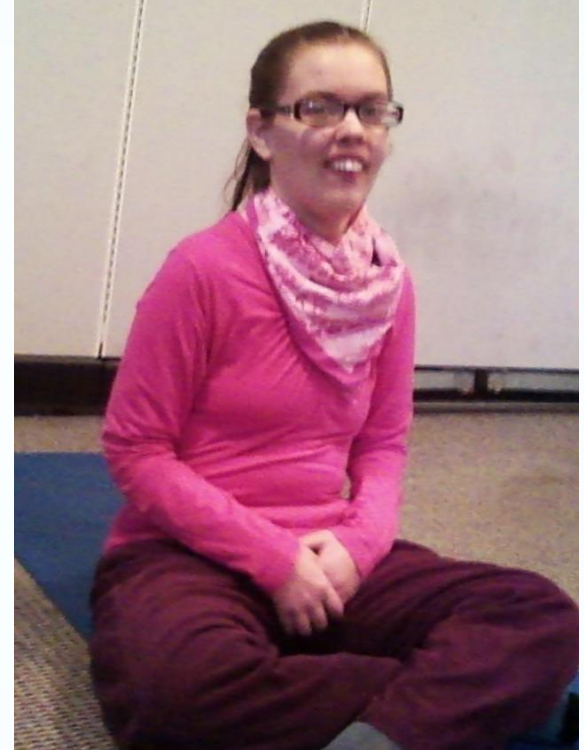
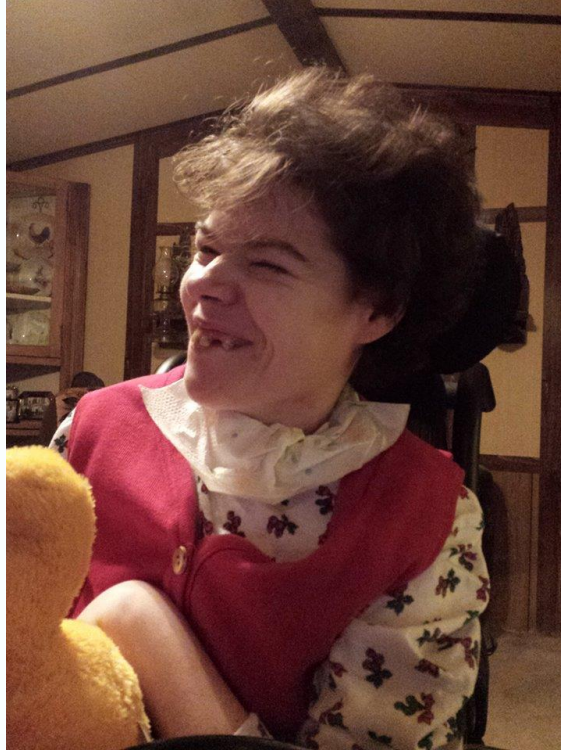


BPAN: Then and Now

Allison Gregory, MS, CGC
Hayflick Lab

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

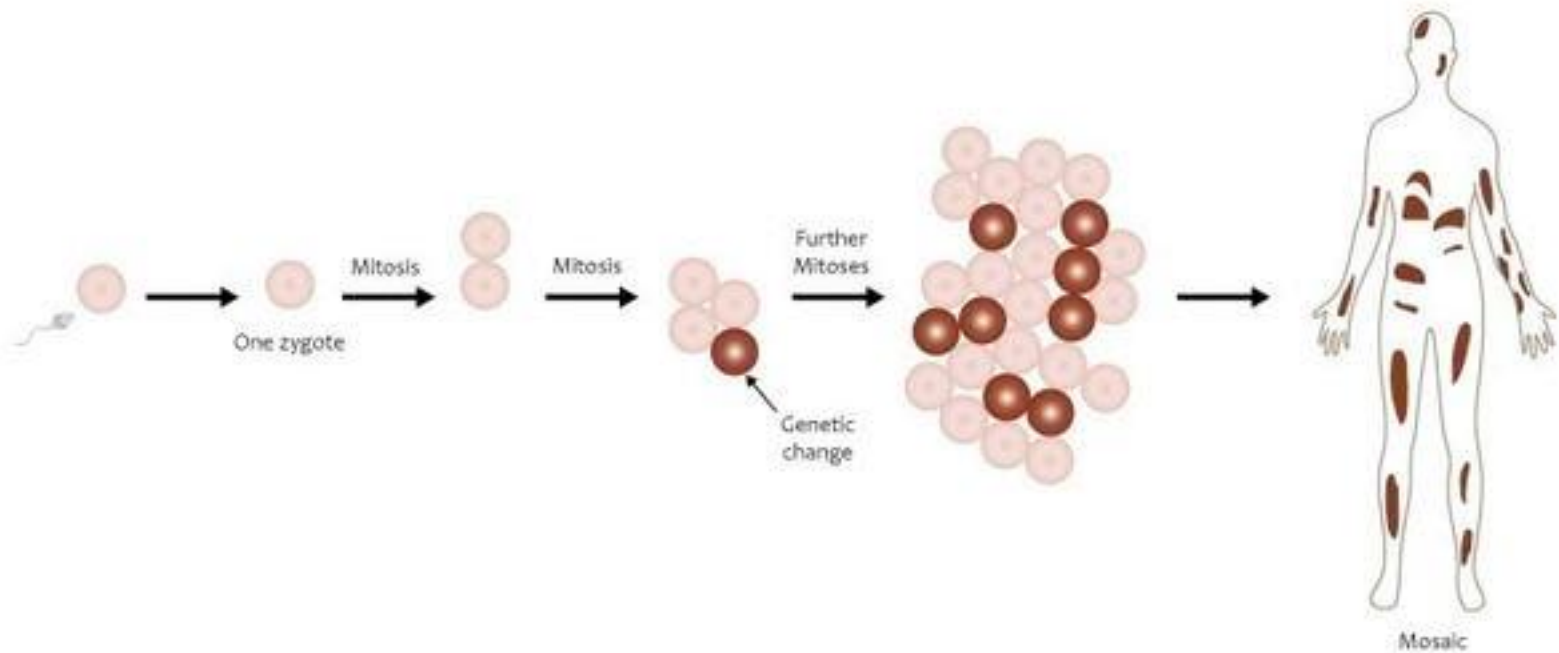
Autophagy



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

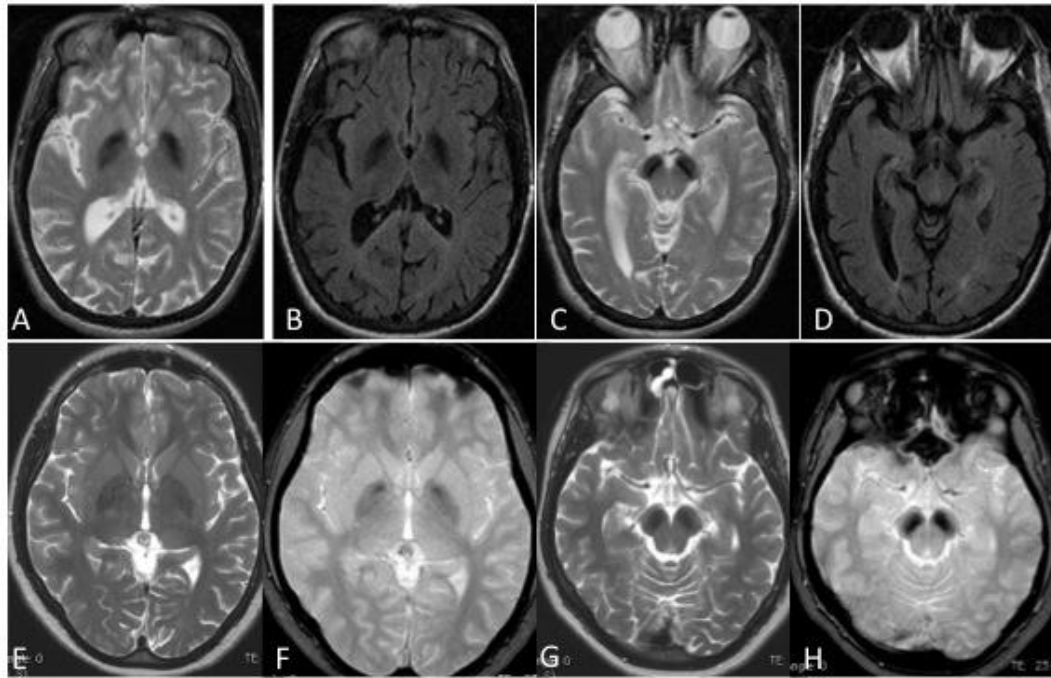
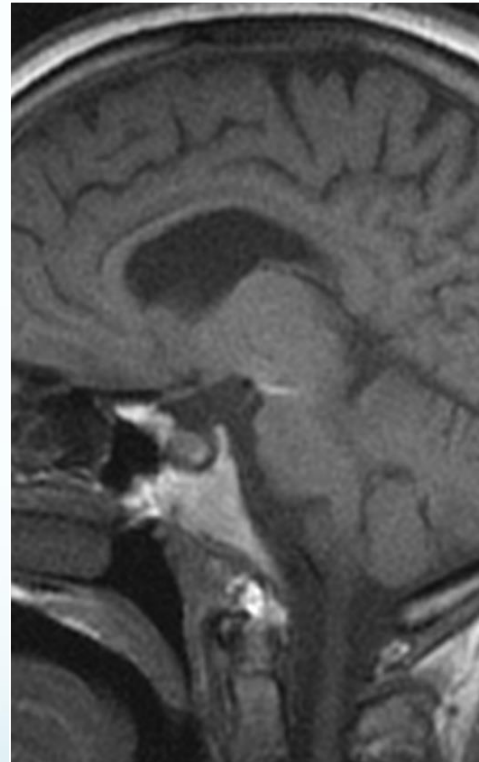
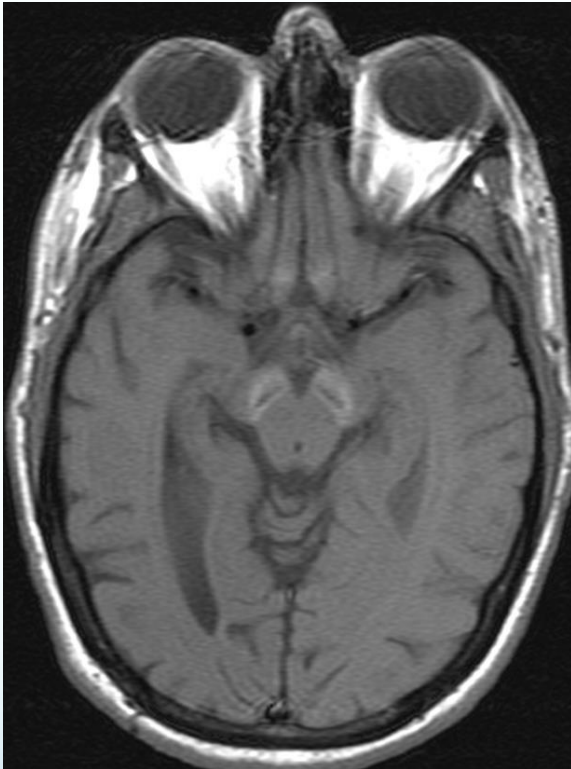


Figure 1

Imaging

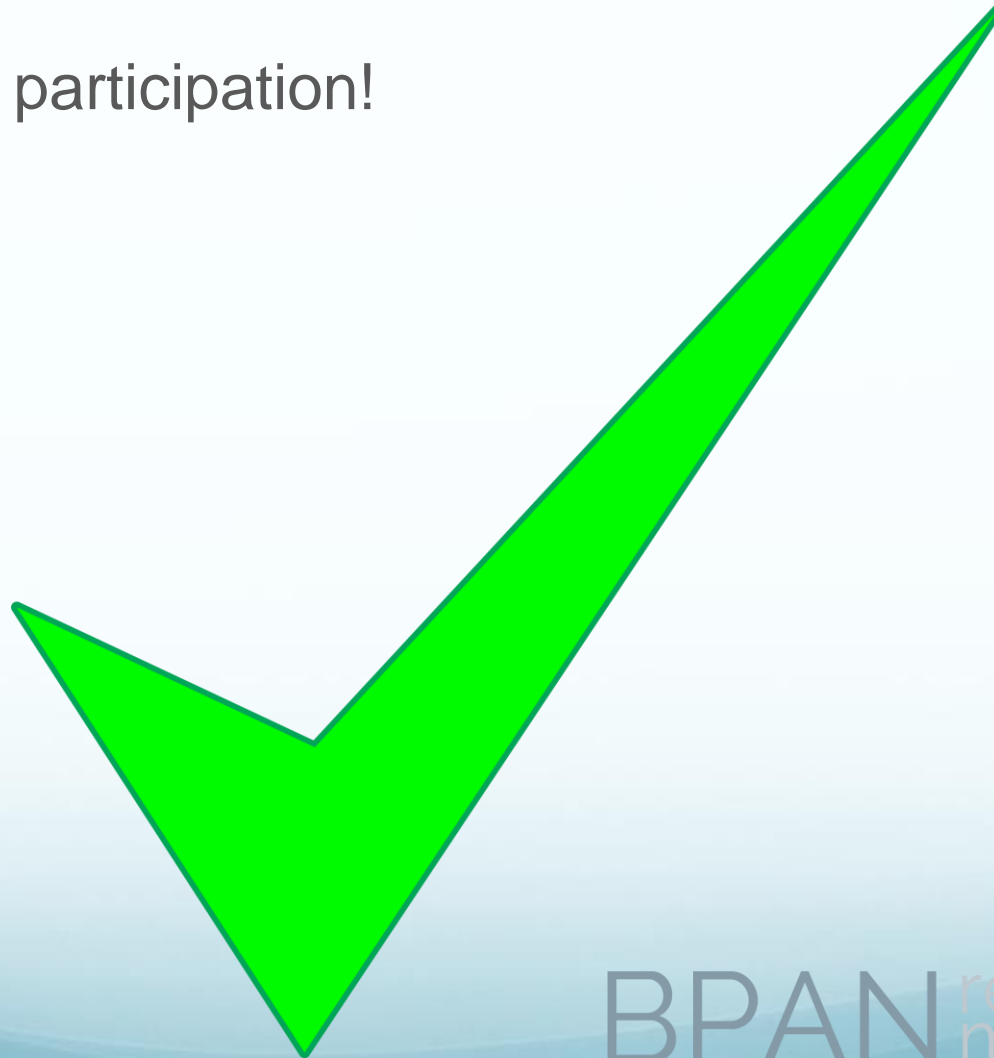


Other tidbits

- 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 

