Figure 1. Phelan-McDermid Syndrome conceptual model

Target patient population

Individuals with Phelan-McDermid Syndrome

Relevant condition process

Phelan-McDermid Syndrome is a result of haploinsufficiency of the SHANK3 gene, resulting from either 22q13.33 deletions encompassing SHANK3 or pathogenic sequence variants.

Caregiver-reported patient impacts

Impacts of sleep disturbance: Bedtime resistance | Need help returning to sleep after waking | Need parent in room/bed to fall asleep | Need medication to sleep | Takes very long time to fall back asleep | Tiredness during the day | Wakes very early | Waking up sweating, screaming, and/or inconsolable

Other impacts: Difficulties at school | Difficulty concentrating | Food refusal | Social avoidance

Signs

Autism spectrum disorder

Autism and/or autistic traits | Decreased social functioning and communication | Hyperactivity | Repetitive behavior|

Communication disturbance | Deficits in non-verbal communication | Deficits in social-emotional reciprocity | Delayed response to verbal cues | Disruptive/antisocial | Does not seem to listen when spoken to directly or refuses to respond to directions | Echolalia | Flat/inappropriate affect | Inattentiveness | Laughs or appears angry for no apparent reasons | Poor eye contact | Random and inappropriate speech | Resistance to change | Responds to imaginary sounds or sights |

Neuropsychiatric signs

Intellectual disability – mild to profound |
Mood cycling | Aggression | Agitation |
Apathy | Appear to be in a stupor | Apraxia |
Behavioral abnormalities | Disinhibited
behavior | Ignorance of consequences |
Impulsivity

Sensory reactivity

Pica | Mouthing, chewing, or teeth grinding | Reduced response to pain | Self-injury | Selfstimulation | Stereotypic movement | Touch aversion

Motor coordination

Ataxia | Balance problems | Unsteady gait

Developmental delays

Delayed to absent speech | Adaptive behavior | Cognitive behavior | Expressive language | Psycho-motor development

Regression

Developmental regression |

Constructive or imaginative play | Expressive language | Fine motor skills | Language | Post psychiatric episodes | Purposeful hand movement | Self-help | Social engagement skills

Gastrointestinal dysfunction

Constipation | Fecal incontinence | Gastroesophageal reflux | Abdominal pain | Choking and gagging | Diarrhea| Vomiting

Sleep disturbance

Difficulty falling asleep | Difficulty staying asleep | Insomnia | Parasomnias | Sleep apnea and sleep disordered breathing

Additional signs

Hypotonia | Seizures | Urinary incontinence | Decreased perspiration | Heat intolerance | Recurrent infections | Restlessness | Tetraparesis | Urinary retention

Other clinical manifestations

Lymphedema | Renal anomalies | Anorexia | Attention deficit hyperactivity disorder | Bipolar disorder I Catatonia or catatonic phase | Congenital heart defects | Depressive episodes | Epilepsy | Manic episodes | Neurologic deterioration | Obsessive-compulsive disorder | Psychiatric disorders | Psychosis | Psychotic symptoms | Schizoaffective disorder | Schizophrenia | Thyroid

dysfunction | Unipolar

major depressive

Caregiver impacts

Caregiver responsibilities
Management of
constipation | Working
with a behavioral
therapist | Long length
of time to toilet training
| Managing pica | Use of
probiotics and
specialized diets |
Worsened behavior of
child due to constipation

Social activities Feeling ostracized from community

Family relationships Impacts to family functioning | Need or desire for genetic testing

Spouse/partner relationship Diminished marital satisfaction

Work impacts
Unemployment

Emotional function
Concern about: Ability to
identify and treat seizures
| EEG and MRI indications
and timing | Aggression |
Toilet-training | Confusion
over EEG results |
Parenting stress |
Restricted parental
freedom and sense of
identity
Worry about: Child's safety
| Regression | How epilepsy

might affect family

Sleep

Awakened by their child during the night |
Becoming drowsy while driving | Child awakens earlier than caregiver |
Difficulty concentrating at work | Feel tired during the day | Irritability due to tiredness | Lack of sleep |
Needing to sleep during the day | Sleep in settings other than their own bed |
Too tired to do the things they want to do

Bold indicates concept was reported with high frequency, in at least four unique peer-reviewed articles. *Italics* indicates domain heading.