Synapse

Volume 15, Issue 3 Summer, 2012

Newsletter of the Spastic Paraplegia Foundation

2012 ANNUAL CONFERENCE

June 8-9, 2012














Letter to the Editor

June 30, 2012

Spastic Paraplegia Foundation, Inc.

To whom it may concern,

Our names are Blake and Gavin Gattuso. We live in Southborough Massachusetts. Your organization has helped our Aunt Meredith Gattuso. She has PLS. We are very grateful for SPF, Inc. and the research that you do to help find a cure for PLS.

For our 10th birthday we asked our friends for donations for SPF, Inc. instead of presents. We couldn't believe how generous people were! We raised $1,110.00! Our dad's company will match the cash donations so Covidien will be sending an additional $435.00 - if our math is right!

We hope this money will help your research to find a cure for PLS and HSP. We felt so good raising money that may contribute to helping our Aunt Meredith.

Thank you for all that you do,

Blake Gattuso and

Gavin Gattuso

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The Spastic Paraplegia Foundation Inc. (SPF) is a national, not-for-profit, voluntary organization. It is the only organization in the Americas dedicated to Primary Lateral Sclerosis (PLS) and Hereditary Spastic Paraplegia (HSP).

Published four times a year for the HSP/PLS community. Available online at www.sp-foundation.org

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Letter from the President

Dear Friends,

I want to welcome you to our late Summer 2012 *Synapse* Newsletter. Besides all of the interesting stories you are about to read, you will be glad to know that a lot of exciting things continue to develop with the Spastic Paraplegia Foundation.

At our very successful June Annual Conference in Virginia, I enjoyed seeing and meeting many of you, learned about new hopes for research, ways to manage HSP & PLS and visited beautiful Washington DC. Our 2013 Annual Conference will be held in Saint Louis, Mo. and our 2014 Annual Conference is currently scheduled to be held in Seattle, WA.

Our board of directors has welcomed the very capable Tina Croghan and Allen Bernard as new members. Tina has been an award winning teacher for many years and promises to provide you with more educational material on HSP and PLS. Allen is a successful writer and will inform and entertain us all about research and news we all want to know about.

Our Board also bids a fond farewell to Beth Anne Shultz who has resigned for personal reasons. Beth Anne has worked tirelessly on many tasks and committees and was a critical part in the success of our recent Annual Conference.

I am pleased to announce that The Spastic Paraplegia Foundation has become a member of the National Organization of Rare Diseases or NORD. This will provide us many new ways to learn from and collaborate with other Rare Disease organizations.

Our Web Site, www.sp-foundation.org, is the face of our Foundation for many people. We are currently working on improving the way our web site looks and operates to provide you with more information that is easier to find. Our improved web site should go live this Fall.

We continue to work with our Scientific Advisory Board and many different doctors, scientists and researchers around the world who take our conditions to heart. We are carefully choosing the best means of investing your donations toward the day we will find cures for our disabilities. I hope you will please keep the Spastic Paraplegia Foundation in mind as you plan your yearend tax deductible donations.

Please enjoy the many great news stories our *Synapse* has for you today. Sincerely,

Frank Davis

President, SPF

2012 Annual Conference

McLean, VA June 8-9, 2012

Over 120 people attended our reception and dinner on Friday night. In addition to attendees from 26 states, Washington, DC and Canada, we were honored to have Peter Macpherson from Australia, Raj Tadla from India, Chris and Sandi Holt from New Zealand plus Mo and Lorraine Charge from the UK. During the reception the guests could take advantage of a Photofun Station to take their picture. The photos can be seen at http://tinyurl.com/SPF-Photos.

Dr. Nazem Atassi spoke to the group about Therapy Development, Stem Cell Research, the Northeast ALS (NEALS) Collaboration and the SPF/NEALS Collaboration. Dr. Atassi emphasized the importance of Biomarkers and how they can improve clinical care and accelerate therapy development. Biomarker research will help with understanding the disease, identifying and testing treatment targets. He also spoke about the stem cell ALS clinical trial at Emory University in Atlanta, GA. The goal of this clinical trial is to see if stem cell therapy is safe. There are several challenges of stem cell treatments such as determining the correct placement of injection, best method of delivery and type of stem cells to use. NEALS facilitates trials in ALS and other motor neuron disorders. The number of subjects in these trials increased tenfold from approximately 200 in 2008 to over 2,000 in 2011. Please check the new NEALS website – www.alsconsortium.org – for current trial and NEALS clinic information. The NEALS and SPF collaboration began in 2010 and is led by Drs. Atassi and Jinsy Andrews. The goals of this collaboration are:

- Improve HSP/PLS clinical care
- Connect HSP/PLS patients with experienced NEALS clinicians
- Launch Biomarkers studies
- Use NEALS infrastructure to plan and conduct HSP/PLS clinical trials
- Encourage NEALS members to submit proposals for a SPF research grant

Frank Davis opened the conference on Saturday morning to a crowd of 156. The main speakers were:

- Craig Blackstone, MD, PhD - NIH/NINDS
- Corey Braastad, PhD - Athena Diagnostics
- Tony Chiodo, MD - University of Michigan
- John Fink, MD - University of Michigan
- Mary Kay Floeter, MD, PhD - NIH/NINDS
- Hiroshi Mitsumoto, MD - Columbia University

On Saturday, the speakers were videotaped and the videos can be found on our website at http://tinyurl.com/SPF-Videos.

In the afternoon, three accessible vehicles were on site for the attendees to compare. Moore Cadillac brought a MV-1 (www.mv1ofvirginia.com/company), Freedom Motors (www.fminow.com) demonstrated a wheelchair van conversion and their converted Honda Element (owned by Annette Lockwood).

In addition to the above demonstration, there were three breakout sessions in the afternoon. The topics were Pediatric Physical Therapy, Adaptive Sports and Caregiving. Please see the article submitted by Jim Brewi about his purchase of a tricycle after attending the Adaptive Sports session.

Dr. Fink Making Great Strides in PLS & HSP

by Allen Bernard

Speaking at this year's annual convention in McLean Virginia, just outside of D.C., Dr. John Fink of the University of Michigan's Neurology department and a leading HSP and PLS researcher announced they may have identified several gene mutations in subjects with PLS.

These results build on those of other investigators that show that mutations are present in at least of subset of PLS subjects. While more testing needs to be done, Dr. Fink is optimistic that this progress may be used to develop a definitive test for PLS as well as provide important clues into mechanisms that cause PLS.

This is important because today PLS is diagnosed based on clinical features alone; often leaving sufferers frustrated because the diagnosis can change if their symptoms change. Also, knowing which gene is responsible for your condition may one day help you as treatments are developed.

Until, now PLS was thought to be a sporadic disease with no known triggers. It is interesting that genes may contribute to PLS even though there is almost always no family history of PLS. This situation is similar to ALS, in which researchers are finding that rare gene mutations contribute to the disorder in a sizable proportion of patients.

Skin cells may lead to faster treatments for HSP

Dr. Fink has also been busy with HSP. His team has found that skin cells could potentially be used in high throughput (HTP) screening of compounds that could be used to develop a treatment for HSP.

Typically, skin cells are taken into the lab and turned into neurons for testing. This process can months; significantly delaying the time it takes to screen compounds against them. What Dr. Fink has discovered is that skin cells from folks with SPG4 can be used directly (instead of converting them into neurons) to study molecular processes involved in SPG4 HSP. He needs to do more testing but, if his early observations are correct, then skin cells, which are easy to obtain, can be used for this purpose. This could lead to more and faster testing of compounds that could be turned into treatments.

Natural history study and gait training

Dr. Fink and his team are also working on a natural history study of HSP and PLS to more accurately measure spastic gait. By looking more closely at spastic gait researchers will be able to better understand the different components that make up spastic gait.

For example, someone may have weakness, spasticity and high muscle tone. To treat the person effectively you need to know in what measure each is present. So if you give someone that has spasticity and weakness a baclofen pump and their primary issue is weakness, that will only help the spasticity and not address the underlying weakness. This means a baclofen pump may not have a major impact on how well they walk.

But, if you have a natural history of the disease that establishes a baseline of the condition compared to a typical person's gait, a scale can be developed to measure each person's particular way of walking. This then gives your doctor a good baseline for measuring the clinical features of your condition.

Once you have this information, then your doctor can prescribe more effective treatments and, just as importantly, researchers can see if the treatments they are working actually work. Without a natural history, it is much harder to tell if improvements are happening and in what degree and why they are happening. In other words, to get where you are going you have to have a starting point.

Gait training is another area Dr. Fink talked about that needs to be explored further as a treatment for spastic gait. This because neuroplasticity studies in other disease like CP have shown the brain actually begins to reorganize itself around a disability. So, for example, in a study of person with a broken arm, an MRI showed that the brain began to reorganize itself to be better at doing things with the good arm. The motor area in side of the brain that controlled the broken and, therefore, immobilized arm, actually got smaller while the side that controlled the person's good arm actually got bigger.

What this could mean for people with spastic gait is gait training may be a way to maintain as much function as possible for as long as possible.

Dr. Fink wrapped up his talk with a Q&A session but the overall tone of his talk was very positive and left most of the folks in attendance feeling pretty good about the advancements being made by the team in Michigan on their behalf.

Our sincere thanks is extended to our speakers, sponsors and exhibitors for their participation and contribution to the success of the 2012 SPF Annual Conference.

Speakers

Brenda Asbury - Caregiver
Craig Blackstone, MD, PhD - NIH/NINDS
Corey Braastad, PhD - Athena Diagnostics
Tony Chiodo, MD - University of Michigan
John Fink, MD - University of Michigan
Mary Kay Floeter, MD, PhD - NIH/NINDS
Hiroshi Mitsumoto, MD - Columbia University
Tom Shultz - Caregiver
Massey Teel - Wintergreen Adaptive Sports
Sara Weiser -Good Beginnings

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Achilles International – Eleanor Cox
Dashaway – Kathi Geisler and Don Wilson
Freedom Motors – Don Malz
MV-1 of Virginia – Rocco Karamoutsos
tobii ATI – Mary deCoen

Team*W*alk - Washington, DC

The Team*W*alk held on the National Mall after our Annual Conference was a CAPITAL success!! Over fifty courageous souls braved a Washington, DC heat wave, and the accompanying high humidity, to walk 'The Walk'! It took two buses to get us all down to the Smithsonian Metro Stop. After a photo-op, courtesy of Gary Lockwood, we began the journey towards the Lincoln Memorial. Many of us stopped along the way to enjoy the Washington Monument, the World War II Memorial, the Vietnam Wall and the Korean War Veterans Memorial. Our last bus run was at 3:20 in the afternoon so a few of our walkers were able to squeeze in a Museum or two after reaching the Lincoln Memorial. Thanks to everyone who participated! We had a great time plus we raised $14,500!

Events and TeamWalks

Spring Fling

Frederick, MD **May 9, 2012**

Submitted by Jim and Barb Spencer

The 12th Annual Spring Fling was held in Frederick, MD the first weekend in May. Over 50 people attended the event hosted by Jim and Barb Spencer. The Spring Fling was originated by Ronnie Grove in Berkley Springs WV. After 10 years, Ronnie "passed the torch" to Jim and Barb last year. They hope to carry it on for years.

The Spring Fling proved to be an opportunity to not only reconnect with friends, but also share and learn. Speakers included a Massage Therapist and Certified Hypnotherapist/ Social Worker who discussed the benefits of Meditation and led the group in a 20 minute session. The day also included small group sessions led by five Licensed Social Workers. Participants with PLS or HSP formed three groups and caregivers were divided into two groups. The small groups allowed for ample time for each person to contribute to the discussion.

A Silent Auction was held throughout the day with the highest bidders announced at the end of the day. The item that brought the highest bid was a wooden hand-crafted framed mirror made be Gene Knicely of Woodstock, VA. The Auction was a success, bringing in over $800 for the SPF.

Since Saturday was May 5th (Cinco de Mayo), a group of about 20 ended the day with dinner and celebration at a Mexican Restaurant in Frederick.

The 13th Annual Spring Fling is planned for the first weekend in May 2013. Mark your calendars for May 3-4, 2013. Barb and Jim are already talking about an educational and fun-filled Spring Fling 2013.

Back: David Lehman, Jim Zalewski, Virginia Buettner, Dorothy Cockrell, Randy LeVier, Annette Lockwood, Danny Tolbert, Bob Miller, Joe Osbourne, Jim Spencer, Judy West, Alene Wendrow
Front: Janet Hawbaker, Diane Sheldon, Gene Knicely, Ronnie Grove, Jerich Jodon, Rich Jodon

MA Connection
June 2, 2012

Submitted by Laurie LeBlanc

We had a small group at our Casual Lunch Connection. Even though the group was small, I feel that it was a great group! We are all different in our level of progression and our abilities but we can still learn a lot from one another. Being able to get and meet other people who understand your challenges is so uplifting! Thanks to John Swain, Nick Mitchell, Jerry Tucker and Marcie Rizzo for joining me!

Dress Down Day
Middletown, CT **June 15, 2012**

Submitted by Kathy Thompson

Farm Hill Elementary School held a Dress Down Day on June 15th to support SPF. A total of $220 was raised during this event. Several members of my family and I have HSP.

Iowa Connection
West Des Moines, Iowa **June 23, 2012**

Submitted by Jackie Wellman

We met for lunch at On the Border on June 23rd. We even had Mari, Ray and Alex White join us from Kansas. Alex was accompanied by his service dog, Hope, who happened to be the best-behaved member of our group. Laurel Yost, her son Chris along and his wife Dixie almost made it to West Des Moines but then had to head back home due to a death in the family. We missed them! For some reason almost all of the SPF members in Iowa have HSP but it was not the topic of discussion. We simply enjoyed each other's company and mostly had fun. David Gibson reminded me that his vote would be canceling mine out in November. I hope everyone and more can make it to the next one.

Left to right: Mari and Ray White, Bruce Stolba, Jennifer Bailey, Kim Richman, Jackie Wellman, David Gibson, Karen Powers with Alex White and Hope in front.

WA Connection
Bellingham WA **June 24, 2012**

Submitted by Jean Chambers

Small group met at the home of Carin and Sal Gurliaccio overlooking Chuckanut Bay, in Bellingham. We had several hours of chatting - sharing things that work and things that don't work. Plus there was an assortment of odd symptoms. I was able to share my enthusiasm about the recent meeting in Washington. Most of the group is looking forward to attending the 2013 meeting, to be held in Phoenix. The possibility of the 2014 meeting being held in Seattle was met with much excitement. Tentative inquiries will be made into possible hotels.

From left to right: David Toperofsky, Carin Gurliaccio, Janice Murphy, Willy Toperofksy, Angela and Dave Irvine and Jean Chambers. Missing – Sal Gurliaccio

KY Connection
Louisville, KY **June 23, 2012**

Submitted by Jane Anne King

The group met at the Holiday Inn at the Louisville Airport on June 23rd. A good time was had by all. Bill Rielly has agreed to organize future Connections in Louisville.

Left to right: Stan & Yvonne Brimmer, Bill & Teresa Reilly, Nisha Litton, and Jane Anne King

Art Walk

Bellingham, WA **August 3, 2012**

Submitted by Carin Gurliaccio

The first Friday of every month, the Downtown Bellingham Art Walk is held from 6-9pm. Several art studios open their doors to the public and often providing music and food. For the Art Walk in August, one of my PTs (Oasis PT) offered me space to set up a table to pass out brochures and talk to interested parties about HSP and PLS.

Upcoming Events

PA Team*W*alk

September 8, 2012 **Philadelphia, PA**

The PA Team*W*alk will be held on Saturday, September 8, 2012 starting at 10:30am. It will be held at Magee Rehabilitation Hospital located at 1513 Race Street. Registration is $10 which includes a Team*W*alk t-shirt, lunch will be provided by the hospital.

If you plan on attending, please contact Helen Kienlen at hmk17@comcast.net.

The Magnificent Mile Race

Sunday, September 16, 2012 at 2pm
300 Hillsborough St, Raleigh, NC

Join us for the Seventh Annual Magnificent Mile Race! The event features a competitive mile race, a recreational mile and two Kid's races. There will also be a street festival with food, fun and prizes.

The Magnificent Mile is the second race in the fall portion of the Second Empire Grand-Prix Series, part of the NC-USATF/Endurance Magazine Champion Series, and the USATF 1-Mile State Championship.

If you have any questions or need more information, please email us at info@magmilerace.com.

CA TeamWalk for our Cures & Connection Weekend

September 21-22, 2012

When: September 22, 2012 (Saturday)
Where: Valley Community Church, 4455 Del Valle Pkwy, Pleasanton, CA
10:00am Social kick-off: Registration, coffee, pastries, juice and water
10:45am Team*W*alk: Walk-n-roll together down Main Street

Noon: Lunch with raffle and closing comments afterwards Join us for a great time of fun, food and camaraderie at our 10th annual California Team*W*alk Connection. At 10:45, we'll walk, stroll and roll together on the sidewalks of Pleasanton's Main Street. We can leisurely take in the shops and even a Farmer's Market. The stroll from the church through downtown and back to the church is an easy walk, go as far as you want or not at all. You can feel free to stay at the church and socialize while you wait to welcome back the walkers 'n rollers.

If you need an accessible room, please call Hem Raju at 925-737-5602 and make your reservations by September 16 to get the special Spastic Paraplegia Foundation room rate of $72/night.

If you plan on attending or have any questions, please email Linda Gentner at lkgentner@aol.com or call at 510-651-5676.

Registration: $10 per person -- a limited quantity of t-shirts will be available.

NY Team*W*alk

September 22, 2012 **Mount Kisco, NY**

The NY Team*W*alk will be on Saturday, September 22, 2012 from 11am-1pm. It will take place at the gazebo on Moger Avenue in Mount Kisco, NY. The gazebo is across from Starbucks and near the Mt Kisco train station.

We will gather at 11am for socialization and around 12pm we will walk (or ride) as a group to the corner before circling back to the original location. Those who do not wish to walk with us can simply stay and socialize. After the walk, a raffle of local business items will be held at the gazebo. This is the 5th Team*W*alk in Mount Kisco and a good time is enjoyed by all. Registration is $10 which includes a Team*W*alk t-shirt and goodie bag.

If you plan on attending or have any questions, please email Ann Lakin at alakin90@gmail.com or call at 914-319-4973.

Note: Team*W*alk is our annual fundraising walkathon. All funds raised support research awards to find our cures. Team*W*alk is a pre-paid event. Participants are encouraged to get sponsors for their participation.

Up Close and Personal

"Pardon Me, Where is the Nearest Restroom?"

By Laura Ratcliff

I don't know how many of you have trouble with incontinence, but it seems to rule my life. As I enter any building I have to ask, "Pardon me, where is your nearest restroom?" I should just make a recording of it and play it for everyone! After I get an answer, I can plan what I need to do in the store or mall doing the things farthest away from the restroom first and rotating by the restroom frequently, just in case.

To make things worse, I am now on a diet that requires that I drink oceans of water! So I'm having a hard time getting to the restroom in time. I don't just "leak" but tend to "gush". And nothing seems able to keep it under control. Yes, I've tried medications and my current one gives me some control, but far from enough, especially with this diet.

The more I worry about it the worse it gets and I seem to lose control as soon as the restroom is in sight. Why is that? Like when I am driving home I get to the driveway, pull in the garage, and lose it as I enter the house.

I think gravity has something to do with it. Perhaps I should crawl, or walk in a hand-stand position? But, if I could do that, I would definitely not need the diet.

Another curious event occurs when I am hurrying into a restroom. My legs refuse to move at even my slow pace. Let's say I normally walk at a snail's pace, but when I need to "go" my pace moves at a chameleon's slow and jerky pace. That not only makes it a more difficult feat, but makes it quite noticeable to others. That's the last thing I need.

I know others have the same challenges, and some worse than mine. I humor myself when I do come home from an outing without any accidents and I say my "pee" prayer. "Thank you for helping me get through this venture without embarrassment and pees help me do the same tomorrow."

Oh, no! The sprinklers went on! Have to go!

Understanding Disability

by Brenda Asbury

- It's not about intent, it's about interpretation.
- From a legal standpoint, that's the bottom line.
- From a moral, ethical, professional belief system, when you pity people, you dis-empower them.
- It's not right to take away someone's choices.
- If they can't do it, they'll let you know, otherwise, you have to respect both them and the law.
- Good intentions can still make people feel terrible.

Vote to Support SPF!!

Everyone willing please use this link to get to the Chase Community Giving page on Facebook. They are giving away **Five Million Dollars** to charities who get the most votes. Basically effortless money for research.

As Frank Davis, SPF President, just said… *"A cure is within reach but it is up to us to do the reaching."* Please help us reach that goal.

Voting takes place between September 6-19, 2012 at http://tinyurl.com/VoteSPF

"If we all did the things we are capable of, we would astound ourselves."

– Thomas Edison

ADAPTIVE SPORTS

submitted by Jim Brewi PLS dx2008/NJ Ambassador

At this year's Annual Conference I attended a breakout session on Adaptive Sports and wanted to share what I heard for those of us who would still like to be active but didn't know there were options available.

Our featured presenter was from a nearby resort that offered accessibility to the physically challenged to both winter sports and water activities in the summer. There are other resorts around the country that offer accessibility, you just have to look for them.

For me the best part was the open discussion that followed with members sharing ways they have found to continue to pursue their outdoor passions, from scuba diving using webbed gloves in lieu of flippers because they can no longer kick, to using an adaptive golf cart where the seat swings out and anchors you in place while allowing you to hit the ball. Many clubs now offer these carts as an option. I was most interested in Kathi Geisler's (HSP) comments regarding her Tricycle (TerraTrike) as I had given up riding a two wheeler for safety reasons about 18 months ago. Kathi is an avid proponent of these trikes as you can see from her pictures, which include going on rides with her service dog as it is good exercise for both. When I got back from the convention I checked out their web www.terratrikes.com to explore further. The challenge you will find is the number of dealers are limited and there was only one in NJ but fortunately for me only a 30 minute drive. I was most concerned with safety, could I get on and off by myself and was it easy to ride? They have a variety of models and pricing can run high for the top of the line models. I settled on the Rambler model which has a little higher platform which makes it easier to get on and off. The brakes allow you to lock them in place which provides stability for getting on and off. Kathi also recommended getting the toe straps which I got or the clip-on shoes which she uses for the most efficient pedaling. I've had mine a couple of weeks now and after the initial adjustment, the ride is very comfortable and FUN and I love being out riding again. I get a lot of smiles from folks on my rides as they try and figure out what is that contraption? I live in an area which has plenty of neighborhood roads for comfortable riding. If you have any other questions you can email me at jbrewi653@aol.com.

Jim Brewi received Community Service Award from PIANJ

The Professional Insurance Agents of New Jersey Inc. announced that James Brewi of North Brunswick, N.J. received the Community Service award at the association's annual conference. The conference was held at the Trump Taj Mahal Resort Casino, June 10-12. Brewi served as regional director of field management for the downstate New York and New Jersey region for Travelers Insurance Co. The PIANJ Community Service Award recognizes individuals who demonstrate a significant commitment to the improvement of his or her community.

Brewi's insurance career spanned from 1976 to his recent retirement from Travelers. During his insurance career he was directly associated with direct service for the independent insurance agent.

In 2008, Brewi was diagnosed with Primary Lateral Sclerosis which causes progressive weakness in the voluntary muscles. Since his diagnosis, Brewi has spent a great deal of time, energy and dedication toward raising funds for the Spastic Paraplegia Foundation Inc.

In 2009, Brewi became Chairperson of the annual Drive "FORE" SPF, a Travelers golf tournament. The first outing raised nearly $140,000. Since then, the event has raised an additional $225,000 for PLS awareness and research.

"Recognizing Jim and his selfless contributions to SPF with this award, is a fitting tribute to this man," said Keith A. Savino, PIANJ president. "This gentleman is an inspiration to us all. I admire his strength, determination and courage."

PIANJ is a trade association representing professional, independent insurance agencies, brokerages and their employees throughout the state.

How Can Federal Employees Help Find Cures?

The Combined Federal Campaign or CFC is a fundraising campaign the Federal Government offers its employees to participate with each year. It is like a United Way campaign where employees pick which non-profits they would like to help each year. The CFC campaign will start the end of August and last through mid October in some locations. Each year **Millions** of dollars are raised through the CFC campaign. The bad news is that the Spastic Paraplegia Foundation doesn't get much of the money raised since we are unknown. Please help us spread the word about the SPF so that we can increase donations received from the CFC. All it takes is for more Federal employees to pick the SPF as a non-profit to donate to. The CFC campaign takes care of the rest. If you know any Federal employees, please ask them to choose the Spastic Paraplegia Foundation during the selection process. The SPF number is 12554. Federal employees will need this number so that SPF can be selected. The following are examples of Federal employees: law enforcement, mail personnel, VA or Veteran's Administration employees, military and many types of governmental jobs.

The best way to get a commitment is to ask personally. If that is too uncomfortable, feel free to send a letter or email. The CFC selection process only happens in the Fall, so now is the time to ask.

Thanks for your help with this great opportunity. If you have any questions, please let me know.

Jim Sheorn jmsheorn@comcast.net or 615-479-7369

Researchers at Baylor College of Medicine Recruiting SPG4 Patients for DNA Study

The laboratory of James Lupski, MD, PhD at Baylor College of Medicine is recruiting patients for a study of SPG4. Eligible individuals are those who have had DNA testing by Athena Diagnostics and have been found to have a "deletion" or "duplication" mutation in the SPG4 gene (also called the "SPAST" gene). This information is listed on the report from Athena. The study will involve providing a blood sample and family tree. If you wish to participate or would like more information, please contact Philip Boone at pmboone@bcm.edu or (713) 798-6873.

HSP Research: The Promise and the Reality

by Allen Bernard *April 2012*

Author's note: *This article is not intended to teach cell biology in any way. The cellular functions I talk about here are vastly oversimplified. Entire text books are devoted to some of the functions I attempt to describe with a single sentence.*

As a writer, I hate using clichés but, in this instance, borrowing Charles Dickens' most famous line is appropriate: "It was the best of times, and it was the worst of times…". Or, put in more modern terms, this is a "good news/bad news" story. It's just a matter of perspective.

First the good news. Researchers working on hereditary spastic paraplegia, better known as HSP, know more today than ever before. They are uncovering new linkages between the proteins that are at the heart of the disorder all the time. This is good because the more common themes you can discover in a disease as complex and mysterious as HSP, the better. These themes, or nodes as they are also called, help cell biologists map the disease and understand why so many different variants -- SPG3A, SPG4, SPG31, etc. -- cause the same common problem: lower limb spasticity and high muscle tone.

This phenotype, or what you and I would call symptoms, cuts across all forms of HSP, both pure and complex. And it is this common phenotype that has led researchers to look for a common cause to the disease -- even though, underneath it all, at least 48 different malfunctioning genes are thought to lie at the heart of the disorder. This is important. From a biological point of view, you would think that so many different genes, which are part of your DNA and provide the instructions the cell needs to make proteins, would cause very different diseases, but that's not how the body works.

This is because proteins work together along complex pathways inside the cell to create energy, remove waste, generate electrical signals, create copies of themselves -- basically, to do everything we need to live, move, breathe, eat, sleep, drive a car…whatever. Now, most cells are extremely small complex structures *(there are over four trillion of them that make up the human body)* that are only now starting to be well understood.

With HSP, researchers and doctors are dealing with one of the most complex and least understood cell types in the body: motor neurons. These cells are found in the motor cortex of the brain. This is where movement begins. These motor neurons have long tails called axons that start, basically, at the top of your head and end at the base of your spine and make up part of your spinal cord. They are one of the longest cells in nature and yet the structures inside these cells are measured in nanometers. To give you some perspective on this, it takes between five and 10 atoms to make one nanometer.

Because of these two vastly different scales – small diameter yet long length – motor neurons are hard to study. You can't just open them up and look at them. They are too small and too intertwined with other parts of the body to put them under a microscope and see what's going on. What this means to folks with HSP *(and, just so you know, my four year old daughter Brianna is one of them),* is this makes HSP incredibly hard to understand and, therefore, to treat…at least for now.

So, for folks hoping for something just around the corner, that's the bad news. There are currently no known drugs that you can take to treat the cause of HSP and, I'm sorry to say, none on the horizon. There are drugs for treating the symptoms like Botox and baclofen but they do nothing to reverse the underlying problem.

Still, I believe, there is more good news than bad to tell in this story.

If you rewind the clock just five years, almost nothing was known about the proteins involved in HSP, how they interacted, what they did or why they did it. Since then much has been learned.

So, what do we know now that will lead to a treatment sooner rather than later? The answer is a lot, but a lot still needs to be discovered and many tests need to be run and many questions need to be answered before you head to the pharmacy to refill your prescription. To create this article I talked at length with five of the world's leading HSP researchers:

Dr. Craig Blackstone at the National Institutes of Health in Bethesda, Maryland;

Dr. Evan Reid at the University of Cambridge in the UK;

Dr. Gerardo Morfini at the University of Illinois, Chicago;

Dr. Joanna Bakowska at Loyola University, Chicago; and

Dr. Michael Hanna at the Texas A&M University, Commerce.

Fortunately for us, there are many, other equally qualified researchers around the world looking at the HSPs with whom these five interact, share knowledge, and learn from.

Okay, now we're going to need a quick bit of science here so we can move on. Genes are basically a set of instructions that tell the cell how to manufacture a protein. Proteins do the work inside of the cell: making energy, removing waste, etc. There are somewhere in the neighborhood of 20,000 to 30,000 proteins that carry out these and all the other functions of life but we are only concerned with a very small number of them.

Depending on the form of HSP, the instructions those genes are putting out are wrong. What this amounts to is you have too much or not enough of a given protein, or you have the right amount of protein but it doesn't work right. In the end, the result is the same: that you have HSP.

Okay, so back to the findings. As I mentioned, researchers keep finding connections between all the different proteins implicated in HSP. The nodes I referred to earlier. Many of you will be all too familiar with the names: atlastin, spastin, maspardin, REEP1, NIPA1, etc. but the vast majority of cases are caused by just three malfunctioning genes: SPG4, SPG3A and SPG31, which code for spastin, atlastin, and REEP1 respectively. Like all HSP genes, these three are very old, having been found in very simple and very ancient life forms, and account for as many as 60 percent of all HSPs. This is actually good news from a cell biology point of view. Here's why.

Fundamental to us all

One of things that HSP has going for it from a treatment point of view is the proteins like atlastin are fundamental to how cells work. Because of this, cell biologists are becoming increasingly interested in studying them so they can increase their knowledge of basic biology. This greatly expands the base of very smart people exploring what these proteins do and how they do it.

For a very rare disease like HSP, this is like hitting a walk-off homerun because it opens the door to unlooked-for-discoveries by researchers outside of the HSP field that could lead to significant breakthroughs in how HSP is understood and treated.

BMP signaling

One of the more promising areas of research is being pursued by Dr. Reid at the University of Cambridge. He and his team are looking at something called the BMP signaling. While BMP stands for bone morphogenic protein, what's really important is it appears that atlastin (SPG3A), spastin (SPG4), maspardin (SPG21), spartin (SPG20), and NIPA1 (SPG6) are all part of the same functional pathway within the motor neuron.

BMP signaling appears to play a key role in how axons grow and what they look like as they branch out into synapses. It is this distal end of the axon, the one at the base of the spine, that connects the neurons in your motor cortex to your legs. If BMP signaling causes HSP's symptoms, then you have a target to go after with drugs. Dr. Reid strongly believes this could be the case but more research needs to be done; particularly in animals; especially in mammals.

The ER (no, not that one…)

Dr. Blackstone's work has led to the realization that spastin, atlastin, REEP1, reticulon2 and possibly NIPA1 are all involved in shaping a very important organelle inside the cell called the endoplasmic reticulum (ER). And this is extremely important from a cell biology point of view because the ER sits at the heart of cell function and is believed to run the length of the axon.

Indeed, before the discovery of atlastin, no one really understood why the ER looked the way it did. Now, HSP has opened a window into this most essential part of the cell. A gateway, if you will, to this and many other areas of cellular function that are now better understood because of HSP.

You may notice that some of these proteins overlap but it isn't clear if ER shaping and BMP signaling are related. Still, this is yet another common point of interaction between two ideas on what is causing HSP. In other words, it gives researchers another place to look for clues that will unravel more of the mystery and teaches them more about how, in this case, the ER is formed, and therefore what is does and, potentially, how to change it.

Casein kinase 2 (CK2)

Working together, the research teams of Dr. Morfini and Dr. Peter Baas at Drexel University in Philadelphia have found a potential target for a treatment of SPG4, spastin. Like Dr. Reid, their findings are preliminary but, if they pan out, they might provide a new framework for the development of treatments that may help prevent motor neuron degeneration in HSP.

Reality check

These are but a few good examples of what researchers are finding. There is more but to talk about it goes well beyond the scope of this article. The important take away here is researchers are finding more and more targets -- functions like axonal transport and structures called microtubules, for example -- to focus on for potential treatments. If just one of these targets proves to be the key to a bona fide treatment, then that is all it takes.

Now, just to be clear, HSP is a very complicated disease with many different forms and no two individuals are affected in exactly the same way so the chances of finding just one pill that cures everyone is remote. But, if 4, 3A and 31 are found to be treatable as a group because of how closely related they are, that would benefit the majority of sufferers.

The squishy side of science

To find this one wonder drug, you might think that money is the end all, be all but it's not. Don't get me wrong on this point, however, more money is definitely better and needed, but perhaps the biggest inhibitor to finding a treatment is lack of good animal models.

While HSP-like symptoms can be created in mice, for example, the phenotype that mice exhibit is less severe than in people and, therefore, harder to measure. Also, mice are just a few inches from head to tail while the cells involved in human HSP are up to a meter long. Mice also take a long time to mature. So when you work with mice, it can take up to a year or more for symptoms to show.

That is why researchers often turn to fruit flies, which share the majority of their genes with humans *(they just have fewer variations of them)* and they reproduce very quickly so you can see results much sooner. But, fruit flies are not people. They can point you in the right direction; give you an idea of what to look for or what questions to ask but they won't serve as a stand in for us.

Researchers like Dr. Morfini also work with squid since their axons can be removed, viewed under a microscope, and react to HSP similarly to our own. Squid have long been used to study other central nervous system (CNS) diseases like ALS and Parkinson's so a lot is known about their basic structure.

This makes squid an important source of information since 99 percent of a motor neuron cell is actually made up of its axon. So axonal transport, or the movement of molecules and proteins up and down the long thin tube that is the axon, is also considered by many in the field to be an good place to look for a cause of HSP. Any disruption of this very finely tuned architecture could result in disease.

Moving the needle

So, the question I'm sure many of you are asking is: "What needs to be done to get from where we are today to a treatment tomorrow?"

Well, while money is not a panacea, more is always needed. More money will buy more animals and hire more research assistants. It can provide seed money for young researchers just getting started and fund "blue sky" ideas that need fleshed out. But money can only do so much. Huntington's, a fatal CNS disease, is very well funded and yet no treatment has been found. Cancer is perhaps an even better example. It's got billions behind it and is still a killer.

Even so, do not be too discouraged, there is still every reason to hope.

I've alluded to the reason for this a few times now in this article. Namely, the proteins involved in HSP are old and integral to the proper functioning of not only motor neurons but many other cells in the body, as well. Atlastin, for example, is found in kidney, liver and skin cells as well as others. Even more interesting is if you have SPG3A HSP, atlastin is mutated in these other cells, and yet, they seem to function just fine. Why is that? No one knows yet.

There are other conditions like Charcot Marie Tooth Type 2b and some neuropathies *(a loss of sensation in the feet and hands that can lead to amputations)* that involve the same proteins as HSP and yet, on the outside, look completely different. This is the type of thing that gets researchers from other fields interested because there must be something very fundamental going on.

ALS and its cousin primary lateral sclerosis (PLS) also have something in common with HSP because of proteins. So, at some point in the future, a researcher in one of these fields or an HSP researcher could uncover a strong bond that could lead to a treatment for both.

HSP is no longer an isolated rare disease with a handful of sufferers that people in the medical community only wonder about. If you take away nothing else from this article, take away this: There are a lot of positive things happening today that weren't happening just a few short years ago that could one day rid us this disease.

As the father of a little girl who really doesn't understand yet why she can't walk like everybody else, this gives me hope. I believe it should give you hope, as well. But, until the day we are free of this disease, life goes on. We smile and cry and persevere. And, in the end, that's what it's all about… HSP or not.

About the Author: *Allen Bernard has written over 1,600 technology, business and science articles in his 14 years as a journalist and editor and is a newly elected board member of the Spastic Paraplegia Foundation and will serve as its newsletter editor going forward.*

Microtubule-targeting drugs rescue axonal swellings in cortical neurons from spastin knock-out mice.

Fassier C, Tarrade A, Peris L, Courageot S, Mailly P, Dalard C, Delga S, Roblot N, Lefevre J, Job D, Hazan J, Curmi PA, Melki J.

Source: UMR CNRS 7224 / Inserm U952 / Université P. & M. Curie, Paris, France;

Abstract: Mutations in SPG4, encoding the microtubule-severing protein spastin, are responsible for the most frequent form of hereditary spastic paraplegia (HSP), a heterogeneous group of genetic diseases characterized by degeneration of the corticospinal tracts. We previously reported that mice harboring a deletion in Spg4, generating a premature stop codon, develop progressive axonal degeneration characterized by focal axonal swellings associated with impaired axonal transport. To further characterize the molecular and cellular mechanisms underlying this mutant phenotype, we have here assessed microtubule dynamics and axonal transport in primary cultures of cortical neurons from spastin mutant mice. We show an early and marked impairment of microtubule dynamics all along the axons of spastin-deficient cortical neurons, which is likely to be responsible for the occurrence of axonal swellings and cargo stalling. Our analysis also reveals that a modulation of microtubule dynamics by microtubule-targeting drugs rescues the mutant phenotype of cortical neurons. Altogether, these results contribute to a better understanding of the pathogenesis of SPG4-linked HSP and ascertain the influence of microtubule-targeted drugs on the early axonal phenotype in a mouse model of the disease.

Role of Kinesin-1 in the Pathogenesis of SPG10, a Rare Form of Hereditary Spastic Paraplegia.

Kawaguchi K.

Abstract: Molecular protein motors play key roles in processes such as intracellular cargo transport and brain wiring, and failure of function can give rise to serious diseases. Kinesin-1, a member of the kinesin superfamily (also known as KIFs) is a two-headed motor protein that uses energy derived from ATP hydrolysis to transport diverse types of intracellular cargo toward the plus-ends of microtubules within axons. Recent studies at the level of a single molecule have provided extensive knowledge on how kinesin-1 moves along microtubules. Further elucidation of kinesin-1 movement may shed light on its influence on axon generation, thereby leading to therapies for diseases such as spastic paraplegia type 10 (SPG10), the subject of this review. SPG10 is an autosomal dominant form of hereditary spastic paraplegia caused by mutations in KIF5A, which encodes one of the isoforms of kinesin-1 (KIF5A, KIF5B, and KIF5C). Although little is known about the cargo of KIF5A, a recent study revealed an axonal transport defect of mitochondria in a KIF5A(-/-) mouse model. This review discusses the consensus moving model of kinesin-1 and the pathogenicity of SPG10 caused by defective KIF5A function.

Novel SPG10 mutation associated with dysautonomia, spinal cord atrophy, and skin biopsy abnormality.

Collongues N, Depienne C, Boehm N, Echaniz-Laguna A, Samama B, Dürr A, Stevanin G, Leguern E, Brice A, Labauge P, de Seze J.

Source: Department of Neurology, University of Strasbourg, Strasbourg, France

Abstract: ***BACKGROUND:*** SPG10 is a rare form of autosomic dominant hereditary spastic paraplegia (HSP) caused by mutations in KIF5A gene, which may be involved in axonal transport.

METHODS: We report the characteristics of a French family with a novel missense mutation c.580 G>C in exon 7 of the KIF5A gene.

RESULTS: The proband and his sister presented with an adult onset HSP, a sensory spinal cord-like syndrome, dysautonomia, and severe axonal polyneuropathy. Contrary to the proband, his sister presented a secondary improvement in spasticity and walking. In the proband, MRI findings consisted in spinal cord atrophy and symmetric cerebral demyelination, whereas the skin biopsy suggested a defect in the number of vesicles and synaptophysin density at the pre-synaptic membrane.

CONCLUSION: This study extends the phenotype of SPG10 and argues for abnormalities in the axonal vesicular transport.

Exome Sequencing Identifies a REEP1 Mutation Involved in Distal Hereditary Motor Neuropathy Type V

Christian Beetz,1 Thomas R. Pieber,2 Nicole Hertel,3 Maria Schabhu¨ttl, 2 Carina Fischer,4 Slave Trajanoski,4 Elisabeth Graf,5 Silke Keiner,6 Ingo Kurth,7 Thomas Wieland,5 Rita-Eva Varga,1 Vincent Timmerman,8 Mary M. Reilly,9 Tim M. Strom,5,10 and Michaela Auer-Grumbach2,*

The distal hereditary motor neuropathies (dHMNs) are a heterogeneous group of neurodegenerative disorders affecting the lower motoneuron.

In a family with both autosomal-dominant dHMN and dHMN type V (dHMN/dHMN-V) present in three generations, we excluded mutations in all genes known to be associated with a dHMN phenotype through Sanger sequencing and defined three potential loci through linkage analysis. Whole-exome sequencing of two affected individuals revealed a single candidate variant within the linking regions, i.e., a splice-site alteration in REEP1 (c.304-2A>G). A minigene assay confirmed complete loss of splice-acceptor functionality and skipping of the in-frame exon 5. The resulting mRNA is predicted to be expressed at normal levels and to encode an internally shortened protein (p.102_139del). Loss-of-function REEP1 mutations have previously been identified in dominant hereditary spastic paraplegia (HSP), a disease associated with upper-motoneuron pathology. Consistent with our clinical-genetic data, we show that REEP1 is strongly expressed in the lower motoneurons as well. Upon exogeneous overexpression in cell lines we observe a subcellular localization defect for p.102_139del that differs from that observed for the known HSP-associated missense mutation c.59C>A (p.Ala20-Glu). Moreover, we show that p.102_139del, but not p.Ala20Glu, recruits atlastin-1, i.e., one of the REEP1 binding partners, to the altered sites of localization.

White and grey matter abnormalities in patients with SPG11 mutations.

França MC Jr, Yasuda CL, Pereira FR, D'Abreu A, Lopes-Ramos CM, Rosa MV, Cendes F, Lopes-Cendes I.

Source: Department of Neurology and Neuroimaging Laboratory, Faculty of Medicine, University of Campinas-UNICAMP, Campinas, São Paulo, Brazil.

Abstract: Background: Mutations in SPG11 are the most frequent known cause of autosomal recessive hereditary spastic paraplegia. Corpus callosum thinning is a hallmark of the condition but little is known about damage to other structures in the CNS. Objective: To evaluate in vivo cerebral damage in patients with SPG11 mutations.Methods5 patients and 15 age and sex matched healthy controls underwent high resolution diffusion tensor imaging (32 directions) and a T1 volumetric (1 mm slices) acquisition protocol in a 3 T scanner (Philips Achieva). These sequences were then analysed through voxel based morphometry (VBM) and tract based spatial statistics (TBSS).Results: Mean age of the patients was 23.6±4.5 years (range 14-45) and mean duration of disease was 12 years (range 5-15). All patients presented with progressive spastic paraplegia and three were already wheelchair bound when first

evaluated. Mutations found were: c.529_533delATATT, c.704_705delAT, c.733_734delAT, c.118C>T and c.7256A>G. VBM identified significant grey matter atrophy in both the thalamus and lentiform nuclei. TBSS analyses revealed reduced fractional anisotropy involving symmetrically subcortical white matter of the temporal and frontal lobes, the cingulated gyrus, cuneus, striatum, corpus callosum and brainstem. Conclusions: Widespread white matter damage in patients with SPG11 mutations has been demonstrated. Grey matter atrophy was prominent in both the thalamus and basal ganglia but not in the cerebral cortex. These findings suggest that neuronal damage/dysfunction is more widespread than previously recognised in this condition.

Microtubule-severing enzymes at the cutting edge.

Sharp DJ, Ross JL.

Abstract: ATP-dependent severing of microtubules was first reported in Xenopus laevis egg extracts in 1991. Two years later this observation led to the purification of the first known microtubule-severing enzyme, katanin. Katanin homologs have now been identified throughout the animal kingdom and in plants. Moreover, members of two closely related enzyme subfamilies, spastin and fidgetin, have been found to sever microtubules and might act alongside katanins in some contexts (Roll-Mecak and McNally, 2010; Yu et al., 2008; Zhang et al., 2007). Over the past few years, it has become clear that microtubule-severing enzymes contribute to a wide range of cellular activities including mitosis and meiosis, morphogenesis, cilia biogenesis and disassembly, and migration. Thus, this group of enzymes is revealing itself to be among the most important of the microtubule regulators. This Commentary focuses on our growing understanding of how microtubule-severing enzymes contribute to the organization and dynamics of diverse microtubule arrays, as well as the structural and biophysical characteristics that afford them the unique capacity to catalyze the removal of tubulin from the interior microtubule lattice. Our goal is to provide a broader perspective, focusing on a limited number of particularly informative, representative and/or timely findings.

Hereditary spastic paraplegias with autosomal dominant, recessive, X-linked, or maternal trait of inheritance.

Finsterer J, Löscher W, Quasthoff S, Wanschitz J, Auer-Grumbach M, Stevanin G.

Source: Krankenanstalt Rudolfstiftung, Wien, Austria; Danube University Krems, Krems, Austria.

Abstract: Hereditary spastic paraplegia (SPG) is a clinically and genetically heterogeneous group of neurodegenerative disorders that are clinically characterised by progressive spasticity and weakness of the lower-limbs (pure SPG) and, majoritorian, additional more extensive neurological or non-neurological manifestations (complex or complicated SPG). Pure SPG is characterised by progressive spasticity and weakness of the lower-limbs, and occasionally sensory disturbances or bladder dysfunction. Complex SPGs additionally include cognitive impairment, dementia, epilepsy, extrapyramidal disturbances, cerebellar involvement, retinopathy, optic atrophy, deafness, polyneuropathy, or skin lesions in the absence of coexisting disorders. Nineteen SPGs follow an autosomal-dominant (AD-SPG), 27 an autosomal-recessive (AR-SPG), 5 X-linked (XL-SPG), and one a maternal trait of inheritance. SPGs are due to mutations in genes encoding for proteins involved in the maintenance of corticospinal tract neurons. Among the AD-SPGs, 40-45% of patients carry mutations in the SPAST-gene (SPG4) and 10% in the ATL1-gene (SPG3), while the other 9 genes are more rarely involved (NIPA1 (SPG6), KIAA0196 (SPG8), KIF5A (SPG10), RNT2 (SPG12), SPGD1 (SPG13), BSCL2 (SPG17), REEP1 (SPG31), ZFYVE27 (SPG33, debated), and SLC33A1 (SPG42, debated)). Among the AR-SPGs, ~20% of the patients carry mutations in the KIAA1840 (SPG11) gene whereas the 15 other genes are rarely mutated and account for SPGs in single families yet (CYP7B1 (SPG5), SPG7 (SPG7), ZFYVE26 (SPG15), ERLIN2 (SPG18), SPG20 (SPG20), ACP33 (SPG21), KIF1A (SPG30), FA2H (SPG35), NTE (SPG39), GJA12/GJC2 (SPG44), KIAA0415 (SPG48) and 4 genes encoding for the AP4-complex (SPG47)). Among the XL-SPGs, 3 causative genes have been identified (L1CAM (SPG1), PLP1 (SPG2), and SLC16A2 (SPG22)). The diagnosis of SPGs is based on clinical, instrumental and genetic investigations. Treatment is exclusively symptomatic.

Reticulon-like-1, the Drosophila ortholog of the Hereditary Spastic Paraplegia gene reticulon 2, is required for organization of endoplasmic reticulum and of distal motor axons.

O'Sullivan NC, Jahn TR, Reid E, O'Kane CJ.

Source: Department of Genetics, University of Cambridge, United Kingdom.

Abstract: Several causative genes for hereditary spastic paraplegia encode proteins with intramembrane hairpin loops that contribute to curvature of the endoplasmic reticulum (ER), but the relevance of this function to axonal degeneration is not understood. One of these genes is reticulon2. In contrast to mammals, Drosophila has only one widely expressed reticulon ortholog, Rtnl1, and we therefore used Drosophila to test its importance for ER organization and axonal function. Rtnl1 distribution overlapped with that of ER, but in contrast to rough ER, was enriched in axons. Loss of Rtnl1 led to expansion of rough or sheet ER in larval epidermis and elevated levels of ER stress. It also caused abnormalities specifically within distal portions of longer motor axons and in their presynaptic terminals, including disruption of smooth ER, the microtubule cytoskeleton, and mitochondria. In contrast proximal axon portions appeared unaffected. Our results provide direct evidence for reticulon function in organization of smooth ER in distal longer axons, and support a model in which spastic paraplegia can be caused by impairment of axonal smooth ER. Our data provide a route to further understanding of both the role of smooth ER in axons, and the pathological consequences of impairment of this compartment.

3D gait analysis in patients with hereditary spastic paraparesis and spastic diplegia: a kinematic, kinetic and EMG comparison.

Piccinini L, Cimolin V, D'Angelo MG, Turconi AC, Crivellini M, Galli M.

Source: IRCCS "E. Medea", "La Nostra Famiglia" Association, Bosisio Parini, Lecco, Italy.

Abstract: The predominant clinical feature of patients with Hereditary Spastic Paraparesis (HSP) is gait disturbance owing to spasticity and weakness of the lower limbs; the spasticity in early-onset disease (infancy or childhood) often cannot be distinguished from mild form of spastic diplegia (SD). The aim of this study was to quantify the gait strategy in HSP and SD children, focusing on the differences between groups as concerns functional limitation during gait. 9 HSP and 16 SD children were evaluated using Gait Analysis; kinematic and kinetic parameters and EMG pattern during walking were identified and calculated to compare the two gait strategies. The results revealed that these two pathologies are characterised by different gait strategies. In particular we found that knee joint, in terms of kinematics and kinetics, and rectus femoris pattern represent discriminatory aspects in order to compare and differentiate gait patterns of HSP and SD children. The findings strongly support the issue that HSP and SD patients need individualised therapeutical program, either neurosurgical or pharmacological treatment, based on the quantification of gait deficiencies and in order to address the peculiarity of their motor limitations and to prevent the onset of compensatory strategies.

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