Down Syndrome Regression Disorder (DSRD)

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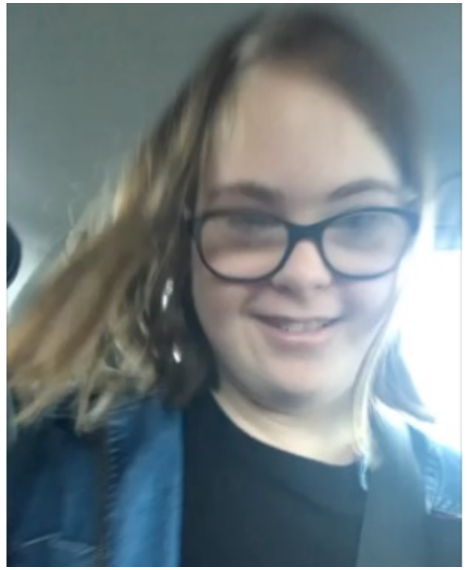
Take-Home messages



Down Syndrome Regression Disorder is…

1. A devastating condition if left untreated.
2. Easily missed, unless you look for it.
3. Treatable.

Brief Case Example

Case Example

Before DSRD

Presented to Emergency Department

Reason for Admission/Presenting Problems

7/7 severe decline in motor function/ deterioration in ADLs unable to walk, talk, Pt hunched drooling coughing/ choking episode this am on breakfast. yes no answer only. Hx: Down Sydnrome normal GCS 15- CT head 7/7 NAD

On examination

Down Syndrome Regression Disorder

The journey to defining a clinical entity

Nomenclature & History

1866 Down syndrome first described

1946 Henry Rollin published case series on 'Catatonic Psychosis': compared 16 affected with 41 unaffected patients with DS

2002 Disintegrative syndrome in young adults (UK: Prasher)

2011 Regression in children and adolescents with DS (USA: Devenny & Matthews)

2011 Catatonia in DS: 2 cases (USA Shannon Jap & Neera Ghaziuddin)

2012 Acute neuropsychiatric disorder: Case series 13 adolescents (Japan: Akahoshi et al)

2013 Developmental regression: Case (USA David Stein et al)

2014 DS Disintegrative Disorder (USA Worley et al) – thyroid autoimmune theory

2016 Rapid Clinical Deterioration (USA Jacobs, Skotko et al) – lists suggested Ix

2019 Unexplained Regression in DS: 35 cases (USA/Aust Stephanie Santoro et al)

2022 Expert consensus on name, assessment and diagnosis (USA/Aust/Spain/Italy) – "**Down syndrome regression disorder**"

Catatonia and regression in Down syndrome

1946 Rollin article

Presenting History:

No previous Hx of behavioural disorder, developed within normal limits for DS.

Age 11-14: alarming and drastic changes, such that families sought institutional care.

Deterioration is rapid across:

- Toileting
- Speech (becomes mute)
- Loss of interest & ability in activities
- Become solitary
- Withdrawal, apathy
- Destructive (tearing up clothes, bed linen, towels)
- Periodic excitement / agitation (throw things etc)

The Clinical Picture

From what has preceded it is evident that the clinical picture of the in a state of fully developed catatonic psychosis is an unattractive one. He is to be seen seated huddled up in some remote corner of the ward or airing court, a fixed, vacant, miserable expression on his face, reddened blepharitic eyes, open-mouthed with a constant stream of saliva dribbling from his cracked lips, with blue acrocyanotic hands idle and immobile hanging at his side or on his lap. There is obviously no capacity for amusement or employment and no trace of animation except when stirred by some inner impulse to an exhibition of catatonic excitement. The enthusiasm for the major events of the day, particularly the appearance of the food trolleys, so clearly manifested by his fellow patients, is unshared by him. He has to be led to table shuffling and unwilling and if capable of feeding himself does so with painful slowness. He is easy prey for the food-snatcher and shows no reaction to this trespass.

The outstanding feature of the picture is an increasing loss of volition. A

Additional catatonic features:
Automatic obedience, waxy flexibility, echolalia and echopraxia
Stereotypy: 4 cases rocking movements, 2 cases hours smoothing creases in bed linen, 1 repetitive rituals with playing cards for hours
Delayed / no response to pain
Weight loss (6.6 lb loss vs. 9lb gain in the unaffected group – despite war-time rationing!)

Prognosis

The prognosis is undoubtedly bad. Once deterioration begins it is usually rapidly progressive. Together with the very definite mental deterioration there is a parallel physical dilapidation.

Figuring it out: starting with a clinical cohort

Unexplained regression in Down syndrome: 35 cases from an international Down syndrome database

Stephanie L. Santoro, MD[1,2], Sheila Cannon, MEd[3], George Capone, MD[4], Cathy Franklin, MBBS, MPhil[5], Sarah J. Hart, PhD, CGC[6], Victoria Hobensack, CPNP-PC[7], Priya S. Kishnani, MD, MBBS[6], Eric A. Macklin, PhD[8], Kandamurugu Manickam, MD, MPH[7], Andrew McCormick, MD[3], Patricia Nash, MD[7], Nicolas M. Oreskovic, MD, MPH[1,2], Vasiliki Patsiogiannis, BA[1], Katherine Steingass, MD[7], Amy Torres, BS[1], Diletta Valentini, MD[9], Kishore Vellody, MD[3] and Brian G. Skotko, MD, MPP[1,2]

GENETICS in MEDICINE | Volume 22 | Number 4 | April 2020

→ Clinical presentation
Abnormal investigation results

Unexplained regression in Down syndrome: Management of 51 patients in an international patient database

Stephanie L. Santoro[1,2] | Nicole T. Baumer[3,4] | Michelle Cornacchia[5] | Catherine Franklin[6] | Sarah J. Hart[7] | Kelsey Haugen[1] | Margaret A. Hojlo[4] | Nora Horick[8] | Priya S. Kishnani[7] | Kavita Krell[1] | Andrew McCormick[9] | Anna L. Milliken[4] | Nicolas M. Oreskovic[1,2] | Katherine G. Pawlowski[4] | Sabrina Sargado[2,4] | Amy Torres[1] | Diletta Valentini[10] | Kishore Vellody[9] | Brian G. Skotko[1,2]

Am J Med Genet. 2022;188A:3049–3062.

AMERICAN JOURNAL OF medical genetics PART A WILEY

→ Treatments used
Most clinically effective treatments

Naming it: Consensus Recommendations

Assessment and Diagnosis of Down Syndrome Regression Disorder: International Expert Consensus

Jonathan D. Santoro[1,2], Lina Patel[3], Ryan Kammeyer[4], Robyn A. Filipink[5], Grace Y. Gombolay[6], Kathleen M. Cardinale[7], Diego Real de Asua[8], Shahid Zaman[9], Stephanie L. Santoro[10], Sammer M. Marzouk[10], Mellad Khoshnood[1], Benjamin N. Vogel[2], Runi Tanna[2], Dania Pagarkar[2], Sofia Dhanani[2], Maria del Carmen Ortega[11], Rebecca Partridge[12], Maria A. Stanley[13], Jessica S. Sanders[14], Alison Christy[15], Elise M. Sannar[3,16], Ruth Brown[17], Andrew A. McCormick[5], Heather Van Mater[18], Cathy Franklin[19], Gordon Worley[20], Eileen A. Quinn[21], George T. Capone[22,23], Brian Chicoine[24], Brian G. Skotko[10,25] and Michael S. Rafii[2,26]*

- Two-round traditional Delphi method survey of an international group of clinicians with experience in treating Down syndrome to develop a standardized approach to clinical care and research
- 27 panelists : 9 medical specialties, 6 different countries
- Target: nomenclature, diagnostic work up and diagnostic criteria
- 78% agreed on nomenclature: **Down Syndrome Regression Disorder** (DSRD)

Characterising it: DSRD Consensus Diagnostic Criteria

Category	Criteria	Possible DSRD	Probable DSRD
Symptom onset	Onset of new neurologic, psychiatric, or mixed symptoms over a period of <12 weeks in previously health individual with Down syndrome	Yes	Yes
Clinical evidence of neurologic dysfunction	1. Altered mental status or behavioral dysregulation - Anorexia/decreased oral intake or hyperphagia - Confusion/disorientation - Inappropriate laughter - Encephalopathy 2. Cognitive decline - Apathy - Abulia and/or avolition - Acute memory impairment (including new difficulty with recall) 3. Developmental regression with or without new autistic features - Social withdrawal - Loss of previously developmental acquired milestones - Inability to perform activities of daily living - Stereotypy - Rigidity around routine changes - Decreased eye contact 4. New focal neurologic deficits on examination and/or seizure 5. Insomnia or circadian rhythm disruption 6. Language deficits - Expressive and/or receptive aphasia - Global aphasia (mutism) - Whispered speech 7. Movement disorder (excluding tics)* - Catatonia - Bradykinesia - Freezing - Gait disturbance 8. Psychiatric symptoms - Anxiety - Delusions or hallucinations - Derealization/depersonalization - Obsessive compulsive tendencies - Aggression/agitation	>3 symptom clusters present	>6 symptom clusters present
Exclusion of other etiologies	Reasonable exclusion of alternative causes of regression including other systemic and central nervous system disorders. Other primary psychiatric disorders are also considered exclusionary	Yes	Yes

*Must be included as one of the symptom clusters for possible or probable diagnosis.

Investigating it: Consensus recommendations for investigations (aim = exclude other causes)

Brain imaging: MRI with and without contrast on a 3T scanner

EEG

Blood tests

- FBE, E/LFT, ESR, CRP, Ammonia, HBA1C, Lipids, B12, Vit D,
- TFTs, Thyroid antibodies
- Celiac serology
- Autoimmune encephalitis panel

Lumbar puncture

- Cell count with differential, total protein, glucose, M/C/S, IgG index, Oligoclonal bands, autoimmune encephalitis panel

Common Conditions to Exclude

Common conditions associated with regression in Down syndrome

- Thyroid disease
- Celiac disease
- Sleep apnea
- Hearing and eye conditions
- Constipation
- Dental problems
- Psychiatric problems – depression, anxiety, psychosis

- CHAP Online: https://www.health.gov.au/resources/publications/adult-comprehensive-health-assessment-program-chap-annual-health-assessment-for-people-with-intellectual-disability?language=en

- DSC2U: https://www.dsc2u.org/

DSC2U
Down Syndrome Clinic to You

Uncommon conditions to exclude (see neurologist)

- Autoimmune encephalitis
- Stroke
- Epilepsy
- Heavy metal toxicity
- Additional genetic disorder associated with regression
- Mitochondrial disorders
- Infection (Lyme, HIV, Syphilis)
- Vitamin deficiencies
- Liver disease
- Electrolyte imbalance
- Mitochondrial disorders
- Organic acidurias
- Fatty acid oxidation disorders
- Urea cycle disorders
- Porphyria
- CDG
- Peroxisome storage disorders
- Lysosomal storage disorders

Building on initial findings: Further research into Neurodiagnostic Abnormalities

Neuroimaging abnormal in 22% (cf. 9% in control group)

- 18% had punctate T2 signal abnormalities (cf. 7% in control group)
- 2.8% Basal ganglia calcification (cf 0.9% in control group)

CSF abnormal in 17% (no control comparison)

- pleocytosis, oligoclonal banding, high IgG index
- elevated neopterin in 6/43

EEG abnormal in 26% (no control comparison)

- focal (3%) or generalized slowing (8.3%)
- focal epileptiform discharges out of any cortex (15% had discharges in frontal or temporal lobes)

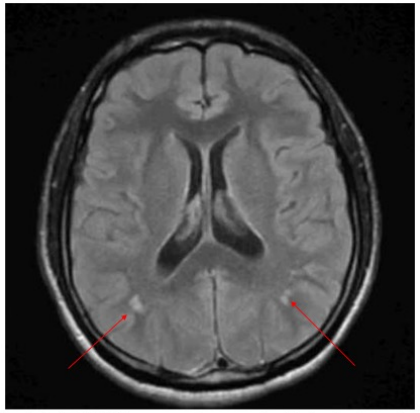


Fig. 3 Axial T2 FLAIR sequence demonstrating T2 signal prolongation along the gray, white junction bilaterally

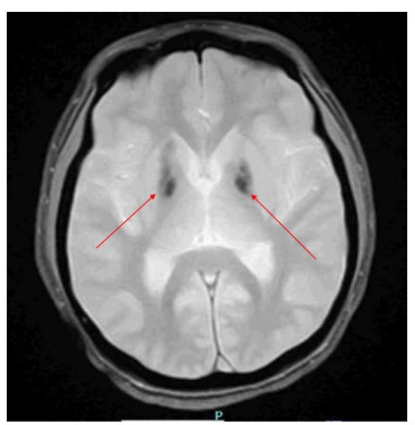


Fig. 4 Axial GRE sequence demonstrating symmetric hypodensities in the bilateral deep gray nuclei consistent with calcification

Santoro JD, Partridge R, Tanna R, et al. Evidence of Neuroinflammation and Immunotherapy Responsiveness in Individuals with Down Syndrome Regression Disorder. J Neurodev Disord. 2022 Updated January 2023 Jun 3;14(1):35. PMID: 35659536. •

Additional Abnormal Findings

Abnormal serum findings

- ANA (13% vs 5%)(p=0.01)
- Thyroid function (less likely: 4% vs 19%) (p=0.01)
- TPO antibodies (37% vs 23%)(p=0.02)
- Cytokine analysis (40% vs 13%): particularly sIL-2 receptor and IL-10 (p=0.02)

Duration of symptoms >3 years was associated with much lower incidence of neurodiagnostic abnormalities (2.8% vs 26.4%)

Literature: Psychiatric findings in DSRD cohorts

Author	Number of cases (n)	Average Age at Diagnosis (yrs)	Anxiety (%)	Depression (%)	Psychosis (%)	Catatonia (%)
Ghaziuddin 2015	4	18.8	0	75	0	100
Miles 2019	7	NS	14	0	0	100
Mircher 2019	30	18-21	33	30	43	37
J Santoro 2022	72	14	62 (symptom)	NS	NS	55
S Santoro 2022	51*	17.6	<----------	---------71-------	----------→	53
Bonne 2023	4	22.5	50	25	50	NS
Smith 2024	9	21.1	NS	NS	NS	100 (inclusion criteria)

ICARDS observational study (Preliminary data)

Test Domain	Name of Test	Abbreviation
Adaptive Function	Adaptive Behaviour Assessment Schedule - 2	ABAS-2
Changes in Adaptive Function Screen	Adaptive Behaviour Dementia Questionnaire	ABDQ
Behaviour in ID Checklist	Developmental Behaviour checklist	DBC
Catatonia severity	Bush Francis Catatonia Rating Scale	BFCRS
Catatonia severity	Catatonia Impact Scale	CIS
Mental Illness in ID Screen	Moss Psychiatric Assessment Schedules (formerly Checklist)	Moss-PAS (Check)
Mental Illness in ID Brief Assessment	Moss Psychiatric Assessment Schedule (formerly Mini PAS-ADD)	Moss-PAS (ID)
Mental Illness in ID Diagnostic Structured Assessment	Moss Psychiatric Assessment Schedule Diagnostic Structured Interview	Moss-PAS (Diag ID)

Demographic data

		Number of DSRD Subjects (Percentage)
Number of subjects		12
Sex	Male	4 (33)
	Female	8 (67)
Race	Caucasian	10 (83)
	Asian	3 (25)
Mean Age	(years)	22.1

ICARDS Psychiatric Scale Profile

ID	MOSS-PAS Anxiety			MOSS-PAS Depression				MOSS-PAS Bipolar			MOSS-PAS Schizophrenia				CLINICAL Catatonia		MOSS-PAS Organic
	Mini	ICD-11	DSM5	Check list	Mini	ICD-11	DSM5	Mini	ICD-11	DSM5	Check list	Mini	ICD-11	DSM5	BFCRS Screening /14	Clinical	Checklist
1	■			■	■		■						■	■	6	■	■
2				■	■	■	■								8	■	■
3	■	S	S	■	■	■	■					■	■	■	6	■	■
4		P	P									■	■	■	7	■	
5		OCD	OCD	■	■	■	■								9	■	■
6				■	■	■	■					■	■	■	6	■	■
7		OCD	OCD	■	■	■	■						■	■	2	■	■
8	■	S	S	■	■	■	■				■	■	■	■	8	■	
9	■			■	■	■	■				■				2	■	■
10				■		■	■				■	■	■	■	5	■	
11				■	■						■	■	■	■	6	■	■
12											■				7	■	
Total	4	5	5	10	9	8	9	0	0	0	5	7	8	8	Mean = 6	12	8

Approach to Management of DSRD

- Early Phase
- Later Phase

Early Stage Management: Education & Support

The skills are not lost – they are just buried

- What is catatonia and how does it affect someone (ie its not behavioural, its mechanical)
- What is DSRD etc
- Hope for improvement
- Reduce demands
- Expect to require significant increased support needs for first 3-6 months at least – document for NDIS

Early Stage Management: Diagnose and Treat

Assess, investigate, treat and education & support to person and family

Assess and investigate *(don't wait!)*

- Confirm diagnosis (physical examination and investigations), identify any mental illness, catatonia
- Swallow assessment may be necessary (catatonia can affect chew and swallow)
- Bush-Francis scale to document catatonia
- Document score out of 10 compared to baseline

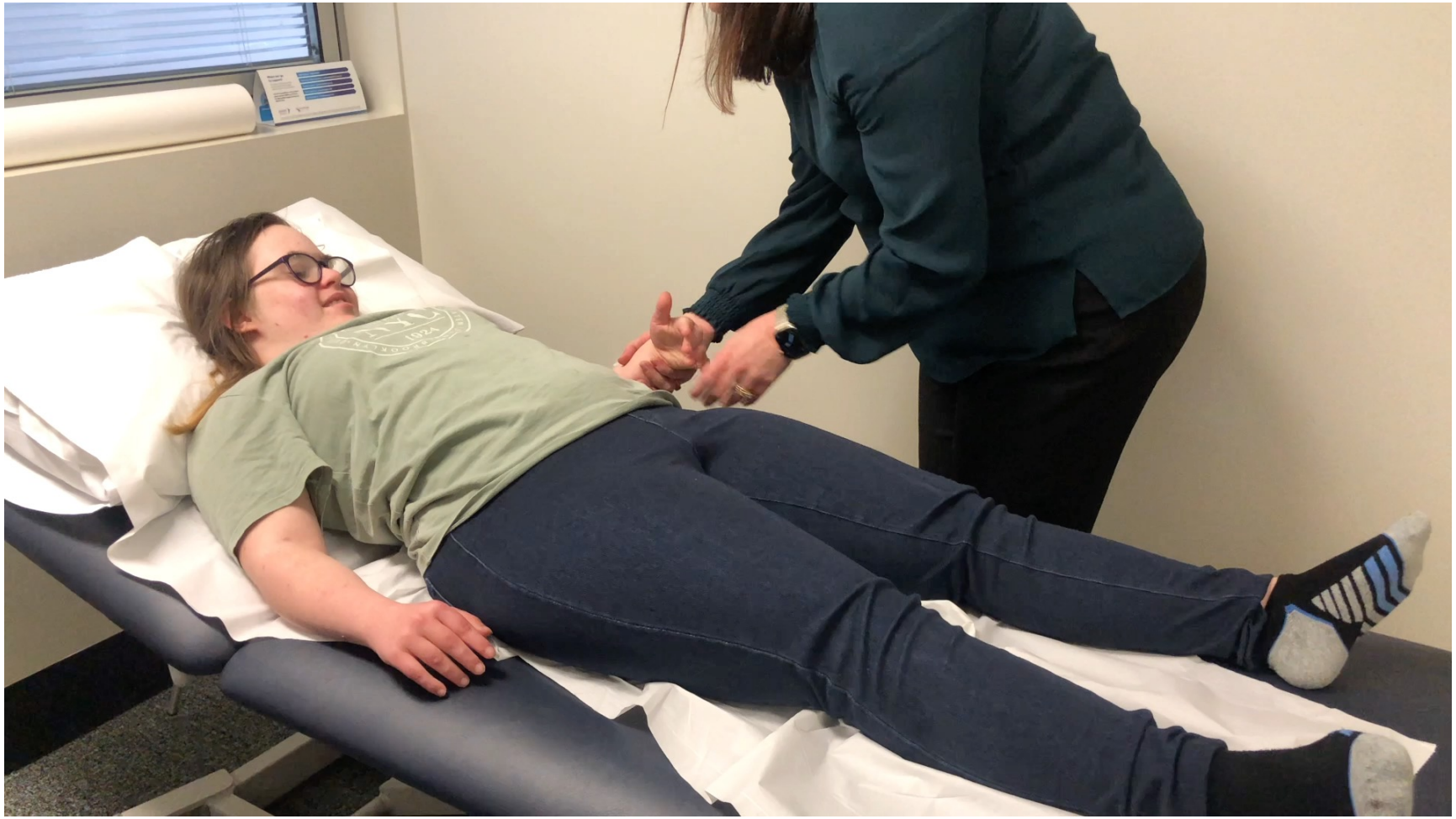
Treat (medications) *(don't delay!)*

- Treat catatonia: lorazepam to max tolerated dose required for best response
- Once catatonia treatment is at its best, consider whether there are any residual depressive or psychotic symptoms
- Consider IVIg
- Consider ECT in severe treatment-refractory cases

Lorazepam

- First-line treatment in catatonia: seems more effective than other benzodiazepines
- I start at 0.5mg bd for a few days, if tolerated (no sedation), increase to 1mg bd then tds then introduce larger doses
- Average dose in large studies = 5mg / day; range 2-20mg
- My clinical experience = most are on 3-6mg / day, a couple on 10-12mg / day
- Instant effect once you hit the right dose
- Tolerance has not been a problem in any of our patients with catatonia (n=25)
- **Don’t** stop suddenly (risk withdrawal) and **Do** store in a safe and secure place!
- IV lorazepam challenge is advocated by some centres but is difficult to access in our healthcare system (and not 100% helpful).

30 mins post first dose lorazepam (the next day)



30 mins post first dose lorazepam (the next day)

ECT

- currently 11 cases in the literature, all case series of ECT for DSRD
- few have comprehensive details of nature of ECT course
- bifrontal is well-tolerated

Effective in all cases but maintenance is often necessary

Full recovery reported in 6/11 patients (compared to 10% rate of full recovery otherwise reported in available literature)

Maintenance ECT treatment appears to be successful in maintaining recovery at, or near to initial response

Maintenance usually also includes ongoing pharmacological management- but consensus is unclear on what this should include

Demographic data and clinical course prior to ECT

- 11 cases reported in the literature, USA based except for 1 in France
- 9 female patients and 2 male patients
- Ages ranged from 15 – 33 years old, with an average age of 24.4 years at presentation
- Variable range of premorbid functional ability

Parameter- prior to ECT treatment	n/11	Range	Mean
Delay to diagnosis	10	2 months – 10 years	4 years
Maximum daily dose of lorazepam	10	3mg – 22mg	11.4 mg
Number of medications trialled	10	2 – 10	5.2
Bush Francis severity score	5	18 – 26	22.2

Treatment outcomes

Patient	Initial response	Relapse	Maintenance treatment	Follow up period
1	Full recovery	Not reported	Not reported	Not stated
2	Full recovery	2 years	Partial relapse at 2 years treated with maintenance lorazepam with good response- close to baseline	6 years
3	Good response, not sustained	1 week	Parents elected not to continue ECT. Maintained on dextromethorphan/quinidine with partial response	5 years
4	Full recovery	6 months	After 2nd relapse was maintained on monthly ECT with full recovery sustained + lorazepam & dextromethorphan/qunidine	5 years
5	Close to baseline	Not reported	Maintained on lorazepam 13mg daily- unable to tolerate dose reduction	3.5 years
6	Good response	3 weeks	Maintained on 3 x ECT treatments at 3 weekly intervals + lorazepam & dextromethorphan/quinidine	2.8 years
7	80% recovery	1 year	Lorazepam + dextromethorphan/quinidine. Considering further ECT	2.5 years
8	Good response	Not reported	On maintenance ECT, intervals not reported + fluoxetine	Not stated
9	Full recovery	2 weeks	Full recovery maintained on 2 weekly maintenance ECT	2.5 years
10	Full recovery	Nil reported	Maintained on lorazepam & memantine	5 months
11	Full recovery	1 week	Maintained full recovery on weekly maintenance ECT	18 months

Later Phase Management

Learning to use skills again

Once the acute symptoms are improved, a rehab approach may be necessary:

- Regular speech therapy to improve communication
- Regular exercise (physio or exercise physiology or personal trainer with experience in disability support)
- 1:1 support is often required to start accessing community again

Support with increased NDIS support requirements is almost always necessary.

Moving forward: the gaps

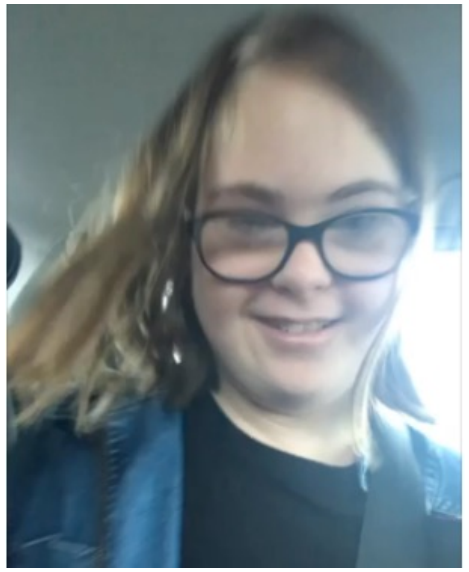
What we know so far…

- The characteristics of the disorder are well described
- There is consensus on the name for the disorder
- A list of consensus investigations has been published
- There are some published findings around possible abnormal screening tests
- Psychosocial stressors may involved in triggering it
- There are case reports and series to suggest that the best treatments are lorazepam, ECT and IVIg (insufficient robust evidence to rank these).

We don't know

- What causes it
- Biomarkers or investigations to definitively confirm the clinical diagnosis
- How IVIg and immune-based treatments work for DSRD – does it mean it is an immune-based condition?

Take-Home messages



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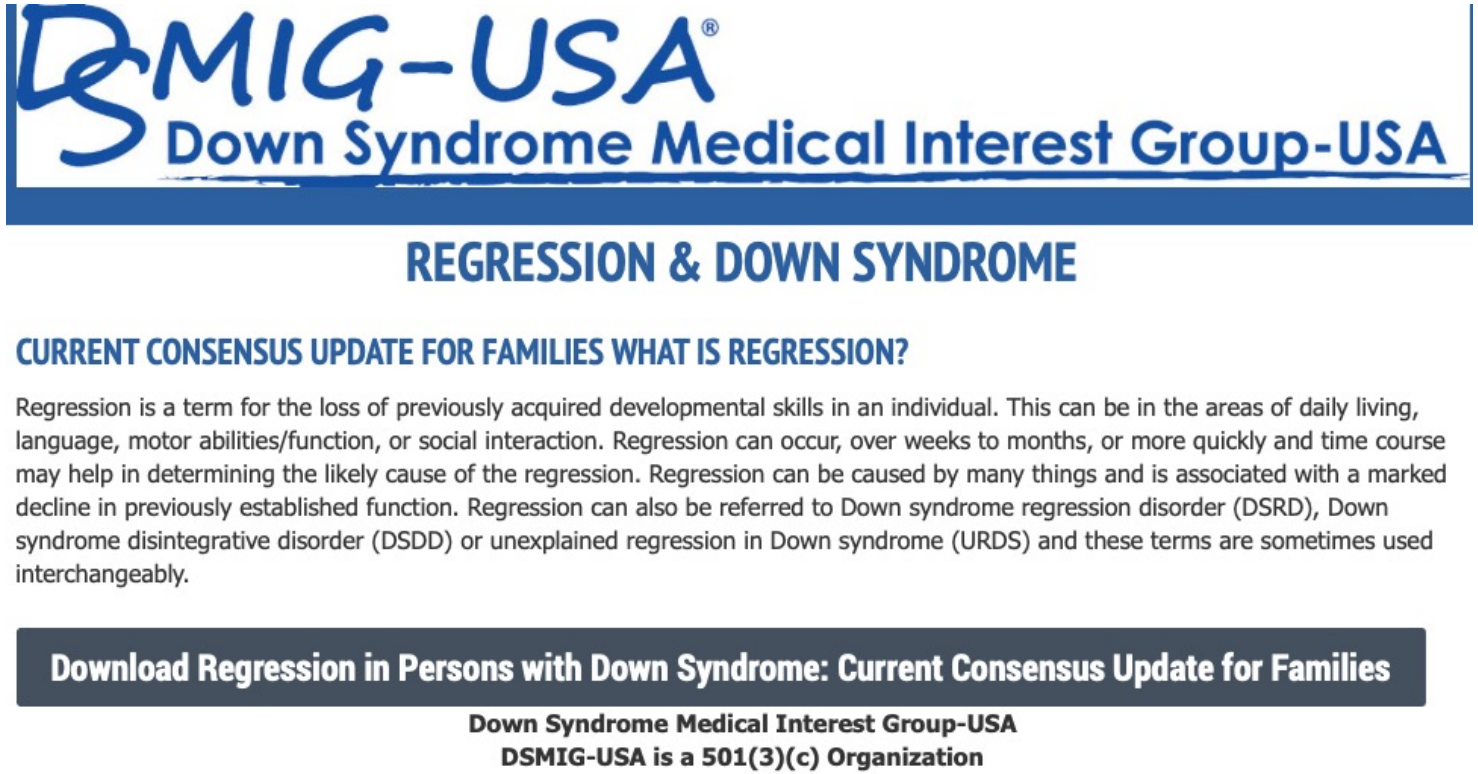
RESOURCES

Resources for Families

DSRD Information for Families

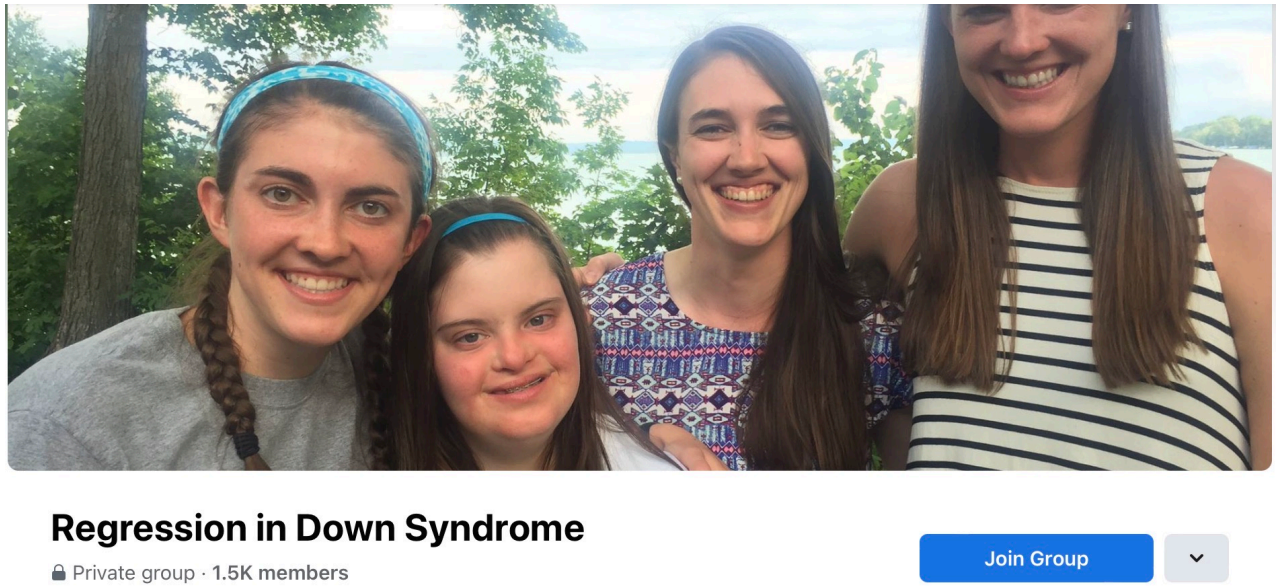


https://www.dsmig-usa.org/Regression

Facebook Group

USA Group (large) – moderated by Dr Eileen Quinn (paediatrician and mother)

https://www.facebook.com/groups/regressionindownsyndrome/

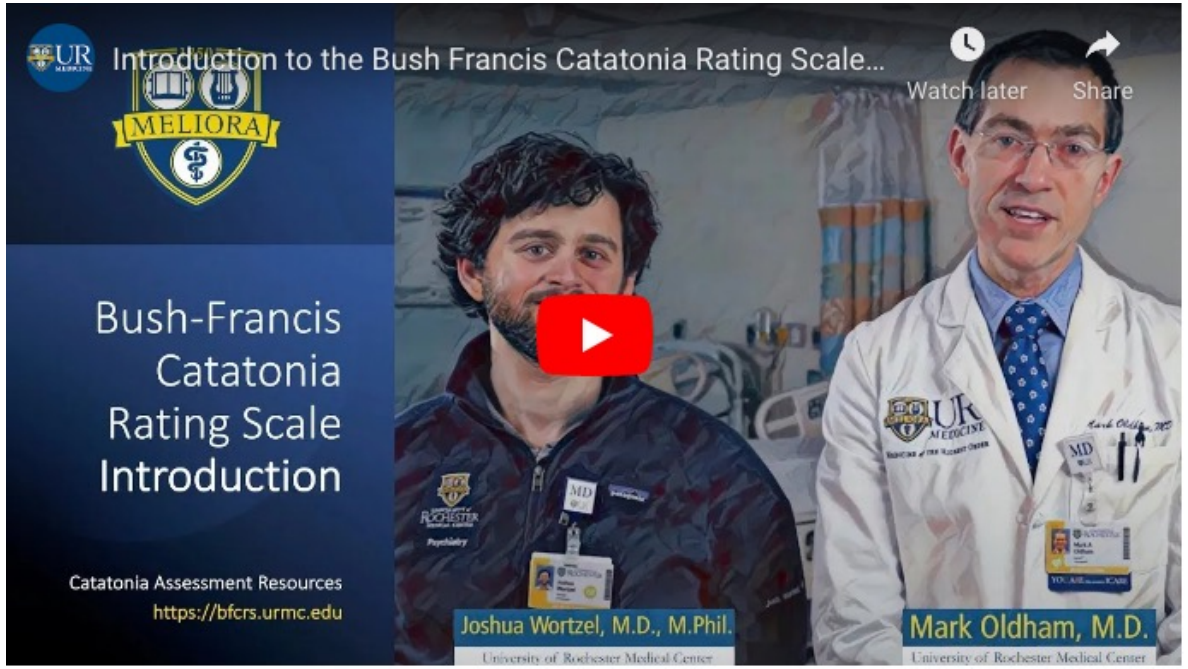


Resources for Health Professionals

Catatonia Examination and Bush-Francis Scale

Bush-Francis Catatonia Scale and Video Training (University of Rochester, USA)

https://www.urmc.rochester.edu/psychiatry/divisions/collaborative-care-and-wellness/bush-francis-catatonia-rating-scale.aspx



Webinars for Medical & Health Professionals

https://www.dsmig-usa.org/Speaker-Series

SESSION V & VI: REGRESSION & DOWN SYNDROME

Date: March 14, 2023 – Part 1 & May 9, 2023 – Part 2
Time: 7:00 – 8:00 PM EST

Individuals with Down syndrome may experience regression in previously acquired skills. This two-part webinar will present panel discussions on regression, with a key focus on Down Syndrome Regression Disorder (DSRD). This condition occurs most commonly between the ages of 10 and 30 years and is associated with loss of skills in language, cognition, behavior, motor and adaptive skills. Discussion will include what we currently know about DSRD diagnosis and management.

Part 1 Speakers	Part 2 Speakers
Eileen A. Quinn, MD UT College of Medicine and Life Sciences **Lina Patel, PsyD** University of Colorado School of Medicine **Robyn Filipink, MD** UPMC's Children's Hospital of Pittsburgh **Dr Cathy Franklin** QCIDD Queensland Centre for Intellectual and Developmental Disability Mater Research Institute - University of Queensland	**Eileen A. Quinn, MD** UT College of Medicine and Life Sciences **Lina Patel, PsyD** University of Colorado School of Medicine **Jonathan Santoro, MD** Assistant Professor of Neurology at CHLA and the Keck School of Medicine at USC **Cassie Karlsson, MD** Director - Child and Adolescent Psychiatry Fellowship Program & Clinical Associate Professor Department of Psychiatry and Behavioral Sciences at UK School of Medicine – Wichita

WATCH PART 1 RECORDING HERE

WATCH PART 2 RECORDING HERE

Clinical papers (Selection)

Overview

Santoro SL, Cannon S, Franklin C, Capone G, et al. Unexplained regression in Down syndrome: 35 cases from an international Down syndrome database. Genet Med. 2020 Apr;22(4):767-776. doi: 10.1038/s41436-019- 0706-8. Epub 2019 Nov 26. PMID: 31767984. • Freely available at: https://www.gimjournal.org/article/S1098-3600(21)01149-7/fulltext

Rosso M, Fremion E, Santoro SL, et al. Down Syndrome Disintegrative Disorder: A Clinical Regression Syndrome of Increasing Importance. Pediatrics. 2020 Jun;145(6):e20192939. doi: 10.1542/peds.2019-2939. PMID: 32471843. • Freely available at: https://publications.aap.org/pediatrics/article/145/6/e20192939/76920/DownSyndrome-Disintegrative-Disorder-A-Clinical

Diagnosis and Assessment

Santoro JD, Patel L, Franklin C, Kammeyer R, et al. Assessment and Diagnosis of Down Syndrome Regression Disorder: International Expert Consensus. Front Neurol. 2022 Jul Ghaziudd15;13:940175. PMID: 35911905. • Freely available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9335003/

Jacobs J, Schwartz A, McDougle CJ, Skotko BG. Rapid clinical deterioration in an individual with Down syndrome. Am J Med Genet Part A. 2016 Jul; 170A(7):1899-1902. PMID: 27149638. • Freely available at: https://onlinelibrary.wiley.com/doi/epdf/10.1002/ajmg.a.37674

Poumeaud F, Mircher C, Smith PJ, Faye PA, Sturtz FG. Deciphering the links between psychological stress, depression, and neurocognitive decline in patients with Down syndrome. Neurobiol Stress. 2021 Feb 5;14:100305. doi: 10.1016/j.ynstr.2021.100305. PMID: 33614867; PMCID: PMC7879042. • Freely available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7879042/

Treatment

Santoro, J.D., Spinazzi, N.A., Filipink, R.A. Franklin, C. *et al.* Immunotherapy responsiveness and risk of relapse in Down syndrome regression disorder. *Transl Psychiatry* **13**, 276 (2023). Doi: 10.1038/s41398-023-02579-z. Freely available at: https://www.nature.com/articles/s41398-023-02579-z

Santoro JD, Partridge R, Tanna R, et al. Evidence of Neuroinflammation and Immunotherapy Responsiveness in Individuals with Down Syndrome Regression Disorder. J Neurodev Disord. 2022 Updated January 2023 Jun 3;14(1):35. PMID: 35659536. • Freely available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9164321/

Santoro SL, Baumer NT, Cornacchia M, Franklin C, …Skotko BG. Unexplained regression in Down syndrome: Management of 51 patients in an international patient database. Am J Med Genet A. 2022 Oct;188(10):3049-3062. doi: 10.1002/ajmg.a.62922. Epub 2022 Aug 4. PMID: 35924793.

Miles JH, Takahashi N, Muckerman J, et al. Catatonia in Down syndrome: systematic approach to diagnosis, treatment and outcome assessment based on a case series of seven patients. Neuropsychiatr Dis Treat. 2019 Sep 20;15:2723-2741. doi: 10.2147/NDT.S210613. PMID: 31571888; PMCID: PMC6759875. • Freely available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6759875/

THE UNIVERSITY OF QUEENSLAND
AUSTRALIA
CREATE CHANGE

Thank you

DrCathyFranklin
Dr Cathy Franklin
DrCathyFranklin
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