Synapse

Volume 15, Issue 2 Spring, 2012

Newsletter of the Spastic Paraplegia Foundation

Forever Friends Memorial Garden

www.mndmemorialgarden.org

Letter from the Editor

Dear Friends,

The spring edition of *Synapse* is brimming with news! A warm welcome is extended to Frank, our new SPF president! Frank has been a member of our community for several years. His willingness to commit to such a vital and time-consuming position for the Spastic Paraplegia Foundation is appreciated! Thank you, Frank.

In other news, check out our "Scientific Bytes" –there are so many that it's more like a "mouthful." The main article, dealing with the "Buyer Be Wary" aspect of stem cell opportunity, provides an in-depth look at the questions and concerns one should ask and be aware of when considering stem cell transplantation. And of course, don't forget to catch up on all the PLS & HSP meetings, connections and events.

I would like to take this opportunity to welcome a new writer for *Synapse*, Ms. Laura J. Ratcliff. She is one of our SPF members from Wyoming, and she will be submitting an article for each publication of *Synapse*. Check out her wryly humorous article in the "Up Close & Personal" section, 'Falling into Life with HSP'!

A reminder for those of you who haven't yet registered for the Annual Conference in June – there's still time to join us at the Hilton McLean in Virginia June 8th and 9th. We'd love to see you on Sunday as well for our Team*W*alk down Constitution Avenue. We'll begin near the Washington Monument and finish with a wonderful view of the Lincoln Memorial!

Beth Anne Shultz, Editor
Bads.spf@wildblue.net

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Volume 15, Issue 2 - Spring 2012

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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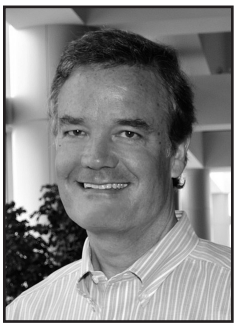
Letter from the President



As the new president of the Spastic Paraplegia Foundation, I want to introduce myself to those of you who I have not yet met. I am 56 years old, have HSP and am currently living in Dallas with my wife Claudia. I worked for thirty years in the direct marketing catalog business in south Texas. I have been secretary on the SPF Board of Directors for six years and have spent the last three years getting a master's degree at SMU.

This is an exciting time to be involved with this organization as our research is unfolding new hope on an almost constant basis. I am looking forward to the opportunity to work with each of you toward that day when together we will celebrate finding a cure for both HSP and PLS.

I have to admit that it will not be easy to follow the dedication and many years of hard work that Annette Lockwood has dedicated as the SPF president. She will remain on the Board of Directors and Jean Chambers will be our new Board Secretary. All other board members will remain. I do hope all of us will allow this change to renew our sense of dedication to the SPF cause. This cause requires that we believe in ourselves and in our capacity to accomplish what at times can seem so difficult; to believe that together, with God's help, we can and will resolve this problem that confronts each of us so personally.

I am especially excited about the SPF Annual Conference scheduled from June 8 to 10, 2012 in the Washington, DC area with the theme "Monumental Hopes & Dreams for a Cure". Washington is one of my favorite cities. The opportunity to hear the latest research about PLS and HSP, to get a chance to meet and talk with so many of you, and to learn new ways to cope with our shared problems in such a fun city is truly a win/win proposition and truly a break that none of us should miss. You will find a current agenda on our web site: www.sp-foundation.org.

Please know that I am always open to hearing any ideas you might have, finding out where you want to pitch in and I look forward to hearing them from you or your state ambassador. Let us keep striving to finish the work we are in.

Sincerely,

Frank Davis

President, SPF

Events and TeamWalks

Monumental Hopes & Dreams TeamWalk

Washington, DC **June 10, 2012**

Over thirty people have signed up for our Team*W*alk in Washington, DC. The cost is $20.00. We will gather near the Smithsonian Metro Stop Sunday morning. Transportation will be provided for those staying at the Hilton, in McLean, Virginia. We will begin our walk on the National Mall with a grand view of the Washington Monument! We'll follow Constitution Avenue until we get an "up close and personal" view of the Lincoln Memorial. Hope you can join us! You may sign up by going to www.sp-foundation.org and registering for the Team*W*alk listed under the Annual Conference Registration Page.

Louisiana Connection - Olive Garden

Baton Rouge, LA **April 21, 2012**

Submitted by Natasha Schaff

Twenty-five of us met at the Olive Garden and spent several hours visiting and exchanging information. Three states were represented within the group: Louisiana, Georgia and Mississippi! Jane Anne and her husband came in from Georgia. Charles Fortenberry, his wife, Milly Fortenberry, his daughter, Shari Fortenberry and his niece Glenda Baustian came to our connection from Mississippi. Members shared information such as the names of physicians who treat HSP and PLS and exercises performed to help increase muscle tone and strength. Jane Anne brought information on different aids and devices to help with day-to-day activities. Charles shared information about stem cell research being performed on animals that seems to help with arthritic issues (in the animals). He is currently pursuing information about this type of research to see where it may lead with regards to an opportunity for people with disorders like HSP and PLS. We hope to have another connection toward the end of the summer so keep an eye out for details in *Synapse* or on the SPF web page.

Oklahoma Connection - State Capitol

Oklahoma City, OK **April 17 2012**

Submitted by Donna Roy

What an awesome day! Lots of people attended the event and many were quite open to hearing about the two bills in question: FAST (4132) and TREAT (2113). It was also a chance to increase awareness for both PLS and HSP. Frank Davis, president of SPF, also attended.

Beta Sigma Phi HSP Connection

Lenexa, Kansas **April 12 2012**

Submitted by Jeri Ragan

Beta Sigma Phi is a service sorority. My sorority sisters had never heard of HSP and wanted to learn more about it. Mari White came to speak at one of our monthly meetings. She and her son, Alex shared their experiences with HSP and we all learned something new!

PLS Dallas – Ft. Worth Connection

Irving, TX **Mar 31, 2012**

Submitted by John Staehle

Several PLSers from the Dallas-Fort Worth area and their families got together on March 31st for a lunch Connection at I Fratelli Ristorante. This is the second such Connection specifically for PLSers who live in north Texas. A total of eight people enjoyed authentic Italian food and great conversation. The PLSers who have been living with their diagnoses for several years were a great help to one who was just recently diagnosed. Attendees shared stories of how they have accommodated the increased difficulty they experience when performing what used to be simple tasks. The group agreed to continue meeting every six months and tentatively set September 29 for the next PLS Connection. In an effort to increase attendance at this Connection, we all agreed to each call a portion of the North Texas PLSers we know about (there are 19 of them) and personally invite them to attend. As that date approaches, John will assign names for each person to contact.

Seated L to R: *Margaret Overly, Jim Thompson, John Staehle, Lois Thompson, Fabio Sampo. Standing: Jeff Smith, Jack Overly, Mauri Overly. (The 4 all the way back are a painting of the restaurant's owners.)*

Virginia Connection

Fairfax, Virginia **February 25, 2012**

Submitted by Annette Lockwood

Sixteen people attended the SPF Connection held on February 25th in Virginia. The group met for lunch at Chevy's Fresh Mex. The Connection was filled with great food and interesting discussions regarding life with HSP or PLS. Volunteers were also solicited for the 2012 Annual Conference and Team*W*alk and several offered their help. The attendees were: John Cobb, Winthrop Cobb, Julie Furgerson, Pamela Hill-Kenya, Iris & Robert Kopach, Annette & Steve Lockwood, Robert Miller, Diane & Janet Sheldon, Barbara & Jim Spencer, Deborah & Ed Thate and Alene Wendrow.

Falling into Life with HSP

Submitted by Laura J. Ratcliff

No one likes to fall; however, falling is nearly an everyday occurrence in my life. Hereditary Spastic Paraplegia is a progressive disease that affects the muscles in your lower body. In my case, the leg muscles feel permanently contracted so I walk with a very stiff gait, but I can walk and for that I am thankful. So you can imagine, my balance is very poor, leading me to fall frequently. I tend to fall without warning and in a very dramatic fashion. Like the time I fell while leaving a bar at a teacher's conference and returned home with a gash on my forehead and a black eye. It was all quite innocent, however, was difficult to explain to my husband and co-workers. And the answer to your question is, "No, I had not been drinking." Another time I was pulling weeds in my garden and fell head first into my small ornamental pond. Do you realize how hard it is to get out of a four foot pond while standing on your head? As I was struggling I saw the headlines flash across our local newspaper, "Local Teacher Drowns in Four Foot Pond". How embarrassing! I finally got out after having swallowed half the water in the pond.

These are only a few of my falls. Not all of them contain humor, like the time I broke my wrist, or the time I took my husband into the emergency room and they wanted to admit me because I looked so bruised and battered. Life is pretty exciting when you can trip on air itself. But this experience has taught me to be thankful for all God has given me. I find myself praying each time I make my way across a patch of ice or climb a flight of stairs. Now I realize all the things there are to be grateful for. I have also developed a slight understanding of those who have mobility challenges. Enjoy what God has given you through Jesus Christ our Lord.

THE ALLERGAN FOUNDATION

A heartfelt thank you goes out to The Allergan Foundation. Due to their support and generosity, the Spastic Paraplegia Foundation was able to print this edition of Synapse at a reduced rate!!

Thank you, Allergan!

Exercise and You

Sit-To-Stand: A Functional Exercise

Contributed by Elizabeth Wrobleski, MPT, PT, HSP

One challenge of exercise is to apply it in everyday activities. Consider using the Sit-to-stand, and subsequently, the Stand-to-sit, for strengthening, balance, weight shifting and ankle/knee control. Getting off a standard height 17" chair without using arms is a good mobility skill to have. There are age norms in the rehab literature as it is often used in assessment of function.

The basic movement sequence is as follows:

1. Sit on a standard chair so that both feet are flat on the floor ready to support the body weight.
2. Cross arms in front over the chest.
3. Keep the low back straight while hinging forward at the hips. Keep the chest up and forward.
4. Come to a full stand and then return to sitting.

Is this easier said than done? What modifications can you incorporate to make this a safe, successful challenge for yourself?

The first variable can be seat height. Initiate your stand from a height greater than 17. Use a high toilet, adjustable commode, a bar stool, added pillows, the firm arm of a couch or even a table edge.

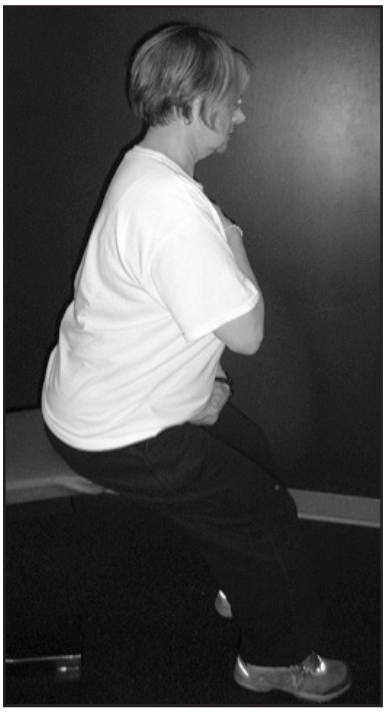
Illustrated is the use of an elastic band above the knees for resistance to facilitate the hip stabilizers. Use weights lifted overhead, placing a balance demand to maintain standing. Other changes can be positioning one foot forward requiring a weight shift to the front foot. Once standing, you can add an actual step or practice trunk turns.

Following through with a controlled Stand-to-sit is important for us so we don't fall back into the chair. Think about "sticking your butt back" as you sit. Pause and hold just before sitting for added work.

This exercise works your glutes and quadriceps muscles. When coming to the stand, don't allow your knees to snap back. This is where controlled lengthening of the hamstrings comes into play. Also, the anterior leg muscles hold the lower leg over the foot as we transition to stand.

As this movement becomes more practiced you can count how many you can do in a given amount of time. Or you can see how long it takes to do a given amount of repetitions. The challenge is to increase the number of repetitions or decrease the amount of time to complete the reps.

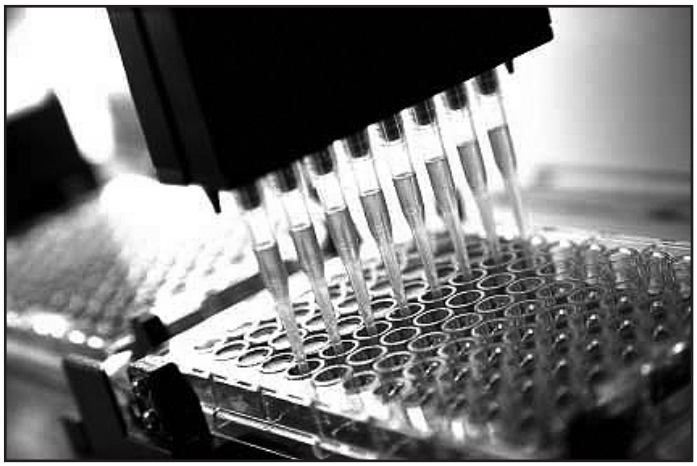
This is a great exercise even if it is necessary to use a chair with arms for a push-to-stand. You can then work on the standing challenges. Consider this exercise good practice for transfers.



PLS Thoughts

Hiroshi Mitsumoto, M.D.,D.Sc.
Columbia University

Patients with primary lateral sclerosis (PLS) have never been prospectively investigated in a systemic way in the past. The reason for this neglect is primarily due to the fact that the disease is so rare, and it takes a long time to get sensible results. Without a good number of patients of PLS to investigate, researchers cannot understand the disease mechanism and develop effective treatment. Five investigators in North America, who have demonstrated a keen interest in PLS by publishing studies *(including Dr. Michael Strong and Dr. Christine Shoesmith at University of Western Ontario, Dr. Richard Barohn at University of Kansas, Dr. Mary Kay Floeter at the National Institute of Neurological Disorders and Stroke, Dr. Mark Singer at University of Texas Southwestern, and Columbia University),* have been studying patients with clinically definite PLS *(more than 5 years but less than 15 years diagnosed)* in a prospective and longitudinal fashion. SPF funded the study in 2009. Currently, we have enrolled 35 patients within these 5 study sites. We are collecting the clinical findings and epidemiological background *(environmental, lifestyle, hobbies, dietary, and psychological profile)* using identical methods. We also have collected DNA, skin fibroblasts, and urine and blood to account for oxidative stress and lipid biomarkers. The analyses of these bio specimens are underway. This SPF-funded study has paved the way for future research and has opened a door for enormous opportunities to expand the investigation of PLS within the field.



Canadian Institutes for Health Research Issues $2.5 Million Grant to Study HSP

Tuesday, March 6, 2012

Ottawa, ON – The Canadian Institutes for Health Research (CIHR) has formed 9 new research teams that will focus on rare diseases. One will focus on HSP. Funding from the CIHR will total $15.4 million over five years, primarily through the Institute of Genetics and the Institute of Nutrition, Metabolism, and Diabetes, while funding from partners will total an additional $1.8 million, also over five years.

The overall objective is to transform fundamental biological research into medical practice and treatments in the area of rare diseases. For example, one team is conducting research on Fabry disease, a rare condition that affects many organ systems. This team will conduct a clinical research trial involving gene therapy, with the ultimate goal of establishing an effective treatment for the disease. The 9 collaborative research teams will investigate a range of issues related to rare diseases, including basic biological science, health services, and policies.

http://checkorphan.org/grid/news/research/research-teams-to-probe-rare-diseases-with-17m-funding

A Patient's Path through the Maze of Stem Cell Transplantation

Courtesy of ALS Worldwide
Article printed and/or paraphrased with permission of Mr. Stephen Byer, Co-Executive Director of ALS Worldwide

An Introduction to the Stem Cell

The first true stem cell was discovered and named in 1908 by the Russian scientist, Alexander Maksimov, who found that certain cells could generate blood cells. In 1963, Canadian researchers Earnest McCullough and James Till described the self-renewing nature of transplanted mouse mesenchymal cells. In 1998, Dr. James Thomson and his colleagues from the University of Wisconsin – Madison announced the successful extraction of stem cells from human embryos in the laboratory. Enormous excitement surrounds these and related discoveries because stem cells have the potential to develop into many different cells, which means they can serve as an internal repair system. When a stem cell divides, it has the potential to either continue functioning as is or become another type of cell with a more specialized function, such as muscle, red blood or brain cell. The most important characteristic of stem cells is their ability to renew, repair or replace worn out or damaged tissue.

We are now, in the late 2000's, faced with a multitude of potential stem cell therapy opportunities for those with ALS and other debilitating diseases and injuries. As a result, an entirely new and complicated collection of terms has emerged in the process. The terminology includes embryonic, adult, fetal, mesenchymal, umbilical cord blood, amniotic, olfactory ensheathing cells, autologous, allogeneic and a whole host of other substrata of stem cells, enough to confuse any patient.

We cannot clarify all of this, but we can try to better identify potential opportunities for stem cell therapies, both by definition and example for the patient community. It is time to view the new paradigm of stem cell technology more carefully and more specifically. Our personal experience has shown us how ALS patients, in their desperation, are often victimized by unfounded, grandiose schemes that lack any scientific basis. The lure is often the inclusion of the words "stem cells," which is effective because of the magical connotation of these words. Though our personal focus is with ALS, we believe this experience is also common for patients suffering from many other debilitating diseases. Therefore, much of the following thoughts, ideas and information are applicable to many other diseases.

In a nutshell, the most important thing to do if considering stem cell transplantation, is to become informed and knowledgeable so that when a decision is made to pursue a particular experimental treatment, it is based on full disclosure and in-depth evaluation of the opportunity being presented, including its benefits and risks.

Definition Terminology

Stem cell therapy is a general term. No one would claim that all medication is either good or bad in itself. In the same way, stem cell-based interventions or procedures cannot be classified as all good or all bad. The value of the intervention depends upon the specifics of each situation and condition. Today, stem cell transplants are routinely used to treat patients with leukemia and other blood cancers so their bodies are able to make new blood cells to replace those destroyed by disease or cancer treatments. By contrast, gene-enhanced stem cell therapy to completely resolve or repair spinal cord injury is clearly something for the future, which will involve extensive research and clinical trials before becoming a standard of medical care.

The existence of a web site, however polished and impressive, does not reflect the existence of an effective or appropriate medical procedure. Do not mistake the qualifications of the marketer for the hopeful qualifications of the clinician or scientist. Unfortunately, there is no absolutely effective "lie detector" when judging the truthfulness or falsehoods of the claims stated in a website. It is worthwhile to ask other qualified resources what they think about the claims in another's website. The final judgment, however, will always fall to the patient.

The best credentials are evidence of a well-constructed and implemented clinical trial. Determine whether or not the institution offering the procedure is nationally and/or internationally accredited. Make certain that authentic documentation of the results of the procedure being considered exist.

Not all types of stem cells are alike, nor do they all offer the same therapeutic potential. With that in mind, following are some, but not all, of the various types of stem cells currently being researched. The challenge is to be able to understand the notable differences between the stem cells' points of origin, their intended uses, and the varying methods of implantation.

The Many Facets of Adult Stem Cells

"Autologous" refers to the stem cells found in most adult tissues, such as bone, skin and blood, and which are also present in the placentas and umbilical cords. These stem cells are also called "somatic," meaning "of the body." This means that stem cells found in the bone marrow of an adult have the potential to become other kinds of cells that pose no risk of rejection if they are utilized in another place in the donor's body.

Allogeneic stem cells are those derived from a healthy donor and transplanted into the patient recipient. In contrast to using autologous cells, the genetic match between donor and recipient is critical so that the risk of rejection of the stem cells is minimized. Extensive testing is always performed to ensure that the risk of rejection is minimized.

Olfactory ensheathing cells (OECs) and autologous mucosal olfactory stem cells (OM-NSCs) are harvested from the lining of the nose and are involved in the sense of smell. Given the right chemical environment, these cells can respond similarly to embryonic stem cells in their ability to transform into many different kinds of cells. They hold the potential for therapeutic applications because they can be easily harvested without harm to the patient. After the cells have been cultured with growth hormone, they are injected into the patient's spinal cord because they have the potential to become neurons.

Mesenchymal stem cells are of particular interest because they have the capacity to differentiate into a variety of tissues. These adult (tissue-specific) stem cells are found in the bone marrow and are able to develop into a variety of cells, including fat, cartilage, bone, tendon, ligaments, muscle, skin and nerve cells. Because they can be obtained in great quantities, they are useful for tissue repair. These stem cells can be obtained and propagated in culture for long periods of time without losing their capabilities to self-renew and differentiate. The fact that these cells can be derived from a small bone marrow sample, induced to multiply in the laboratory, and then given back to the same patient without risk of rejections makes their usage compelling.

Hematopoietic stem cells are adult cells obtained from a patient's own blood, and are frequently used to treat life-threatening conditions such as leukemia, lymphoma and cancer. These are the cells that can be isolated from the blood or bone marrow, renewed, and differentiated into a variety of specialized cells. Hematopoietic stems cells can differentiate into white blood cells that fight infections and were the first stem cells to be used successfully in therapies to treat blood cancers such as leukemia.

Transplantation Procedures

The next step is to understand how stem cells can be transplanted into the patient. For ALS patients, the need is to replace and/or repair damaged and deceased neurons in the brain and spinal cord. This involves surgical procedures that require careful scrutiny.

Brain

Adult and fetal stem cells have been transplanted into the brain in clinical trials of ALS and other conditions for some time now in various countries, including China, Hong Kong, Mexico, Scotland, Italy and the United States. As the practice has generally transitioned from donor to patient cells, the health risks to the patients have been dramatically diminished and the potential benefits have become more obvious because donor cells virtually eliminate the concerns of rejection and infection. These injections are made with the hope of repairing and/or replacing damaged and deceased neurons. This type of procedure appears to have its greatest impact on the upper motor neurons, those in the brain, and far less impact on lower motor neurons, which are those in the spinal cord.

Spinal Cord

There are several current safety and efficacy regulations in effect that govern the use of stem cell transplants into the spinal cord for ALS. Done earlier, without apparent success, in Italy, China, Argentina, and elsewhere, clinical trials of stem cell insertion into the spinal cord are now underway at Emory University in Atlanta, Georgia; the Mayo Clinic in Rochester, Minnesota; Portugal; Israel and elsewhere.

Brain and Spinal Cord

In our view, brain and spinal cord injection of stem cells for the purpose of replacement and/or repair of damaged or deceased neurons hold the greatest potential for eventual success for the ALS patient. However, both must maintain minimally invasive procedures for the stability, safety and well-being of the patient.

Other Methods

Intravenous, intramuscular and subcutaneous injection of stem cells have, until now, shown no benefit to ALS patients and have largely been the treatment offered by untested, unproven, disreputable, opportunistic and unaffiliated stem cell clinics and individual practitioners. Current efforts incorporating intravenous and intramuscular stem cell injections appear promising only when used in conjunction with other forms of delivery.

Current Stem Cell Clinical Studies

On any given day, at any given moment, there are more than 200 stem cell clinics and facilities either opening or closing their doors, making grandiose statements about their capabilities and enticing a vulnerable patient community. However, there are legitimate research efforts being conducted today that hold promise and deserve to be investigated. The common factors of these "second generation studies" are the supervision of a government oversight board, the effective use of an institutional review board, the support of a major teaching institution or hospital, and the adherence to accepted clinical trial standards of practice. These include, but are not limited to, use of control groups (either historical or placebo), informed consent, clearly defined pre- and post-procedure observation and concurrent reportage.

Caveat Emptor: Let the Buyer Beware Appearances Can Be Deceiving

Anyone can launch a beautiful web site, include impressive photographs, write "Doctor" before his name or list credentials from well-known institutions. Whether the information presented is true must be ascertained by the patient. Take the time to investigate. Find the physical location utilizing Google street view. Sometimes a great deal can be discovered in a very brief period of time by simply plugging in the address.

SYNAPSE APPEAL

If you would like to help defray the printing costs for Synapse or fund medical research, please use the enclosed envelope to make a donation. Every little bit helps.

If you prefer to read *Synapse* online, please send an email to information@sp-foundation.org

Evaluate the Stem Cell Clinic or Facility

Practice due diligence. Check references for the physicians and scientists involved in the research protocol. Information about where they received their training and their curricula vitae should be readily available, preferably posted right on the web site

A major institution with an impressive reputation should be providing oversight. This can be a university or a research institute, but it should be one that can be researched. The reputation of the institution is important as well. Its involvement in medical research should have a verifiable history.

Legitimate research organizations have previously published research documentation that is readily available and willingly shared. Even though a new research activity may have recently been launched, a history of past successes should exist.

As with any rapidly advancing technology, multiple sources of information must be found and considered. Triangulating between knowledgeable medical professionals, proven patient experiences and independent judgments from other resources such as dedicated not-for-profit organizations is necessary.

Consideration of the Stem Cell Protocol and/or Treatment

Patients should fully understand the risks involved and the level of safety provided in the trial. If the trial claims to treat several different diseases with the same procedure, it is likely that the facility is offering empty promises to a most vulnerable population. Ask questions about the scientific underpinnings of the treatment, why they believe in their procedure and what they hope to achieve. At the same time, it is not possible for any one doctor or scientist to know about everything that is currently being offered. The finest neurologists, scientists and physicians are the first to say they cannot possibly know all research protocols currently underway, nor can they give an informed opinion about those protocols. This means that your own investigation is of paramount importance in order to make an informed decision.

Quick Reference Guide

Ask yourself these seven very important questions. If any single answer isn't forthcoming, verifiable by outside sources, or is 'no', then walk away.

- Did the physician/scientist receive training from a reputable institution?
- Is the physician/scientist/researcher affiliated with a reputable institution?
- Is there proper internal and external oversight for the procedure?
- Are the claims reasonable and believable and supported by objective data?
- Does the facility openly explains risks, is candid about reasonable expectations and has a single or limited disease focus?
- Does the facility provide information about its process and procedures?
- Do the clinical trials collect data and provide careful examinations before and after treatment?

Promising Adult and Embryonic Stem Cell Research in the United States

United States government funding for stem cell research, whether embryonic or adult, is essential for major scientific accomplishments to be achieved and for research to prevail. Government funding often initiates the most basic, highest expense and riskiest biological work. The following is a partial list of research organizations in the United States that are currently involved in both adult and embryonic stem cell research as therapies for conditions other than ALS.

- Geron Corp recently received U.S. Food and Drug Administration approval to start testing its experimental human embryonic stem cell therapy in people with new spinal cord injuries – the first trial of the controversial cells in humans.
- StemCells, Inc. recently said its human neural stem cells helped improve movement in mice being treated for spinal injuries. The Palo Alto, California-based company planned to start human trials in 2011.
- Advanced Cell Technology, Inc. recently received orphan drug status from the FDA for retinal stem cells to treat Stargardt's Macular Dystrophy, which can lead to blindness.
- Neuralstem, Inc., Rockville, MD, filed an investigational new drug application with the FDA to begin a Phase I safety clinical trial for chronic spinal cord injury with its spinal cord stem cells. It is also testing its cells in patients with ALS.
- Aastrom Biosciences, Inc. is working on ways to take a patient's own cells and use them to treat heart disease. These are in advanced trials in patients.
- ThermoGenesis Corp, supplies products and services that process and store adult stem cells. The company is a leader in cryopreservation systems.
- Osiris Therapeutics, Inc. is testing stem cells taken from bone marrow in patients with Crohn's disease and Graft vs Host Disease.
- Aldagen, Inc., a private company, announced results from a Phase I clinical trial of ALD-201, a stem cell treatment for heart failure. Many companies are working to find ways to use stem cells to regenerate damaged heart tissue.
- Celgene Corp., better known for blood cancer treatments, has an experimental stem cell treatment for Crohn's disease in Phase I clinical trials.
- International Stem Cell Corp. in California is trying to make human stem cells via parthenogenesis, in which an unfertilized egg begins to divide and grow as if it were fertilized by sperm. It positions its potential products as alternatives to embryonic stem cells.

Evaluating a Clinical Trial: Questions to Ask

- Have data about the procedure been published in peer-reviewed scientific journals?
- Is the therapeutic protocol subject to the scrutiny and oversight of an independent Ethics Committee and/or Institutional Review Board (IRB)?
- Does the protocol have a license or a formal authorization by the national governmental licensing body?
- Has the protocol been developed exclusively for ALS or any other singular condition or is it a "one size fits all" treatment that is being offered for a myriad of diseases?
- Finally, is any or all of the total cost of the procedure borne by the hospital or other facility at which it is offered?

"Dedicated to the honor and memory of Benjamin Saul Byer and all ALS patients and their families who have become part of our lives" – Barbara and Stephen Byer

TDP-43 pathology in a case of hereditary spastic paraplegia with a NIPA1/SPG6 mutation

Martinez-Lage M, Molina-Porcel L, Falcone D, McCluskey L, Lee VM, Van Deerlin VM, Trojanowski JQ.

Acta Neuropathol. 2012 Feb 3. [Epub ahead of print]

Source: *Department of Pathology and Laboratory Medicine, Center for Neurodegenerative Disease Research (CNDR), University of Pennsylvania Health System, 3400 Spruce St, Philadelphia, PA, 19104, USA*

ABSTRACT: Mutations in NIPA1 have been described as a cause of autosomal dominant hereditary spastic paraplegia (HSP) known as SPG6. We present the first neuropathological description of a patient with a NIPA1 mutation, and clinical phenotype of complicated HSP with motor neuron disease-like syndrome and cognitive decline. Postmortem examination revealed degeneration of lateral corticospinal tracts and dorsal columns with motor neuron loss. TDP-43 immunostaining showed widespread spinal cord and cerebral skein-like and round neuronal cytoplasmic inclusions. We ruled out NIPA1 mutations in 419 additional cases of motor neuron disease. These findings suggest that hereditary spastic paraplegia due to NIPA1 mutations could represent a TDP-43 proteinopathy.

Ongue's Motor Evoked Potentials in the Diagnosis of Primary Lateral Sclerosis (PLS): Preliminary Report

Bocci T, Briscese L, Giorli E, Pecori C, Sartucci F
J Neurol Sci. 2012 Feb 17 [Eppub ahead of print]

Source: *Department of Neuroscience, Unit of Neurology, Pisa University Medical School, Pisa, Italy; Department of Neuroscience, Neurology and Clinical Neurophysiology Section, Siena University Medical School,Siena, Italy.*

ABSTRACT

BACKGROUND: Primary Lateral Sclerosis (PLS) is an adult-onset neurodegenerative disorder due to a selective loss of precentral pyramidal neurons. Our purpose was to evaluate preferential impairment of pyramidal tract to bulbar muscles in patients with PLS and identify a valuable electrophysiological method to help clinicians in the differential diagnosis from Amyotrophic Lateral Sclerosis (ALS).

MATERIALS AND METHODS: We recorded Motor Evoked Potentials (MEPs) from tongue's and anterior tibialis muscles in six patients with PLS and compared the results, in terms of Central Motor Conduction Time (CMCT), amplitude of MEPs and duration of contralateral silent period (cSP), with those obtained both from ten age-matched healthy volunteers and ten patients affected by ALS.
Results: For lower limbs, CMCT resulted significantly increased in PLS and ALS samples compared with healthy subjects; we did not disclose any difference between ALS and PLS groups. Instead for tongue's recordings, CMCT, absolute amplitude of MEPs and cSP were significantly altered in PLS patients towards both ALS patients and healthy volunteers.

CONCLUSIONS: We showed that tongue's MEPs are selectively impaired in PLS. This technique could be helpful to differentiate patients with PLS from those affected by upper motor neuron-predominant variants of ALS. Tongue's MEPs could represent an interesting electrodiagnostic test, potentially useful for the diagnosis of PLS.

The N355K atlastin 1 mutation is associated with hereditary sensory neuropathy and pyramidal tract features.

Leonardis L, Auer-Grumbach M, Papic L, Zidar J.
Eur J Neurol. 2012 Feb 16

Source: Institute of Clinical Neurophysiology, Division of Neurology, University Medical Center Ljubljana, Ljubljana, Slovenia Department of Internal Medicine, Division of Endocrinology and Metabolism, Medical University Graz, Graz, Austria.

ABSTRACT

BACKGROUND AND PURPOSE: Mutations in atlastin-1 (ATL-1), a gene known to cause pure, early-onset autosomal dominant hereditary spastic paraplegia SPG3A, have been recently reported to cause hereditary sensory neuropathy I (HSN I). We describe the detailed clinical and electrophysiologic findings in the first family with ulcero-mutilating sensory neuropathy carrying the c. C1065A, p.N355K mutation inATL-1. Methods: Detailed clinical and electrophysiologic studies were performed in affected and at-risk family members. Motor and sensory nerve conductions studies (NCS) were carried out in upper and lower limbs. ATL-1 was screened for mutations by direct sequencing. Results: Ten patients were found to carry the N355K mutation.

With the exception of the two youngest patients, all had trophic skin changes in the feet consisting mainly of painless ulcers. Frequently, amputation of toes, feet, or even more proximal parts of the lower legs became necessary. A variable degree of increased muscle tone was observed in younger patients, whilst some older affected individuals only presented with hyperreflexia of patellar tendon reflexes. NCS revealed signs of an axonal motor and sensory neuropathies. Conclusions: Our family carrying the N355K ATL-1 mutation, which was initially diagnosed as HSN I, enlarges the SPG3A phenotype. We therefore suggest that patients with HSN I excluded for more common causes of HSN I, and in particular, affected individuals who exhibit additional pyramidal tract features should also be screened for mutations in ATL-1.

Mutation in the AP4B1 gene cause hereditary spastic paraplegia type 47 (SPG47)

Bauer P, Leshinsky-Silver E, Blumkin L, Schlipf N, Schroder C, Schicks J, Lev D, Riess O, Lerman-Sagie T, Schols L.

Department of Medical Genetics, University of Tubingen, Tubingen, Germany

Neurogenetics, 2012 Feb

ABSTRACT

We recently identified a new locus for spastic paraplegia type 47 (SPG47) in a consanguineous Arabic family with two affected siblings with progressive spastic paraparesis, intellectual disability, seizures, periventricular white matter changes and thin corpus callosum. Using exome sequencing, we now identified a novel AP4B1 frameshift mutation (c.664delC) in this family. This mutation was homozygous in both affected siblings and heterozygous in both parents. The mutant allele was absent in 316 Caucasian and 200 ethnically matched control chromosomes. We propose that AP4B1 mutations cause SPG47 and should be considered in early onset spastic paraplegia with intellectual disability.

"We are not human beings having a spiritual experience. We are spiritual beings having a human experience"

– Pierre Teilhard de Chardin

Loss of Drosophila melanogaster p21-activated kinase 3 suppresses defects in synapse structure and function caused by spastin mutations

Ozdowski EF, Gayle S, Bao H, Zhang B, Sherwood NT

Genetics. 2011 Sep

Source: *Department of Biology/Institute for Genome Sciences and Policy, Duke University, Durham, North Carolina 27710, USA*

ABSTRACT

Microtubules are dynamic structures that must elongate, disassemble, and be cleaved into smaller pieces for proper neuronal development and function. The AAA ATPhase Spastin severs microtubules along their lengths and is thought to regulate the balance between long, stable filaments and shorter fragments that need extension or are transported. In both Drosophila and humans, loss of Spastin function results in reduction of synaptic connections and disabling motor defects. To gain insight into how spastin is regulated, we screened the Drosophila melanogaster genome for deletions that modify a spastin overexpression phenotype, eye size reduction. One suppressor region deleted p21-activated kinase 3 (pak3), which encodes a member of the Pak family of actin-regulatory enzymes, but whose in vivo function is unknown. We show that pakk3 mutants have only mild synaptic defects at the larval neuromuscular junction, but exhibit a potent genetic interaction with spastin mutations. Aberrant bouton morphology, microtubule distribution, and synaptic transmission caused by spastin loss of function are all restored to wild type when pak3 is simultaneously reduced. Neuronal overexpression of pak3 induces actin-rich thin projections, suggesting that it functions in vivo to promote filopodia during presynaptic terminal arborization. Pak3, therefore regulates synapse development in vivo, and when mutated, suppresses the synaptic defects that result from spastin loss.

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Alu elements mediate large SPG11 gene rearrangements: further spatacsin mutations

Conceicao Pereira M, Loureiro JL, Pinto-Basto J, Brandao E, Margarida Lopes A, Neves G, Dias P, Geraldes R, Martins IP, Cruz VT, Kamsteeg EJ, Brunner HG, Coutinho P, Sequeiros J, Alonso I.

Genet Med. 2012 Jan

Source: UnIGENe, IBMC, Porto, Portugal [2] CGPP, IBMC, Porto, Portugal

ABSTRACT

Purpose: Hereditary spastic paraplegias compose a group of neurodegenerative disorders with a large clinical and genetic heterogeneity. Among the autosomal recessive forms, spastic paraplegia type 11 is the most common. Methods: To better understand the spastic paraplegia type 11 mutation spectrum, we studied a group of 54 patients with hereditary spastic paraplegia. Mutation screening was performed by PCR amplification of SPG11 coding regions and intron boundaries, followed by sequencing. For the detection of large gene rearrangements, we performed multiplex ligation-dependent probe amplification. Results: We report 13 families with spastic paraplegia type 11 carrying either novel or previously identified mutations. We describe a complex entire SPG11 rearrangement and show that large gene rearrangements are frequent among patients with spastic paraplegia type 11. Moreover, we mapped the deletion breakpoints of three different large SPG11 deletions and provide evidence for Alu microhomology-mediated exon deletion. Conclusion: Our analysis shows that the high number of repeated elements in SPG11 together with the presence of recombination hotspots and the high intrinsic instability of the 15q locus all contribute toward making this genomic region more prone to large gene rearrangements. These findings enlarge the amount of data relating repeated elements with neurodegenerative disorders and highlight their importance in human disease and genome evolution.

"Your time is limited, so don't waste it living someone else's life. Don't be trapped by dogma — which is living with the results of other people's thinking. Don't let the noise of others' opinions drown out your own inner voice. And most importantly, have the courage to follow your heart and intuition. They somehow already know what you truly want to become. Everything else is secondary."

– Steve Jobs

Psychometric properties of functional mobility tools in hereditary spastic paraplegia and other childhood neurological conditions

Adair B, Said CM, Rodda J, Morris ME

Dev Med Child Neurol. 2012 Apr 24

Source: Department of Physiotherapy, The University of Melbourne, Victoria Hugh Williamson Gait Laboratory, The Royal Children's Hospital, Parkville, Victoria, Australia

ABSTRACT:

Aim: To evaluate studies on the psychometric properties of measurement tools used to quantify functional mobility in children with hereditary spastic paraplegia (HSP) and other childhood neurological conditions. Method: Two independent reviewers identified measures previously used by clinicians to quantify functional mobility. Because our primary interest was HSP, the first search identified measurement tools in studies that included those with HSP. To enhance the generalizability, the second search examined the reliability, validity, and responsiveness of tools in children with a range of neurological conditions such as cerebral palsy, spinal muscular atrophy, Down syndrome, and traumatic brain injury. The Consensus-bases Standards for the Selection of Health Measurement Instruments was used to rate the methodological quality of identified articles.

RESULTS:

The Gillette Functional Assessment Questionnaire (FAQ), the Functional Mobility Scale (FMS), the Gross Motor Function Measure (GMFM), the Rivermead Motor Assessment and the Walking Index for Spinal Cord Injury II were identified for quantifying functional mobility. The FMS and GMFM were reliable, valid, and responsive to changes across a range of childhood neurological conditions. The FAQ was reliable and valid for measuring functional mobility in similar populations.

INTERPRETATION:

The FAQ, FMS, and GMFM are valid, reliable, and responsive measures in children with a range of neurological conditions.

Primary lateral sclerosis as progressive supranuclear palsy: Diagnosis by diffusion tensor imaging

Coon EA, Whitwell JL, Jack CR Jr, Josephs KA

Mov Disord. 2012 Apr 19

Source: Department of Neurology (Behavior Neurology), Mayo Clinic, Rochester, Minnesota, USA.

ABSTRACT

BACKGROUND:
Evaluating the integrity of white matter tracts with diffusion tensor imaging may differentiate primary lateral sclerosis from progressive supranuclear palsy.

METHOD:
Thirty-three prospectively recruited subjects had standardized evaluations and diffusion tensor imaging: 3 with primary lateral sclerosis who presented with features suggestive of progressive supranuclear palsy, 10 with probable or definite progressive supranuclear palsy, and 20 matched controls. We compared fractional anisotropy of the corticospinal tract, superior cerebellar peduncles, and body of the corpus callosum between groups.

RESULTS:
Both the primary lateral sclerosis and progressive supranuclear palsy subjects showed reduced fractional anisotropy in superior cerebellar peduncle and body of the corpus callosum compared with controls, but only primary lateral sclerosis subjects showed reductions in the corticospinal tracts. A ratio of corticospinal tract/superior cerebellar peduncle best distinguished the disorders ($P<.02$).

CONCLUSIONS:
The corticospinal tract/superior cerebellar peduncle ratio is a marker to differentiate primary lateral sclerosis from progressive supranuclear palsy.

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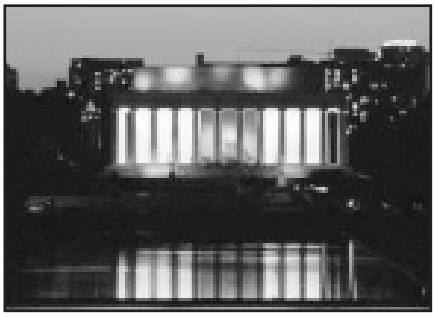
If you and your family still have energy to spare, the Lincoln & World War II Memorials, the White House, the Capitol and the Smithsonian Museums are all just minutes away! Make plans to attend – we can't wait to see you!!!



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