# Unmasking Mood and Anxiety Disorders in Down Syndrome: The Role of Accurate Identification and SSRI Response

Hailey Hayes, MD[1], Emma Rutledge[1], Emily Meudt, MD[1,2], Jill C. Fodstad[1,2]
[1]Indiana University School of Medicine, Department of Psychiatry
[2]Indiana University Health

## Introduction

- Internalizing concerns, like mood and anxiety disorders, are frequently misidentified in patients with Down Syndrome (DS) as memory issues, developmental or cognitive regression, or behavioral dysregulation[1,2], leading to gaps in psychiatric intervention[1]. Accurate identification of mental health symptoms is critical.[3]
- A chart review of adults with DS found that 82% responded to Selective Serotonin Reuptake Inhibitors (SSRIs), standard evidenced-based pharmacotherapy for mood disorders,[2] once depression was identified and treated.[5]
- This case series explores the diagnosis of mood and anxiety disorders in individuals with DS and their response to Sertraline (an SSRI) after presenting to a DS-specialty clinic for other presenting concerns.

## Case Demographics

| Case | Age | Sex | Race | Ethnicity |
|---|---|---|---|---|
| 1 | 13 | F | Black or African American | Hispanic/ Latino |
| 2 | 42 | M | White | Hispanic/ Latino |
| 3 | 23 | F | White | Non-Hispanic |
| 4 | 36 | F | Black or African American | Non-Hispanic |
| 5 | 14 | F | White | Non-Hispanic |

*Cohort's age range suggests that difficulties in diagnosing mood and anxiety symptoms in persons with DS can occur across various ages, from adolescence to adulthood.*

## Presenting Concerns, Baseline Data, Diagnostic Impressions, and Treatment

| | Case 1 | Case2 | Case 3 | Case4 | Case 5 |
|---|---|---|---|---|---|
| **Referral Concern** | Frequent meltdowns, aggression | Suspected dementia | Down Syndrome Regression Disorder | Down Syndrome Regression Disorder | Frequent meltdowns, reduced communication |
| **Behavioral Presentation** | Persistent behavioral dysregulation | Declining cognition, withdrawal, apathy, irritability | Forgetfulness, irritability, decline in function, sleep changes, agitation | Aggression | Phobias, Anxiety, selective mutism |
| **Previous Psychiatric Diagnoses** | PTSD | None | None | ADHD, Autism | None |
| **Prior Medication Trials** | Guanfacine ER 3mg, Hydroxyzine 25 mg, Risperidone 10mg BID | None | None | Mixed-amphetamine Salts | None |
| **GAD-7 Score** | 10 | 4 | 3 | ----- | 9 |
| **PHQ-2 Score** | ----- | 0 | 2 | ----- | 1 |
| **Diagnosis Provided** | MDD | MDD | MDD | GAD | Anxiety disorder, unspecified |
| **Optimized Medication Treatment** | Sertraline 25 mg | Sertraline 50 mg | Sertraline 40 mg | Sertraline 12.5 mg | Sertraline 25 mg |
| **Other Treatment** | None | None | Mirtazapine discontinued due to irritability | None | Fluoxetine10 mg discontinued due to insomnia |
| **Subjective Improvements** | ↑ Mood<br>↑ Communication<br>↓ Aggression<br>↑ Sleep<br>↓ Irritability | ↑ Cognition<br>↓ Irritability<br>↑ Playfulness<br>↑ Energy<br>↑ Independence<br>↓ Isolation | ↑ Motivation<br>↓ Withdrawal<br>↑ Communication<br>↑ Relaxed Affect and Behavior | ↑ Sleep<br>↑ Motivation<br>↑ Interaction with Family<br>↓ Irritability<br>↓ Startle Response | ↑ Sleep<br>↓ Agitation<br>↓ Irritability<br>↑ Energy<br>↑ Relaxed Affect and Behavior in Public |

*Notes:* PTSD = post traumatic stress disorder; ADHD = attention deficit/hyperactivity disorder, ER = extended release; mg = milligrams; BID = twice a day; GAD-7 = Generalized Anxiety Disorder-7, a 7 item anxiety disorder screening tool with total scores ≥ 10 being a positive screen; PHQ-2 = Patient Health Questionnaire-2, a 2-iten depression screening tool with a total score ≥ 3 being a positive screen; MDD = major depression disorder; GAD = Generalized Anxiety Disorder; ----- = measure not completed at intake.

## Conclusions

- Anxiety and mood disorders exist across the lifespan in DS, but frequently mask as behavioral, memory, or regression symptoms, making comprehensive assessment an absolute necessity.[1-3,5]
- Standard tools (PHQ-2; GAD-7) may be inadequate; in 0 cases did either align with the clinical diagnosis. Relying on parent report may underestimate severity.
- Traditional medications like SSRIs (specifically Sertraline) may be effective for individuals with DS of various ages once accurate diagnoses are established.

## Future Directions

- Urgent need for RCTs of Sertraline in people with DS.
- The GAD-7 and PHQ-2 are not validated for the persons with DS. Accurate assessment tools that align with the needs of the DS community are needed.

**References**

1. Stein, D. S., Munir, K. M., Karweck, A. J., Davidson, E. J., & Stein, M. T. (2013). Developmental Regression, Depression, and Psychosocial Stress in an Adolescent with Down Syndrome. *Journal of Developmental & Behavioral Pediatrics*, *34*(3), 216–218. https://doi.org/10.1097/dbp.0b013e318280b2d2
2. Bonne, S., Iftimovici, A., Mircher, C., Conte, M., Louveau, C., Legrand, A., Danset-Alexandre, C., Cannarsa, C., Dehel, A., Consoli, A., Krebs, M., Ellul, P., & Chaumette, B. (2023). Down syndrome regression disorder, a case series: Clinical characterization and therapeutic approaches. *Frontiers in Neuroscience*, *17*, 1126973. https://doi.org/10.3389/fnins.2023.1126973
3. Palumbo, M. L., & McDougle, C. J. (2018). Pharmacotherapy of Down syndrome. *Expert Opinion on Pharmacotherapy*, *19*(17), 1875–1889. https://doi.org/10.1080/14656566.2018.1529167
4. Cleare, A., Pariante, C., Young, A., Anderson, I., Christmas, D., Cowen, P., Dickens, C., Ferrier, I., Geddes, J., Gilbody, S., Haddad, P., Katona, C., Lewis, G., Malizia, A., McAllister-Williams, R., Ramchandani, P., Scott, J., Taylor, D., Uher, R., & Meeting, T. M. O. T. C. (2015). Evidence-based guidelines for treating depressive disorders with antidepressants: A revision of the 2008 British Association for Psychopharmacology guidelines. *Journal of Psychopharmacology*, *29*(5), 459–525. https://doi.org/10.1177/0269881115581093
5. Thom, R. P., Palumbo, M. L., Thompson, C., McDougle, C. J., & Ravichandran, C. T. (2021). Selective Serotonin Reuptake Inhibitors for the Treatment of Depression in Adults with Down Syndrome: A Preliminary Retrospective Chart Review Study. *Brain Sciences*, *11*(9), 1216. https://doi.org/10.3390/brainsci11091216