 CdLS Foundation

Neurodevelopmental Disorders and Behavioral Management in Cornelia de Lange Syndrome (CdLS)

Siddharth Srivastava, M.D.
siddharth.srivastava@childrens.harvard.edu
Department of Neurology
Boston Children’s Hospital

June 13, 2019
Outline

• Background
• Language Disorders
• Attention Deficit Hyperactivity Disorder
• Anxiety/Depression
• Aggression/Self-Injury
• Conclusions
• Non-medication interventions can be effective too, but I will try to focus on medications for this talk

• The information presented here is a combination of anecdotal and observational data from individuals with CdLS, and extrapolated data from other neurodevelopmental disorders

• In general, there is a great need for evidence-based research on neurobehavioral interventions for CdLS
Background
CdLS

- CdLS is associated with distinct facial features, intellectual disability, autism spectrum disorder, and multiple systemic features
- Behavioral features such as hyperactivity, aggression, and anxiety are common
Significance

- Challenging behaviors and developmental concerns can affect the quality of life for individuals with CdLS and their families.

- Addressing these concerns early on – through medications, therapies, or other interventions – may help optimize long-term neurodevelopmental outcomes.
Development

- Motor
- Language
- Socialization
- Cognition
- Behavior/Mood

Cerebral Palsy
Language Disorder*
Autism
Intellectual Disability
ADHD*
Anxiety/Depression*
Aggression/Self-Injury*
Language affects our ability to interface with the rest of the world (e.g., socialize, communicate)

Expressive Language
Ability to communicate

Receptive Language
Ability to understand
Language and Cognition

Intellectual Disability

6 year old, IQ = 50

Developmental age (years)

Cognitive age equivalent

Language age equivalent

Intellectual Disability PLUS Language Disorder

6 year old, IQ = 50

Developmental age (years)

Cognitive age equivalent

Language age equivalent
Language Disorders
Language Disorders Treatment

- Individual Speech/Language Therapy
- Play/Social Groups
- Augmentative and Alternative Communication (AAC)
AAC

- AAC refers to the use of special devices that allow children to communicate even in the absence of spoken speech.
- These devices can be high tech or low tech.
- AAC is especially useful for children who are non-verbal.
Attention Deficit Hyperactivity Disorder (ADHD)
ADHD

• ADHD is characterized by impairment of attention, distractibility, hyperactivity, and impulsivity

• Symptoms must be present in two or more settings (e.g., home, school)

• Symptoms must cause functional impairments (e.g., social, academic)
ADHD Treatment

Non-Medication

Behavioral Therapy

Medication

Methylphenidate Products (Stimulants)

Dextroamphetamine Products (Stimulants)

Non-Stimulant Products
ADHD Medications

Treatment may require a trial-and-error approach

- “Start low, go slow”
- Main side effects are decreased appetite, disrupted sleep
- Wait at least 1 week before deciding whether a new medication or dose change is ineffective
## ADHD Medications

<table>
<thead>
<tr>
<th></th>
<th>Pill (can’t crush/chew)</th>
<th>Capsule (can open up and sprinkle onto food)</th>
<th>Chewable Pill (can chew)</th>
<th>Liquid</th>
<th>Patch</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>METHYLPHENIDATE PRODUCTS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short Acting</td>
<td>Focalin Ritalin</td>
<td></td>
<td>Methylin Chewable</td>
<td>Methylin Solution</td>
<td></td>
</tr>
<tr>
<td>Long Acting</td>
<td>Concerta Ritalin SR</td>
<td>Focalin XR</td>
<td></td>
<td>Quillivant XR</td>
<td>Daytrana</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ritalin LA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metadate CD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>AMPHETAMINE PRODUCTS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short Acting</td>
<td>Adderall</td>
<td></td>
<td></td>
<td>ProCentra</td>
<td></td>
</tr>
<tr>
<td>Long Acting</td>
<td>Vyvanse Dexedrine</td>
<td>Adderall XR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>NON-STIMULANT PRODUCTS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short Acting</td>
<td>Clonidine Guanfacine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long Acting</td>
<td>Gunfacine ER Clonidine ER Atomoxetine</td>
<td></td>
<td></td>
<td>Clonidine patch</td>
<td></td>
</tr>
</tbody>
</table>
General Approach to Treatment of ADHD in CdLS
Anxiety and Depression
Anxiety and Depression

- Symptoms can include irritability, excessive worry, perseveration, social avoidance

- Anxiety and depression can be difficult to recognize, especially with increasing levels of intellectual disability associated with CdLS
Anxiety and Depression Treatments

Non-Medication
- Exploration of Exacerbating Factors

Medication
- Selective Serotonin Reuptake Inhibitors
- Other Antidepressants (SNRIs, NRIs, NDRIs)
- Benzodiazepines
Anxiety and Depression Medication

• A selective serotonin reuptake inhibitors (SSRI) may help anxiety and mood issues in CdLS

• **CAVEAT:** SSRIs can lead to **behavioral activation** and **worsening agitation** in some individuals

• It may be prudent to avoid benzodiazepines for the management of anxiety due to risk of dependency and paradoxical agitation
General Approach to Treatment of Anxiety and Depression in CdLS
Aggression/Self-Injury
Aggression/Self-Injury

- Aggressive/self-injurious behaviors include head-banging, hand-biting, and excessive scratching.
- They can be a source of significant parental distress for families affected by CdLS.
Aggression/Self-Injury Treatment

• Aggressive, self-injurious behaviors require a full behavioral assessment in order to identify triggers.

• Sometimes undiagnosed medical problems – such as reflux, dental issues – can worsen aggression/self-injury.
Aggression/Self-Injury Medications

- **Second-generation neuroleptics (such as risperidone)** may be an option for CdLS
- Other second-generation neuroleptics to consider include aripiprazole, quetiapine, and olanzapine
- In some individuals, a mood stabilizer (valproate, lithium) may be beneficial, though the data is limited
Aggression/Self-Injury Medications

- **CAVEAT:** Neuroleptics are potent medications, with potential for serious side effects, such as **metabolic syndrome** and **weight gain**
General Approach to Treatment of Aggression in CdLS
Conclusions

- There is a spectrum of neurodevelopmental disorders associated with CdLS
  - Intellectual Disability
  - Autism
  - Language Disorder
  - Cerebral Palsy
- Identifying the target behavioral symptom(s) can help tailor medication management:
  - Hyperactivity
  - Anxiety/Depression
  - Aggression/Self-Injury
- There is a great need to study what medications work and don’t work for individuals with CdLS
Acknowledgements

- Families / CdLS Foundation
- Dr. Marco Grados
- Dr. Alex Kolevzon, Phelan-McDermid Syndrome Foundation Project ECHO (https://www.pmsf.org/echo-project/)
- Dr. Mustafa Sahin
THANK YOU