SUBJECTIVE COGNITIVE COMPLAINTS FOLLOWING ELECTROCONVULSIVE THERAPY FOR DEPRESSION

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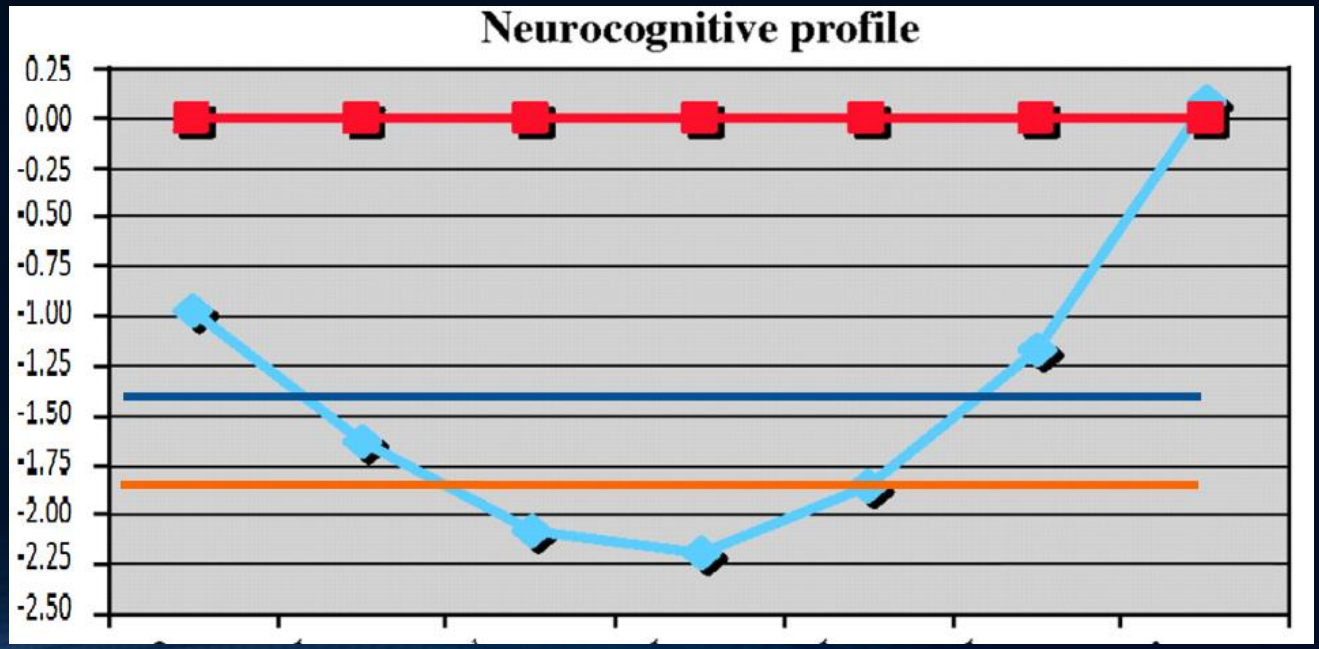
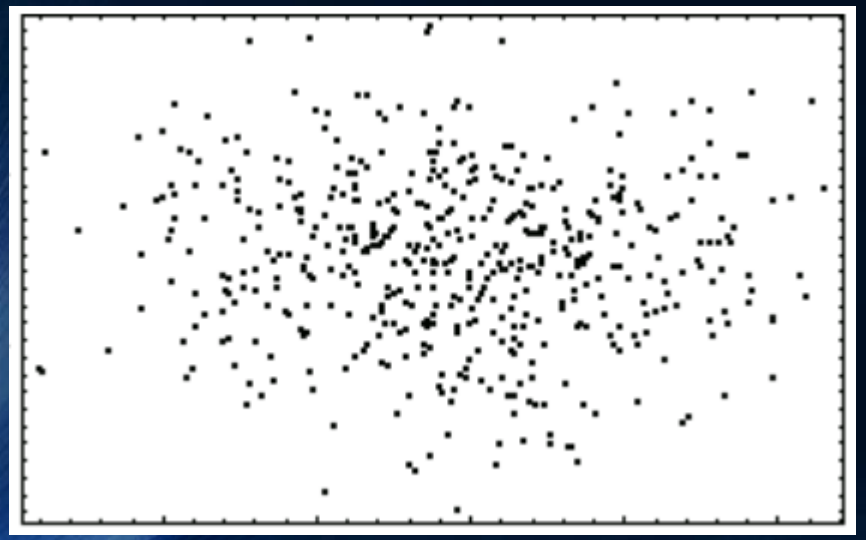
Cognition & depression

- Acute depression: recognised cognitive deficits (e.g., Rock et al., 2014; Snyder, 2013 meta-analyses)
  - generally **moderate** and affecting **executive functions**, **sustained attention** and **memory**
  - **large** deficits in **inhibition** and **fluency** and **moderate** deficits in between-tasks **shifting** & **working memory**



Cognition & depression

- Acute depression: recognised cognitive deficits
- Cognitive deficits **present from the 1st** depressive **episode**: characterised by the same pattern (e.g., Lee et al., 2012; Ahern & Semkovska, 2017)
  - Some deficits **persist** following remission



- However, the **lack of association** between **subjective** cognitive complaints and **objective** cognitive performance is a consistent finding
  (e.g., Lahr et al., 2007; Mohn & Rund, 2016; Srisurapanont et al., 2018; Svendsen et al., 2011)

ECT, cognition, subjective complaints & depression

- Reports of ECT-associated cognitive deficits are almost as old as the therapy
  - Improvement of techniques has resulted in less pronounced objectively measured deficits
  - Reports subjective complaints less consistent
- **Effect of ECT** on subjective complaints
  - **Deleterious**: e.g., Hughes et al., 1981; Brus et al., 2017
  - **None**: e.g., Frith et al., 1983; Semkovska et al., 2016
  - **Advantageous**: Coleman et al., 1996; Sienaert et al., 2009
- **Effect of electrode placement**
  - **Bilateral = more complaints** than unilateral: Fleminger et al., 1970; Semkovska et al., 2016
  - **None**: Coleman et al., 1996; Brus et al., 2017

The patient voice

- Over 70 years of research on subjective ECT-related complaints
  - predictions?
  - complaints: sine wave > brief pulse
  - Some patients will complain
  - Some evidence that individuals with persisting depressive symptoms following ECT are more likely to report subjective cognitive complaints
- How can all this research inform clinical practice?

Aims

(1) Estimate the **rate of patients** presenting cognitive complaints following ECT for depression attributable to treatment

(2) Estimate the **degree of pre-post ECT change in cognitive complaints**

(3) Evaluate the independent effects of potential **mediators** on both these variables

- Age & gender
- Time interval between end of ECT and subjective report
- Persisting depressive symptoms
- Objective cognitive burden
- Treatment parameters: electrode placement, number of ECT sessions & dosage

(4) Evaluate the **strength of the association** between **depression** and **cognitive complaints** **following ECT**

Methods

PRISMA guidelines for systematic reviews and meta-analyses (Moher et al., 2009)

- Search strategy: MEDLINE, EMBASE, PsycARTICLES, PsycINFO, and CINAHL from 1972 to November 2017, using the terms:

  “electroconvulsive therapy” or ECT

  AND 'depression' or 'depressive' or ‘depressed’ or ‘MDD’

  AND 'cognitive side effects' or 'side-effects' or 'subjective memory' or 'complaint' or 'complain' or 'subjective' or “self-report” or “patient-report” or “patient-reported” or 'self-reported' or 'self-rating' or 'self-rated'

Methods

Inclusion criteria :

- adults (age≥18)
- treated with brief or ultra-brief ECT for a Major Depressive Episode;
- reported subjective cognitive complaints either as:
  - (a) rates of patients complaining about ECT-associated cognitive deficits
  - (b) change in subjective cognitive complaints following ECT (pre-post design)

Methods

Exclusion criteria :

- redundant reports
- case series
- cognition only objectively measured
- severe psychiatric comorbidity (e.g., schizophrenia)
- neurological disorder (e.g., Parkinson)

Methods

Recorded variables

- Number of samples (k) per study and participants (n) per sample
- Patients' rates of cognitive complaints
- Type of cognitive complaint (e.g., memory, concentration)
- Pre- and post- means and SD (or pre-post ECT change) on the subjective scale
- Type of subjective complaint scale used
- Where available: moderator details, i.e., age, interval between end of ECT and subjective report, etc.
- Where available: statistics for the association between post-ECT depressive symptoms severity and subjective cognitive complaints report

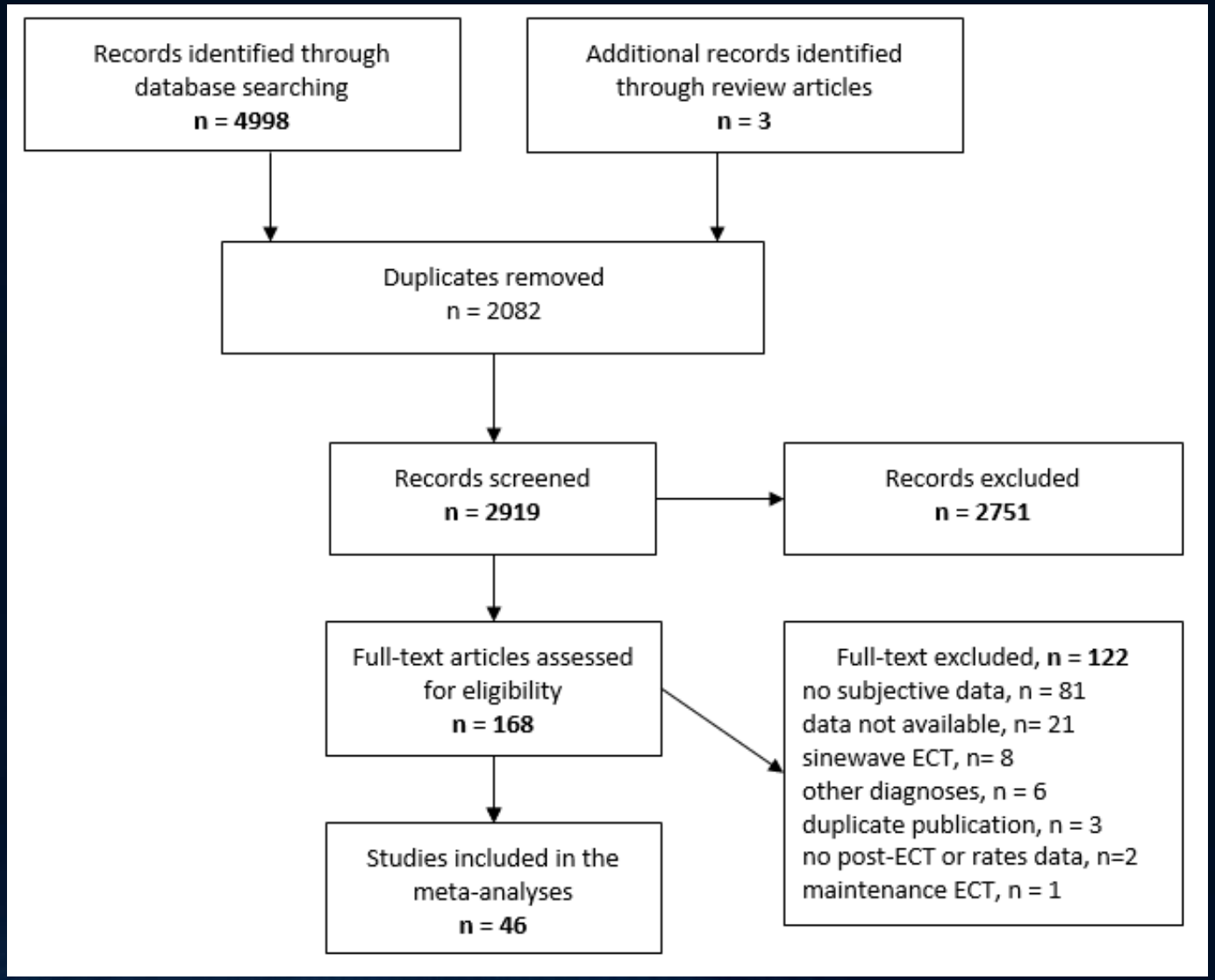
Methods

Statistical analyses

- Three sets of met-analyses were run for estimating
  1. Rates for patients presenting with cognitive complaints following ECT
  2. Change in cognitive complaints, i.e., effect size=(Mean post-ECT-Mpre-ECT)/Sdpi

     → positive effect size = complaints at **post**-ECT **<** **pre**-ECT
  3. Strength of the post-ECT correlation between subjective complaints and depression
- Random effects model for calculating the 3 main effects
- Mixed effects model were used for the moderator analyses

Results – studies selection



1. Results – rates of patients complaining

- **14** studies including **33** rates estimates (**k**) and **2006** patients (**n**)
- Samples ranging 6 to 732 participants, mean n=100.2
- ECT-related cognitive complaint reported

Memory	**93%**
Confusion	**21%**
General cognition	**7%**
Concentration	**7%**
Thinking	**7%**
Feeling slowed down	**7%**

1. Results – rates of patients complaining

- **14** studies including **33** rates estimates (**k**) and **2006** patients (**n**)
- Samples ranging 6 to 732 participants, mean n=100.2

k	Mean estimated rate	95% confidence interval		z	p	heterogeneity	
33	42.0	35.3	49.0	-2.247	0.025	I^2=92%	p<0.001

Electrode placement	k	Mean estimated rate	95% confidence interval		Model z	Model p
Bitemporal	12	40.3	37.4	43.3	-2.82	0.005
Mixed	17	46.7	44.1	49.4		

1. Results – rates of patients complaining

Moderator	Range	Mean
Interval (days)	0.1 to 180	15.5
Age (years)	39.6 to 68.5	55.0
Gender (%women)	0 to 100	60.4
Number of ECT sessions	6.2 to 15.4	9.11
Mean improvement in depressive symptoms	14.1 to 73.7	30.0
Cognitive burden (pooled change from pre-ECT)	-92.71 to 10.94	-16.5
Electrical dosage (mC)	105 to 800	230

1. Results – rates of patients complaining

Moderator	k	z	p
Interval (days)	33	**0.14**	0.89
Age (years)	32	**-1.04**	0.30
Gender (%women)	32	**-0.85**	0.39
Number of ECT sessions	25	**2.68**	**0.007**
Mean improvement in depression	23	**-1.60**	0.10
Cognitive burden	17	**0.99**	0.32
Electrical dosage	17	**0.41**	0.68

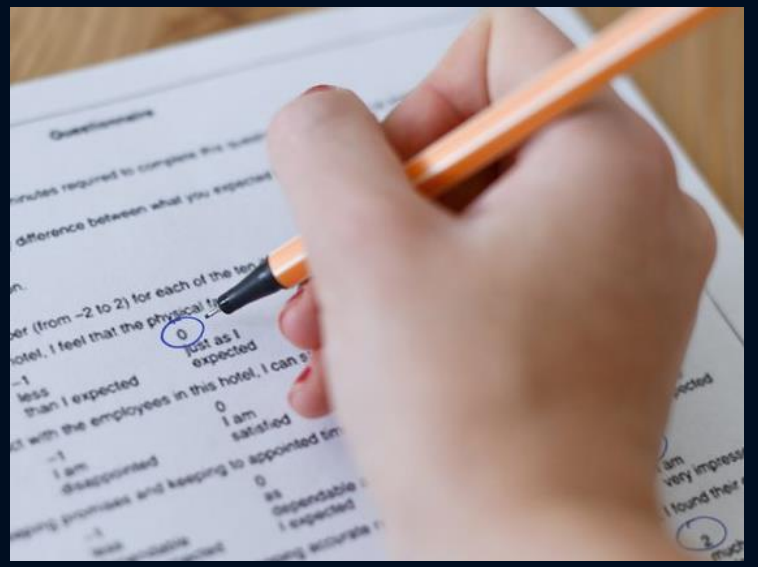
2. Results – change in cognitive complaints post-ECT

- **39** studies including **108** samples (**k**) and **2283** patients (**n**)
- Samples ranging 10 to 202 participants, mean n=39

2. Results – change in cognitive complaints post-ECT

- Subjective cognitive complaints questionnaire used

Squire Subjective Memory Questionnaire (SSMQ)	44%
Cognitive subscale of the Columbia Subjective Side Effect Scale (CSSES)	24%
Severity of memory impairment (GMy)	19%
Cognitive Failures Questionnaire	11%
Severity of cognitive impairment	2%
Severity of thinking impairment	1%



Cognitive Failures Questionnaire

	Very often	Quite often	Occasionally	Very rarely	Never
1. Do you read something and find you haven't been thinking about it and must read it again?	4	3	2	1	0
2. Do you find you forget why you went from one part of the house to the other?	4	3	2	1	0
3. Do you fail to notice signposts on the road?	4	3	2	1	0
4. Do you find you confuse right and left when giving directions?	4	3	2	1	0
5. Do you bump into people?	4	3	2	1	0
6. Do you find you forget whether you've turned off a light or a fire or locked the door?	4	3	2	1	0
7. Do you fail to listen to people's names when you are meeting them?	4	3	2	1	0
8. Do you say something and realize afterwards that it might be taken as insulting?	4	3	2	1	0
9. Do you fail to hear people speaking to you when you are doing something else?	4	3	2	1	0
10. Do you lose your temper and regret it?	4	3	2	1	0
11. Do you leave important letters unanswered for days?	4	3	2	1	0

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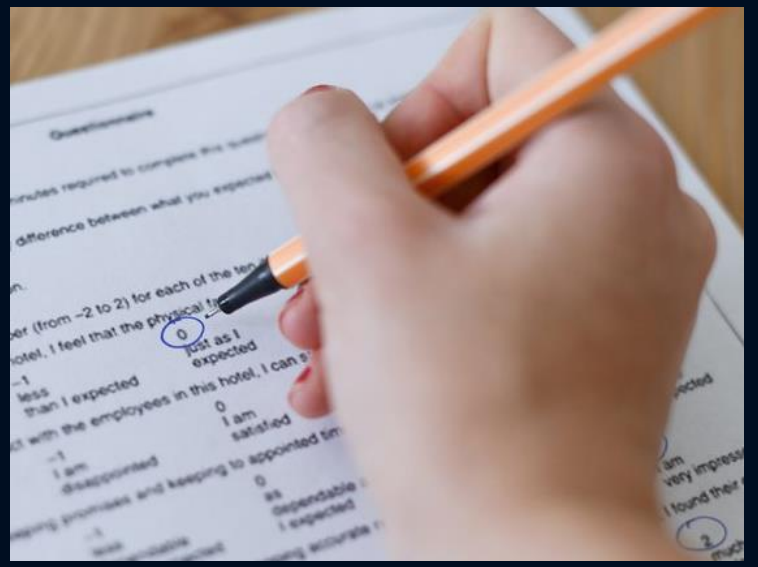

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k	Mean estimated change	95% confidence interval		z	p	heterogeneity	
108	-0.135	-0.28	0.001	-1.82	0.069	I^2=94%	p<0.001

Electrode placement	k	Change estimate	Model z	Model p
Bitemporal	41	-0.29	2.27	0.32
Right Unilateral	39	0.0		
Mixed	28	-0.20		

2. Results – change in cognitive complaints post-ECT

k	Mean estimated change	95% confidence interval		z	p	heterogeneity	
108	-0.135	-0.28	0.001	-1.82	0.069	I=94%	p<0.001

Scale used	k	Change estimate	95% confidence interval		z	p	Model Q	Model p
CFQ	12	-0.053	-0.25	.14	-0.52	0.59	-56.8	<0.001
CSSES	26	-0.61	-0.98	-0.24	-3.20	<0.001		
GMy	20	-0.89	-1.22	-0.56	-5.32	<0.001		
SSMQ	47	0.50	0.28	0.73	4.36	<0.001		

2. Results – change in cognitive complaints post-ECT

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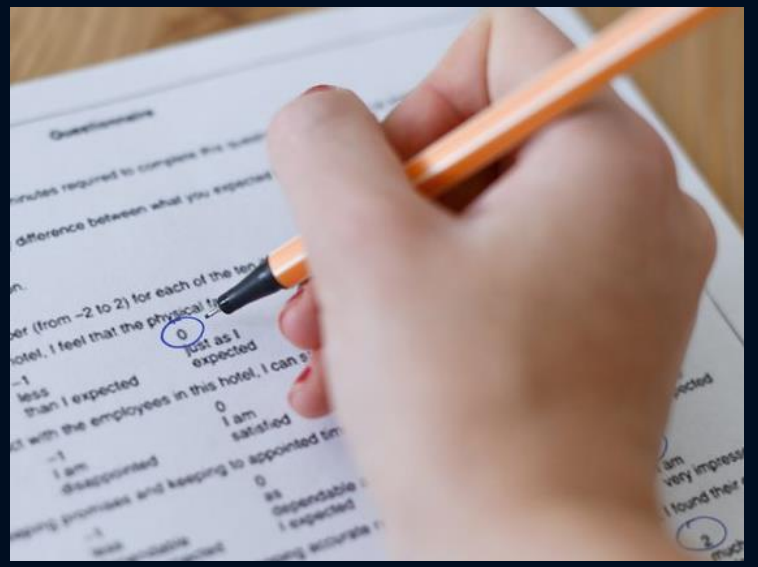

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	z	p
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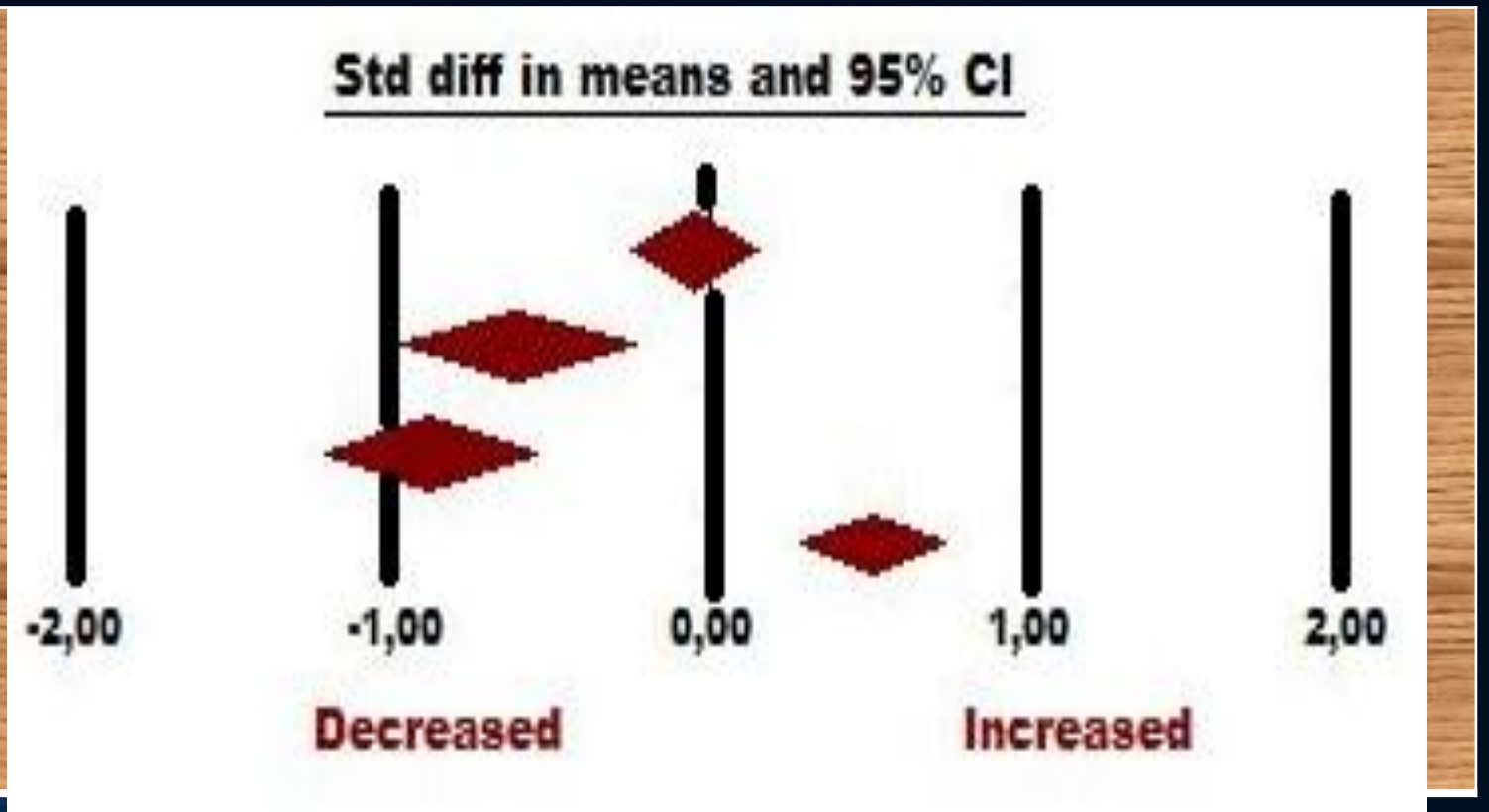

2. Results – change in cognitive complaints post-ECT

Moderator	Range	Mean
Interval (days)	0.13 to 657	45.6
Age (years)	37.7 to 68.3	54.0
Gender (%women)	37.0 to 80	62.7
Number of ECT sessions	5.0 to 23.0	10.1
Mean improvement in depressive symptoms	0.36 to 54.0	18.8
Cognitive burden (pooled change from pre-ECT)	-133.8 to 56.2	-1.72
Electrical dosage (mC)	98 to 1008	281

2. Results – change in cognitive complaints post-ECT

Moderator	k	z	p
Interval (days)	108	**0.08**	0.94
Age (years)	108	**3.02**	**0.003**
Gender (%women)	104	**2.59**	**0.009**
Number of ECT sessions	91	**0.33**	0.74
Mean improvement in depression	84	**2.65**	**0.008**
Cognitive burden	60	**1.54**	0.12
Electrical dosage	63	**0.41**	0.68

2. Results – change in cognitive complaints post-ECT

Within subgroups moderators effect

Time interval

Scale	k	z	p
CFQ	12	-0.13	0.90
CSSES	26	1.90	0.058
GMy	20	-1.10	0.27
SSMQ	47	-0.94	0.35

Electrode placement	k	z	p
Bitemporal	41	3.43	<0.001
RUL	39	-1.43	0.15
Mixed	28	1.00	0.31

Compared to pre-ECT cognitive complaints and as **time interval** increases:

- For BL ECT only, less complaints
- (less complaints with CSSES)

2. Results – change in cognitive complaints post-ECT

Within subgroups moderators effect

Age

Scale	k	z	p
CFQ	12	-0.41	0.68
CSSES	26	0.94	0.35
GMy	20	3.22	0.001
SSMQ	47	2.13	0.033

Electrode placement	k	z	p
Bitemporal	41	1.58	0.11
RUL	39	2.40	0.017
Mixed	28	3.89	<0.001

Compared to pre-ECT cognitive complaints and as **age** increases:

- For RUL and mixed ECT, less complaints
- less complaints with GMy and SSMQ

2. Results – change in cognitive complaints post-ECT

Within subgroups moderators effect

Gender

Scale	k	z	p
CFQ	12	0.64	0.52
CSSES	26	6.33	<0.0001
GMy	16	2.69	0.007
SSMQ	45	0.48	0.63

Electrode placement	k	z	p
Bitemporal	38	1.22	0.22
RUL	37	1.19	0.23
Mixed	27	3.65	<0.001

Compared to pre-ECT cognitive complaints and as **% women in sample** increases:

- For mixed ECT only, less complaints
- less complaints with CSSES & GMy

2. Results – change in cognitive complaints post-ECT

Within subgroups moderators effect

Number of ECT

Scale	k	z	p
CFQ	11	3.02	0.003
CSSES	26	0.026	0.98
GMy	12	-2.96	0.003
SSMQ	40	0.20	0.84

Electrode placement	k	z	p
Bitemporal	36	1.86	0.063
RUL	33	-1.39	0.17
Mixed	22	0.11	0.91

Compared to pre-ECT cognitive complaints and as **the number of sessions** increases:

- No significant effect of electrode placement
- less complaints with CFQ, but more complaints with GMy

2. Results – change in cognitive complaints post-ECT

Within subgroups moderators effect

Depressive symptoms

Electrode placement	k	z	p
Bitemporal	35	-2.36	0.018
RUL	31	-2.50	0.012
Mixed	18	-0.53	0.60

Scale	k	z	p
CFQ	8	Not enough data	
CSSES	26	-0.21	0.83
GMy	14	-1.70	0.09
SSMQ	34	-3.20	<0.001

Compared to pre-ECT cognitive complaints and as **depressive symptoms** decrease:

- For both BL & RUL ECT, less complaints
- With SSMQ, less complaints

2. Results – change in cognitive complaints post-ECT

Within subgroups moderators effect

Stimulus intensity (mC)

Electrode placement	k	z	p
Bitemporal	25	-2.79	0.005
RUL	33	-2.00	0.045
Mixed	18	-0.53	0.60

Scale	k	z	p
CFQ	6	Not enough data	
CSSES	23	2.71	0.007
GMy	9	Not enough data	
SSMQ	24	-0.79	0.43

Compared to pre-ECT cognitive complaints and as **stimulus intensity** decreases:

- For both BL & RUL ECT, less complaints
- With CSSES, more complaints

2. Results – change in cognitive complaints post-ECT

Within subgroups moderators effect

Cognitive burden

Electrode placement	k	z	p
Bitemporal	26	0.34	0.74
RUL	21	0.55	0.58
Mixed	13	-0.51	0.61

Scale	k	z	p
CFQ	4	Not enough data	
CSSES	16	0.93	0.35
GMy	9	Not enough data	
SSMQ	30	0.72	0.47

Compared to pre-ECT cognitive complaints and as **cognitive burden** increases:

- No significant effect of electrode placement
- No significant effect of scale used

3. Results – relationship between change in depression and change in cognitive complaints post-ECT

- 13 studies including 24 samples (**k**) and 1121 patients (**n**)
- Samples ranging 20 to 360 participants, mean n=62.3

k	Mean correlation	95% confidence interval		z	p	heterogeneity	
24	-0.51	-0.55	-0.46	-17.2	<0.0001	I^2=0%	p=0.65

- Fail-safe n=3156
- Higher symptoms' improvement moderately correlates with lower cognitive complaints post-ECT

Conclusions – subjective complaints & patients' demographics

- **Pre-post change in severity of subjective complaints**
  - **Increased age** associated with **less post-ECT complaints**: consistent with recent Swedish register study of subjective complaints (Brus et al., 2017; n=1212) and previous meta-analytical results on objective cognitive effects (Semkovska et al., 2011)

> higher age predicted smaller decrease in cognitive performance in verbal learning ($p = 0.0001$), in visual recognition ($p < 0.0001$) and in semantic memory retrieval ($p = 0.047$), whereas it predicted

  - **Increased % female** in sample associated with less cognitive complaints post-ECT, especially when patients are asked how severely ECT has affected their memory/cognition (GMy & CSSES)

Conclusions – subjective complaints & ECT technique

- **Rates of patients complaining** about ECT-associated cognitive problems correlate with the **number of ECT sessions**
- **Electrode placement** does **not** appear to affect neither the rate of patients complaining nor the pre-post change in subjective complaints
  - **except** for the interaction with time: patients who have received bitemporal ECT complain less as the time interval between the end of ECT and the subjective report increases
- **Pre-post change** **in subjective cognitive complaints** appears to be sensitive to:
  - Some **treatment parameters**: number of sessions & stimulus intensity **when patients specifically asked to report the severity of ECT-associated** memory/cognitive impairment (GMy or CSSES)

Conclusions – subjective complaints & persisting depressive symptoms

- **Pre-post change in subjective cognitive complaints** appears to be sensitive to:
  - Persisting depression **when measured as subjective severity** of memory impairment **compared to 'personal's best** functioning' (SSMQ)
- All studies that directly compare these variables find a **significant negative association**

Conclusions – subjective cognitive complaints

- **No association with objectively measured cognition**
  - Consistent with other studies in both depression and ECT
  - But this might be linked to the study's limitations:

    (a) global cognitive burden pooled (vs specific cognitive functions, e.g., attention, memory, etc.)

    (b) number of interactions tested: **more complex interactions might better explain subjective complaints**

    e.g., objective cognitive function might interact with persisting depressive symptoms and ECT treatment parameters

Conclusions – subjective cognitive complaints

- Scales used show **differential sensitivity** **to individual characteristics**
  - CSSES & GMy might be more appropriate to assess specifically ECT-associated memory complaints
  - SSMQ: assess subjective memory related to clinical state
  - CFQ: little evidence to support its usefulness in ECT research

- An **useful clinical indicator & potential psychoeducation tool**

Thank you for your attention!

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