Familial Spastic Paraparesis (FSP)

- FSP is genetically and clinically a heterogeneous group of motor disorders.
- The main clinical feature is weakness and spasticity in the lower extremities that may be progressive.
Familial Spastic Paraparesis

- Due to mutations in genes encoding for proteins involved in the maintenance of corticospinal tract neurons

- These mutations cause distal axonopathy of the longest corticospinal tract axons but other nerve pathways may also be affected

Classification of FSPs

- **Mutated Gene:** SPG3A=ATL1, SPG4=SPAST, SPG6=NIPA1, ...

- **Mode of inheritance:** Autosomal Dominant, Autosomal Recessive, X-linked

- **Clinical presentation:**
  - Clinical Manifestations:
    - Uncomplicated or Pure: Neuro signs limited to lower limbs, Urinary urgency due to spastic bladder and mild vibration/proprioceptive sensory deficit in lower limbs
    - Complicated: Present with additional neurological and MRI abnormalities (i.e., ataxia, peripheral neuropathy, cognitive impairment, thin corpus callosum, etc.)
  - Age of onset:
    - Early (infantile vs. childhood/adolescence) vs. Late

FSP Inheritance

- Over 70 genetic loci have been identified

- FSP may be inherited as:
  - Autosomal dominant: 65% (usually “pure”)
  - Autosomal recessive: 17%
  - Sporadic: 18%
  - X-linked

De Bot, et al. Neurology 2010
FSP suspected if...

- the child has spastic paraparesis and no obvious cause that can be identified by history or imaging (MRI) of brain and spinal cord
- there is a positive family HX

Unfortunately, a family history of HSP is absent in the majority of patients with childhood onset HSP. Many of these patients may be misdiagnosed as spastic diplegia type of Cerebral Palsy

Prevalence of FSP and other facts

- FSP prevalence = 4.3 to 9.8/100,000
  - CP = 300-400/100,000
- “Pure” forms account for 70-80% of the AD-SPGs

AD-SPGs:
- Most common is SPG4 (40-45% of the Pure AD-HSP)
- SPG3A = 10% of AD-HSP cases but this incidence increases in early onset cases
- SPG31 = 4.5-6.5% of AD-SP cases

Importance of Finding Out Genetic Cause

- Provides information about prognosis
- Prevents further additional burdensome and potentially costly diagnostic evaluation
- Allows for genetic counseling
- May help prevent potential complications
- Allows for potential selection in clinical research trials
Two clinical courses of pediatric FSP

- **Infantile onset**
  - Gross motor delay present from the beginning of life

- **Childhood onset**
  - Normal early gross motor development with subsequent loss of gross motor skills and development of spasticity

ICF: International Classification of Functioning, Disability and Health

- **Health Condition** (FSP)
  - Body function & structure (Impairment)
  - Activities (Limitation)
  - Participation (Restriction)
  - Environmental Factors
  - Personal Factors

Assessment of Motor Impairment

- **NEGATIVE**
  - Weakness
  - Poor selective motor control
  - Sensory deficits
  - Balance and Coordination problems
  - Musculo-skeletal deformities
  - Contractures
  - Bony torsions
  - Joint dislocations

- **POSITIVE**
  - Abnormal reflexes
  - Hypertonia (spasticity, dystonia)
  - Involuntary movements
Functional Disability Rating for FSP

- **Grade 0**: asymptomatic, no evidence of gait disturbance, no functional limitation
- **Grade 1**: noticeably abnormal gait but without significant functional limitation and no need for an assistive device
- **Grade 2**: moderate gait disturbance causing functional limitations but no consistent use of an assistive device
- **Grade 3**: marked gait abnormality causing significant functional limitation requiring a consistent use of cane, crutches, or walker or occasional use of a wheelchair (less than 10% of the time and only for long distances)
- **Grade 4**: marked gait abnormality requiring frequent use of a wheelchair (11 to 50% of the time) but still able to walk short distances using other assistive devices
- **Grade 5**: marked functional impairment, unable to walk with crutches, requiring a wheelchair more than 50% of the time.

*Hedera P, et al. Neurology 1999*

Measuring Impairment in Pediatric FSP

The Spastic Paraplegia Rating Scale (SPRS)

A reliable and valid measure of disease severity

R. Schöle, MD, T. Holland-Letz, MSc, S. Ellings, MD, J. Kassubeck, MD, T. Klopstock, MD; V. Mull, MD; S. Orso, MD; B. Wüstem, MD, and L. Solito, MD

Neurology 2006:67:430-434

DOI 10.1212/01.wnl.0000278342.53336.90

Treatment Paradigm

- **Patient**
- **Family**
- **Treating Team**

**GOALS**
**GOALS**

- Task Specific Training
- Strengthening
- Orthosis
- Casting
- Ortho Surgery
- Adaptive Equipment
- Mobility Aids
- Tone Management

**Treatment Paradigm**

**Gait Analysis in Patients with FSP**

- Well reported in the CP population, but limited in patients with FSP, particularly children
- Two primary areas in literature to date:
  - Differentiating FSP and CP
  - Treatment outcomes in FSP (often case studies)

**Gait Differences in FSP vs. CP**

- Prolonged hip extension in FSP (Wolf)
- Increased internal hip rotation in CP (Piccinini)
- Prolonged knee ext. in midstance in FSP (Cimolin, Piccinini, Wolf)
- Increased DF in FSP (Piccinini)
- Prolonged ankle plantar flexion in FSP (Wolf)
- Large trunk tilt velocities appear unique in some HSP (Wolf)
- Increased trunk movements in FSP vs. increased upper extremity compensations in CP patients (Bonnefoy-Mazure)
Treatment Outcomes in FSP

- **Intrathecal Baclofen**
  - Normative changes in phase coupling (interaction between thigh, shank and foot) injection (Dan)
  - Improvement in self-selected speed, step and stride length, knee and ankle kinematics, and ankle kinetics. (Molteni – case study)

- **Functional Electrical Stimulation (FES)**
  - Common Peroneal Nerve: increased dorsiflexor torque, improves toe clearance and dorsiflexion in swing phase, improves walking speed

- **Hydrotherapy Treatment**
  - Significant increase in walking speed
  - Increased ability to perform compensatory strategies rather than achieve typical kinematic and kinetic patterns

- **Robot-assisted training**
  - Improvements in walking speed and balance
  - No changes in gait kinematics and kinetics

Role of Motion Analysis

- **To provide comprehensive, qualitative assessment of function for treatment decision making**
  - Physical Examination
    - Passive/Active ROM
    - Tone and Spasticity Assessment
  - Gross Motor Function
  - Gait Analysis
    - With or without orthoses
    - Oxygen consumption
    - Community Ambulation Levels