Brief or ultrabrief? That is the question!

A review of the evidence for 0.5 msec pulse width ECT

Dr Shane Gill

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This presentation

- Will attempt to define the current status of 0.5 ms PW ECT in regard to the evidence
- Will cover the following areas:
  - What is the quality of evidence for 0.5 ms PW ECT?
  - Is 0.5 ms PW a wider version of ultrabrief ECT or a narrower version of brief pulse ECT?
  - Does 0.5 ms PW ECT have a role in RUL ECT?
  - Does 0.5 ms PW ECT have a role in BL ECT?
  - What further research do we need in 0.5 ms PW ECT?
  - If we are going to use 0.5 ms PW now, how should it be used?
What is the quality of evidence for 0.5 ms PW ECT?
The evidence for 0.5 ms PW
Systematic reviews and metanalyses

• There are no meta-analyses or systematic reviews involving ECT delivered with 0.5 ms PW ECT

– In contrast, for other PWs, there are systematic reviews/meta-analyses for:
  
  • 1ms high dose RUL vs 1ms BT¹
  • RUL 0.3 ms vs 1 ms²
  • 1 ms BF vs 1ms BT³

The evidence for 0.5 ms PW
Randomized controlled trials

• There are no double blind randomized controlled trials comparing 0.5 ms PW ECT with other pulse widths

  – In contrast, for other PWs, there are RCT’s for:
    
    • BT 1.5 ms vs BT 0.3 ms vs RUL 1.5 ms vs RUL 0.3 ms
    
    • RUL 0.3 ms vs 1 ms

The evidence for 0.5 ms PW
Stimulus Dose Relative to Seizure Threshold

• The optimum stimulus dose relative to seizure threshold (SDRST) has not been characterized for 0.5 ms PW, for any placement
  
  – In contrast, for other PWs, there are RCT’s studying SDRST for:
    • RUL and BT 1 ms at threshold vs 2.5x ST¹
    • RUL 1 ms at 2.5x ST vs 6x ST²
    • RUL 0.3 ms 4x ST vs 7x ST v 10x ST³, and in studies at 6x ST and 8x ST

So what is the evidence for 0.5 ms PW ECT?
The evidence for 0.5 ms PW
Comparison trials

- There are some comparison trials for 0.5 ms PW ECT
- Seizure Threshold 0.5 ms PW c.f. other PWs
  - Swartz (2000): 0.5 ms lower ST than 1 ms (LART)
  - Rosa (2013): 0.5 ms same ST as 0.3 ms (RUL)
  - Isenberg (2016): 0.5 ms lower ST than 2 ms (BT)
- Animal models of electro-convulsive shock (ECS)
  - O’Donovan (2014): no difference in models of clinical response or cognitive SE in 0.5 ms vs 0.3 ms
- Computational modelling of ECT stimuli
  - Bai (2012): 0.6 ms stimulus produced more focal and less intense stimulation than a 1 ms stimulus
Comparison trials with 0.5 ms PW
Efficacy and side effects

• **Clinical Efficacy**

  • Niemantsverdriet (2011): 0.25 ms and 0.5 ms BT equally effective, albeit with a very slow response (mean no of treatments in course = 17 and 13 respectively) - suggesting both are UB

  • Brus (2017) retrospective chart review in Sweden found UB (0.3 ms) remission rate was 29%, the 0.5 ms remission rate was 44% and the 1 ms PW remission rate was 56% - suggesting a linear relationship between PW and efficacy
Comparison trials with 0.5 ms PW
Efficacy and side effects

• Cognitive side effects
  
  • Warnell (2011) compared end of course MMSE scores with 0.5 ms BT (mean 29) than 1 ms BT (mean 23) suggesting less impairment in 0.5 ms BT
  
  • Ithal (2015) compared 0.5 ms BT with 1 ms BT in schizophrenia. Autobiographical memory was less impaired in 0.5 ms group at trend level (p = 0.06)
Other notable studies using a 0.5 ms pulse width

- Bjølseth and Dybedal (2015 & 2016)
  - Compared 0.5 ms RUL with 0.5 ms BF
  - Remission rates 51% and 39% respectively (ns difference) – somewhat lower than usually reported with 1 ms PW
  - Both had minimal cognitive side effects
  - Compare with Sienaert in 2009 - found remission rates for 0.3 ms RUL and 0.3 ms BF to be 44% and 34% respectively, also with minimal cognitive side effects

- Tor (2017) compared response rates in schizophrenia between 0.5 ms RUL, 0.5 ms BT and 1 ms BF – with no difference in mean response rates, around 64%, between groups
Conclusion #1

0.5 ms PW ECT shares more in common with 0.3 ms PW than 1 ms PW and should be considered a variant of UB ECT, not of BP ECT

- 0.5 ms PW ECT has lower seizure thresholds than 1 ms (and wider) ECT but a similar ST to 0.3 ms ECT
- Animal studies show 0.3 and 0.5 ms PW to have similar effects
- Studies using 0.5 ms PW show slower response times (and longer courses) than ECT with 1 ms PW – the same pattern as has been shown with 0.3 ms RUL c.f. 1 ms RUL.
- 0.5 ms PW ECT seems probably to have fewer cognitive side effects than 1 ms PW (as does 0.3 ms PW)
Conclusion #2

0.5 ms PW ECT is likely to have a limited role in RUL ECT

- 0.3 ms RUL ECT has a much better evidence base as a cognitive sparing alternative to 1 ms PW ECT, and should be 1st choice when sparing cognition is the priority.
- 1 ms RUL ECT (at 5-6x ST) has a much better evidence base of efficacy (shown to be non-inferior to BT) and is 1st choice if speed of response is the priority.
- It is possible that 0.5 ms RUL might be the best of both worlds – the efficacy of RUL 1ms and SE of RUL 0.3 ms, but it might equally be the worst of both worlds – the efficacy of 0.3 ms and the SE of 1 ms. We simply don’t know.
- RUL 0.5 ms is undoubtedly effective – with a similar efficacy to RUL 0.3 ms – so it may have a second line role when either 0.3 ms or 1 ms are unsuitable.
Conclusion #3

0.5 ms PW ECT’s major role, if it to have one, is likely to be in bilateral (esp. BT) ECT, where it might become the “ultrabrief option” for BT ECT that 0.3 ms is for RUL ECT

• 0.3 ms BT was shown to be ineffective (Sackheim 2008), and 0.3 ms BF was shown to have lower response rates and be even slower in response time than 0.3 ms RUL (Sienaert 2009), so 0.3 ms shouldn't be used in BL ECT. 0.5 ms is likely to be as brief as you can go in BL ECT.

• The evidence suggests 0.5 ms BT ECT has fewer cognitive SE than 1 ms BT ECT and is effective (e.g. Brus, Tor), although there are no head to head RCT’s to tell us if it is equally effective, or if less effective, by how much.

• It is worth noting that 0.5 ms is the default factory PW setting for Thymatron and the Thymatron manual does explicitly recommend using 0.5 PW for BL ECT
Conclusion #4

We need to do more research to characterize 0.5 ms PW in order for it to stand alongside 0.3 ms RUL and 1 ms RUL, BF and BT as 1st line options

- We need RCTs comparing 0.5 ms PW with 1 ms PW for each of the 3 major placements, to see how it compares in terms of efficacy and cognitive SE, and to determine for which placements it has the best role. My guess: BT
- We need to characterize the optimum SDRST for 0.5 ms PW, in terms of best balance between efficacy and SE.
  - Since 6-8x ST is optimum for 0.3 ms RUL and 4-6x for 1 ms RUL, 6 x ST is a safe guess for RUL 0.5 ms
  - The optimum SDRST for BT and BF is likely to be > 1.5x ST, given the less intense stimulation with 0.5 ms (e.g. Bai). My guess is around 2x ST for BT and 3x ST for BF - if you go higher you may lose the cognitive advantage of using it
How should 0.5 ms PW be used in current ECT practice?

- If 0.3 ms RUL has been less effective, but 1 ms RUL has had too many SE, RUL 0.5 ms may be worth a trial in the hope of achieving a better balance between efficacy and SE. If using 0.5 ms RUL, use a 6 x ST dose.

- If a bilateral placement is indicated (e.g. RUL ECT has been less effective), but cognitive sparing is a priority, consider 0.5 ms BT rather than 1 ms BT. There is less evidence supporting 0.5 ms BF. For BT ECT, probably use 2-3x ST, maybe slightly higher if using BF rather than BT.

- If efficacy (esp speed of response) is the priority, then 1 ms RUL 5-6x ST, or 1ms BL ECT 1.5x ST (e.g. if RUL unsuitable) probably should be used.

- Despite the paucity of formal evidence, the anecdotal testimony of those who use 0.5 ms PW is that it is effective and the SE profile is favourable.