MANAGING ATAXIA: SOUP TO NUTS

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National Ataxia Foundation
PRESENTER DISCLOSURES

- Susan L. Perlman M.D.
- The following personal financial relationships with commercial interests relevant to this presentation existed during the past 12 months:
  - No relationships to disclose or list
  - But Dr. Perlman/UCLA has been a site for clinical trials sponsored by Edison, EryDel, Grifols, Horizon, Pfizer, Reata, Shire/Viropharma, and Teva.
SO, YOU HAVE ATAXIA
GETTING IN THE DRIVERS SEAT

Instruction Manual
*User Information

It can help to have a co-pilot

If your UI even vaguely resembles an airplane cockpit, you’re doing it wrong.

John Gruber
WELCOME TO MY OFFICE

• Obtaining a diagnosis
• Selecting your care team
• Medication
• Exercise
• Nutrition
• Equipment
• Support services
• Getting information
OBTAINING A DIAGNOSIS

• “I feel off balance, clumsy, dizzy/woozy…” Inner ear, vision, neuropathy. Medical or medication issues.
• “I have a tremor…” Do not assume it is Parkinson’s disease (Dr. WebMD).
• “I have had unexplained falls…” Weakness, foot drop, trick knee. Fainting, seizures.
• “My father, mother, brother, sister, third cousin twice removed had a walking problem, but it was due to alcohol, back injury, arthritis, old age…”

• All of these scenarios deserve a trip to a neurologist for a good neurologic examination and brain MRI scan (or CT scan if you have a pacemaker).
• Brain MRI can rule out brain tumor, stroke, MS—and may help rule in ataxia.
BRAIN MRI

A small amount of cerebellar atrophy

A large amount of atrophy in cerebellum and brainstem
Mittal and Machado 2014
OTHER LAB WORK
EVERYONE SHOULD HAVE DONE

- Even if you have a strongly positive family history of ataxia, it is a good idea to be checked for a few common, simple, treatable things—or some rarer things that might look like what you have (courtesy of Dr. Brent Fogel):

- A spinal tap might be necessary if an infection, inflammation, chemical imbalance, or spinal fluid pressure problems are suspected.

<table>
<thead>
<tr>
<th>General Studies (All Patients)</th>
<th>1st Line Tests</th>
<th>2nd Line Tests</th>
<th>3rd Line Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Additional work-up to be directed by age, clinical exam, family history, imaging, and other testing.]</td>
<td>Chem 10, CBC, LFTs, uric acid ESR, ANA, RPR TSH, Hgb A1c, Vit B12, MMA, HC, Folate, Vit E D3 VLCFA, phytanic acid Urine heavy metals</td>
<td>Lactate, Pyruvate, Ammonia, Copper, Ceruloplasmin, ACE, CK, SPEP, Ketones, Fasting Lipids, SSA/SSB, Anti-gliadin (non-deamindated) Anti-GAD Anti-thyroid Lyme, HTLV I/II, HIV CSF Studies ( Cultures, IgG synthesis, oligoclonal bands, lactate, other specific tests)</td>
<td>Plasma Amino Acids Urine Organic Acids Lysosomal Screen -------------------------------- Brain PET scan MR Spectroscopy Conjunctival Biopsy Bone Marrow Biopsy</td>
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</table>
1-5% of ataxians with no family history may have a common ataxia gene. Exome sequencing may uncover more genes.

<table>
<thead>
<tr>
<th>Common Adult Genetic Ataxias</th>
<th>SCA1, 2, 3, 6, 7, 8 SCA17, DRPLA FXTAS, FRDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common Pediatric Genetic Ataxias</td>
<td>AT FRDA AOA1, AOA2</td>
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</table>
THE EFFECTS OF A HIDDEN CANCER

<table>
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<tr>
<th>Paraneoplastic disorders</th>
<th>Malignancy workup (CT chest, abdomen, pelvis, mammogram, testicular ultrasound, body PET scan)</th>
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<tbody>
<tr>
<td></td>
<td>Paraneoplastic antibody testing (blood or spinal fluid)</td>
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</table>
MULTIPLE SYSTEM ATROPHY

- 80% of MSAs start with Parkinsonian symptoms; 20% of MSAs start with ataxia.
- 25% of patients with sporadic cerebellar ataxia will go on develop MSA (non-levodopa responsive Parkinsonism, blood pressure instability, early bladder dysfunction) within 5 years of onset of ataxia, especially if >50y/o.
- Erectile dysfunction can precede ataxia by 5-10 years.
- Notable cerebellar disability is seen within 2-3 years.
- REM sleep disturbances, obstructive sleep apnea, and stridor are common.
- Uncommon are: onset after age 75, family history of ataxia or Parkinsons, classic pill-rolling rest tremor, chorea (involuntary twitches), slowed or limited eye movements, dementia.
- Important to identify MSA early, as there are drug trials in development.
SELECTING YOUR CARE TEAM

• A primary care physician/healthcare provider
• A neurologist

You may see the following only once, but they have important input for ataxia:
• A second opinion neurologist who specializes in ataxia
• A geneticist
• A physical therapist and/or equipment-orthotics specialist
• An occupational therapist
• A speech and swallowing therapist
• A nutritionist
• A social worker or psychologist
• Other sub-specialists for associated problems (ophthalmologist, cardiologist, pulmonary or sleep specialist, pain management specialist)
MAYO CLINIC STUDY ABOUT WHAT PEOPLE WANT IN A DOCTOR

- Confident: "The doctor's confidence gives me confidence."
- Empathetic: "The doctor tries to understand what I am feeling and experiencing, physically and emotionally, and communicates that understanding to me."
- Forthright: "The doctor tells me what I need to know in plain language and in a forthright manner."
- Humane: "The doctor is caring, compassionate, and kind."
- Personal: "The doctor is interested in me more than just as a patient, interacts with me, and remembers me as an individual."
- Respectful: "The doctor takes my input seriously and works with me."
- Thorough: "The doctor is conscientious and persistent."
• There are still no cures for ataxia, but symptoms can be treated.
• Give any new medication at least a month to work.
  The dose may need to be increased.
• Report side effects right away. You may reduce the dose, but don’t stop the medication until you speak with your doctor, unless you are having an allergic reaction.
• Taking care of your general health, exercising regularly, and possibly using an anti-oxidant vitamin, might slow up progression of ataxia.
• Discuss with your doctor any exciting new treatments you may be hearing about… before trying them.
• If you are depressed, talk to someone about it and consider medication.
• **Goals for all—no falls, no choking, no infections, restful sleep, good energy, no pain.**
DRUGS FOR SYMPTOMS OF ATAXIA
THESE ARE ALL OFF-LABEL

Reported in the medical literature for ataxia
*possibly also neuroprotective

- Amantadine
- Buspirone
- L-5-hydroxytryptophan
- Memantine *
- Physostigmine
- Riluzole *
- Tandospirone *
- Thyrotropin releasing factor *
- Varenicline

For tremor, myoclonus, nystagmus

- 4-aminopyridine
- Baclofen
- Carbamazepine
- Clonazepam
- Gabapentin
- Isoniazid
- Levetiracetam
- Piracetam
- Primidone
- Propranolol
- Valproic acid
- Zonisamide
- Botulinum toxin shots
- Surgery, stimulators

- Fluoxetine (speech, swallowing) *
- Meclizine, Scopolamine, Ondansetron (vertigo)
- Acetazolamide, 4-aminopyridine *, Dilantin, Flunarizine (episodic ataxia)
DRUGS FOR SYMPTOMS OF ATAXIA

THESE ARE ALSO OFF-LABEL

For Fatigue
- Pyridostigmine
- Amantadine
- Selegiline
- Methyphenidate
- Modafinil, Armodafinil
- Fluoxetine, Sertraline, other energizing anti-depressants
- Caffeine
- Creatine, Carnitine
- Anti-oxidant vitamins

Non-drug approaches as well
- Look for other illnesses, drug side effects
- Good nutrition.
- Conditioning exercise.
- Weight management.
- Pain control.
- Sleep hygiene.
- Energy conservation.
- Lifestyle modification.
- Emotional health

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• Friday, April 1, 10:30am Physical Therapy
  
  Jennifer Keller, PT Motion Analysis Lab, Kennedy Krieger Institute Baltimore, MD

• Goals of Rehabilitation (PT, OT, Speech Therapy):
  • safe mobility (including driving)
  • independence in activities of daily living
  • intelligible speech or other communication
  • safe swallow or other nutrition
  • safe airway
  • control of deconditioning, fatigue, and pain
• Weight maintenance.
• Supplements for documented deficiencies.
• Enough fiber to stabilize bowel function.
• Carefully chosen pre-exercise supplements used in moderation, if desired.
• Gluten-free diet if you are gluten sensitive—other uses optional.
• Other restrictive diets (ketogenic, vegan, etc.) must be assessed by a nutrition specialist to avoid micronutrient deficiencies.

• There are no diets proven to cure ataxia.
• **Sunday, April 2, 10:45am** Using an iPad for Aided Communication: Augmentative and Alternative Communication Options and Technology
Nancy Harrington, MA, CCC-SLP Florida Alliance for Assistive Services

• Occupational therapists are helpful for aids to activities of daily living, driver evaluations.
• Physical therapists can recommend aids to gait, bracing, mobility devices, transfer devices, appropriate seating.

• Videogame playing has been shown to help hand coordination.
• Friday, April 1, 11:00am Disability Decisions and Applying
  Jon Rodis & Kathleen Kane, Esq. for SSDI Winthrop, MA
• Friday, April 1, 11:30am The Ataxia Rollercoaster: How to Have a Smoother Ride with the Ups, Downs & Loop-the-Loops of Life
  Ellen Sichel, BS CEO of Custom Calm, LLS, Atlanta, GA
• Saturday, April 2, 10:00am Detours Ahead: Life with Ataxia
  Nygel Lenz NAF Support Group Leader, Clearwater, FL

Genetic counseling, Psychosocial Counseling, Home Health Assistance, Legal Aid, Support Groups Disability decisions, insurance issues, financial concerns may require professional help.
GETTING INFORMATION

• The Internet—7 million hits for “ataxia”
• National Ataxia Foundation website and its links
• ClinicalTrials.gov

• Your healthcare provider
• Your “co-pilot”
• Other ataxians—social media; support groups; Birds of a Feather

• Control the flow of information you are getting so as not to drown.
GETTING INVOLVED TO MASTER ATAXIA

• Join the National Ataxia Foundation
• Sign up in the Registry
• Find a Support Group or Ambassador near you
• Explore social media…carefully
• Volunteer for studies and clinical trials.
• Empower your doctor—if your doctor knows that there are things that can be done, s/he will be a stronger member of your team.
• Use information to open dialogues—with family, friends, healthcare providers, fellow ataxians…
• Keep a short list of whom to ask when you have questions.
QUICK LINKS

• CoRDS **Registry**--http://www.sanfordresearch.org/cords/
  The NAF website has a link to this, as well as lists of ataxia doctors.

To find a **research center near you:**
• CRC-SCA--Phuong Deleyrolle, RN-Coordinator pdeleyrolle@ufl.edu
• CCRN-FA-- info@curefa.org (484) 879-6160 (also has a registry just for FA)

To find **research studies near you:**
• ClinicalTrials.gov—type in “ataxia” and select “open studies”.
  The first 50 studies that come up are most applicable.
• ClinicalTrials.gov—type in “multiple system atrophy” and select “open studies”.
  The first 30 studies that come up are the most applicable.
• The research centers above should also have information about studies and trials.
• New studies are opening up all the time—natural history, biomarker, genetic, treatment.
PHARMACEUTICAL COMPANIES WITH ATAXIA DRUGS IN THE PIPELINE

- Anavex
- Astra-Zeneca—MSA (currently active)
- Ataxion
- Bioblast
- Biohaven
- EryDel—A-T
- Ionis
- Steminent

- And others that have not yet gone public.

Primary target is FA--
- BioMarin
- Chondrial
- Edison
- Gene therapies—Annapurna, Voyager, Agilis, Bamboo, IGBMC
- Horizon
- RaNA
- Reata
- Retrotope
- Shire/Viropharma
- STATegics
LOCATIONS FOR THE Astra-Zeneca MSA DRUG TRIAL

• Contact: AstraZeneca Clinical Study Information Center 1-877-240-9479
  information.center@astrazeneca.com
• Stanford
• New Haven
• Tampa
• Boston
• Ann Arbor
• Rochester, MN
• NYC
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- Robert Baloh, M.D. (Neuro-Otology)
- The George Bartzokis, M.D. Group (Neuroimaging, Biomarkers)
- Yvette Bordelon, M.D., Ph.D. (Huntington’s disease, Biomarkers, Drug Trials)
- Stephen Cederbaum, M.D. (Medical Genetics, Metabolic Disorders)
- Giovanni Coppola, M.D. (Molecular Genetics)
- Ming Guo, M.D., Ph.D. (Drosophila)
- Michelle Hamilton, M.D., Juan Alejos, M.D., and associates (Cardiology)
- Joanna Jen, M.D., Ph.D. (Episodic Ataxias, Drug Trials)
- Arik Johnson, Psy.D. (Psychology)
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- Nagmeh Dorrani, M.S. — Genetic Counselor (310) 206-6581
UCLA NEUROGENETICS CLINICAL RESEARCH TEAM
• **National Ataxia Foundation**—
  • sponsor of grants for our internal database, our DNA bank, and our web-based database project.

• **Muscular Dystrophy Association** and
  • **Friedreich’s Ataxia Research Alliance**—
  • sponsors of the grant for the collaborative project on “Clinical Outcome Measures in Friedreich’s Ataxia”.

• **The Smith Family Foundation; The Lapin Family Fund; The Bettencourt Fund**

• And to our patients and their families for their willingness to work with us and to share with us their ideas and hopes.