

Detailed Research Summary

Source: Vermeulen K, Staal WG, van Bokhoven H, Egger JMI, Kleefstra T. *Sleep disturbance as a precursor of severe regression in Kleefstra Syndrome suggests a need for firm and rapid pharmacological treatment.*

Clinical Neuropharmacology. 2017;40(4):185-188. [DOI link](#)

Background

- Psychosis is a severe mental health condition involving hallucinations, delusions, and disordered thinking.
 - The EHMT1 gene (linked to Kleefstra Syndrome, KS) is also implicated in some cases of schizophrenia.
 - Regression — loss of previously acquired skills — has been reported in adolescents and young adults with KS.
 - Sleep disturbance may act as an early warning sign.
 - Standard practice in intellectual disability (ID) is to use **low starting doses** of antipsychotics, titrating slowly to reduce side effects.
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Case Reports

Case 1: Female, 19 (KS, ADHD, ASD)

- Gradual sleep disturbance after pneumonia → awake 72 hours, hyperactive, aggressive, not eating.
- Low-dose benzodiazepines ineffective.
- Higher dose olanzapine normalised sleep in 24 hours.
- Regression: loss of continence, reduced language, increased self-injury.
- Developmental age: fell from 2 years at 12 y/o → 17 months six months later.

Case 2: Female, 23 (KS, ASD, major depression at 18)

- Severe sleep disturbance.
- Low-dose aripiprazole (2mg) ineffective; led to major regression (loss of dressing, reading, writing, hygiene, and sentence speech).
- Higher dose (15mg) restored sleep, improved mood, halted regression.
- Developmental age: 3y10m at 19 → 2y5m one year later. Some recovery of skills.

Case 3: Female, 23 (KS, ASD, psychosis at 20)

- Triggered by grandfather's death. Severe sleep disturbance + hallucinations and delusions.
 - Multiple low/normal dose antipsychotics ineffective.
 - Over 2 years: lost speech, literacy, continence, ability to dress, swim.
 - At 22: psychiatric inpatient; higher-dose treatment restored sleep, improved psychosis, stopped further decline.
 - Developmental age fell from 3 years at 16 → 15 months at 22.
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Authors' Key Points

1. Sleep disturbance is common in KS, especially at adolescence/early adulthood, and may precede rapid regression.
 2. Regression coincides with the critical period for psychiatric disorders (psychosis, bipolar disorder, depression).
 3. Case studies show that **adequate, immediate treatment with second-generation antipsychotics** can halt regression.
 - Clozapine: most effective, but with serious side effects.
 - Olanzapine: useful for ID patients, available in melt-in-mouth form.
 4. High-normal doses appear more effective than low-dose protocols typically used in ID.
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Clinical Implications

- When individuals with KS present with **sudden severe sleep disturbance and psychiatric symptoms**, treatment should mirror **standard psychosis protocols in the general population** (adequate doses, not ID-specific "low and slow" dosing).
- This approach may help **reduce regression, preserve function, and improve quality of life**.