerative disorders. The review focuses particularly on clinical and genetic features and molecular mechanisms. Conditions discussed in detail include idiopathic torsion dystonia (DYT1), focal dystonias (DYT7) and mixed dystonias (DYT6 and DYT13), dopa-responsive dystonia, myoclonus dystonia, rapid-onset dystonia parkinsonism, Fahr disease, Aicardi-Goutieres syndrome, Hallervorden-Spatz syndrome, X-linked dystonia parkinsonism, deafness-dystonia syndrome, mitochondrial dystonias, neuroacanthocytosis and the paroxysmal dystonias/dyskinesias.

Update on dystonia.

**Abstract**

**PURPOSE OF REVIEW:** This review considers the recent literature pertaining to the clinical features, genetics, neuropathology and treatment of dystonia syndromes.

**RECENT FINDINGS:**

The term dystonia indicates at the same time a clinical phenotype and a collection of neurological syndromes mainly of genetic origin. The physical signs contributing to the phenomenology of dystonia have been recently assembled into a coherent set. The molecular genetics of primary dystonia syndromes (DYT1 and DYT6) have been the object of extensive analysis, providing converging views on their causative mechanisms. The relationship between genotype, phenotype, and endophenotypes has been explored for hereditary and sporadic dystonia syndromes. Neurophysiological studies on DYT1 and DYT6 patients, as well as on nonmanifesting carriers, have demonstrated the presence of altered synaptic plasticity. Several recent data indicate a role of dopamine and acetylcholine (ACh) transmission in the pathophysiology of primary dystonia.

**SUMMARY:**

Recent findings have led to novel, testable hypotheses on cellular mechanisms and physiopathological abnormalities underlying dystonia. Neurophysiological studies, imaging data and animal models support the view that corticostriatal, cerebellar, and dopaminergic dysfunctions converge to produce the pathophysiological abnormalities of dystonia.


Abnormal plasticity in dystonia: Disruption of synaptic homeostasis.

**Abstract**

Work over the past two decades lead to substantial changes in our understanding of dystonia, which was, until recently, considered an exclusively sporadic movement...
disorder. The discovery of several gene mutations responsible for many inherited forms
of dystonia has prompted much effort in the generation of transgenic mouse models
bearing mutations found in patients. The large majority of these rodent models do not
exhibit overt phenotypic abnormalities, or neuronal loss in specific brain areas.
Nevertheless, both subtle motor abnormalities and significant alterations of synaptic
plasticity have been recorded in mice, suggestive of an altered basal ganglia circuitry.
In addition, robust evidence from experimental and clinical work supports the
assumption that dystonia may indeed be considered a disorder linked to the disruption
of synaptic "scaling", with a prevailing facilitation of synaptic potentiation, together
with the loss of synaptic inhibitory processes. Notably, neurophysiological studies from
patients carrying gene mutations as well as from non-manifesting carriers have shown
the presence of synaptic plasticity abnormalities, indicating the presence of specific
endophenotypic traits in carriers of the gene mutation. In this survey, we review
findings from a broad range of data, obtained both from animal models and human
research, and propose that the abnormalities of synaptic plasticity described in mice
and humans may be considered an endophenotype to dystonia, and a valid and
powerful tool to investigate the pathogenic mechanisms underlying this movement
disorder. This article is part of a Special Issue entitled "Advances in dystonia".

27. Neuromodulatory control of striatal plas... [Curr Opin Neurobiol. 2011] - PubMed -
NCBI Free PMC Article (Full Text)


Neuromodulatory control of striatal plasticity and behavior.

Lerner TN, Kreitzer AC.

Source
Gladstone Institute of Neurological Disease, San Francisco, CA, USA.

Abstract
Excitatory synapses onto projection neurons in the striatum, the input nucleus of the
basal ganglia, play a key role in regulating basal ganglia circuit function and are a
major site of long-term synaptic plasticity. Here, we review the mechanisms and
regulation of both long-term potentiation and long-term depression at these synapses.
In particular, we highlight the role that neuromodulators play in determining the
strength and direction of plasticity, which ultimately shapes the balance of activity in
basal ganglia circuits and regulates motor behavior.

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PMID: 21333525 [PubMed - indexed for MEDLINE] PMCID: PMC3092792 Free PMC
Article

28. Convergent evidence for abnormal striatal syna... [Neurobiol Dis. 2010] - PubMed -
NCBI Free PMC Article (Full Text)

Convergent evidence for abnormal striatal synaptic plasticity in dystonia.

**Peterson DA, Sejnowski TJ, Poizner H.**

Source

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Abstract

Dystonia is a functionally disabling movement disorder characterized by abnormal movements and postures. Although substantial recent progress has been made in identifying genetic factors, the pathophysiology of the disease remains a mystery. A provocative suggestion gaining broader acceptance is that some aspect of neural plasticity may be abnormal. There is also evidence that, at least in some forms of dystonia, sensorimotor "use" may be a contributing factor. Most empirical evidence of abnormal plasticity in dystonia comes from measures of sensorimotor cortical organization and physiology. However, the basal ganglia also play a critical role in sensorimotor function. Furthermore, the basal ganglia are prominently implicated in traditional models of dystonia, are the primary targets of stereotactic neurosurgical interventions, and provide a neural substrate for sensorimotor learning influenced by neuromodulators. Our working hypothesis is that abnormal plasticity in the basal ganglia is a critical link between the etiology and pathophysiology of dystonia. In this review we set up the background for this hypothesis by integrating a large body of disparate indirect evidence that dystonia may involve abnormalities in synaptic plasticity in the striatum. After reviewing evidence implicating the striatum in dystonia, we focus on the influence of two neuromodulatory systems: dopamine and acetylcholine. For both of these neuromodulators, we first describe the evidence for abnormalities in dystonia and then the means by which it may influence striatal synaptic plasticity. Collectively, the evidence suggests that many different forms of dystonia may involve abnormal plasticity in the striatum. An improved understanding of these altered plastic processes would help inform our understanding of the pathophysiology of dystonia, and, given the role of the striatum in sensorimotor learning, provide a principled basis for designing therapies aimed at the dynamic processes linking etiology to pathophysiology of the disease.

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PMID: 20005952 [PubMed - indexed for MEDLINE] PMCID: PMC2846420 Free PMC Article

29. The basal ganglia and cerebellum interact in the expression of dystonic movement. [Brain. 2008] - PubMed - NCBI Free PMC Article (Full Text)


The basal ganglia and cerebellum interact in the expression of dystonic movement.

Neychev VK, Fan X, Mitev VI, Hess EJ, Jinnah HA.
Source
Department of Neurology, Johns Hopkins University, Baltimore, MD 21287, USA.

Abstract
Dystonia is a neurological disorder characterized by excessive involuntary muscle contractions that lead to twisting movements or abnormal posturing. Traditional views place responsibility for dystonia with dysfunction of basal ganglia circuits, yet recent evidence has pointed towards cerebellar circuits as well. In the current studies we used two strategies to explore the hypothesis that the expression of dystonic movements depends on influences from a motor network that includes both the basal ganglia and cerebellum. The first strategy was to evaluate the consequences of subthreshold lesions of the striatum in two different animal models where dystonic movements are thought to originate from abnormal cerebellar function. The second strategy employed microdialysis to search for changes in striatal dopamine release in these two animal models where the cerebellum has been already implicated. One of the animal models involved tottering mice, which exhibit paroxysmal dystonia due to an inherited defect affecting calcium channels. In keeping with prior results implicating the cerebellum in this model, surgical removal of the cerebellum eliminated their dystonic attacks. In contrast, subclinical lesions of the striatum with either 6-hydroxydopamine (6OHDA) or quinolinic acid (QA) exaggerated their dystonic attacks. Microdialysis of the striatum revealed dystonic attacks in tottering mice to be associated with a significant reduction in extracellular striatal dopamine. The other animal model involved the induction of dystonia via pharmacological excitation of the cerebellar cortex by local application of kainic acid in normal mice. In this model the site of stimulation determines the origin of dystonia in the cerebellum. However, subclinical striatal lesions with either 6OHDA or QA again exaggerated their generalized dystonia. When dystonic movements were triggered by pharmacological stimulation of the cerebellum, microdialysis revealed significant reductions in striatal dopamine release. These results demonstrate important functional relationships between cerebellar and basal ganglia circuits in two different animal models of dystonia. They suggest that expression of dystonic movements depends on influences from both basal ganglia and cerebellum in both models. These results support the hypothesis that dystonia may result from disruption of a motor network involving both the basal ganglia and cerebellum, rather than isolated dysfunction of only one motor system.

PMID: 18669484 [PubMed - indexed for MEDLINE] PMCID: PMC2724906 Free PMC Article

30. Short-term and long-term plasticity at corti... [Behav Brain Res. 2009] - PubMed - NCBI


Short-term and long-term plasticity at corticostriatal synapses: implications for learning and memory.

Abstract
The striatum is the major division of the basal ganglia, representing the input station of the circuit and arguably the principal site within the basal ganglia where information processing occurs. Striatal activity is critically involved in motor control and learning. Many parts of the striatum are involved in reward processing and in various forms of learning and memory, such as reward-association learning. Moreover, the striatum appears to be a brain center for habit formation and is likely to be involved in advanced stages of addiction. The critical role played by the striatum in learning and cognitive processes is thought to be based on changes in neuronal activity when specific behavioral tasks are being learned. Accordingly, excitatory corticostriatal synapses onto both striatal projecting spiny neurons and interneurons are able to undergo the main forms of synaptic plasticity, including long-term potentiation, long-term depression, short-term forms of intrinsic plasticity and spike timing-dependent plasticity. These specific forms of neuroplasticity allow the short-term and long-term selection and differential amplification of cortical neural signals modulating the processes of motor and behavioral selection within the basal ganglia neural circuit.


Dopamine-mediated regulation of corticostriatal synaptic plasticity.
Calabresi P, Picconi B, Tozzi A, Di Filippo M.

Abstract
The striatum represents the main input into the basal ganglia. Neurons projecting from the striatum receive a large convergence of afferents from all areas of the cortex and transmit neural information to the basal ganglia output structures. Corticostriatal transmission is essential in the regulation of voluntary movement, in addition to behavioural control, cognitive function and reward mechanisms. Long-term potentiation (LTP) and long-term depression (LTD), the two main forms of synaptic plasticity, are both represented at corticostriatal synapses and strongly depend on the activation of dopamine receptors. Here, we discuss possible feedforward and feedback mechanisms by which striatal interneurons, in association with striatal spiny neurons and endogenous dopamine, influence the formation and maintenance of both LTP and LTD. We also propose a model in which the spontaneous membrane oscillations of neurons projecting from the striatum (named 'up' and 'down' states), in addition to the pattern of release of endogenous dopamine, bias the synapse towards preferential...
induction of LTP or LTD. Finally, we discuss how endogenous dopamine crucially influences changes in synaptic plasticity induced by pathological stimuli, such as energy deprivation.


Encoding of aversion by dopamine and the nucleus accumbens.

McCutcheon JE, Ebner SR, Loriaux AL, Roitman MF.

Source

Department of Psychology, University of Illinois at Chicago Chicago, IL, USA.

Abstract

Adaptive motivated behavior requires rapid discrimination between beneficial and harmful stimuli. Such discrimination leads to the generation of either an approach or rejection response, as appropriate, and enables organisms to maximize reward and minimize punishment. Classically, the nucleus accumbens (NAc) and the dopamine projection to it are considered an integral part of the brain's reward circuit, i.e., they direct approach and consumption behaviors and underlie positive reinforcement. This reward-centered framing ignores important evidence about the role of this system in encoding aversive events. One reason for bias toward reward is the difficulty in designing experiments in which animals repeatedly experience punishments; another is the challenge in dissociating the response to an aversive stimulus itself from the reward/relief experienced when an aversive stimulus is terminated. Here, we review studies that employ techniques with sufficient time resolution to measure responses in ventral tegmental area and NAc to aversive stimuli as they are delivered. We also present novel findings showing that the same stimulus - intra-oral infusion of sucrose - has differing effects on NAc shell dopamine release depending on the prior experience. Here, for some rats, sucrose was rendered aversive by explicitly pairing it with malaise in a conditioned taste aversion paradigm. Thereafter, sucrose infusions led to a suppression of dopamine with a similar magnitude and time course to intra-oral infusions of a bitter quinine solution. The results are discussed in the context of regional differences in dopamine signaling and the implications of a pause in phasic dopamine release within the NAc shell. Together with our data, the emerging literature suggests an important role for differential phasic dopamine signaling in aversion vs. reward.

PMID: 23055953 [PubMed] PMCID: PMC3457027 Free PMC Article


Basolateral amygdala modulates terminal dopamine release in the nucleus accumbens and conditioned responding.


Source
Department of Psychology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599, USA.

Abstract

BACKGROUND:
Dopamine signaling in the nucleus accumbens (NAc) is essential for goal-directed behaviors and primarily arises from burst firing of ventral tegmental area neurons. However, the role of associative neural substrates such as the basolateral amygdala (BLA) in regulating phasic dopamine release in the NAc, particularly during reward seeking, remains unknown.

METHODS:
Male Sprague-Dawley rats learned to discriminate two cues: a discriminative stimulus (DS) that predicted sucrose reinforcement contingent upon a lever press and a nonassociated stimulus (NS) that predicted a second lever never reinforced with sucrose. Following training, a test session was completed in which NAc dopamine was measured using fast-scan cyclic voltammetry in conjunction with inactivation of the ipsilateral BLA (gamma-aminobutyric acid agonists; baclofen/muscimol) to determine the contribution of BLA activity to dopamine release in the NAc core during the task.

RESULTS:
Under vehicle conditions, DS and NS presentation elicited dopamine release within the NAc core. The DS evoked significantly more dopamine than the NS. Inactivation of the BLA selectively attenuated the magnitude of DS-evoked dopamine release, concurrent with an attenuation of DS-evoked conditioned approaches. Other behavioral responses (e.g., lever pressing) and dopamine release concomitant with those events were unaltered by BLA inactivation. Furthermore, neither ventral tegmental area electrically stimulated dopamine release nor the probability of high concentration dopamine release events was altered following BLA inactivation.

CONCLUSIONS:
These results demonstrate that the BLA terminally modulates dopamine signals within the NAc core under specific, behaviorally relevant conditions, illustrating a functional mechanism by which the BLA selectively facilitates responding to motivationally salient environmental stimuli.

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PMID: 20044074 [PubMed - indexed for MEDLINE] PMCID: PMC2849914 Free PMC Article

Source
Medical Center Boulevard, Department of Physiology and Pharmacology, Wake Forest University School of Medicine, Winston-Salem, NC 27157, USA.
ebudygin@wfubmc.edu

Abstract
Aversive stimuli have a powerful impact on behavior and are considered to be the opposite valence of pleasure. Recent studies have determined some populations of ventral tegmental area (VTA) dopaminergic neurons are activated by several types of aversive stimuli, whereas other distinct populations are either inhibited or unresponsive. However, it is not clear where these aversion-responsive neurons project, and whether alterations in their activity translate into dopamine release in the terminal field. Here we show unequivocally that the neurochemical and anatomical substrates responsible for the perception and processing of pleasurable stimuli within the striatum are also activated by tail pinch, a classical painful and aversive stimulus. Dopamine release is triggered in the dorsal striatum and nucleus accumbens (NAc) core by tail pinch and is time locked to the duration of the stimulus, indicating that the dorsal striatum and NAc core are neural substrates, which are involved in the perception of aversive stimuli. However, dopamine is released in the NAc shell only when tail pinch is removed, indicating that the alleviation of aversive condition could be perceived as a rewarding event.

Aversive Stimuli Differentially Modulate Real-Time Dopamine Transmission Dynamics within the Nucleus Accumbens Core and Shell. Badrinarayan A, Wescott SA, Vander Weele CM, Saunders BT, Couturier BE, Maren S, Aragona BJ.

Source
Neuroscience Graduate Program and Department of Psychology, University of Michigan, Ann Arbor, Michigan 48109-1043.

Abstract
Although fear directs adaptive behavioral responses, how aversive cues recruit motivational neural circuitry is poorly understood. Specifically, while it is known that dopamine (DA) transmission within the nucleus accumbens (NAc) is imperative for
mediating appetitive motivated behaviors, its role in aversive behavior is controversial. It has been proposed that divergent phasic DA transmission following aversive events may correspond to segregated mesolimbic dopamine pathways; however, this prediction has never been tested. Here, we used fast-scan cyclic voltammetry to examine real-time DA transmission within NAc core and shell projection systems in response to a fear-evoking cue. In male Sprague Dawley rats, we first demonstrate that a fear cue results in decreased DA transmission within the NAc core, but increased transmission within the NAc shell. We examined whether these changes in DA transmission could be attributed to modulation of phasic transmission evoked by cue presentation. We found that cue presentation decreased the probability of phasic DA release in the core, while the same cue enhanced the amplitude of release events in the NAc shell. We further characterized the relationship between freezing and both changes in DA as well as local pH. Although we found that both analytes were significantly correlated with freezing in the NAc across the session, changes in DA were not strictly associated with freezing while basic pH shifts in the core more consistently followed behavioral expression. Together, these results provide the first real-time neurochemical evidence that aversive cues differentially modulate distinct DA projection systems.


Prefrontal/accumbal catecholamine system determines motivational salience attribution to both reward- and aversion-related stimuli.

Ventura R, Morrone C, Puglisi-Allegra S.

Source
Santa Lucia Foundation, European Centre for Brain Research (CERC), Via del Fosso di Fiorano 65, 00143 Rome, Italy. rossella.ventura@cc.univaq.it

Abstract
Recent evidence suggests that rewarding and aversive stimuli affect the same brain areas, including medial prefrontal cortex and nucleus accumbens. Although nucleus accumbens is known to respond to salient stimuli, regardless of their hedonic valence, with selective increased dopamine release, little is known about the role of prefrontal cortex in reward- and aversion-related motivation or about the neurotransmitters involved. Here we find that selective norepinephrine depletion in medial prefrontal cortex of mice abolished the increase in the release of norepinephrine by prefrontal cortex and of dopamine by nucleus accumbens that is induced by food, cocaine, or lithium chloride and impaired the place conditioning induced by both lithium chloride (aversion) and food or cocaine (preference). This is evidence that prefrontal cortical norepinephrine transmission is necessary for motivational salience attribution to both reward- and aversion-related stimuli through modulation of dopamine in nucleus accumbens, a brain area involved in all motivated behaviors.
37. **Real-time chemical responses in the nucleus acc... [Nat Neurosci. 2008] - PubMed - NCBI** [Free PMC Article](Full Text)


Real-time chemical responses in the nucleus accumbens differentiate rewarding and aversive stimuli.

Roitman MF, Wheeler RA, Wightman RM, Carelli RM.

Source
Department of Psychology, University of Illinois, Chicago, Illinois 60607, USA.

mroitman@uic.edu

Abstract
Rewarding and aversive stimuli evoke very different patterns of behavior and are rapidly discriminated. Here taste stimuli of opposite hedonic valence evoked opposite patterns of dopamine and metabolic activity within milliseconds in the nucleus accumbens. This rapid encoding may serve to guide ongoing behavioral responses and promote plastic changes in underlying circuitry.

PMID: 18978779 [PubMed - indexed for MEDLINE] PMCID: PMC3171188 [Free PMC Article] 

38. **Prefrontal/accumbal catecholamine system determines motivational salience attribution to both reward- and aversion-related stimuli** (Full Text)


Neuroscience
Prefrontal/accumbal catecholamine system determines motivational salience attribution to both reward- and aversion-related stimuli

Rossella Ventura,*‡‡ Cristina Morrone,*§ and Stefano Puglisi-Allegra*§

This article has been cited by other articles in PMC.

**ABSTRACT**
Recent evidence suggests that rewarding and aversive stimuli affect the same brain areas, including medial prefrontal cortex and nucleus accumbens. Although nucleus accumbens is known to respond to salient stimuli, regardless of their hedonic valence, with selective increased dopamine release, little is known about the role of prefrontal cortex in reward- and aversion-related motivation or about the neurotransmitters involved. Here we find that selective norepinephrine depletion in medial prefrontal...
cortex of mice abolished the increase in the release of norepinephrine by prefrontal
cortex and of dopamine by nucleus accumbens that is induced by food, cocaine, or
lithium chloride and impaired the place conditioning induced by both lithium chloride
(aversions) and food or cocaine (preference). This is evidence that prefrontal cortical
norepinephrine transmission is necessary for motivational salience attribution to both
reward- and aversion-related stimuli through modulation of dopamine in nucleus
accumbens, a brain area involved in all motivated behaviors.

39. Activation of nucleus accumbens NMDA receptors differentially affects appetitive or
aversive taste learning and memory (Full Text)


Published online 2012 April 19. doi: 10.3389/fnbeh.2012.00013

Activation of nucleus accumbens NMDA receptors differentially affects appetitive or
aversive taste learning and memory

Luis Núñez-Jaramillo,1 José A. Rangel-Hernández,2 Belén Burgueño-Zúñiga,2 and
María I. Miranda2,*

This article has been cited by other articles in PMC.

Abstract

Taste memory depends on motivational and post-ingestional consequences; thus, it can
be aversive (e.g., conditioned taste aversion, CTA) if a novel, palatable taste is paired
with visceral malaise, or it can be appetitive if no intoxication appears after novel taste
consumption, and a taste preference is developed. The nucleus accumbens (NAC) plays
a role in hedonic reactivity to taste stimuli, and recent findings suggest that reward and
aversions are differentially encoded by the activity of NAC neurons. The present study
examined whether the requirement for N-methyl-D-aspartate (NMDA) receptors in the
NAC core during rewarding appetitive taste learning differs from that during aversive
taste conditioning, as well as during retrieval of appetitive vs. aversive taste memory,
using the taste preference or CTA model, respectively. Bilateral infusions of NMDA (1
μg/μl, 0.5 μl) into the NAC core were performed before acquisition or before retrieval
of taste preference or CTA. Activation of NMDA receptors before taste preference
training or CTA acquisition did not alter memory formation. Furthermore, NMDA
injections before aversive taste retrieval had no effect on taste memory; however, 24 h
later, CTA extinction was significantly delayed. Also, NMDA injections, made before
familiar appetitive memory retrieval, interrupted the development of taste preference
and produced a preference delay 24 h later. These results suggest that memory
formation for a novel taste produces neurochemical changes in the NAC core that have
differential requirements for NMDA receptors during retrieval of appetitive or aversive
memory.
Encoding of Aversion by Dopamine and the Nucleus Accumbens

James E. McCutcheon,1 Stephanie R. Ebner,1 Amy L. Loriaux,1 and Mitchell F. Roitman1,*

Abstract
Adaptive motivated behavior requires rapid discrimination between beneficial and harmful stimuli. Such discrimination leads to the generation of either an approach or rejection response, as appropriate, and enables organisms to maximize reward and minimize punishment. Classically, the nucleus accumbens (NAc) and the dopamine projection to it are considered an integral part of the brain's reward circuit, i.e., they direct approach and consumption behaviors and underlie positive reinforcement. This reward-centered framing ignores important evidence about the role of this system in encoding aversive events. One reason for bias toward reward is the difficulty in designing experiments in which animals repeatedly experience punishments; another is the challenge in dissociating the response to an aversive stimulus itself from the reward/relief experienced when an aversive stimulus is terminated. Here, we review studies that employ techniques with sufficient time resolution to measure responses in ventral tegmental area and NAc to aversive stimuli as they are delivered. We also present novel findings showing that the same stimulus – intra-oral infusion of sucrose – has differing effects on NAc shell dopamine release depending on the prior experience. Here, for some rats, sucrose was rendered aversive by explicitly pairing it with malaise in a conditioned taste aversion paradigm. Thereafter, sucrose infusions led to a suppression of dopamine with a similar magnitude and time course to intra-oral infusions of a bitter quinine solution. The results are discussed in the context of regional differences in dopamine signaling and the implications of a pause in phasic dopamine release within the NAc shell. Together with our data, the emerging literature suggests an important role for differential phasic dopamine signaling in aversion vs. reward.

Hedonic and nucleus accumbens neural responses to a natural reward are regulated by aversive conditioning

doi: 10.1101/lm.1869710

Hedonic and nucleus accumbens neural responses to a natural reward are regulated by aversive conditioning
Mitchell F. Roitman,1,6,7 Robert A. Wheeler,2,6 Paul H.E. Tiesinga,3,4 Jamie D. Roitman,1 and Regina M. Carelli2,5

This article has been cited by other articles in PMC.

Abstract
The nucleus accumbens (NAc) plays a role in hedonic reactivity to taste stimuli. Learning can alter the hedonic valence of a given stimulus, and it remains unclear how the NAc encodes this shift. The present study examined whether the population response of NAc neurons to a taste stimulus is plastic using a conditioned taste aversion (CTA) paradigm. Electrophysiological and electromyographic (EMG) responses to intraoral infusions of a sucrose (0.3 M) solution were made in naïve rats (Day 1). Immediately following the session, half of the rats (n = 6; Paired) received an injection of lithium chloride (0.15 M; i.p.) to induce malaise and establish a CTA while the other half (n = 6; Unpaired) received a saline injection. Days later (Day 5), NAc recordings during infusions of sucrose were again made. Electrophysiological and EMG responses to sucrose did not differ between groups on Day 1. For both groups, the majority of sucrose responsive neurons exhibited a decrease in firing rate (77% and 71% for Paired and Unpaired, respectively). Following conditioning, in Paired rats, EMG responses were indicative of aversion. Moreover, the majority of responsive NAc neurons now exhibited an increase in firing rate (69%). Responses in Unpaired rats were unchanged by the experience. Thus, the NAc differentially encodes the hedonic value of the same stimulus based on learned associations.

42. Basolateral amygdala modulates terminal dopamine release in the nucleus accumbens and conditioned responding (Full Text)

Biol Psychiatry. Author manuscript; available in PMC 2011 April 15.

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Basolateral amygdala modulates terminal dopamine release in the nucleus accumbens and conditioned responding

Joshua L. Jones1, Jeremy J. Day,1 Brandon J. Aragona,1 Robert A. Wheeler,1 R. Mark Wightman,2,3 and Regina M. Carelli1,3

The publisher's final edited version of this article is available at Biol Psychiatry
See other articles in PMC that cite the published article.

Abstract
Background

Dopamine signaling in the nucleus accumbens (NAc) is essential for goal-directed behaviors and primarily arises from burst firing of ventral tegmental area (VTA)
neurons. However, the role of associative neural substrates such as the basolateral amygdala (BLA) in regulating phasic dopamine release in the NAc, particularly during reward-seeking, remains unknown.

Biological substrates of reward and aversion: a nucleus accumbens activity hypothesis

Neuropharmacology. Author manuscript; available in PMC 2010 January 1.

Published in final edited form as:
Published online 2008 July 15. doi: 10.1016/j.neuropharm.2008.06.075

Biological substrates of reward and aversion: a nucleus accumbens activity hypothesis

William A. Carlezon, Jr.1 and Mark J. Thomas2

The publisher's final edited version of this article is available at Neuropharmacology
See other articles in PMC that cite the published article.

Abstract
The nucleus accumbens (NAc) is a critical element of the mesocorticolimbic system, a brain circuit implicated in reward and motivation. This basal forebrain structure receives dopamine (DA) input from the ventral tegmental area (VTA) and glutamate (GLU) input from regions including the prefrontal cortex (PFC), amygdala (AMG), and hippocampus (HIP). As such, it integrates inputs from limbic and cortical regions, linking motivation with action. The NAc has a well-established role in mediating the rewarding effects of drugs of abuse and natural rewards such as food and sexual behavior. However, accumulating pharmacological, molecular, and electrophysiological evidence has raised the possibility that it also plays an important (and sometimes underappreciated) role in mediating aversive states. Here we review evidence that rewarding and aversive states are encoded in the activity of NAc medium spiny GABAergic neurons, which account for the vast majority of the neurons in this region. While admittedly simple, this working hypothesis is testable using combinations of available and emerging technologies, including electrophysiology, genetic engineering, and functional brain imaging. A deeper understanding of the basic neurobiology of mood states will facilitate the development of well-tolerated medications that treat and prevent addiction and other conditions (e.g., mood disorders) associated with dysregulation of brain motivation systems.

CREB activity in the nucleus accumbens shell controls gating of behavioral responses to emotional stimuli


Published online 2002 August 6. doi: 10.1073/pnas.172091899
Neurobiology
CREB activity in the nucleus accumbens shell controls gating of behavioral responses to emotional stimuli


This article has been cited by other articles in PMC.

ABSTRACT
The transcription factor cAMP response element (CRE)-binding protein (CREB) has been shown to regulate neural plasticity. Drugs of abuse activate CREB in the nucleus accumbens, an important part of the brain's reward pathways, and local manipulations of CREB activity have been shown to affect cocaine reward, suggesting an active role of CREB in adaptive processes that follow exposure to drugs of abuse. Using CRE-LacZ reporter mice, we show that not only rewarding stimuli such as morphine, but also aversive stimuli such as stress, activate CRE-mediated transcription in the nucleus accumbens shell. Using viral-mediated gene transfer to locally alter the activity of CREB, we show that this manipulation affects morphine reward, as well as the preference for sucrose, a more natural reward. We then show that local changes in CREB activity induce a more general syndrome, by altering reactions to anxiogenic, aversive, and nociceptive stimuli as well. Increased CREB activity in the nucleus accumbens shell decreases an animal's responses to each of these stimuli, whereas decreased CREB activity induces an opposite phenotype. These results show that environmental stimuli regulate CRE-mediated transcription within the nucleus accumbens shell, and that changes in CREB activity within this brain area subsequently alter gating between emotional stimuli and their behavioral responses. This control appears to be independent of the intrinsic appetitive or aversive value of the stimulus. The potential relevance of these data to addiction and mood disorders is discussed.

Enhanced Striatal Sensitivity to Aversive Reinforcement in Adolescents versus Adults.

Galván A, McGlennen KM.

Source
University of California-Los Angeles.

Abstract
Neurodevelopmental changes in mesolimbic regions are associated with adolescent risk-taking behavior. Numerous studies have shown exaggerated activation in the striatum in adolescents compared with children and adults during reward processing. However, striatal sensitivity to aversion remains elusive. Given the important role of the
striatum in tracking both appetitive and aversive events, addressing this question is critical to understanding adolescent decision-making, as both positive and negative factors contribute to this behavior. In this study, human adult and adolescent participants performed a task in which they received squirts of appetitive or aversive liquid while undergoing fMRI, a novel approach in human adolescents. Compared with adults, adolescents showed greater behavioral and striatal sensitivity to both appetitive and aversive stimuli, an effect that was exaggerated in response to delivery of the aversive stimulus. Collectively, these findings contribute to understanding how neural responses to positive and negative outcomes differ between adolescents and adults and how they may influence adolescent behavior.

46. [A patient with focal dystonia induced by... [Rinsho Shinkeigaku. 2005] - PubMed - NCBI


[A patient with focal dystonia induced by golf and presenting a decrease in activity of cerebral motor cortex on task].

[Article in Japanese]
Tanaka M, Ohyagi Y, Kawajiri M, Taniwaki T, Tobimatsu S, Furuya H, Yoshiura T, Kira J.

Source
Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University.

Abstract
We here report a 45-year-old man with left arm focal dystonia induced by golf. He was a swimming instructor. From 35 years of age, he swung a golf club for 4 hours everyday. At 37 years of age, he noted difficulties in moving left arm when swinging, and developed involuntary movement of left arm toward his back thereafter. His involuntary movement was exacerbated even in several years after stopping both golf and swimming. Neurologically, simultaneous contraction was observed in left triceps and biceps muscles and his left arm dropped when raising arm to front. A 'sensory trick' was also observed. Thus, he was diagnosed as having a rare focal dystonia, and its clinical characteristics and course were basically different from those of 'yips', a focal dystonia that is characterized by anxiety and distal dominant dystonia presenting only on golf. Magnetic resonance imaging (MRI), FDG-positron emission CT (FDG-PET), C11-Raclopride PET and 99mTc-single photon emission CT (SPECT) revealed no abnormality in cerebral cortex and basal ganglias. However, motor evoked potentials (MEPs) were not evoked bilaterally when magnetic stimulation was applied on primary motor cortex. On functional MRI (fMRI), 40 seconds raising left arm task-induced activation in the right primary motor, supplementary motor, and premotor areas was apparently decreased, while left motor areas, the normal side, were reasonably activated. Motor-associated areas are generally overactivated by task in focal dystonia patients whereas excitability in primary motor area is decreased in idiopathic generalized dystonia. Therefore, dystonia of the present case appears to be similar to
focal dystonia clinically but may partly have a mechanism similar to idiopathic generalized dystonia as shown in the fMRI studies.

47. **Task-specific Dystonias** (Full Text)

Ann N Y Acad Sci. Author manuscript; available in PMC 2009 March 9.

Published in final edited form as:
doi: 10.1196/annals.1444.012

Task-specific Dystonias

Diego Torres-Russotto and Joel S. Perlmutter a,b

The publisher's final edited version of this article is available at Ann N Y Acad Sci

Abstract

Task-specific dystonias are primary focal dystonias characterized by excessive muscle contractions producing abnormal postures during selective motor activities that often involve highly skilled, repetitive movements. Historically these peculiar postures were considered psychogenic but have now been classified as forms of dystonia. Writer’s cramp is the most commonly identified task-specific dystonia and has features typical of this group of disorders. Symptoms may begin with lack of dexterity during performance of a specific motor task with increasingly abnormal posturing of the involved body part as motor activity continues. Initially, the dystonia may manifest only during the performance of the inciting task, but as the condition progresses it may also occur during other activities or even at rest. Neurological exam is usually unremarkable except for the dystonia-related abnormalities. Although the precise pathophysiology remains unclear, increasing evidence suggests reduced inhibition at different levels of the sensorimotor system. Symptomatic treatment options include oral medications, botulinum toxin injections, neurosurgical procedures, and adaptive strategies. Prognosis may vary depending upon body part involved and specific type of task affected. Further research may reveal new insights into the etiology, pathophysiology, natural history, and improved treatment of these conditions.


51 Pages of PubMed articles by M Hallet, almost entirely concerning dystonias.

Results: 1 to 20 of 1033

1. *Dystonia: abnormal movements result from loss of inhibition.*
Hallett M.
PMID: 14509648 [PubMed - indexed for MEDLINE]
Related citations

2. **Physiology of dystonia.**
Hallett M.
PMID: 9750898 [PubMed - indexed for MEDLINE]

3. **Abnormal cortical motor excitability in dystonia.**
Ikoma K, Samii A, Mercuri B, Wassermann EM, Hallett M.
PMID: 8628484 [PubMed - indexed for MEDLINE]

4. **Dystonia and the supplementary sensorimotor area.**
Hallett M, Toro C.
PMID: 8615228 [PubMed - indexed for MEDLINE]

5. **Disturbed surround inhibition in focal hand dystonia.**
Sohn YH, Hallett M.
PMID: 15455393 [PubMed - indexed for MEDLINE]

6. **Generation of movement-related potentials in the supplementary sensorimotor area.**
Hallett M, Toro C.
PMID: 8615195 [PubMed - indexed for MEDLINE]

7. **Neurophysiology of tics.**
Hallett M.
PMID: 11530431 [PubMed - indexed for MEDLINE]

8.
H-reflex recovery curve and reciprocal inhibition of H-reflex in different kinds of dystonia.
Panizza M, Lelli S, Nilsson J, Hallett M.
PMID: 2330111 [PubMed - indexed for MEDLINE]
Related citations

9.
The neurophysiology of dystonia.
Hallett M.
PMID: 9605716 [PubMed - indexed for MEDLINE]
Related citations

10.
Spatial discrimination is abnormal in focal hand dystonia.
Bara-Jimenez W, Shelton P, Hallett M.
PMID: 11134387 [PubMed - indexed for MEDLINE]
Related citations

11.
Abnormal somatosensory homunculus in dystonia of the hand.
Bara-Jimenez W, Catalan MJ, Hallett M, Gerloff C.
PMID: 9818942 [PubMed - indexed for MEDLINE]
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12.
Congenital mirror movements. Abnormal organization of motor pathways in two patients.
Brain. 1991 Feb;114 ( Pt 1B):381-403.
PMID: 2004248 [PubMed - indexed for MEDLINE]
Related citations

13.
Akinesia in Parkinson's disease. II. Effects of subthreshold repetitive transcranial motor cortex stimulation.
PMID: 8190293 [PubMed - indexed for MEDLINE]
Related citations

14.
Akinesia in Parkinson’s disease. I. Shortening of simple reaction time with focal, single-pulse transcranial magnetic stimulation.
PMID: 8190292 [PubMed - indexed for MEDLINE]
Related citations

15.
Movement-related electroencephalographic desynchronization in patients with hand cramps: evidence for motor cortical involvement in focal dystonia.
Toro C, Deuschl G, Hallett M.
PMID: 10762156 [PubMed - indexed for MEDLINE]
Related citations

16.
Parkinson revisited: pathophysiology of motor signs.
Hallett M.
PMID: 12442661 [PubMed - indexed for MEDLINE]
Related citations

17.
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PMID: 8848963 [PubMed - indexed for MEDLINE]
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18.
Symptomatic and essential palatal tremor. 3. Abnormal motor learning.
Deuschl G, Toro C, Valls-Solé J, Hallett M.
J Neurol Neurosurg Psychiatry. 1996 May;60(5):520-5.
Related citations

19.
Depression of motor cortex excitability by low-frequency transcranial magnetic stimulation.
PMID: 9153480 [PubMed - indexed for MEDLINE]
Related citations

20.
Functional coupling and regional activation of human cortical motor areas during simple, internally paced and externally paced finger movements.
Related citations
51 more pages.

49. Disordered plasticity in the primary somatosensory cortex in focal hand dystonia (Full Text)

Published online 2009 January 16. doi: 10.1093/brain/awn348

Disordered plasticity in the primary somatosensory cortex in focal hand dystonia
Yohei Tamura,1,2 Yoshino Ueki,1 Peter Lin,1 Sherry Vorbach,1 Tatsuya Mima,3 Ryusuke Kakigi,4 and Mark Hallett1

This article has been cited by other articles in PMC.

Abstract
Interventional paired associative stimulation (PAS) can induce plasticity in the cortex, and this plasticity was previously shown to be disordered in the primary motor cortex in focal hand dystonia (FHD). This study aimed to test whether associative plasticity is abnormal in the primary somatosensory cortex (S1) in FHD and whether PAS modulates excitatory or inhibitory interneurons within the cortex. Ten FHD patients and 10 healthy volunteers were studied. We investigated the changes in single- and double-pulse somatosensory-evoked potentials before and after PAS, which consisted of peripheral electrical nerve stimulation and subsequent transcranial magnetic stimulation over S1. Four sessions of somatosensory-evoked potentials recordings were performed: before PAS, and immediately, 15 and 30 min after PAS. We compared the time course of the somatosensory-evoked potentials between the FHD and healthy groups. In the single-pulse condition, the P27 amplitudes were significantly higher in FHD immediately after PAS than before PAS, while no changes were observed in healthy subjects. In the double-pulse condition, significant differences in the suppression ratio of P27 were found immediately after and 15 min after PAS, while there were no significant differences in healthy subjects. The P27 suppression tended to normalize toward the level of the healthy volunteer group. In FHD, PAS transiently induced an abnormal increase in excitability in S1. In addition, intracortical inhibition in S1 was found to increase as well. This abnormal plasticity of the intracortical neurons in S1 may contribute to the pathophysiology of dystonia.
Surround inhibition depends on the force exerted and is abnormal in focal hand dystonia

S. Beck,1,2 M. Schubert,3 S. Pirio Richardson,1,4 and M. Hallett1

This article has been cited by other articles in PMC.

Abstract
There is evidence that surround inhibition (SI), a neural mechanism to enhance contrast between signals, may play a role in primary motor cortex during movement initiation, while it is deficient in patients with focal hand dystonia (FHD). To further characterize SI with respect to different force levels, single- and paired-pulse transcranial magnetic stimulation was applied at rest and during index finger movement to evoke potentials in the nonsynergistic, abductor pollicis muscle. In Experiment 1, in 19 healthy volunteers, SI was tested using single-pulse transcranial magnetic stimulation. Motor-evoked potentials at rest were compared with those during contraction using four different force levels [5, 10, 20, and 40% of maximum force (Fmax)]. In Experiments 2 and 3, SI and short intracortical inhibition (SICI) were tested, respectively, in 16 patients with FHD and 20 age-matched controls for the 10% and 20% Fmax levels. SI was most pronounced for 10% Fmax and abolished for the 40% Fmax level in controls, whereas FHD patients had no SI at all. In contrast, a loss of SICI was observed in FHD patients, which was more pronounced for 10% Fmax than for 20% Fmax. Our results suggest that SI is involved in the generation of fine finger movements with low-force levels. The greater loss of SICI for the 10% Fmax level in patients with FHD than for the 20% Fmax level indicates that this inhibitory mechanism is more abnormal at lower levels of force.
The pathophysiology of dystonia has been best studied in patients with focal hand dystonia. A loss of inhibitory function has been demonstrated at spinal, brainstem and cortical levels. Many cortical circuits seem to be involved. One consequence of the loss of inhibition is a failure of surround inhibition, and this appears to directly lead to overflow and unwanted muscle spasms. There are mild sensory abnormalities and deficits in sensorimotor integration; these also might be explained by a loss of inhibition. Increasing inhibition may be therapeutic. A possible hypothesis is that there is a genetic loss of inhibitory interneurons in dystonia and that this deficit is a substrate on which other factors can act to produce dystonia.


Motor training as treatment in focal hand dystonia.

Zeuner KE, Shill HA, Sohn YH, Molloy FM, Thornton BC, Dambrosia JM, Hallett M.

Source

Human Motor Control Section, Medical Neurology Branch, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland 20892-1428, USA.

Abstract

Focal hand dystonia may arise as a result of aberrant plasticity from excessive repetitive use. Improvement might be possible with appropriate motor training. Focusing on trying to decrease abnormal overflow of movement to fingers not involved in a task, we developed a motor training program for individualized finger movements. Ten patients with writer's cramp participated in the motor training program. Evaluation was done with the Fahn dystonia scale, kinematic analysis of handwriting, transcranial magnetic stimulation (TMS), and electroencephalography (EEG). Clinical improvement of dystonia was significant using the Fahn dystonia scale, and 6 patients reported an improvement in writing. The handwriting analysis showed a trend for improvement after training in simple exercises. There were no changes in cortical excitability measured by TMS and EEG. Whereas this method of motor training for 4 weeks led to mild subjective improvement and some improvement in handwriting, it is not sufficient to reverse motor cortex abnormalities measured by TMS and EEG.

2004 Movement Disorder Society.
Short intracortical and surround inhibition are selectively reduced during movement initiation in focal hand dystonia.

Beck S, Richardson SP, Shamim EA, Dang N, Schubert M, Hallett M.

Source
Human Motor Control Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland 20892-1428, USA. becksa@ninds.nih.gov

Abstract
In patients with focal hand dystonia (FHD), pathological overflow activation occurs in muscles not involved in the movement. Surround inhibition is a neural mechanism that can sharpen desired movement by inhibiting unwanted movement in adjacent muscles. To further establish the phenomenon of surround inhibition and to determine whether short intracortical inhibition (SICI) reflecting inhibition from the local interneurons in primary motor cortex (M1), might play a role in its genesis, single- and paired-pulse transcranial magnetic stimulation (TMS), and Hoffmann reflex testing were applied to evaluate the excitability of the relaxed abductor pollicis brevis muscle (APB) at various intervals during a movement of the index finger in 16 patients with FHD and 20 controls. Whereas controls showed inhibition of APB motor-evoked potential (MEP) size during movement initiation and facilitation of APB MEP size during the maintenance phase, FHD patients did not modulate APB MEP size. In contrast, SICI remained constant in controls, but FHD patients showed reduced SICI during movement initiation. The H(max)/M(max) ratio in control subjects increased during movement initiation. The results provide additional evidence for the presence of surround inhibition in M1, where it occurs only during movement initiation, indicating that different mechanisms underlie movement initiation and maintenance. Thus, surround inhibition is sculpted both in time and space and may be an important neural mechanism during movement initiation to counteract increased spinal excitability. SICI may contribute to its generation, because in patients with FHD, the lack of depression of APB MEP size is accompanied by a reduction in SICI.

54. Adaptation motor learning of arm movements in patients with cerebellar disease. (Full Text)


Adaptation motor learning of arm movements in patients with cerebellar disease.

G Deuschl, C Toro, T Zeffiro, S Massaquoi, and M Hallett

This article has been cited by other articles in PMC.

Abstract
OBJECTIVE--To design a test of motor learning using arm movements in normal subjects and patients with cerebellar disease. METHODS--Elbow angle was continuously displayed as a cursor (a dot) on a computer screen, and subjects made ballistic elbow flexion and extension movements to try to move the cursor between
two targets on the screen. The relation between the arm movement and its visual feedback was changed, and the subjects reacted by adapting the amplitude of their movements in subsequent trials. RESULTS—The consecutive errors showed exponential learning curves during adaptation, which were quantified by their steepness. Ten patients with isolated cerebellar or olivopontocerebellar degeneration had less steep learning curves than normal subjects, indicating a failure of adaptation motor learning in cerebellar disease. The results show that this test may be useful for the analysis of motor learning.


Hand cramps: clinical features and electromyographic patterns in a focal dystonia.

**Cohen LG, Hallett M.**

**Source**

Human Motor Control Section, National Institute of Neurological and Communicative Disorders and Stroke, Bethesda, MD 20892.

**Abstract**

We studied 19 patients with hand cramps, including writer's cramp, typist's cramp, piano, and guitar player's cramp. EMGs were recorded while patients performed the task triggering the cramps. Ten patients with dystonic cramps had EMGs with generalized muscle spasms with co-contraction of agonist and antagonist muscles. In three patients with simple cramps that involved one to three fingers, specific muscle groups showed co-contracting bursts that lasted longer than normal. The physiological abnormalities support the interpretation that hand cramp is a focal dystonia, characterized by both excessive muscle activity and defective fine motor control.


Movement-related cortical potentials in writer's cramp.

**Deuschl G, Toro C, Matsumoto J, Hallett M.**

**Source**

Human Motor Control Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD 20892-1428, USA.

**Abstract**

Movement-related cortical potentials in response to simple, self-paced, brisk index finger abduction movements were recorded in patients with simple and complex writer's cramp and compared with those of age-matched control subjects. Analysis of the movement-related cortical potential waveforms showed that the
Bereitschaftspotential, the peak of the negative slope, and the frontal peak of the motor potential did not differ in the two groups, except for the average amplitude of the early part of the negative-slope peak, which was decreased in the patient group during the interval of 300 to 200 msec prior to electromyographic onset. This finding was restricted to the electrodes overlying the contralateral and midline central electrodes. Movement-related cortical potentials from patients and control subjects could be equally accounted for by a four-dipole source model with sources located in the contralateral and ipsilateral sensorimotor regions and the supplementary motor area. There was a trend for a reduction in the strength of the sensorimotor sources active during the premotor period in the patient group, but the difference did not reach a significant level for any individual source. No differences were found between the movement-related cortical potentials elicited by movements of the affected and unaffected hand, or between those of patients with simple or complex hand cramps. This result suggests a deficiency of contralateral motor cortex activation just prior to the initiation of voluntary movements in patients with focal dystonia.

57. Sensory training for patients with focal hand dys... [Ann Neurol. 2002] - PubMed - NCBI


Sensory training for patients with focal hand dystonia.

Zeuner KE, Bara-Jimenez W, Noguchi PS, Goldstein SR, Dambrosia JM, Hallett M.

Source
Medical Neurology Branch, National Institute of Neurological Disorders and Stroke, Bethesda, MD 20892-1428, USA.

Abstract
Some patients with focal hand dystonia have impaired sensory perception. Abnormal sensory processing may lead to problems with fine motor control. For patients with focal hand dystonia who demonstrate sensory dysfunction, sensory training may reverse sensory impairment and dystonic symptoms. We studied the efficacy of learning to read braille as a method of sensory training for patients with focal hand dystonia. Sensory spatial discrimination was evaluated in 10 patients who had focal hand dystonia and 10 age- and gender-matched controls with a spatial acuity test (JVP domes were used in this test). Clinical dystonia evaluation included the Fahn dystonia scale and time needed to write a standard paragraph. Each individual was trained in braille reading at the grade 1 level for 8 weeks, between 30 and 60 minutes daily, and was monitored closely to ensure that reading was done regularly. Both controls and patients demonstrated improvement on the spatial acuity test. Patients showed a significant mean difference from baseline to 8 weeks on the Fahn dystonia scale. Sixty percent of the patients shortened the time they needed to write a standard paragraph. Improved sensory perception correlated positively with improvement on the Fahn dystonia scale. We conclude that training in braille reading improves deficits in spatial discrimination and decreases disability in patients with focal hand dystonia.


Pathophysiology of dystonia.

**Hallett M.**

**Source**

Human Motor Control Section, NINDS, NIH, Bethesda, MD, USA. [hallettm@ninds.nih.gov](mailto:hallettm@ninds.nih.gov)

**Abstract**

Understanding of the pathophysiology of dystonia derives primarily from studies of focal dystonias. Physiological investigations have revealed a number of abnormalities that may reflect the genetic substrate that predisposes certain individuals to develop dystonia. There is a loss of inhibition in the central nervous system, and a loss of surround inhibition specifically. Plasticity is increased, and there are sensory abnormalities. Which of these disorders is primary is uncertain.


Changes in brain anatomy in focal hand dystonia.


**Source**

Human Motor Control Section, Medical Neurology Branch, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD 20892-1428, USA.

**Abstract**

No consistent cerebral anatomical abnormality has ever been reported in primary focal hand dystonia (FHD). The present voxel-based morphometry study showed a significant bilateral increase in gray matter in the hand representation area of primary somatosensory and, to a lesser extent, primary motor cortices in 36 patients with unilateral FHD compared with 36 controls. The presence of anatomical changes in the perirolandic cortex for the unaffected hand as well as that for the affected hand suggests that these disturbances may be, at least in part, primary.

60. The role of inhibition from the left dorsal premotor cortex in right-sided focal hand dystonia. [Brain Stimul. 2009] - PubMed - NCBI


The role of inhibition from the left dorsal premotor cortex in right-sided focal hand dystonia.

**Beck S, Houdayer E, Richardson SP, Hallett M.**
The left dorsal premotor cortex (PMd) plays an important role in movement selection and is abnormally activated in imaging studies in patients with right-sided focal hand dystonia (FHD).

OBJECTIVE:
The aims of this study were to assess the role of left PMd in patients with FHD and in the genesis of surround inhibition, which is deficient in FHD.

METHODS:
Single- and paired-pulse transcranial magnetic stimulation (TMS) was applied during different phases of an index finger movement using the abductor pollicis brevis muscle (APB), a surrounding, nonsynergistic muscle, as target muscle. To look at the effect of PMd on the primary motor cortex (M1), a subthreshold conditioning pulse was applied to PMd 6 milliseconds before stimulation over M1.

RESULTS:
There was surround inhibition during movement initiation in controls, but not in FHD patients. In contrast, FHD patients, but not controls, showed premotor-motor inhibition (PMI) at rest. During movement, PMI was absent in both groups.

CONCLUSIONS:
We conclude that PMI does not appear to play a key role in the formation of surround inhibition in normal subjects, because it was not enhanced during movement initiation. However, in FHD, inhibition from PMd on M1 was abnormally increased at rest and declined during movement initiation. The behavior of PMd can therefore partly explain the loss of surround inhibition in the FHD patients. The functional significance of increased PMI at rest is not clear, but might be an attempt of compensation for losses of inhibition from other brain areas.

The N30 component of somatosensory evoked potentials in patients with dystonia.

Reilly JA, Hallett M, Cohen LG, Tarkka IM, Dang N.

Source
Human Motor Control Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD 20892.

Abstract
We recorded short-latency median nerve somatosensory evoked potentials (SEPs) in 10 patients with dystonia (6 with focal dystonia, 3 with generalized dystonia, and 1 with
segmental dystonia) and compared them with those of 10 normal controls. The EEG was recorded from 29 sites on the scalp with linked earlobe electrodes for reference. Latencies and amplitudes of P15, postcentral N20 and P45, and frontal N30 were evaluated. The latencies of all potentials were the same in patients and controls. The amplitudes of P15, N20 and P45 were also the same in both groups, but the N30 amplitude of the patients was larger than of the controls. The amplitude of N30 did not vary from the affected side to the unaffected side. Previous work has shown decreased N30 amplitude in patients with Parkinson's disease. Changes in N30 amplitude may be indicative of abnormal excitatory effects on cortex resulting from disorders of the basal ganglia.


Mapping the basal ganglia: fMRI evidence for somatotopic representation of face, hand, and foot.

Maillard L, Ishii K, Bushara K, Waldvogel D, Schulman AE, Hallett M.

Abstract

OBJECTIVE: To noninvasively investigate the somatotopy of the basal ganglia in humans.

METHODS: Functional MRI, 1.5-T, was performed on six normal right-handed volunteers during simple acoustically paced motor tasks involving the right hand, foot, and face.

RESULTS: In a single-subject analysis, statistical parametric maps showed overlapping activation extending along the anteroposterior extent of the left lentiform nucleus (LLN) for the hand, foot, and face representations. Within the LLN, the centers of gravity of each body part, reflecting both the extent and gradient of activation, were all located in the retrocommissural portion of the putamen. Their spatial relationship followed a similar pattern across subjects-face was medial to toes and fingers, toes were dorsal and rostral to fingers.

CONCLUSIONS: The somatotopic organization of hand, face, and foot representation in the human lentiform nucleus suggests a triangular pattern, rather than the linear pattern seen in primate studies. The overlap observed between the distinct body parts differs from the cortical sensorimotor representation, indicating a different organizational concept of the basal ganglia.
Plasticity of cortical inhibition in dystonia is impaired after motor learning and paired-associative stimulation.

Meunier S, Russmann H, Shamim E, Lamy JC, Hallett M.

Abstract
Artificial induction of plasticity by paired associative stimulation (PAS) in healthy volunteers (HV) demonstrates Hebbian-like plasticity in selected inhibitory networks as well as excitatory networks. In a group of 17 patients with focal hand dystonia and a group of 19 HV, we evaluated how PAS and the learning of a simple motor task influence the circuits supporting long-interval intracortical inhibition (LICI, reflecting activity of GABA(B) interneurons) and long-latency afferent inhibition (LAI, reflecting activity of somatosensory inputs to the motor cortex). In HV, PAS and motor learning induced long-term potentiation (LTP)-like plasticity of excitatory networks and a lasting decrease of LAI and LICI in the motor representation of the targeted or trained muscle. The better the motor performance, the larger was the decrease of LAI. Although motor performance in the patient group was similar to that of the control group, LAI did not decrease during the motor learning as it did in the control group. In contrast, LICI was normally modulated. In patients the results after PAS did not match those obtained after motor learning: LAI was paradoxically increased and LICI did not exhibit any change. In the normal situation, decreased excitability in inhibitory circuits after induction of LTP-like plasticity may help to shape the cortical maps according to the new sensorimotor task. In patients, the abnormal or absent modulation of afferent and intracortical long-interval inhibition might indicate maladaptive plasticity that possibly contributes to the difficulty that they have to learn a new sensorimotor task.
Abstract
We tested whether task-dependent modulation of inhibition within the motor cortex is impaired in patients with dystonia. Paired-pulse transcranial magnetic stimulation (TMS) at an interstimulus interval of 2 ms was used to measure the effect of two different tasks on cortical inhibition (SICI) in dystonic and normal subjects. In two experiments, SICI of the fourth dorsal interosseus (4DIO) and abductor pollicis brevis (APB) muscles were measured prior to and at the end of the training task. In the first experiment, subjects performed a nonselective task consisting of abducting the thumb, where the APB acted as agonist and the 4DIO as synergist. In the second experiment, the function of the 4DIO was changed as the subjects were asked to consciously inhibit this muscle while abducting the thumb (selective task). Therefore, while the APB was activated in both tasks, the 4DIO was activated in the nonselective task but was in the inhibitory surround in the selective task. We found that performance of the selective but not the nonselective task resulted in increased SICI in the 4DIO of normal but not in dystonic subjects. We conclude that task-dependent SICI is disturbed in patients with dystonia.

65. Left Parietal Activation Related to Planning, Executing and Suppressing Praxis Hand Movements (Full Text)

Clin Neurophysiol. Author manuscript; available in PMC 2010 May 1.

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Left Parietal Activation Related to Planning, Executing and Suppressing Praxis Hand Movements

Lewis Wheaton,1,2 Esteban Fridman,1 Stephan Bohlhalter,1 Sherry Vorbach,1 and Mark Hallett1

The publisher's final edited version of this article is available at Clin Neurophysiol
See other articles in PMC that cite the published article.

Abstract
Objective

We sought to investigate the activity of bilateral parietal and premotor areas during a Go/No Go paradigm involving praxis movements of the dominant hand.

Methods

A sentence was presented which instructed subjects on what movement to make (S1; for example, “Show me how to use a hammer.”). After an 8-s delay, “Go” or “No
Go” (S2) was presented. If Go, they were instructed to make the movement described in the S1 instruction sentence as quickly as possible, and continuously until the “Rest” cue was presented 3 s later. If No Go, subjects were to simply relax until the next instruction sentence. Event-related potentials (ERP) and event-related desynchronization (ERD) in the beta band (18–22 Hz) were evaluated for three time bins: after S1, after S2, and from −2.5 to −1.5 s before the S2 period.

Results

Bilateral premotor ERP was greater than bilateral parietal ERP after the S2 Go compared with the No Go. Additionally, left premotor ERP was greater than that from the right premotor area. There was predominant left parietal ERD immediately after S1 for both Go and No Go, which was sustained for the duration of the interval between S1 and S2. For both S2 stimuli, predominant left parietal ERD was again seen when compared to that from the left premotor or right parietal area. However, the left parietal ERD was greater for Go than No Go.

Conclusion

The results suggest a dominant role in the left parietal cortex for planning, executing, and suppressing praxis movements. The ERP and ERD show different patterns of activation and may reflect distinct neural movement-related activities.

Significance

The data can guide further studies to determine the neurophysiological changes occurring in apraxia patients and help explain the unique error profiles seen in patients with left parietal damage.

66. Abnormal Reorganization of Functional Cortical Small-World Networks in Focal Hand Dystonia (Full Text)


Published online 2011 December 13. doi: 10.1371/journal.pone.0028682

Abnormal Reorganization of Functional Cortical Small-World Networks in Focal Hand Dystonia

Seung-Hyun Jin,1,2 Peter Lin,1 and Mark Hallett1,*

This article has been cited by other articles in PMC.

Abstract

We investigated the large-scale functional cortical connectivity network in focal hand dystonia (FHD) patients using graph theoretic measures to assess efficiency. High-resolution EEGs were recorded in 15 FHD patients and 15 healthy volunteers at rest and during a simple sequential finger tapping task. Mutual information (MI) values of wavelet coefficients were estimated to create an association matrix between EEG
electrodes, and to produce a series of adjacency matrices or graphs, G, by thresholding with network cost. Efficiency measures of small-world networks were assessed. As a result, we found that FHD patients have economical small-world properties in their brain functional networks in the alpha and beta bands. During a motor task, in the beta band network, FHD patients have decreased efficiency of small-world networks, whereas healthy volunteers increase efficiency. Reduced efficient beta band network in FHD patients during the task was consistently observed in global efficiency, cost-efficiency, and maximum cost-efficiency. This suggests that the beta band functional cortical network of FHD patients is reorganized even during a task that does not induce dystonic symptoms, representing a loss of long-range communication and abnormal functional integration in large-scale brain functional cortical networks. Moreover, negative correlations between efficiency measures and duration of disease were found, indicating that the longer duration of disease, the less efficient the beta band network in FHD patients. In regional efficiency analysis, FHD patients at rest have high regional efficiency at supplementary motor cortex (SMA) compared with healthy volunteers; however, it is diminished during the motor task, possibly reflecting abnormal inhibition in FHD patients. The present study provides the first evidence with graph theory for abnormal reconfiguration of brain functional networks in FHD during motor task.

67. Functional coupling of human cortical sensorimotor are... [Brain. 1999] - PubMed - NCBI (Full Text)

Brain. 1999 May;122 ( Pt 5):855-70.

Functional coupling of human cortical sensorimotor areas during bimanual skill acquisition.

Andres FG, Mima T, Schulman AE, Dichgans J, Hallett M, Gerloff C.

Source

Human Motor Control Section, National Institutes of Health, Bethesda, MD 20892, USA.

Abstract

Bimanual co-ordination of skilled finger movements is a high-level capability of the human motor system and virtually always requires training. Little is known about the physiological processes underlying successful bimanual performance and skill acquisition. In the present study, we used task-related coherence (TRCoh) and task-related power (TRPow) analysis of multichannel surface EEG to investigate the functional coupling and regional activation of human sensorimotor regions during bimanual skill acquisition. We focused on changes in interhemispheric coupling associated with bimanual learning. TRCoh and TRPow were estimated during the fusion of two overlearned unimanual finger-tapping sequences into one novel bimanual sequence, before and after a 30-min training period in 18 normal volunteers. Control experiments included learning and repetition of complex and simple unimanual finger sequences. The main finding was a significant increase in interhemispheric TRCoh selectively in the early learning stage (P < 0.0001).
Interhemispheric TRCoh was also present during the unimanual control tasks, but with lower magnitude, even if learning was involved. Training improved bimanual sequence performance (from 58.3+/-24.1 to 83.7+/-15.3% correct sequences). After training, interhemispheric (bimanual) TRCoh decreased again, thereby approaching levels similar to those in the unimanual controls. We propose that the initial increase in TRCoh reflects changes in interhemispheric communication that are specifically related to bimanual learning and may be relayed through the corpus callosum. The present data might also offer a neurophysiological explanation for the clinical observation that patients with lesions of the corpus callosum may show deficits in the acquisition of novel bimanual tasks but not necessarily in the execution of previously learned bimanual activities.

68. The pathophysiology of focal hand dystonia (Full Text)

J Hand Ther. Author manuscript; available in PMC 2010 April 1.

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The pathophysiology of focal hand dystonia

Peter T. Lin and Mark Hallett

The publisher's final edited version of this article is available at J Hand Ther
See other articles in PMC that cite the published article.

Abstract
Focal hand dystonia is a disabling movement disorder, often task-specific, that leads to impaired hand use. In addition to a genetic predisposition, environmental risk factors including repetitive use and musculoskeletal constraints are contributory. Although the underlying cause is unknown, recent studies have identified several key mechanisms that may play a part in its genesis. Failure of inhibition, abnormal sensorimotor integration, and maladaptive plasticity seem to be important. Understanding the underlying physiology may lead to the design of novel therapies.


Brain. 1998 Jul;121 ( Pt 7):1195-212.

The pathophysiology of primary dystonia.

Berardelli A, Rothwell JC, Hallett M, Thompson PD, Manfredi M, Marsden CD.
Source
Department of Neurological Sciences, Università di Rome La Sapienza and Mediterranean Neurological Institute, Neuromed, Pozzilli (IS), Italy.

Abstract
Co-contraction and overflow of EMG activity of inappropriate muscles are typical features of all dystonic movements whether voluntary or involuntary. Voluntary movements are slow and more variable than normal, and there is particular difficulty switching between component movements of a complex task. Reduced spinal cord and brainstem inhibition is common to many reflex studies (long-latency reflexes, cranial reflexes and reciprocal inhibition). These reflex abnormalities may contribute to the difficulties in voluntary movements but cannot be causal as they can occur outside the clinically involved territory. Clinical and neurophysiological studies have emphasized the possible role of sensory feedback in the generation of dystonic movements. Abnormalities of cortical and basal ganglia function have been described in functional imaging and neurophysiological studies of patients with dystonia and in animal models of primary dystonia. Studies of cortical function have shown reduced preparatory activity in the EEG before the onset of voluntary movements, whilst magnetic brain stimulation has revealed changes in motor cortical excitability. Functional imaging of the brain in primary dystonia has suggested reduced pallidal inhibition of the thalamus with consequent overactivity of medial and prefrontal cortical areas and underactivity of the primary motor cortex during movements. These findings are supported by preliminary neuronal recordings from the globus pallidus and the thalamus at the time of stereotaxic surgery in patients with dystonia. All this evidence suggests that primary dystonia results from a functional disturbance of the basal ganglia, particularly in the striatal control of the globus pallidus (and substantia nigra pars reticulata). This causes altered thalamic control of cortical motor planning and executive areas, and abnormal regulation of brainstem and spinal cord inhibitory interneuronal mechanisms.


An update on psychogenic movement disorders.

Ellenstein A, Kranick SM, Hallett M.

Source

Human Motor Control Section, Medical Neurology Branch, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD 20892-1428, USA. ellensteina@ninds.nih.gov

Abstract

Psychogenic movement disorders (PMD) and other conversion disorders (CD) with apparent neurologic signs (neurologic CD) plague patients and perplex physicians. Due to a lack of objective evidence of underlying brain lesions, CD were largely abandoned by neurologists and remained poorly understood psychiatric diagnoses throughout most of the 20th century. Modern neuroscience now supports increasingly comprehensive biological models for these complex disorders, definitively establishing their place in both neurology and psychiatry. Although it is often clinically useful to distinguish a movement disorder as either "organic" or "psychogenic," this dichotomy is
difficult to defend scientifically. Here we describe the neuroimaging and
neurophysiologic evidence for dysfunctional neural networks in PMD, explain the
diagnostic potential of clinical neurophysiologic testing, discuss the promising if
increasingly complex role of neuropsychiatric genetics, and review current treatment
strategies.


Psychogenic movement disorders.
Hallett M, Weiner WJ, Kompoliti K.
Source
Human Motor Control Section, NINDS, NIH, Bethesda, MD 20892-1428, USA.
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Abstract
Psychogenic movement disorders are common, but the diagnosis may be
difficult. Visual appearance alone is typically not sufficient to make a diagnosis,
but such information is certainly important. That a movement is bizarre can be
helpful, but still must be considered thoughtfully since organic movement
disorders can have endless variety. The diagnosis should rest on positive findings
such as paroxysmal nature, maximum severity at or near onset, variability of
tremor direction, frequency and amplitude, entrainment of tremor, distractability
and suggestibility, and wildly swaying gait and balance problems with no
falling. Psychogenic parkinsonism often poses a problem because of the
relatively high frequency of overlap of psychogenic and organic disease. In
regard to psychogenic parkinsonism, there are special features to look for. There
might be tremor with kinetic movement as well as rest and posture, and finger
tremor might be absent. With sequential movements, the sequence effect is
typically lacking. Extreme slowness and grunting with great effort may be seen.
Improvement in arm swing while running, a feature of organic parkinsonism,
may not be seen.


Psychogenic movement disorders.
Schrag A, Lang AE.
Source
Royal Free and University College Medical School, University College London,
London, UK. a.schrag@medsch.ucl.ac.uk

Abstract
PURPOSE OF REVIEW:
This review focuses on recent studies assessing clinical features and laboratory findings that may help diagnose psychogenic movement disorders, and the ongoing controversy about the relationship of these disorders with preceding peripheral injury.

RECENT FINDINGS:
'Organic' movement disorders may still be misdiagnosed as psychogenic. Probably more commonly, however, psychogenic movement disorders are underdiagnosed. Most features typically associated with recognized movement disorders, including geste antagoniste or treatment-induced dyskinesias, can be seen in psychogenic movement disorder, and abnormal movements that would not normally be considered psychogenic or produced by psychological factors, such as palatal tremor, may occur on a psychogenic basis. On the other hand, psychiatric features are sometimes seen in neurologically based movement disorders. The diagnostic criteria for psychogenic movement disorders provide a degree of diagnostic certainty based on a combination of clinical and psychiatric features. Laboratory investigations can help exclude specific diagnoses, such as Parkinson's disease with (123I)beta-CIT single photon emission computed tomography, and neurophysiological methods can demonstrate characteristic features of psychogenic movement disorders, such as entrainment or suppression of psychogenic tremor with contralateral hand movements. However, some tests reported to differentiate psychogenic from neurological movement disorders may have incomplete specificity; for example, psychogenic tremor may not always be associated with complete coherence of tremor frequency. An ongoing controversy surrounds movement disorders following peripheral injuries, but recent evidence suggests that such patients should always be screened for the presence of a psychogenic movement disorder.

SUMMARY:
Psychogenic movement disorder continues to be a difficult diagnosis to make and is likely to be underrecognized. Clinical and laboratory features are emerging, however, that support this diagnosis. The controversy regarding posttraumatic movement disorders continues, but a diagnosis of a psychogenic movement disorder should be actively sought in such patients.

73. Psychogenic movement disorders: frequency, clinical profile, and characteristics. (Full Text)


Psychogenic movement disorders: frequency, clinical profile, and characteristics.

S A Factor, G D Podskalny, and E S Molho

This article has been cited by other articles in PMC.

Abstract

Of 842 consecutive patients with movement disorders seen over a 71 month period, 28 (3.3%) were diagnosed as having a documented or clinically established psychogenic
movement disorder. Tremor was most common (50%) followed by dystonia, myoclonus, and parkinsonism. Clinical descriptions of various types are reviewed. Clinical characteristics common in these patients included distractability (86%), abrupt onset (54%), and selective disabilities (39%). Distractability seems to be most important in tremor and least important in dystonia. Other diagnostic clues included entrainment of tremor to the frequency of repetitive movements of another limb, fatigue of tremor, stimulus sensitivity, and previous history of psychogenic illness. On examination, 71% had other psychogenic features. Over 60% had a clear history of a precipitating event and secondary gain and 50% had a psychiatric diagnosis (usually depression). Twenty five per cent of patients presented with combined psychogenic movement disorder and organic movement disorder; 35% resolved and this subgroup had a shorter duration of disease than those who are unresolved. Psychogenic movement disorder represents an uncommon diagnosis among patients with movement disorders. The ability to make a diagnosis rests on the presence of a multitude of clinical clues and therapeutic action should be taken as early as possible.

74. Jinnah, HA, Dystonia Coalition, Treatment Strategies for Dystonia: Medical and Surgical, American Academy of Neurology, Spring 2010

The clinical manifestations of the dystonias are extremely varied. Dystonias occur in children and adults. They may involve one body region or many. They may be progressive, static, task-specific, or paroxysmal. The causes of these varied clinical manifestations are equally varied. Dystonias may be inherited or acquired, with a broad array of known underlying biological mechanisms. Considering the clinical and etiological heterogeneity, it is not surprising that responses to different treatments also vary widely. The heterogeneity makes the design of a universal treatment algorithm challenging.

Although systematic and evidence-based reviews for treatments of dystonia have been published,[1-3] many commonly used treatments have not been subject to rigorous clinical trials. Much evidence comes from small controlled trials, unblinded or uncontrolled observations, retrospective reviews, or anecdotal reports, and personal experience. In the absence of definitive evidence, recommendations regarding treatments reflect a combination of all available evidence combined with the experience of providers who treat large numbers of dystonia patients.

Multiple lengthy reviews covering treatments for dystonia have been published already. [4-8] This summary was developed as a practical synopsis and is organized into three parts. The first part provides a synopsis of the most common treatment options available, both medical and surgical. The second part provides a synopsis of how the diagnosis of different types of dystonia influences the selection of treatment options. The third part includes a summary and conclusions, along with future goals for the development and testing of novel therapies.

Available Treatment Options:

- Oral Medications
Procedures and Neurosurgical Interventions

Treatment Strategies for Different Populations:

- Before Starting Treatment
- Specific Treatments for Special Populations
- General Treatment Strategy

Summary and Future Prospects

Selected References

75. rarediseasesnetwork.epi.usf.edu/dystonia/documents/03NEDMRFORDPressRelease2009-10-01.pdf

Dystonia Medical Research Foundation, Press Release, NIH Awards New Grant to Develop Better Treatments for Focal Dystonias (Oct. 2009)

October 1, 2009 – Officials at the National Institutes of Health (NIH) have announced the funding of a five year award aimed at forming a multicenter Dystonia Coalition to advance clinical research on primary focal dystonias, including Cervical Dystonia, Spasmodic Dysphonia, Blepharospasm, and others. Leading the Coalition will be H. A. Jinnah, MD, PhD, Professor of Neurology and Human Genetics at Emory University in Atlanta, GA.

Dystonia is a neurological movement disorder that causes muscles to contract and spasm involuntarily. It affects men, women and children. Dystonia can be generalized, affecting many major muscle groups and resulting in twisting, repetitive movements and abnormal postures. Or dystonia can be more focal, affecting a specific part of the body such as legs, arms, hands, neck, face, mouth, or vocal cords. Currently, it is estimated that at least 300,000 individuals in North America suffer from dystonia, making it more common than Huntington’s disease, muscular dystrophy, and ALS. There is no known cure.

The $6 million award will allow the Dystonia Coalition to cultivate a better understanding of the primary focal dystonias and find better therapies. This includes projects to develop a better understanding of their natural history, establish instruments appropriate for monitoring disease severity in clinical trials, and develop proper diagnostic criteria. The creation of a biorepository to store biological samples to support future research is also planned, making these resources available to investigators worldwide. The Coalition will bring together the most committed dystonia researchers in North America and Europe, along with dystonia patient advocacy groups.

The Dystonia Medical Research Foundation (DMRF) will play an integral role by providing logistical and planning support for the Coalition. The Foundation is well-poised to serve in this capacity as it is the largest and most established patient support organization devoted to dystonia.
“Dystonias are rare and devastating diseases, with limited and sometimes inadequate treatment options,” explains Dr. Jinnah. “Funding of the Dystonia Coalition will allow us to address unmet needs in focal dystonia research, as well as make resources available to other investigators that will help to advance the field.”

“We are delighted about the funding of the Dystonia Coalition and pleased that Dr. Jinnah will be leading this effort,” says Mahlon R. DeLong, MD, Scientific Director of the DMRF. “This is a unique opportunity to provide much-needed attention to these rare diseases. The DMRF is proud to play a role in this important effort.”

The Dystonia Medical Research Foundation is dedicated to advancing research for more treatments and ultimately a cure, promoting awareness and education and supporting the needs and well being of affected individuals and families. To learn more about dystonia, contact the Dystonia Medical Research Foundation at 1-800-377-3978 or www.dystonia-foundation.org.

76. AAN Annual Meeting Programs: 7SM.001 - The Dystonias: Diagnosis, Treatment, and Update on Causes -- American Academy of Neurology (March 2013)

7SM.001 - The Dystonias: Diagnosis, Treatment, and Update on Causes

**Event Time:**
Friday March 22, 2013 6:30 am to 8:30 am

**Topic(s):** Movement Disorders

**Director(s):** H. Jinnah MD, PhD

**Description:** Dystonia is one of the least understood and most often misdiagnosed movement disorders. Using video demonstrations, faculty will address the clinical spectrum and classification of the dystonias; current concepts regarding the underlying causes; strategies for diagnostic evaluation; and medical and surgical treatment strategies.

**Completion Message:** Participants should be familiar with the varied clinical manifestations of the dystonias; the classification of the dystonias; the many causes for dystonia and a diagnostic approach; current understanding of the etiology and pathogenesis of dystonia; and treatment options.


Extreme task specificity in writer's cramp.
Shamim EA, Chu J, Scheider LH, Savitt J, Jinnah HA, Hallett M.
Source
Human Motor Control Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland, USA.
shamime@mail.nih.gov

Abstract
BACKGROUND:
Focal hand dystonia may be task specific, as is the case with writer's cramp. In early stages, task specificity can be so specific that it may be mistaken for a psychogenic movement disorder.

METHODS:
We describe 4 patients who showed extreme task specificity in writer's cramp. They initially only had problems writing either a single letter or number. Although they were largely thought to be psychogenic, they progressed to typical writer's cramp.

CONCLUSIONS:
Early recognition of this condition may provide an opportunity for early initiation of treatment.

78. Is writer's cramp caused by a deficit of senso... [Exp Brain Res. 2001] - PubMed - NCBI


Is writer's cramp caused by a deficit of sensorimotor integration?
Writer's cramp is a highly specific movement disorder in which handwriting is impaired while most other manual skills are often unaffected. On the basis of abnormal findings in experiments measuring the control of grip forces, it has been suggested that writer's cramp is caused by a deficit of sensorimotor integration. The aim of our study was to determine whether there is a functional link between sensory deficits, abnormalities in the control of grip force, and handwriting disorders. We compared the grip force and handwriting performance of writer's cramp patients with that of control subjects and with that of a stroke patient suffering a purely somatosensory deficit of his dominant hand (patient S1). We found that: (1) writer's cramp patients and patient S1 had elevated grip-force levels; (2) training reduced the grip force to near-normal levels in all writer's cramp patients but not in S1; (3) effortful writing performance also induced increased grip-force levels in healthy subjects; and (4) patient S1 had normal handwriting movements. These findings suggest that the elevated pretraining grip-force levels of writer's cramp patients might be a consequence of their effortful writing style and do not reflect a deficit of sensorimotor integration. Moreover, the good handwriting performance of patient S1 shows that a severe somatosensory deficit is not a sufficient condition for a handwriting disorder. These findings disagree with the sensorimotor explanation of writer's cramp.

Pathophysiology of writer's cramp. [Hum Mov Sci. 2006] - PubMed - NCBI


Pathophysiology of writer's cramp.

Hallett M.

Source

Human Motor Control Section, NINDS, NIH Building 10, Room 5N226 Bethesda, MD 20892-1428, USA. hallettm@ninds.nih.gov

Abstract

Writer's cramp is a task-specific focal hand dystonia. The abnormality of task specificity is a curious one and indicates that we need to learn more about the coupling of motor programs and their effectors. Writer's cramp appears to be triggered by spending much time writing by an individual with a fertile physiological substrate for producing the disorder. The fertile background, which is likely genetic, may be a decrease of inhibition, an increase of plasticity or an impairment in sensory function. Recent pathophysiological findings have implications for new therapies.

Etiology of musician's dystonia: familial or envir... [Neurology. 2009] - PubMed - NCBI

(Full Text)
Neurology. 2009 Apr 7;72(14):1248-54.

Etiology of musician's dystonia: familial or environmental?


Source

Institute of Music Physiology and Musicians' Medicine, Hanover University of Music and Drama, Hanover, Germany.

Abstract

OBJECTIVE:
To test the hypothesis that there is familial aggregation of dystonia and other movement disorders in relatives of patients with musician's dystonia (MD) and to identify possible environmental triggers.

METHODS:
The families of 28 index patients with MD (14 with a reported positive family history of focal task-specific dystonia [FTSD] and 14 with no known family history [FH-]) underwent a standardized telephone screening interview using a modified version of the Beth Israel Dystonia Screen. Videotaped neurologic examinations were performed on all participants who screened positive and consensus diagnoses established. All patients were investigated for DYT1 dystonia and suitable families were tested for linkage to DYT7. All family members were administered questionnaires covering potential triggers of FTSD.

RESULTS:
A diagnosis of dystonia was established in all 28 index patients and in 19/97 examined relatives (MD: n = 8, other FTSD: n = 9, other dystonias: n = 2), 5 of whom were members of FH- families. In 27 of the 47 affected individuals, additional forms of dystonia were seen; other movement disorders were observed in 23 patients. In total, 18 families were multiplex families with two to four affected members. Autosomal dominant inheritance was compatible in at least 12 families. The GAG deletion in DYT1 was absent in all patients. Linkage to DYT7 could be excluded in 1 of the 11 informative families. With respect to potential environmental triggers, there was no significant difference between patients with MD/FTSD compared to unaffected family members.

CONCLUSION:
Our results suggest a genetic contribution to musician's dystonia with phenotypic variability including focal task-specific dystonia.

Table tennis dystonia. [Mov Disord. 2010] - PubMed - NCBI


Table tennis dystonia.
Le Floch A, Vidailhet M, Flamand-Rouvière C, Grabli D, Mayer JM, Gonce M, Broussolle E, Roze E.

Source
Service de Neurologie, Hôpital Nîmes, Nîmes, France.

Abstract
Focal task-specific dystonia (FTSD) occurs exclusively during a specific activity that usually involves a highly skilled movement. Classical FTSD dystonias include writer's cramp and musician's dystonia. Few cases of sport-related dystonia have been reported. We describe the first four cases of FTSD related to table tennis (TT), two involving professional international competitors. We also systematically analyzed the literature for reports of sport-related dystonia including detailed clinical descriptions. We collected a total of 13 cases of sport-related dystonia, including our four TT players. Before onset, all the patients had trained for many years, for a large number of hours per week. Practice time had frequently increased significantly in the year preceding onset. As TT is characterized by highly skilled hand/forearm movements acquired through repetitive exercises, it may carry a higher risk of FTSD than other sports. Intensive training may result in maladaptive responses and overwhelm homeostatic mechanisms that regulate cortical plasticity in vulnerable individuals. Our findings support the importance of environmental risk factors in sport-related FTSD, as also suggested in classical FTSD, and have important implications for clinical practice.

(c) 2010 Movement Disorder Society.


Task-specific hand dystonia: can too much plasticity be bad for you?

Quartarone A, Siebner HR, Rothwell JC.

Source
Department of Neuroscience, Psychiatric and Anaesthesiological Sciences, University of Messina, 98125 Messina, Italy. angelo.quartarone@unime.it

Abstract
Patients with occupational hand dystonias have task-specific involuntary co-contraction and overflow of activity to inappropriate muscles. This interferes with highly skilled movements such as handwriting (writer's cramp) or playing a musical instrument (musician's cramp). Transcranial stimulation methods that probe mechanisms of synaptic plasticity in the motor cortex show an abnormal modifiability of sensorimotor circuits in patients with writer's cramp, probably because homeostatic control of the range of modification is deficient. We argue that during skilled motor practice, this leads to an excessive tendency to form associations between sensory inputs and motor outputs (abnormal potentiation) and to a failure to weaken already existing associations (deficient depotentiation). Deficient homeostatic control might be
an important mechanism that triggers maladaptive reorganization and produces symptoms of occupational hand dystonias.

83. **Homeostatic-like plasticity of the primary motor hand area is impaired in focal hand dystonia.**


Homeostatic-like plasticity of the primary motor hand area is impaired in focal hand dystonia.

**Quartarone A, Rizzo V, Bagnato S, Morgante F, Sant'Angelo A, Romano M, Crupi D, Girlanda P, Rothwell JC, Siebner HR.**

**Source**

Department of Neuroscience, Psychiatric and Anaesthesiological Sciences, University of Messina, Italy. [angelo.quartarone@unime.it](mailto:angelo.quartarone@unime.it)

**Abstract**

The excitability of inhibitory circuits in patients with writer's cramp is reduced at multiple levels within the sensorimotor system, including the primary motor hand area (M1). Although this may play a major role in the pathophysiology of writer's cramp, it is still unclear what factors may cause the imbalance between inhibition and excitation to arise. One possibility is that homeostatic mechanisms that keep cortical excitability within a normal physiological range are impaired. In eight patients with writer's cramp and eight healthy age-matched controls, we combined low-frequency repetitive transcranial magnetic stimulation (rTMS) with transcranial direct current stimulation (TDCS) to probe regional homeostatic plasticity of the left M1. Confirming our previous study (Siebner et al., J Neurosci 2004; 24: 3379-85), 'facilitatory' preconditioning of the M1 with anodal TDCS enhanced the inhibitory effect of subsequent 1 Hz rTMS on corticospinal excitability. Conversely, 'inhibitory' preconditioning with cathodal TDCS reversed the after effect of 1 Hz rTMS, producing an increase in corticospinal excitability. The results were quite different in patients with writer's cramp. Following preconditioning with TDCS, 1 Hz rTMS induced no consistent changes in corticospinal excitability, indicating a loss of the normal 'homeostatic' response pattern. In addition, the normal inhibitory effect of preconditioning with cathodal TDCS was absent. The present data suggest that homeostatic mechanisms that stabilize excitability levels within a useful dynamic range are impaired in patients with writer's cramp. We propose that a faulty homeostatic response to acute increases in corticospinal excitability favours maladaptive motor plasticity. The role of homeostatic-like plasticity in the pathophysiology of task-specific dystonias warrants further study.

84. **Abnormal associative plasticity of the human motor cor...** *Brain.* 2003 Dec;126(Pt 12):2586-96. Epub 2003 Sep 23.

Abnormal associative plasticity of the human motor cortex in writer's cramp.
Quartarone A, Bagnato S, Rizzo V, Siebner HR, Dattola V, Scalfari A, Morgante F, Battaglia F, Romano M, Girlanda P.

Source

Department of Neurosciences, Psychiatric and Anaesthesiological Sciences, University of Messina, Italy. angelo.quartarone@unime.it

Abstract

Low-frequency median nerve stimulation, paired with suprathreshold transcranial magnetic stimulation (TMS) over the optimal site for activation of the abductor pollicis brevis (APB) muscle induces a long-lasting increase in the excitability of corticospinal output neurons, if median nerve stimulation is given 25 ms before TMS. Here we employed this protocol of stimulation to assess associative plasticity of the primary motor hand area in 10 patients with writer's cramp and 10 age-matched controls. Motor evoked potentials (MEPs) were recorded from right APB muscle and right first dorsal interosseus (FDI) muscle. Resting and active motor threshold, mean MEP amplitude at rest, short-latency intracortical inhibition (SICI) at an interstimulus interval of 2 ms and the duration of the cortical silent period (CSP) were assessed immediately before and after associative stimulation. In both groups, associative stimulation led to an increase in resting MEP amplitudes which was more pronounced in the right APB muscle. Compared with healthy controls, stimulation-induced facilitation of MEP amplitudes was stronger in patients with writer's cramp. In addition, only patients showed a slight decrease of resting and active motor thresholds after conditioning stimulation. In both groups, associative stimulation induced a prolongation of CSP in the APB and FDI muscles, which was significant only in the APB muscle in healthy controls. Associative stimulation had no effects on SICI in patients and healthy controls. Taken together, in patients with writer's cramp, the motor system exhibited an abnormal increase in corticospinal excitability and an attenuated reinforcement of intracortical inhibitory circuits that generate the CSP in response to associative stimulation. This altered pattern of sensorimotor plasticity may favour maladaptive plasticity during repetitive skilled hand movements and, thus, may be of relevance for the pathophysiology of writer's cramp and other task-specific dystonias.


Musician's focal dystonia.

Tubiana R.

Source

Institute De La Main, Clinique Jouvenet, 6 Square Jouvenet, Paris 75016, France.

Abstract

Focal dystonia is probably the most disabling professional disorder in musicians, as it decreases the technical level of performances and may end a career. The instrumentalist is progressively unable to control the movement of one or more fingers when playing. Although, the exact cause of the disorder is still debated, it seems that
focal dystonia is the consequence of several factors. Musician's focal dystonia poses difficult problems of diagnosis and of therapy, which are discussed in this article.

86. Focal dystonia in musicians: phenomenology, pathophysiology, triggering factors, and treatment. 

Altenmüller E, Jabusch HC. 
Source 
Institute for Music Physiology and Musicians' Medicine, University for Music and Drama, Hannover. altenmueller@hmt-hannover.de 
Abstract 
Musician's dystonia is a task-specific movement disorder that manifests itself as a loss of voluntary motor control in extensively trained movements. Approximately 1% of all professional musicians develop musician's dystonia, and in many cases, the disorder terminates the careers of affected musicians. The pathophysiology of the disorder is not completely clarified. Findings include 1) reduced inhibition at different levels of the central nervous system, 2) maladaptive plasticity and altered sensory perception, and 3) alterations in sensorimotor integration. Epidemiological data demonstrate a higher risk for those musicians who play instruments requiring maximal fine-motor skills. For instruments where workload differs across hands, focal dystonia appears more often in the more intensely used hand. In psychological studies, musicians with dystonia have more anxiety and perfectionist tendencies than healthy musicians. These findings strengthen the assumption that behavioral factors may be involved in the etiology of musician's dystonia. Preliminary findings also suggest a genetic contribution to focal task-specific dystonia with phenotypic variations including musician's dystonia. Treatment options include pharmacological interventions, such as trihexyphenidyl or botulinum toxin-A, as well as retraining programs and ergonomic changes in the instrument. Patient-tailored treatment strategies may significantly improve the situation of musicians with focal dystonia. Positive results after retraining and unmonitored technical exercises underline the benefit of an active involvement of patients in the treatment process. Only a minority of musicians, however, return to normal motor control using the currently available therapies.

87. Restoring balance in focal limb dystonia with... 

Restoring balance in focal limb dystonia with botulinum toxin. 
Sheean G. 
Source
Abstract
Focal task-specific dystonia of the hand is rare in the general population, where it usually manifests as writer's cramp, but seems relatively common among musicians. The disability may be so severe as to prevent writing altogether or to end a professional musician's career. The cause is usually unknown but it is thought to be primarily a basal ganglia disorder with dysfunction of cortical-striatothalamic-cortical circuits. Abnormalities have been found in cortical movement preparation, intracortical inhibition, sensory and motor maps, and patterns of cortical activation during movement. Much evidence supports disordered processing of sensory information with disturbed sensorimotor integration. Underlying this may be maladaptive neural plasticity mechanisms. Treatment is difficult. Oral medications are generally ineffective and have troublesome side-effects. Intensive rehabilitation techniques based on neural plasticity theory show promise but are rarely available and are time-intensive. Botulinum toxin injections appear to be effective in writer's cramp and musician's dystonia, at least initially; long-term benefit is less common. Despite definite improvement, some patients abandon treatment because the gain is insufficient for meaningful function: this is particularly so for musicians. Much of the benefit from botulinum toxin injection comes from simply reducing muscle overactivity through muscle paralysis, restoring balance to motor control. However, some evidence suggests that botulinum toxin injections can produce transient improvement in some of the various cortical abnormalities described, probably through alteration of sensory input from the periphery, by direct and indirect means. These changes in cortical function might be usefully combined with those brought about by sensorimotor retraining programs, but such studies are awaited.

88. Pathophysiological differences between musician's dystonia... [Brain. 2005] - PubMed - NCBI (Full Text)


Pathophysiological differences between musician's dystonia and writer's cramp.
Source
Sobell Department of Motor Neuroscience and Movement Disorders, Institute of Neurology, Queen Square, London, UK. k.rosenkranz@ion.ucl.ac.uk

Abstract
Focal hand dystonia (FHD) has been suggested to be a maladaptive response of the brain to repetitive performance of stereotyped and attentionally demanding hand movements. However, not all patients with FHD have a strict history of excessive hand use; for example, patients with musician's dystonia (MD) spend many hours per day with their attention focused on instrumental practice, whereas many patients with writer's cramp (WC) have a history of average hand use. The present experiments test whether seven MD and six WC patients have different pathophysiological deficits by
examining the spatial pattern of sensorimotor organization in the motor cortex. Two control groups were used, eight healthy non-musicians and eight healthy musicians. The latter served to control for physiological adaptation of the brain to musical training. We used focal vibration of a single hand muscle to produce sensory input whilst the excitability of corticospinal outputs to the vibrated and other hand muscles was evaluated with transcranial magnetic stimulation. In healthy non-musicians, vibration increases the amplitude of motor-evoked potentials and decreases the short-latency intracortical inhibition (SICI) in the vibrated muscle, whilst having the opposite effect on the non-vibrated hand muscles. The pattern of sensorimotor interaction was abnormal in both patient groups. However, the nature of the deficit differed between them. While vibration had little effect on cortical excitability in WC, it strongly reduced SICI in all hand muscles irrespective of spatial organization in MD. In the healthy musicians we found an organization intermediate between that of healthy non-musicians and MD. The data are consistent with a model in which musical practice in healthy musicians leads to beneficial changes in organization of the motor cortex, but in MD these progress too far and begin to interfere with movement rather than assist it. The fact that sensory input had no effect on motor output in patients with WC suggests that sensory information from the hand may play a smaller role in provoking pathological changes in WC than in MD.


An fMRI study of musicians with focal dystonia during tapping tasks.


Source

Department of Rehabilitation for Sensory Functions, Research Institute, National Rehabilitation Center for Persons with Disabilities, Tokorozawa, Saitama, Japan. 
kadotahiroshi@gmail.com

Abstract

Musician's dystonia is a type of task specific dystonia for which the pathophysiology is not clear. In this study, we performed functional magnetic resonance imaging to investigate the motor-related brain activity associated with musician's dystonia. We compared brain activities measured from subjects with focal hand dystonia and normal (control) musicians during right-hand, left-hand, and both-hands tapping tasks. We found activations in the thalamus and the basal ganglia during the tapping tasks in the control group but not in the dystonia group. For both groups, we detected significant activations in the contralateral sensorimotor areas, including the premotor area and cerebellum, during each tapping task. Moreover, direct comparison between the dystonia and control groups showed that the dystonia group had greater activity in the ipsilateral premotor area during the right-hand tapping task and less activity in the left cerebellum during the both-hands tapping task. Thus, the dystonic musicians showed
irregular activation patterns in the motor-association system. We suggest that irregular neural activity patterns in dystonic subjects reflect dystonic neural malfunction and consequent compensatory activity to maintain appropriate voluntary movements.


Regaining motor control in musician's dystonia by restoring sensorimotor organization.

Rosenkranz K, Butler K, Williamon A, Rothwell JC.

Source
Sobell Department of Motor Neuroscience and Movement Disorders and Department of Clinical and Experimental Epilepsy, UCL Institute of Neurology, London W1N 3BG, United Kingdom. k.rosenkranz@ion.ucl.ac.uk

Abstract
Professional musicians are an excellent model of long-term motor learning effects on structure and function of the sensorimotor system. However, intensive motor skill training has been associated with task-specific deficiency in hand motor control, which has a higher prevalence among musicians (musician's dystonia) than in the general population. Using a transcranial magnetic stimulation paradigm, we previously found an expanded spatial integration of proprioceptive input into the hand motor cortex [sensorimotor organization (SMO)] in healthy musicians. In musician's dystonia, however, this expansion was even larger. Whereas motor skills of musicians are likely to be supported by a spatially expanded SMO, we hypothesized that in musician's dystonia this might have developed too far and now disrupts rather than assists task-specific motor control. If so, motor control should be regained by reversing the excessive reorganization in musician's dystonia. Here, we test this hypothesis and show that a 15 min intervention with proprioceptive input (proprioceptive training) restored SMO in pianists with musician's dystonia to the pattern seen in healthy pianists. Crucially, task-specific motor control improved significantly and objectively as measured with a MIDI (musical instrument digital interface) piano, and the amount of behavioral improvement was significantly correlated to the degree of sensorimotor reorganization. In healthy pianists and nonmusicians, the SMO and motor performance remained essentially unchanged. These findings suggest that the differentiation of SMO in the hand motor cortex and the degree of motor control of intensively practiced tasks are significantly linked and finely balanced. Proprioceptive training restored this balance in musician's dystonia to the behaviorally beneficial level of healthy musicians.

91. Sensorimotor skills and focal... [J Neurol Neurosurg Psychiatry. 2011] - PubMed - NCBI

Sensorimotor skills and focal dystonia are linked to putaminal grey-matter volume in pianists.

Granert O, Peller M, Jabusch HC, Altenmüller E, Siebner HR.

Source

Department of Neurology, University Hospital Schleswig-Holstein, Kiel Campus, Arnold-Heller-Str 3, Building No 41, Kiel D-24105, Germany. o.granert@neurologie.uni-kiel.de

Abstract

BACKGROUND:
Focal hand dystonia has been associated with morphometric changes and distorted somatotopic representations in the putamen.

OBJECTIVE:
The authors used voxel-based morphometry (VBM) to identify regions in the putamen where grey-matter volume is associated with musician's dystonia (MD) or the skill level of piano playing in professional pianists.

METHODS:
In 11 pianists with MD affecting the right hand and 12 healthy pianists without dystonia, the authors performed high-resolution T1-weighted MRI of the brain. The authors also measured the temporal variability of key strokes during scale playing with the right hand to characterise the individual skill level of piano playing. Statistical comparisons of the normalised and smoothed grey-matter maps were performed to test for dystonia and performance-related structural changes in the putamen.

RESULTS:
During scale playing, the timing of consecutive key strokes was more variable in MD patients than in non-dystonic pianists. Regional grey-matter volume in the middle part of left and right putamen increased with timing variability during piano playing in pianists with and without MD. Between-group comparisons revealed that MD patients had a larger grey-matter volume in the right middle putamen compared with healthy musicians.

CONCLUSION:
In highly trained pianists with and without MD, the volume of the associative motor territory in the middle putamen reflects both the skill level of piano playing and the presence of dystonia. While a smaller volume is associated with better timing skills, a relative expansion is correlated with the presence of focal task-specific hand dystonia.

92. EEG oscillatory patterns are associated with erro... [Neuroimage. 2011] - PubMed - NCBI


EEG oscillatory patterns are associated with error prediction during music performance and are altered in musician's dystonia.

Ruiz MH, Strübing F, Jabusch HC, Altenmüller E.
Skilled performance requires the ability to monitor ongoing behavior, detect errors in advance and modify the performance accordingly. The acquisition of fast predictive mechanisms might be possible due to the extensive training characterizing expertise performance. Recent EEG studies on piano performance reported a negative event-related potential (ERP) triggered in the ACC 70 ms before performance errors (pitch errors due to incorrect keypress). This ERP component, termed pre-error related negativity (pre-ERN), was assumed to reflect processes of error detection in advance. However, some questions remained to be addressed: (i) Does the electrophysiological marker prior to errors reflect an error signal itself or is it related instead to the implementation of control mechanisms? (ii) Does the posterior frontomedial cortex (pFMC, including ACC) interact with other brain regions to implement control adjustments following motor prediction of an upcoming error? (iii) Can we gain insight into the electrophysiological correlates of error prediction and control by assessing the local neuronal synchronization and phase interaction among neuronal populations? (iv) Finally, are error detection and control mechanisms defective in pianists with musician's dystonia (MD), a focal task-specific dystonia resulting from dysfunction of the basal ganglia-thalamic-frontal circuits? Consequently, we investigated the EEG oscillatory and phase synchronization correlates of error detection and control during piano performances in healthy pianists and in a group of pianists with MD. In healthy pianists, the main outcomes were increased pre-error theta and beta band oscillations over the pFMC and 13-15 Hz phase synchronization, between the pFMC and the right lateral prefrontal cortex, which predicted corrective mechanisms. In MD patients, the pattern of phase synchronization appeared in a different frequency band (6-8 Hz) and correlated with the severity of the disorder. The present findings shed new light on the neural mechanisms, which might implement motor prediction by means of forward control processes, as they function in healthy pianists and in their altered form in patients with MD.
Musician's dystonia (MD) is a task-specific movement disorder characterized by a loss of voluntary motor control in highly trained movements like piano playing. Its underlying pathophysiology is defined by deficient functioning of neural pathways at different levels of the central nervous system. However, a few studies have examined the brain responses associated with executive functions such as error monitoring in MD. We recorded the electroencephalogram (EEG) in professional pianists during the performance of memorized music sequences at fast tempi. Event-related potentials (ERPs) locked to pitch errors were investigated in MD and a control group. In MD patients, significantly larger error-related brain responses before and following errors were observed as compared with healthy pianists. Our results suggest that in MD, the generalized degraded neural activity at all levels of the central nervous system is manifested in specific neural correlates of the executive functions that monitor an overlearned sensorimotor performance.


Focal dystonia: advances in brain imaging and understanding of fine motor control in musicians.

Altenmüller E.
Source
University for Music and Drama, Hannover Institute for Music Physiology and Musicians' Medicine, Hohenzollernstr. 47, Hannover D-30161, Germany. altenmueller@hmt-hannover.de

Abstract
This article reviews the neuroanatomic and neurophysiologic foundations of music performance and learning. Music performance is regarded as complex voluntary sensorimotor behavior that becomes automated during extensive practice with auditory feedback. It involves all motor, somatosensory, and auditory areas of the brain. Because of the life-long plasticity of neuronal connections, practicing a musical instrument results first in a temporary and later in a stable increase in the amount of nerve tissue devoted to various component tasks. Motor and somatosensory brain regions corresponding to specific subtasks of music performance are larger in musicians starting younger than age 10 years than in the general population. In rare cases, overuse of movement patterns may induce a degradation of motor memory that results in a loss of voluntary control of movements, called musician's cramp. Specific therapeutic options for this condition are reviewed.


Alteration of digital representations in somatosensory cortex in focal hand dystonia.

Abstract

Focal hand dystonia involves a loss of motor control of one or more digits; it is associated with the repetitive, synchronous movements of the digits made by musicians over periods of many years. Magnetic source imaging revealed that there is a smaller distance (fusion) between the representations of the digits in somatosensory cortex for the affected hand of dystonic musicians than for the hands of non-musician control subjects. The data suggest that use-dependent susceptibility to digital representation fusion in cortex may be involved in the etiology of focal dystonia. A successful therapy for the condition has been developed based on this consideration.

96. Human brain mapping in dystonia reveals both endo... [Ann Neurol. 2001] - PubMed - NCBI


Human brain mapping in dystonia reveals both endophenotypic traits and adaptive reorganization.

Meunier S, Garnero L, Ducorps A, Mazières L, Lehéricy S, du Montcel ST, Renault B, Vidailhet M.

Source

Department of Clinical Neurophysiology, Pitié-Salpêtrière Hospital, Paris, France.
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Abstract

Dystonia has a wide clinical spectrum from early-onset generalized to late-onset sporadic, task-specific forms. The genetic origin of the former has been clearly established. A critical role of repetitive skilled motor tasks has been put forward for the latter, while underlying vulnerability traits are still being searched for. Using magnetoencephalography, we looked for structural abnormalities reflecting a preexisting dysfunction. We studied finger representations of both hands in the primary sensory cortex, as compared in 23 patients with unilateral task-specific dystonia and 20 control subjects. A dramatic disorganization of the nondystonic hand representation was found in all patients, and its amount paralleled the severity of the dystonic limb motor impairment. Abnormalities were also observed in the cortex coding the dystonic limb representation, but they were important only in the most severely affected patients. The abnormal cortical finger representations from the nondystonic limb appear to be endophenotypic traits of dystonia. That finger representations from the dystonic limb were almost normal for the less severely affected patients may be due to intrinsic beneficial remapping in reaction against the primary disorder.


Abnormal somatosensory homunculus in dystonia of the hand.

Bara-Jimenez W, Catalan MJ, Hallett M, Gerloff C.

Source
Human Motor Control Section, Medical Neurology Branch, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD 20892-1428, USA.

Abstract
Abnormalities of the sensory system have been proposed as causative factors for dystonia. By mapping the human cortical hand somatosensory area of 6 patients with focal dystonia of the hand, we found an abnormality of the normal homuncular organization of the finger representations in the primary somatosensory cortex (S1). Although a remote antecedent event or even a developmental anomaly cannot entirely be ruled out, our findings may support the concept that abnormal plasticity is involved in the development of dystonia.

Spatial discrimination is abnormal in focal hand d... [Neurology. 2000] - PubMed - NCBI


Spatial discrimination is abnormal in focal hand dystonia.

Bara-Jimenez W, Shelton P, Hallett M.

Source
Human Motor Control Section, Medical Neurology Branch, National Institute of Neurological Disorders and Stroke, Bethesda, MD 20892-1428, USA.

Abstract
BACKGROUND:
In patients with focal hand dystonia, abnormal digit representations in the primary somatosensory cortex (S1) could be the result of enlarged and overlapping receptor fields, as suggested by an animal model of dystonia. A possible clinical correlate of this S1 abnormality is a disturbed spatial discrimination capability.

OBJECTIVE:
To test the hypothesis that somatosensory spatial discrimination is abnormal in focal hand dystonia.

METHODS:
Seventeen patients with focal hand dystonia underwent a quantitative evaluation of somatosensory spatial frequency (gap detection, JVP domes, applied to the distal phalanx of the index finger) and single-touch localization (Von Frey monofilaments, applied to the middle phalanx of the index finger).

RESULTS:
Compared with control subjects, patients had a decreased performance in both the gap detection (p = 0.004) and the localization (p = 0.013) tasks. The extent of spatial frequency abnormality correlated with age in both groups.
CONCLUSIONS:
These findings, together with a previously shown temporal discrimination deficit, support a role for sensory dysfunction in the pathophysiology of dystonia.


Role of the somatosensory system in primary dystonia.
Tinazzi M, Rosso T, Fiaschi A.
Source
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Abstract
The pathophysiology of dystonia is still not fully understood, but it is widely held that a dysfunction of the corticostriatal-thalamocortical motor circuits plays a major role in the pathophysiology of this syndrome. Although the most dramatic symptoms in dystonia seem to be motor in nature, marked somatosensory perceptual deficits are also present in this disease. In addition, several lines of evidence, including neurophysiological, neuroimaging and experimental findings, suggest that both motor and somatosensory functions may be defective in dystonia. Consequently, abnormal processing of the somatosensory input in the central nervous system may lead to inefficient sensorimotor integration, thus contributing substantially to the generation of dystonic movements. Whether somatosensory abnormalities are capable of triggering dystonia is an issue warranting further study. Although it seems unlikely that abnormal somatosensory input is the only drive to dystonia, it might be more correlated to the development of focal hand than generalized dystonia because local somesthetic factors are more selectively involved in the former than in the latter where, instead it seems to be a widespread deficit in processing sensory stimuli of different modality. Because basal ganglia and motor areas are heavily connected not only with somatosensory areas, but also with visual and acoustic areas, it is possible that abnormalities of other sensory modalities, such as visual and acoustic, may also be implicated in the pathophysiology of more severe forms of primary dystonia. Further studies have to be addressed to the assessment of the role of sensory modalities and their interaction on the pathophysiology of different forms of primary dystonia.


Dystonia: a disorder of motor programming or motor execution?
Kanovský P.
Source
Abstract

For some time, dystonia has been seen as purely a motor disorder. Relatively novel concepts published approximately 10 years ago also presumed that in the development of dystonic dyskinesias, only motor behaviour was abnormal. Neurophysiological observations of various types of dystonic disorders, which were performed using sophisticated electromyography, polymyography, H-reflex examination, long-latency reflex, etc., as well as new insights into the behaviour of dystonia, have urged the inclusion of sensory (particularly somatosensory) mechanisms into the pathophysiological background of dystonia. The major role has been considered to be played by abnormal proprioceptive input by means of the Ia proprioceptive afferents, with the source of this abnormality found in the abnormal processing of muscle spindle afferent information. However, neurophysiological investigations have also provided evidence that the abnormality in the central nervous system is located not only at the spinal and subcortical level, but also at the cortical level; specifically, the cortical excitability and intracortical inhibition have been revealed as abnormal. This evidence was revealed by SEP recordings, paired transcranial magnetic stimulation recordings, and BP and CNV recordings. The current concept of dystonic movement connects the abnormal function of somatosensory pathways and somatosensory analysers with the dystonic performance of motor action, which is based on the abnormality of sensorimotor integration.

101. One-Hz repetitive transcranial magnetic stimulation... [Mov Disord. 2004] - PubMed - NCBI


One-Hz repetitive transcranial magnetic stimulation of the premotor cortex alters reciprocal inhibition in DYT1 dystonia.

Huang YZ, Edwards MJ, Bhatia KP, Rothwell JC.

Source

The Sobell Department of Motor Neuroscience and Movement Disorders, Institute of Neurology, University College London, Queen Square, London, United Kingdom.

Abstract

Repetitive transcranial magnetic stimulation (rTMS) can produce long-lasting effects not only underneath the site of stimulation, but also at distant connected sites. This study aimed to assess how low frequency rTMS over the premotor area might affect abnormalities in spinal motor function in patients with generalised dystonia associated with the DYT1 gene mutation. We assessed reciprocal inhibition (RI) in a group of 8 manifesting carriers of the DYT1 gene (DYT1) and 10 healthy controls. All subjects then received 20 minutes of 1 Hz rTMS over the premotor area, and RI was assessed again. Before rTMS, the second and third phases of RI were abnormal in DYT1 subjects compared to controls. After 20 minutes of 1 Hz rTMS over the premotor area, a significant increase in inhibition was noted in the third and possibly the first phase of
RI in the DYT1 group. No changes in RI were observed in control subjects after rTMS. We have shown for the first time to date that reducing cortical excitability in patients with dystonia using rTMS can produce corresponding changes in abnormal spinal motor output. These findings make a case for further exploring rTMS as a tool to modulate abnormal cortical and spinal excitability in individuals with dystonia and even as a potential form of treatment for dystonic symptoms.

102. Restoration of motor inhibition through an abnorm... [Mov Disord. 2010] - PubMed - NCBI (Full Text)


Restoration of motor inhibition through an abnormal premotor-motor connection in dystonia.

Huang YZ, Rothwell JC, Lu CS, Wang J, Chen RS.

Source

Department of Neurology, Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Taipei, Taiwan.

Abstract

To clarify the rationale for using rTMS of dorsal premotor cortex (PMd) to treat dystonia, we examined how the motor system reacts to an inhibitory form of rTMS applied to the PMd in healthy subjects and in a group of patients with focal hand dystonia and DYT1 gene carriers. Continuous theta burst transcranial magnetic stimulation (cTBS) with 300 and 600 pulses (cTBS300 and cTBS600) was applied to PMd, and its after-effects were quantified by measuring the amplitude of MEPs evoked by single pulse transcranial magnetic stimulation (TMS) over the primary motor cortex (M1), short interval intracortical inhibition/facilitation (SICI/ICF) within M1, the third phase of spinal reciprocal inhibition (RI), and writing tests. In addition, in DYT1 gene carriers, the effects of cTBS300 over left PMd on MEPs were studied in separate experiments. In healthy subjects, cTBS300 and cTBS600 over PMd suppressed MEPs for 30 min or more and cTBS600 decreased SICI and RI. In contrast, neither form of cTBS over PMd had any significant effect on MEPs, while cTBS600 increased effectiveness of SICI and RI and improved writing in patients with writer's cramp. NMDYT1 had a normal response to cTBS300 over left PMd. We suggest that the reduced PMd to M1 interaction in dystonic patients is likely to be due to reduced excitability of PMd-M1 connections. The possible therapeutic effects of premotor rTMS may therefore involve indirect effects of PMd on SICI and RI, which this study has shown can be normalised by cTBS.

103. Area 5 influences excitability within the primary m... [PLoS One. 2011] - PubMed - NCBI (Full Text)


Area 5 influences excitability within the primary motor cortex in humans.

Premji A, Rai N, Nelson A.
Abstract
In non-human primates, Brodmann's area 5 (BA 5) has direct connectivity with primary motor cortex (M1), is largely dedicated to the representation of the hand and may have evolved with the ability to perform skilled hand movement. Less is known about human BA 5 and its interaction with M1 neural circuits related to hand control. The present study examines the influence of BA 5 on excitatory and inhibitory neural circuitry within M1 bilaterally before and after continuous (cTBS), intermittent (iTBS), and sham theta-burst stimulation (sham TBS) over left hemisphere BA 5. Using single and paired-pulse TMS, measurements of motor evoked potentials (MEPs), short interval intracortical inhibition (SICI), and intracortical facilitation (ICF) were quantified for the representation of the first dorsal interosseous muscle. Results indicate that cTBS over BA 5 influences M1 excitability such that MEP amplitudes are increased bilaterally for up to one hour. iTBS over BA 5 results in an increase in MEP amplitude contralateral to stimulation with a delayed onset that persists up to one hour. SICI and ICF were unaltered following TBS over BA 5. Similarly, F-wave amplitude and latency were unaltered following cTBS over BA 5. The data suggest that BA 5 alters M1 output directed to the hand by influencing corticospinal neurons and not interneurons that mediate SICI or ICF circuitry. Targeting BA 5 via cTBS and iTBS is a novel mechanism to powerfully modulate activity within M1 and may provide an avenue for investigating hand control in healthy populations and modifying impaired hand function in clinical populations.

Source
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