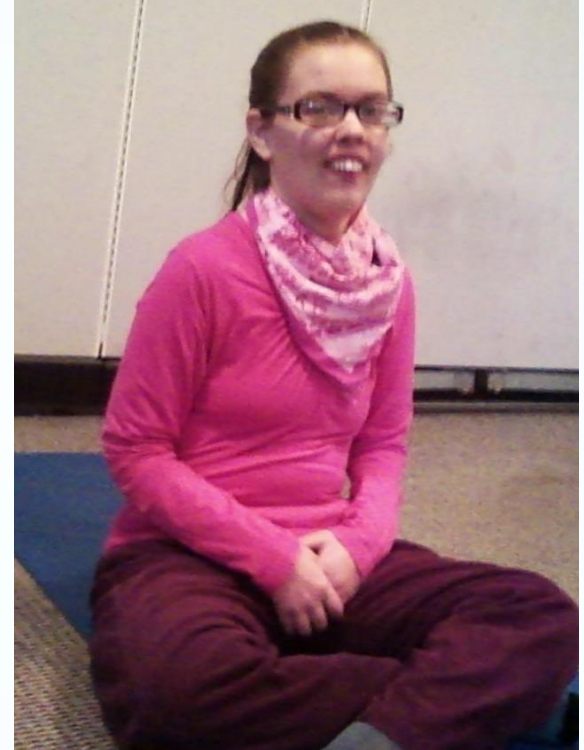
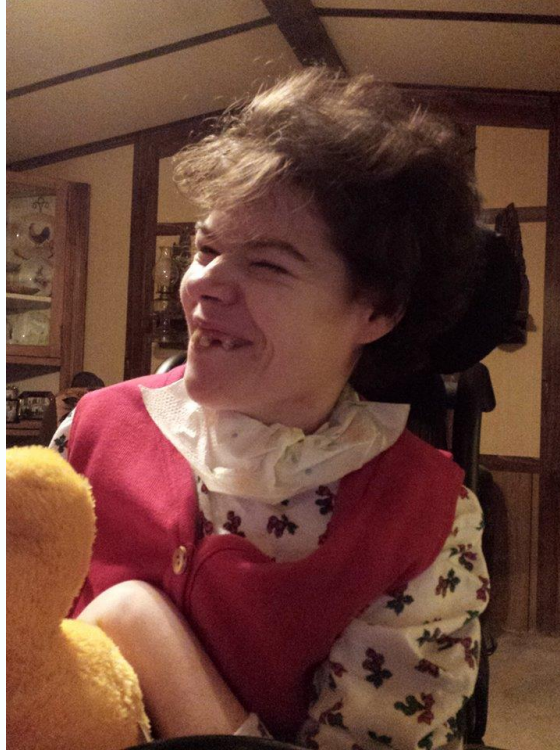


# BPAN: Then and Now

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# Objectives

- What we knew in the beginning
- What we know now
- How you can help



Smile

# What we learned

- The gene *WDR45* is located on the X chromosome
- The gene acts in a dominant manner
- Gene changes are usually sporadic; rarely they can be inherited
- The gene is involved in a process called autophagy



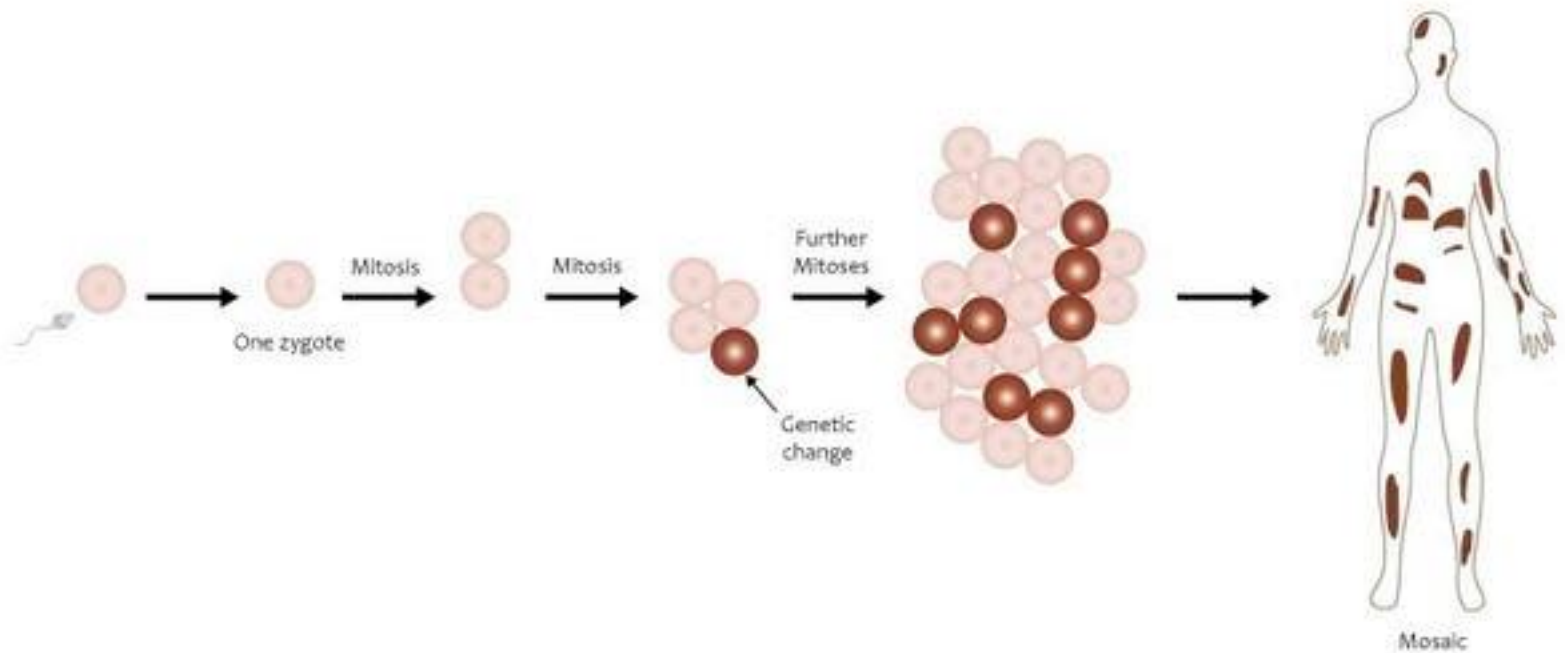
# Autophagy



# Factors contributing to variation

- Mosaicism
- X-inactivation

# What is mosaicism?



# What is x-inactivation?

- All females are mosaics for the X chromosome. In each cell, only one copy is working and the other is “turned off.”
- This can be skewed in either direction.
- It is basically a different type of mosaicism





# Then

- Our original “cohort” of BPAN patients consisted mainly of young adults and adults who were referred to us because of brain iron on MRI
- NOW: we are finding patients in completely different ways, mainly after whole exome testing

# Now

- New data on younger kids with BPAN found through whole exome testing
- What will these kids look like as adults? We don't entirely know...
- What is ascertainment bias?

# New data highlights

- From 16 girls and 3 boys ages 2-18
- Developmental delay is early and universal
- About half had a formal autism diagnosis at some point (mainly because of absent language, stimulation/sensory-seeking behaviors)
- Speech—majority have no expressive language to very limited language. There are exceptions.



# Highlights

- Walking ranged from “on time” to some who have never walked. A broad, unsteady walk is common, especially at first. Stairs can be tricky.
- Seizures—nearly all of the 19 have had them. Often start as febrile and will change over time. Management is a big issue.
- Sleep—nearly all report some sort of sleep issue (waking in night, trouble getting back to sleep, seems to change with age)



# Highlights

- Muscle tone: hypotonia or “floppiness” is common early on. Dystonia and spasticity seem to come later in childhood for some.
- GI issues: constipation, GERD, several with unexplained elevated liver enzymes. Most seem to be doing OK with feeding; a few young kids have g-tubes
- Most not potty-trained or partially trained



# Imaging

- Early delayed myelination or “hypomyelination” in several
- Agenesis or “thin” corpus callosum
- Several with small heads, some meeting definition of “microcephaly”
- Iron can be recognizable during childhood

# Imaging

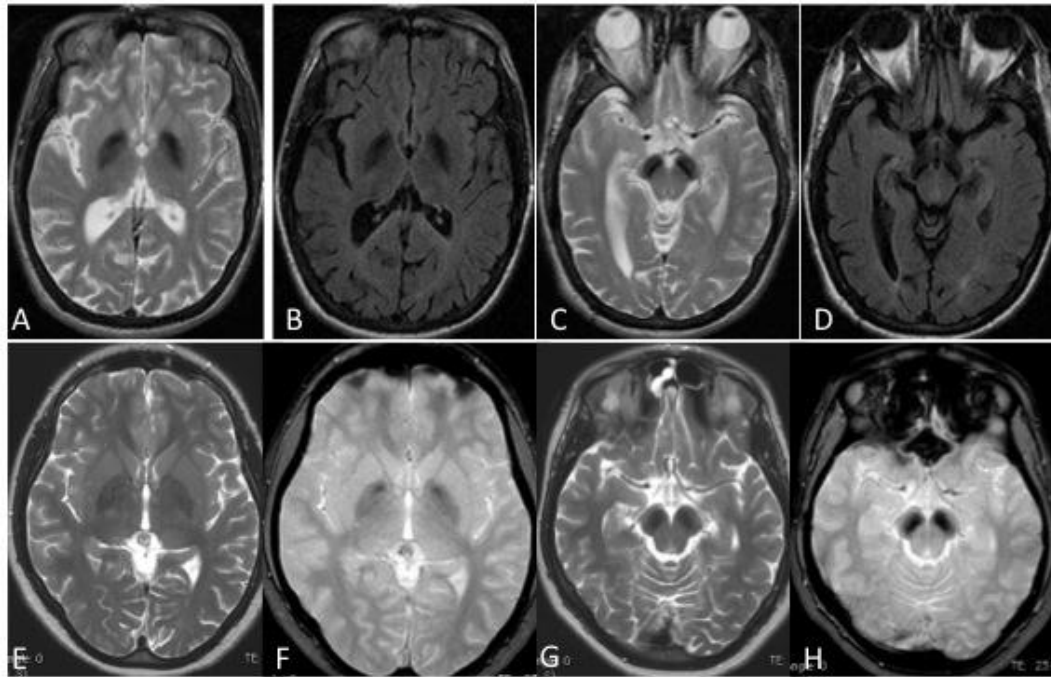
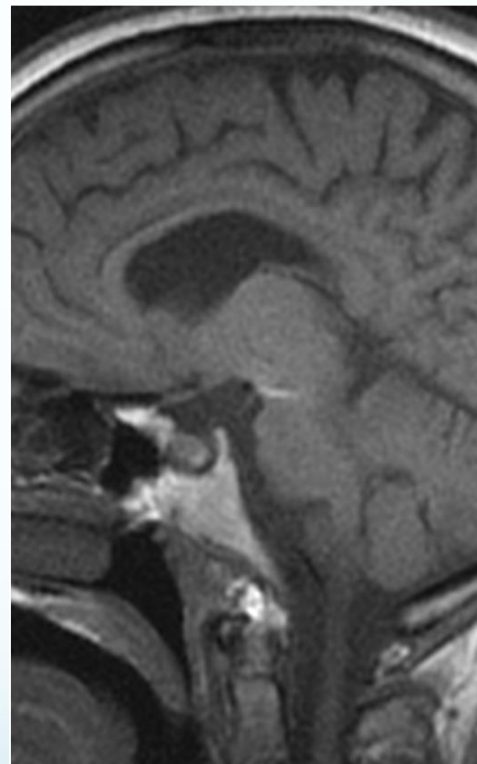
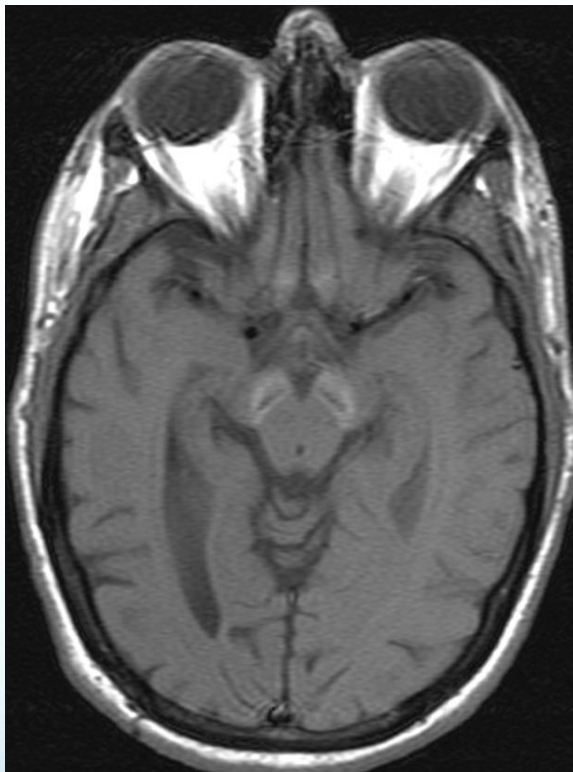


Figure 1

# Imaging



# Other tidbits

- Are there common facial features?
- Precocious puberty or early development?
- Hyperventilation and other Rett-like behaviors (teeth grinding, hand-flapping)
- Behavior/emotional control?

# How you can help

- Research participation!



# Consider brain tissue donation



BPAN research  
meeting





