What we’ve learned from the KAND natural history study

July 9, 2021
Lia Boyle, PhD
Chung lab, Columbia University
A Precision Medicine Approach to KAND

1. Characterization
2. Modeling
3. Understanding the model
4. Developing therapies
5. Implementing therapies
A Precision Medicine Approach to KAND

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2. Modeling
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Outline

• Chung lab KAND history
• Natural history study: why is it important?
• Background on our study
• What’s in a name? KAND vs SPG30 vs NESCAV
• Refresher on overall symptoms
• New symptom information from our follow up survey
• Focus on seizures
• How you can participate
KAND worldwide

25 different countries – and counting!
Why do we need a natural history study?

• Helps clinicians and scientists understand disease progression
• Important for identifying and developing best clinical practices
• Identifies factors that affect disease severity
• A critical step in clinical trial readiness
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Participating in the study makes sure your voice is heard and your family is represented
What’s in a name: KAND vs NESCAV vs SPG30
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KAND affects the whole body

**Cognition, Epilepsy & Behavior**
- Developmental delay/intellectual disability: 92%
- Epilepsy: 42%
- Autism: 24%
- Attention deficit/hyperactivity disorder: 19%
- Obsessive compulsive disorder: 5%

**Vision & Eyesight**
- Optic nerve atrophy: 50%
- Cortical visual impairment: 20%
- Strabismus: 26%
- Cataracts: 8%

**Stomach & Digestion**
- Reflux: 40%
- Diarrhea: 17%
- Constipation: 39%

**Urinary & Reproductive**
- Irregularity in genitalia: 13%
- Kidney problems: 3%

**Neurological & Musculoskeletal**
- Hypotonia: 84%
- Hypertonia/spasticity: 81%
- Peripheral neuropathy: 27%
- Scoliosis: 14%

**Growth**
- Short stature: 13%
- Absence of growth hormone: 3%

Data from Boyle et al., *HGG Advances*, 2021
How symptoms can appear: an example

7 year old boy

20 year old woman
How symptoms can appear: an example

7 year old boy

20 year old woman

- First seizure at 4
How symptoms can appear: an example

7 year old boy

20 year old woman
- First seizure at 4
- Optic nerve atrophy at 10
How symptoms can appear: an example

7 year old boy
- First seizure at 6

20 year old woman
- First seizure at 4
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KAND natural history follow up survey

- Participants eligible if initial study interview completed ≥1 year ago
- Follow up surveys received for 74 participants
- Average age at initial interview: 9.5 years old
- Average age at follow up: 11.3 years old
- Roughly equal males and females with similar age distribution
- 47 unique variants
Age at follow up

Caroline Mebane, Scott Robinson
Hypertonia/spasticity by age

Caroline Mebane

n=60
Hypertonia/spasticity by age

Caroline Mebane  
n=60
Hypertonia/spasticity by age

Caroline Mebane

n=60
Hypertonia/spasticity by age

Caroline Mebane

n=60
Hypotonia by age

Caroline Mebane
Hypotonia by age

Caroline Mebane

n=66
Clumsiness/discoordination by age

Caroline Mebane

n=62
Optic nerve atrophy by age

Caroline Mebane

n=71
Cortical visual impairment by age

Percent

Age (years)

% With Symptom At Age
% With Data At Age

Caroline Mebane

n=74
Abnormal neuroimaging by age

Caroline Mebane

n=67
Type of neuroimaging abnormalities

Caroline Mebane

n=45
Seizure history by age

Caroline Mebane

n=71
Seizures in KAND: Rare Epilepsy Network survey

- Survey designed by Rare Epilepsy Network (REN) to better characterize rare epilepsies
- 101 participants (95% response rate!)
- 45% of participants reported at least one seizure

Jennifer Bain, MD, PhD
Who gets seizures?

Jennifer Bain, MD, PhD
Who gets seizures?

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Who gets seizures?

Jennifer Bain, MD, PhD
Age at first seizure

Jennifer Bain, MD, PhD
Age at first seizure

Jennifer Bain, MD, PhD
Age at first seizure

How many people

How many people

1-2
3-4
5-6
8-10
14-17
18-19
27

Age (years)

Jennifer Bain, MD, PhD
How many had a seizure in the last 6 months?

• Out of the participants with any seizure history, 54% had at least one seizure in the last 6 months

Jennifer Bain, MD, PhD
Who had a seizure in the last 6 months?

Jennifer Bain, MD, PhD
What types of seizures do we see?

Jennifer Bain, MD, PhD
Anti-seizure medication use

Maintenance medication
- Yes 78%
- No 22%

Rescue medication
- Yes 54%
- No 46%

Jennifer Bain, MD, PhD
# Anti-seizure maintenance medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levetiracetam (<em>Keppra</em>)</td>
<td>69</td>
</tr>
<tr>
<td>Clobazam (<em>Onfi</em>)</td>
<td>33</td>
</tr>
<tr>
<td>Lamotrigine (<em>Lamictal</em>)</td>
<td>28</td>
</tr>
<tr>
<td>Carbamazepine (<em>Tegretol</em>)</td>
<td>22</td>
</tr>
<tr>
<td>Valproic acid/Valproate</td>
<td>22</td>
</tr>
<tr>
<td>Medical marijuana/Cannabis/Cannabinoid/CBD/THC</td>
<td>19</td>
</tr>
<tr>
<td>Clonazepam (<em>Klonopin</em>)</td>
<td>14</td>
</tr>
<tr>
<td>Phenytoin (<em>Dilantin</em>)</td>
<td>14</td>
</tr>
<tr>
<td>Lorazepam (<em>Ativan</em>)</td>
<td>11</td>
</tr>
<tr>
<td>Topiramate (<em>Topamax</em>)</td>
<td>11</td>
</tr>
</tbody>
</table>

**Others:** lacosamide, oxcarbazepine, vigabatrin, zonisamide, ACTH, eslicarbazepine, gabapentin, phenobarbital, prednisone, pregabalin, perampanel

Jennifer Bain, MD, PhD
What this tells us

• Not everyone with KAND has the same challenges
• Some symptoms (e.g., hypertonia) are more common than others (e.g., cortical visual impairment)
• Different symptoms arise at different times
• We still have a lot to learn
Still to learn

• How does the condition change over time?
• Does this differ by genetic variant?
• What treatments do or do not work?
What we need from you

• Keep us updated: fill out your Year 3 Follow Up Survey
  • Survey sent out September 7th, 2021
  • Sent to people in the study for more than 6 months
  • Medical history update as well as Vineland Adaptive Behavior Scale update

• Send us your records
  • Reports: MRI reports, EEG reports, OCT reports
  • Original images and data: MRIs, EEGs

• Help us keep in touch
  • Give us your updated contact information

• Keep an eye out for more opportunities in the future, both virtual and in person…
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  Contact us at kif1a_study@cumc.columbia.edu!
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Chung lab

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Scott Robinson
Laura Hamm

Jennifer Bain, MD, PhD

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