Is it safe and ethical to use ECT in children?

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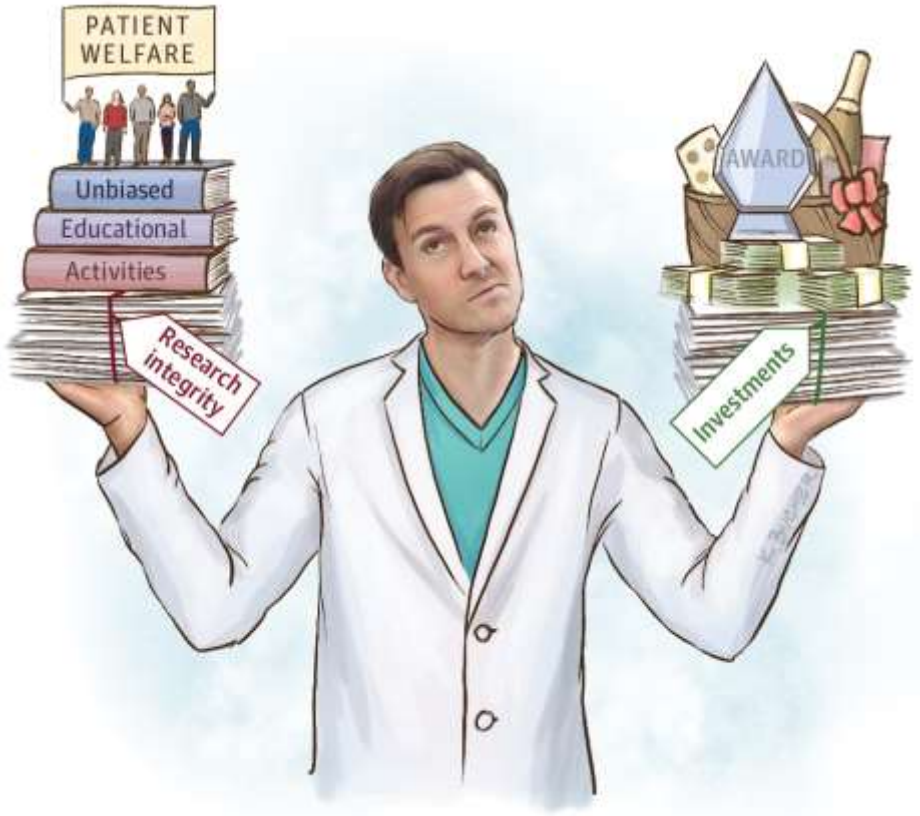
Disclosures

No conflicts of interest



UN-convention – Rights of the Child (1989)

Article 24

The right of the child to the enjoyment of the highest attainable standard of health and to facilities for the treatment of illness and rehabilitation of health.

Case 13-year old girl

Kjærholm et al., Ugeskr Læger 2023;185:V11220696

”It is as if I no longer have an appearance, I just see a corpse.”

”I feel I cannot think, I do not exist, I have been overtaken by a demon.”

”I just think the demon is everything og when it is not here, then I am nothing, I am a corpse.”

”My brain has become smaller and smaller and now it is completely gone, I am brain-dead.”

Cotards syndrome

- A rare neuropsychiatric condition (200 known cases worldwide?)
- Pathophysiology unknown – neural misfiring in fusiform face area / amygdala, neural disconnection ?
- Risk associated to patients with kidney dysfunction and treatment with aciclovir/valaciclovir
- Not described in ICD or DSM manuals
- First described by Dr. Jules Cotard in 1882 – ”le délire des négations” - ”the delirium of negation”
- Nihilistic delusions that range from a belief that one has lost organs, blood, or body parts to insisting that one has lost one's soul or is dead, non-existence concerning one's own body, delusions of immortality.
- Associated with severe depression, anxious melancholia, schizophrenia, dementia, encephalopathy, multiple sclerosis, Parkinson's disease, stroke, subdural bleeding, epilepsy, and migraine.
- ECT appears more effective than psychopharmacological treatment (in adults)

- *Tomasetti et al, Int rev Psych. 2020*
- *Berrios et al. Acta Psych Scand 1995*
- *Debruyne et al, Current Psychiatry Reports, 2010*
- *Helldén A, Odar-Cederlöf I, Larsson K et al. Death delusion. BMJ 2007; 335:1305.*

13-year old girl, case description

Kjærholm et al., Ugeskr Læger 2023;185:V11220696

- Admitted to inpatient unit after suicide attempt by strangulation.
- Familial dispositions: none
- Pre-morbid: quiet, shy, normal school attendance and hobbies
- During the one year prior to admission: Became sad and isolated herself. Developed anorexia. Later during admission, she described that during this period, a voice had ordered her not to eat, and she described having experienced increasing hallucinations and the development of paranoid, bizarre and nihilistic delusions
- Admission: Hallucinations. Nihilistic delusions and delusions of control/passivity phenomena. Severely depressed and tormented. Negative symptoms. Bed-ridden, needed full support for toilet, meals and personal hygiene. Limited speech, rejected visit from family. Normal body weight and no eating disordered thoughts.

13-year old girl, assessments

Kjærholm et al., Ugeskr Læger 2023;185:V11220696

- Psychopathological evaluation, parent reports and observation of symptoms and function in in-patient care.
- MRI-scan of cerebrum, EEG, blood lab work, genetic assessments – no abnormal findings

13-year old girl, treatment

Kjærholm et al., Ugeskr Læger 2023;185:V11220696

- Antidepressants – initially sertralin 200 mg/d, limited effect
- Addition of antipsychotic: first aripiprazole 25 mg/d, then quetiapine 900 mg/day, then olanzapine 25 mg/day, limited effect
- ECT bitemporal X 3 per week. A total of 25 sessions. Satisfactory seizure response.
- Few transient side effects
- Patient status improved with less withdrawal, better interaction, more initiative, less self-neglect and less self-harm.
- PANSS total score (range 30-210): decreased from 102 (pre-ECT) to 72 (post-ECT)
- After ECT, treatment with clozapine.
- Discharged after 11 months in partial remission to 24-hour placement and treatment.

ECT in Denmark, age distribution

2008-2014:

Hundrup, J ECT 2017

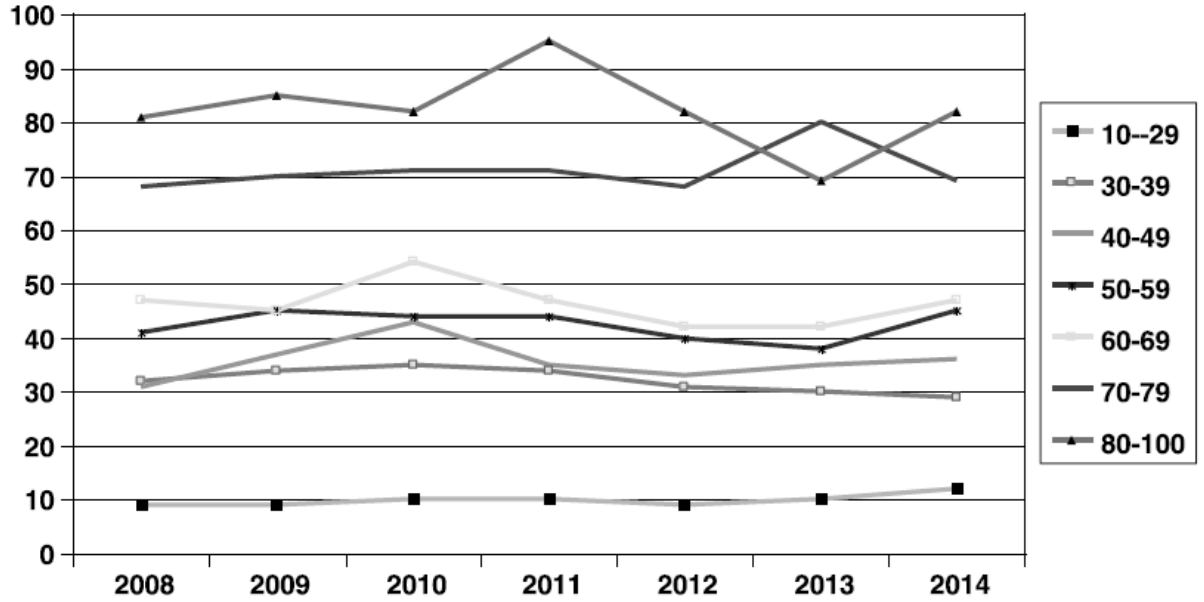


FIGURE 1. Annual number of patients in ECT per 100,000 inhabitants (>10 years) in Denmark in relation to age, 2008–2014.

2000-2019: a total of 25 patients < 18 years were treated with ECT
(unpublished data, related to update of *Hundrup et al. , J ECT 2017*)

Review of ECT studies in youth 1942-1996

Ray & Walter, Annu Prog Child Psychiatry Child Dev. 1998;223–236

Improvement rates (clinically assesed) immediately after ECT:

Depression 63%

Mania 80%

Schizophrenia 42%

Catatonia 80%

-similar to results in adults.

Electroconvulsive therapy in children and adolescents: A systematic review of current literature and guidelines

Døssing & Pagsberg, J ECT 2021

P: Children and adolescents with psychiatric disorders

I: Electroconvulsive therapy

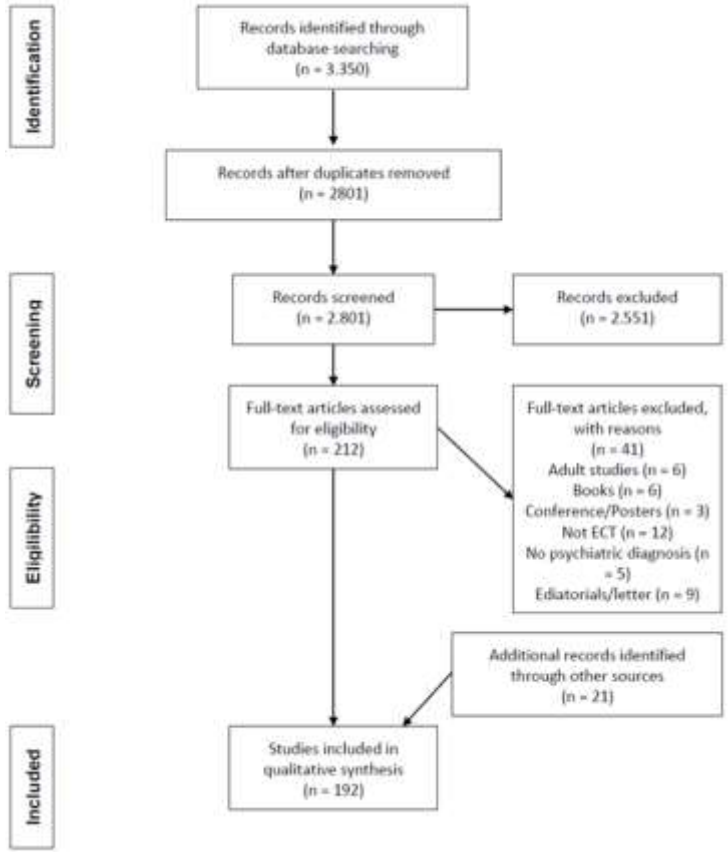
C: Treatment as usual/None

O: Symptom improvement

Period: 01.03.1996-13.01.2020

Results: Total, 192 studies. Case studies (52), overview/review articles (49), retrospective studies (49)

-no RCTs



ECT in youth - overall synthesis of results

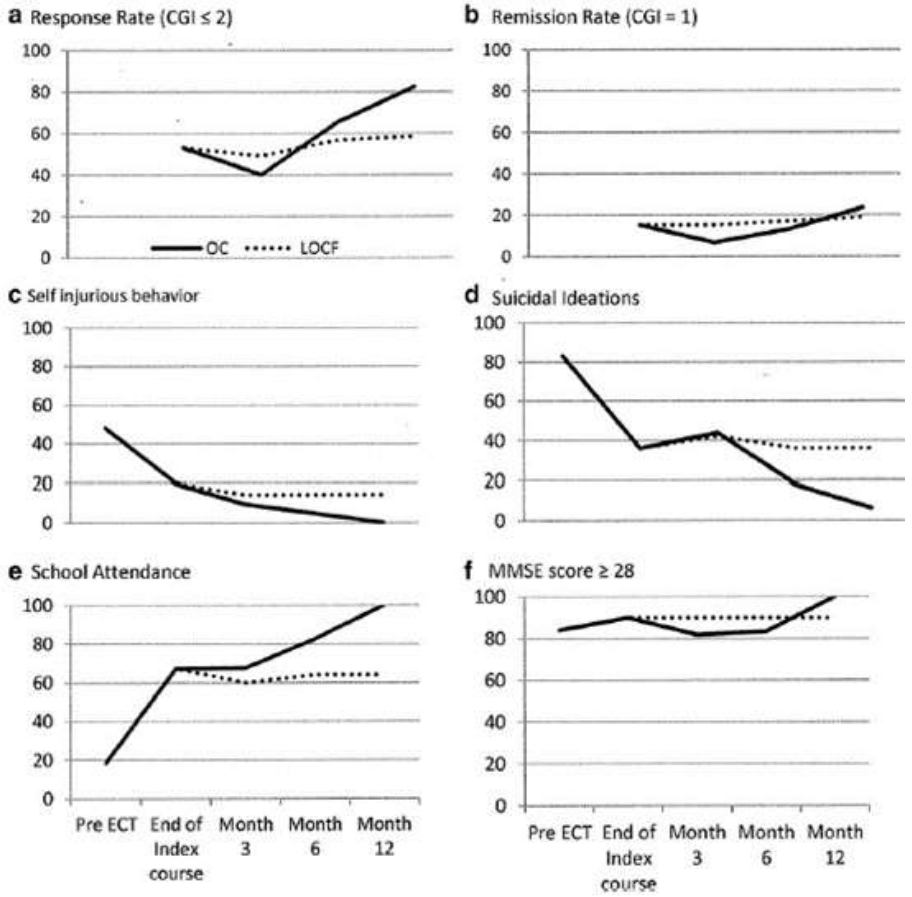
TABLE 2. Overview of Indications of ECT in Children and Adolescents, Based on Disorder

	No. Studies	Rey and Walter, Effect Range	Effect Range (Included in Review)	Conclusions
Mood disorders	23	63% for depression, 80% for mania	77%–100% for depression, 75%–100% for bipolar. More limited for acute mania.	High response rate, several studies
Catatonia	33	80% for catatonia	75%–76%	High response rate, heterogeneous patient group
Schizophrenia	16	42% for schizophrenia	54% (75 combined with antipsychotics)	Modest effect, it seems to be safe
ID	8	Not included	67%–79%	No controlled studies, small no. studies
SIB and aggression	4	Not included	No larger studies conducted	Uncertain effect

Other indications: primarily NMS and anti-NMDAR, but no larger studies exist.

ECT - affective disorders in youth

Ghaziuddin et al 2020 (see fig): Retrospective study, N= 54 youth with refractory depressive or bipolar disorder treated with ECT. At 12 months: response rate 82.4%, remission 23.5%, decreased suicidality, improved school attendance



ECT catatonia in youth

- Appears highly effective (>75%)
- Heterogenious syndrome, complicates external validity of studies
- APA/AACAP recommends ECT for catatonia regardless of aetiology (+malignant catatonia and malignant neuroleptic syndrome)
- Review, *Consoli et al 2010*: n=59 cases of youth with catatonia. Favorable reponse in 76%.
- Has been used with effect in cases of catatonia with co-morbid autism spectrum disorder, Downs syndrome, fragile X syndrome.

ECT – schizophrenia in youth

- Overall more modest response compared to mood disorders and catatonia

- *Zhang, 2012, see fig*: case-control study

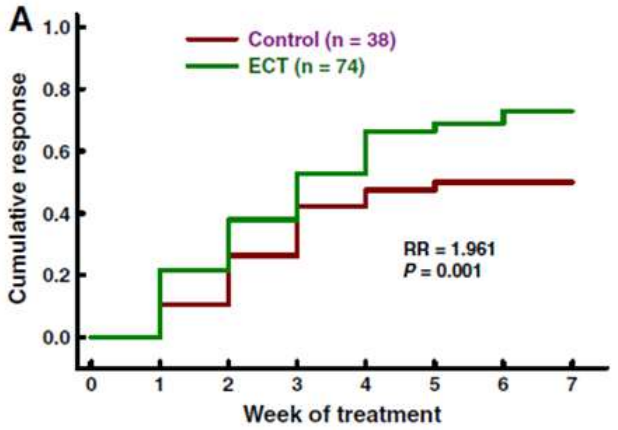
N=112, age 13-20 y.

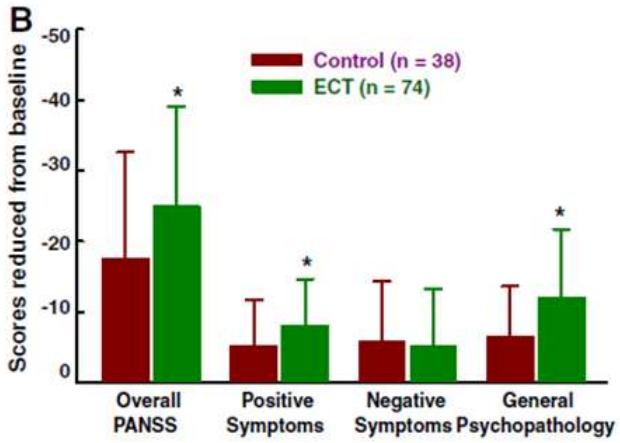
Response rates

(min. 30 % reduction on PANSS total score):

AP+ECT = 74%

AP = 50%





Zhang 2012

ECT – across conditions in youth

Table 1: Comparison of findings from the two age groups of ECT recipients

	Adults (>20 years) (n=56)	*Adolescents (≤20 years) (n=13)*
Age, years (average, SD)	49.6 (16.6)	17.1 (1.9)
Diagnosis %		
Schizophrenia	25.0	38.5
Schizoaffective	12.5	30.8
Bipolar	19.7	7.7
Major depression	42.9	23.1
Reason for referral to ECT (%)		
Lack of response and/or side effects of pharmacotherapy	85.5	46.2
Pharmacotherapy before being referred to ECT (average number of trials, SD)		
Antidepressants	2.1 (1.8)	0.7 (0.8)
Antipsychotic	1.4 (1.5)	1.6 (1.4)
Atypical antipsychotic	0.6 (0.9)	0.6 (1)
Mood stabilizers	0.6 (0.8)	0.3 (0.8)
ECT characteristics		
Number of treatments per course (average, SD)	19.9 (12.7)	13.2 (8.8)
Intensity (average %, SD)	54 (21.1)	25 (13.2)
Response to ECT (%)		
Highly effective	34.6	44.4
Moderately effective	42.3	33.3

Bloch et al 2008

Puffer et al, 2016: n=51, 16.8 y, mood/schizophrenia/catatonia. 77% much/very much improvement by CGI-I.

Benson et al 2019: youth mean age 21y, varied conditions, significant improvement, based on BSIS scores

Maoz et al, 2018: n=36, 12-19 y, mood/schizophrenia/catatonia. 72.2% much/very much improvement by CGI-I

ECT – other indications in youth

Combinations of severe treatment-resistant disorders and/or catatonia/mood disorders/schizophrenia:

Severe aggression

Severe self-harm

Severe anorexia nervosa

Autism spectrum dirorders /mental retardation

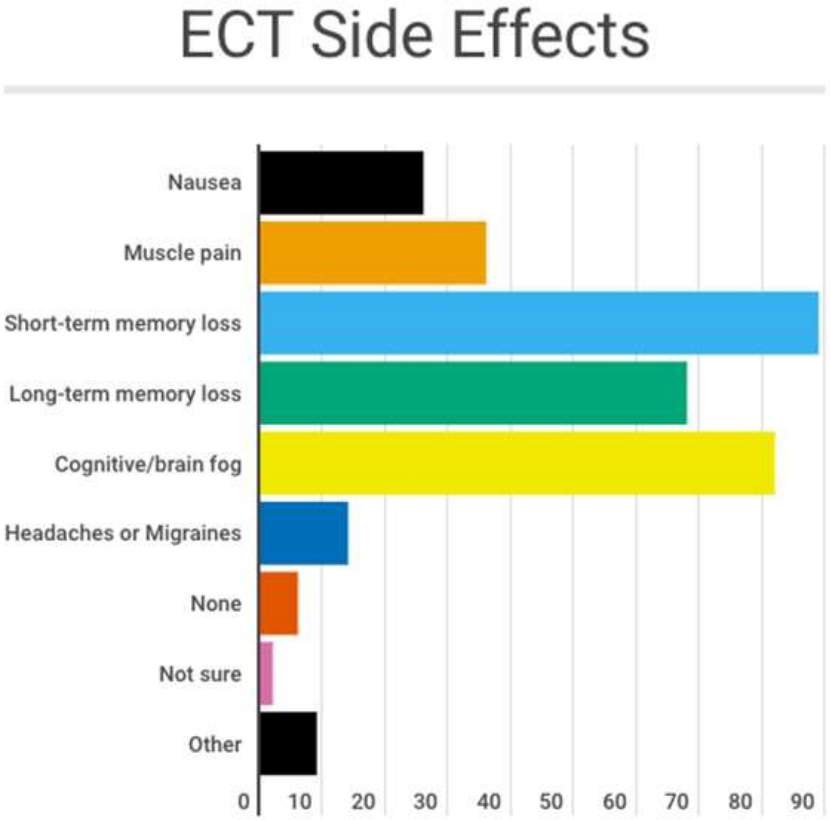
Severe OCD

Autoimmune encephalitis (anti-NMDAR)

Delirium

ECT – side effects in youth

- Similar side effects in adolescents as for adults.
- The literature has few data on longterm cognitive deficits in youth. The few studies show similar level as adults *(Swartz 2009, Ghazziudin 2000), 2*-5 y follow-up.
- Adolescents may be more prone to prolonged (10%) or tardive seizures (rare) *(Kutcher 1995, Hill 1997)*
- Contraindications are the same as for adults.



Conclusion review

- Lack of high-quality studies on ECT i youth
- Studies in this review: evidence overall rated as of low to very low quality according to GRADE
- Probable publication bias (few studies with lack of effect)
- Concerns about the impact on the developing brain
- No absolute contraindications for ECT in youths
- Longer-term cognitive side effects has not been found, but limited data
- ECT may be considered for youth in severe, treatment-resistant disorders, especially mood disorders, catatonia, schizophrenia. Especially in older adolescents.

Newer data:

Electroconvulsive Therapy in Children and Adolescents in Germany—A Case Series From 3 University Hospitals, *Karl et al. J ECT Dec 2022*

Objective Electroconvulsive therapy (ECT) is a well-established, safe, and efficacious treatment for severe psychiatric disorders. In children and adolescents, it is used much less frequently than in adults, likely because of a lack of knowledge.

Methods We retrospectively analyzed all patients aged 12 to 17 years who completed a course of ECT at 3 psychiatric university hospitals in Germany between 2010 and 2020. Clinical Global Impression Severity (CGI-S) scores were assessed based on electronic medical records. Changes in CGI-S scores were assessed using a paired samples *t* test. Predictors for response and remission were assessed using binomial logistic regression.

Results We included 32 patients. The CGI-S scores improved significantly from before to after ECT treatment (6.9 vs 3.9, $t = 10.0$, $P < 0.01$). A total of 40.6% of patients responded (CGI ≤ 3) and 21.9% remitted (CGI ≤ 2). The number of ineffective medication trials in the 6 months before ECT treatment was significantly associated with response (odds ratio, 0.54; $P = 0.028$) and remission (odds ratio, 0.31; $P = 0.048$). Five patients reported subjective cognitive adverse effects, 2 patients exhibited a prolonged seizure, 1 patient reported headaches, and 1 patient experienced a mild allergic reaction after anesthesia with etomidate. A total of 65.6% of patients experienced no adverse effects at all.

Conclusions This retrospective analysis found ECT to be effective and safe in children and adolescents irrespective of their main diagnosis. The reported data point to the importance of an early use of ECT for severe psychiatric diseases in child and adolescent psychiatry.

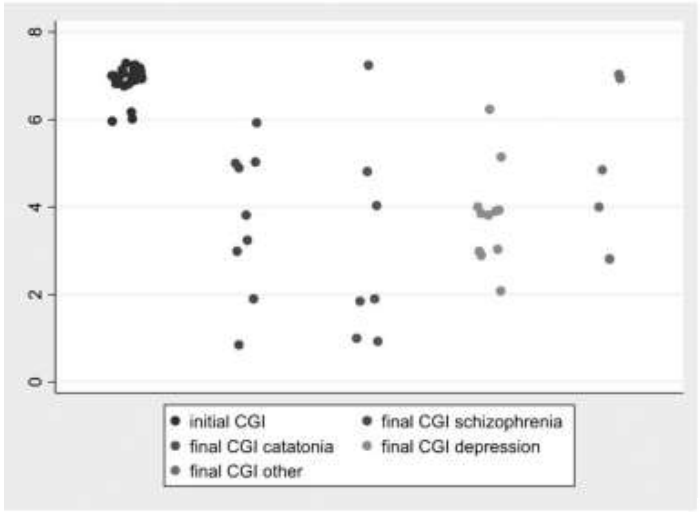


FIGURE 1. The CGI-S before and after the ECT series by main diagnosis. full color online

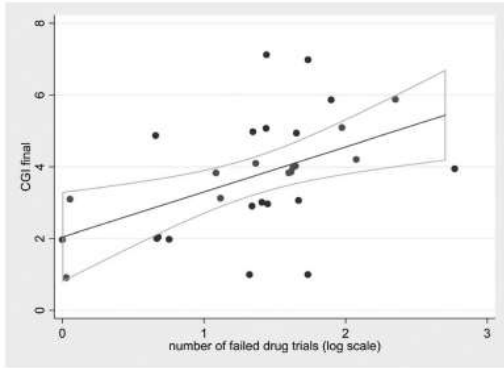


FIGURE 2. The CGI-S score after the ECT series (CGI final) shows a significant linear correlation (Spearman) with the number of failed drug trials in the 6 months before ECT ($r = 0.24$, $P = 0.005$). full color online

Newer reviews – important highlights on youths

Catatonia and ECT across the lifespan,
Karl S , Sartorius A, Aksay SS, Sch research 2023

The fear of harming the developing brain - existing data confirm the transient nature of potential cognitive side effects or memory impairment during the ECT also in children and adolescents (Karl et al., 2022).

The overlap between the symptoms of catatonia, autism, and psychosis has been referred to as an “iron triangle”. This hypothesis might reflect a kind of common final pathway of all three disorders for very severe cases (Shorter and Wachtel, 2013).

This diagnostic overlap might lead to catatonia being misinterpreted as symptoms of autism, and thus ECT is falsely not considered as a true therapeutic option. The same applies to self-injurious behavior (SIB), which is a frequently observed phenomenon in autism spectrum disorders.

In addition to an acute course of ECT, maintenance ECT has also been found to be safe and useful. Maintenance ECT is often necessary to prevent relapse in catatonia and prolonged maintenance ECT may provide sustained improvement without cognitive side effects (Ghaziuddin et al., 2021).

Youth - a lower seizure threshold compared with adults. This makes it necessary to start ECT treatment with a lower charge to determine the seizure threshold using the titration method. Very low charges however are associated with a higher risk for developing prolonged seizures.

Table 3: Overview of indications for ECT in children and adolescents, based on guidelines

	NIH/NICE	ACAAP	APA
General indications	Severe symptoms after an adequate trial of other treatment options has proven ineffective and/or when the condition is considered to be potentially life-threatening	Failure to respond to at least two adequate trials of appropriate psychopharmacological agents accompanied by other appropriate treatment modalities.	Other viable treatments have been ineffective or if other treatments cannot be administered safely
Mood disorders	Yes, for major depression or prolonged and/or severe manic episode	Yes, severe, persistent major depression or mania with or without psychotic features	Yes, major depressive disorder or mania
Schizophrenia	Not recommended	Yes, schizoaffective disorder, or, less often, schizophrenia	Yes
Catatonia	Yes	Yes	Yes

User perspectives (few data)

- Patients with schizophrenia < 18 y:
  79% experienced improvement with ECT
  80% (No ECT) vs. 84% (ECT) would chose ECT if indicated for them

- Parents to patients with schizophrenia < 18 y:
  74% experienced that ECT had improved mental health in their children/adolescents.94,7% (No ECT) vs. 100% (ECT) wanted ECT for their children if indicated.

De la Serna 2015, Flamarique 2017

Treating children with electroconvulsive therapy. By Chris Rogers and Marshall Corwin, BBC News, New York. 19 May 2017

Seventeen-year-old Jonah Lutz is severely autistic. He's also prone to outbursts of violent behaviour, in which he sometimes hits himself repeatedly.

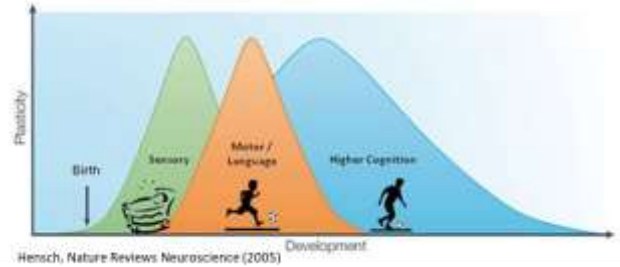
His mother, Amy, is convinced that if it wasn't for electroconvulsive therapy - ECT - he would now have to be permanently institutionalised for his own safety, and the safety of those around him.

Amy and husband Andy tried countless traditional treatments using medication or behavioural therapy before finally turning to ECT - a treatment that first began to be used on children like Jonah a decade ago, in parts of the US. Each session alleviates his symptoms for up to 10 days at a time - but it's not a cure.

https://www.bbc.com/news/magazine-39961472

Discussion

Is it safe and ethical to use ECT in children?



Hensch, Nature Reviews Neuroscience (2005)

ECT is safe and effective in adults. Difficult to directly extrapolate to youth.
-how does is affect the developing brain?

Very limited evidence in youth. No RCTs. Publication bias? Very limited clinical experience.

Guidelines point to the use of ECT in youth in severe treatment-resistant cases and in life-threatening cases.

Some indications of a possible positive user perspective.

May assist child- and adolescent psychiatry in severe cases:

Children have the right to the highest attainable standard of health.

Child- and adolescent psychiatry face psychopharmacological challenges concerning limited studies and evidence and few approvals (then off-label use), lower efficacy of certain drugclasses (antipsychotics and antidepressants), increased side effects such as metabolic, endocrine, neuromotor (antipsychotics), suicidality (antidepressants).

Research is needed. Clinical studies (efficacy and safety, including long term) as well as preclinical studies (brain development). Clinical training and experience is needed.

Thank you for your attention and for inviting me to Malmö and meeting the NACT society