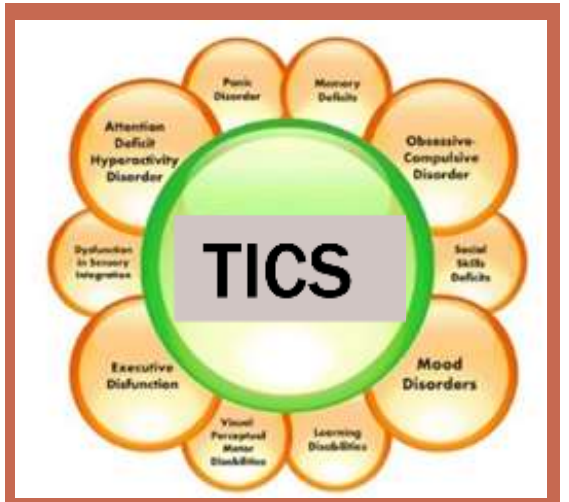
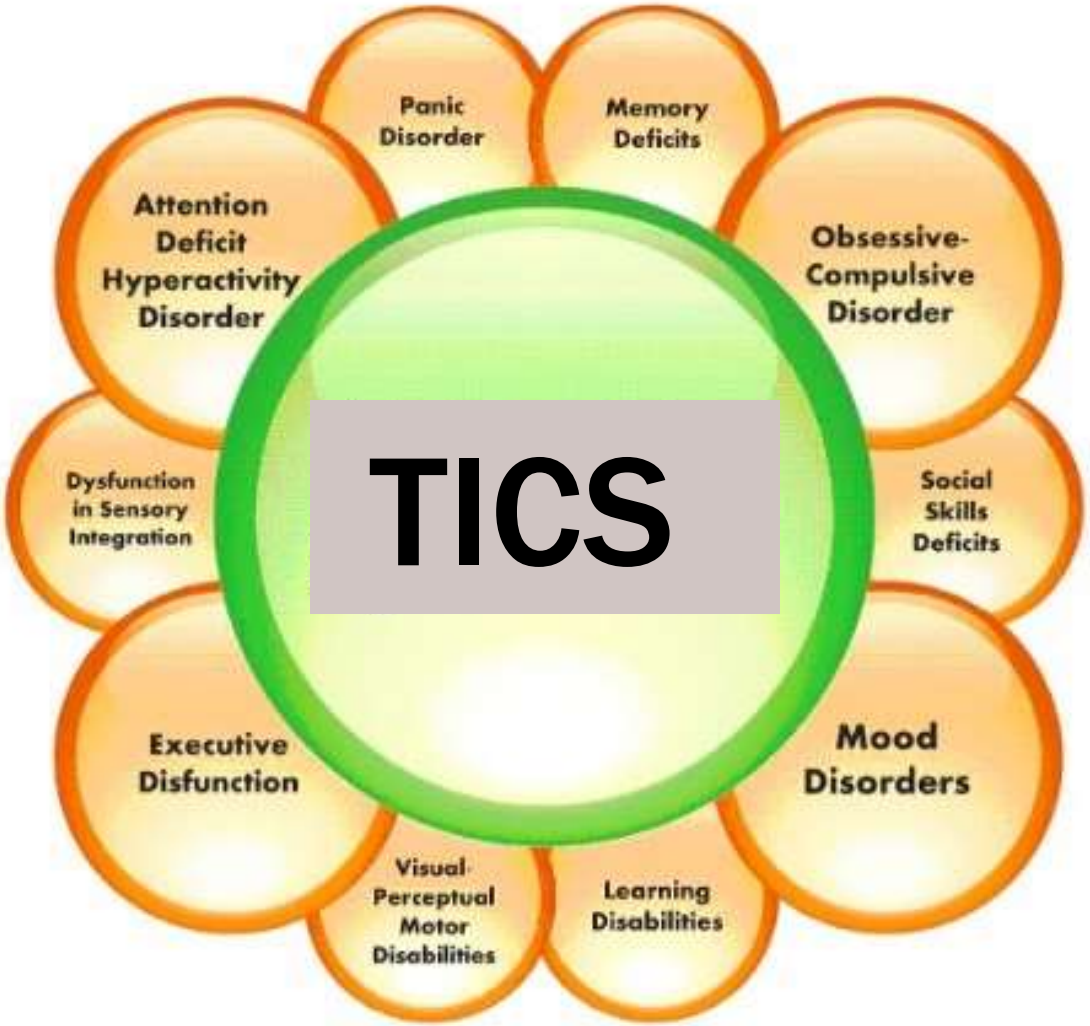
PHARMACOLOGICAL MANAGEMENT OF TIC DISORDERS AND CO-MORBIDITIES

Joe Kilgariff
Trainee Advanced clinical Practitioner
NMP/ Behavioural Therapist



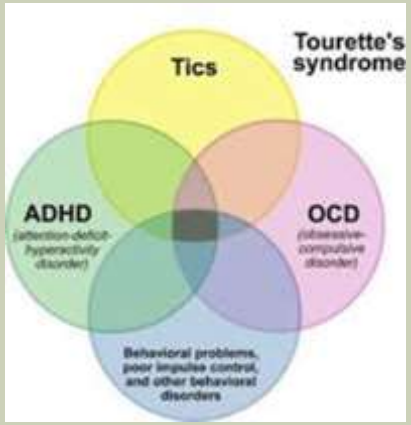
PHARMACOLOGICAL MANAGEMENT OF TICS AND CO MORBIDITIES.

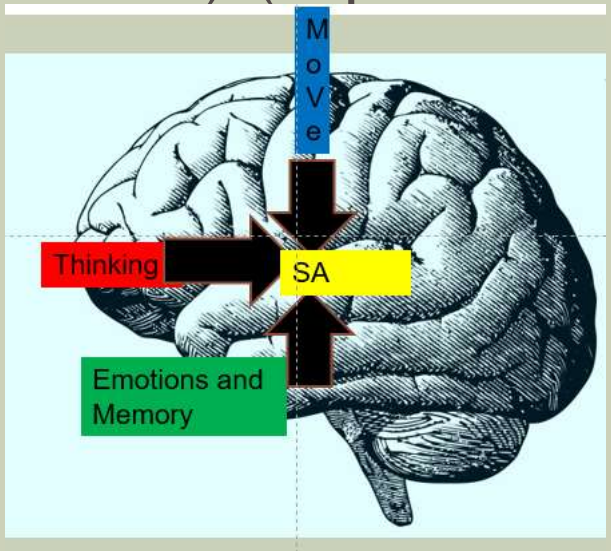


MEDICATION

- First rule - treatments should be main symptom targeted and often the symptom which is causing most impairment / distress to the child. which might not be the tics themselves but could be social based, school based, friendship based etc.

- Tics vs ADHD vs ASD vs OCD/B's - generally shared neurology (frontostriatal loop)
- (patients can have very separate thoughts to parents wishes – there can be quite a few hidden factors (such as intrusive thoughts, bullying, obsessions etc). (important to speak separately if possible)





TIC MEDICATION

- 4 Main sources

- 1) Hollis et al (2016)clinical effectiveness and patient perspective of different treatment stratergies for tics in children and adolescents with tourette syndrome: - a systematic review and qualitative analysis: Health Technol Assess Jan 20 (4), 1-450. https://www.journalslibrary.nihr.ac.uk/hta/hta20040/#/abstract
- 2) Besag,F. Vasey, M.J. Kim, L. Chowdhury, U and Stern, S. Pharmacological treatment for Tourette syndrome in children and adults: What is the quality of the evidence? A systematic review. Journal of Psychopharmacology. (2021) 1-25. https://journals.sagepub.com/doi/10.1177/02698811211032445?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed
- 3) European clinical guidelines for Tourette syndrome and other tic
- disorders—version 2.0. Part III: pharmacological treatment. *European Child & Adolescent Psychiatry* (2022) 31:425–441 https://doi.org/10.1007/s00787-021-01899-z
- Maudsley Prescribing guidelines 14th ed. (Taylor, D. M., Barnes, T. R. E., & Young, A. H. (2021). The Maudsley prescribing guidelines in psychiatry (14th ed.). John Wiley & Sons).

TIC MEDICATION - SUMMARY

- "The first preference should be given to psychoeducation and to behavioural approaches, as it strengthens the patients' self-regulatory control and thus his/her autonomy. Because behavioural approaches are not effective, available, or feasible in all patients, in a substantial number of patients pharmacological treatment is indicated, alone or in combination with behavioural therapy".
- The largest amount of evidence supports the use of dopamine blocking agents, preferably aripiprazole because of a more favourable profile of adverse events than first- and second-generation antipsychotics. Aripiprazole is often the drug of first choice both in children and adults in Europe (ES - 0.74).
- However in cases of co-existing attention deficit hyperactivity disorder (ADHD), clonidine and guanfacine considered effective (ES - 0.72)
- Maudsley Prescribing guidelines in Uk – (14th ed) favours Clonidine and Guanfacine as first line due to side effect profile in tic disorder treatment of children.

- Besag, et al 2021

- “There are relatively few placebo-controlled trials of commonly prescribed medications. Studies are often of poor quality and short duration. There is evidence for the efficacy of each medication, but no drug is clearly superior. Clonidine and guanfacine are better tolerated than antipsychotics, but less effective”.
- “Pharmacological interventions frequently achieve short-term efficacy, but the evidence that medication is the best long-term solution remains questionable”.

- (based on 17 RCT’s)

MEDICATION FOR TICS – FIRST LINE

- Centrally acting α2 Adrenergic agonists - action on presynaptic receptors (Clonidine) or Post synaptic receptors (Guanfacine), Increasing nor-adrenergic release and improving frontal striatal signalling, modulating working memory function and supporting cognitive flexibility.

Clonidine	Guanfacine
Slower initial dosing	Faster initial dosing
Slower titration – more increments	Faster titration – 1mg, 2mg, 3mg 4mg
More evidence and available research	Less evidence – hardly any for tics
Cheaper - £4-18 pound per 112 tablets - (4x25mcg a day)	More expensive - £56 (1mg) - £76 (4mg) per month
Less interactions	More interactions CYP3A4 inducers CYP3A4 and CYP3A5 inhibitors QT prolonging medicinal products
Less selective - Clondine is a non selective α2 agonists (and Imidazoline receptor agonist (sympathetic NS) (more antihypertensive / less NA regulation	More selective – Guanfacine is a selective α2A agonists (Elbe, 2020) (more NA regulation / less antihypertensive)
More subtle dosing -	Much less subtle dosing

CLONIDINE VS GUANFACINE

- Both helpful for ADHD. Guanfacine better in this respect
- Clonidine - 3-5mcg/kg in two-three divided doses Initiated at 25mcg nocte, then generally increased in 25mcg increments. Majority at night.
- Guanfacine (INTUNIV) - initially 1mg once daily at night. Titrated up to 4mg children and 7mg adolescents (depending on weight) [SmPC) .
- Titrate with low doses - **Start low – go Slow -** weekly to fortnightly increments if possible. (Treat like ASD for sensitivity).

TIC MEDICATION CONT.

- Antipsychotic medication is used as second line treatment for those children that do not respond to clonidine from a tic severity point of view. Effective in adults population and with OCD/B comorbidities.
- Aripiprazole used first unless co-morbid ASD with Challenging behaviour or anxiety / arousal – then Risperidone.
- Quetiapine (sedation), haloperidol (treatment resistive), Olanzapine (mood stabalisation).
- Aripiprazole – initiated - 0.5 - 1mg OD nocte – target range 5-10mg
- Risperidone – initiated - 0.25-0.5mg OD nocte – target range 2-4mg

ADHD - MEDICATION

FIRST LINE IF APPROPRIATE = METHYLPHENIDATE

% of short vs long acting

100%
(Mph Hcl - Instant release)

Test dose, top up dose following extended release or if higher potency is needed.

22/78
(Osmotic PR)

First line extended release- milder side effects profile – 10-12 hrs duration

30/70
(Equasym XL)

Sits in between Delmosart PR and Medkinet XL 8-10 hrs duration.

50/50
(Medikinet XL)

Higher potency - used when early morning speed of onset is preferable.6-8 hrs duration.

If Stimulants not effective or not tolerated or problematic to tics.

Atomoxetine (STRATTERA)
If tics do not require Treating

Clonidine, Guanfacine (INTUNIV)
If tics do require treating
Or clinician prefers.

If Methylphenidate is tolerated and effective but suboptimal response

Lisdexamfetamine (Elvanse)
Or instant release sulphate

MOOD AND ANXIETY

- Fluoxetine has a better evidence base for depression (initially 4mg – target 20mg – max 60mg)
- Sertraline has a better evidence base for anxiety (initially 25mg – target 100mg – max 200mg).
- (change from one to other if ineffective for either)
- Both used to treat OCD (max doses often required) + OCB's (obsessive compulsive behaviours linked to tic disorders)
- Sleep – Melatonin – up to 10mg. Clonidine, Promethazine.

REFERENCES

1) *Besag,F. Vasey, M.J. Kim, L. Chowdhury, U and Stern, S. Pharmacological treatment for Tourette syndrome in children and adults: What is the quality of the evidence? A systematic review. Journal of Psychopharmacology. (2021) 1-25.*

2) Hollis et al (2016)clinical effectiveness and patient perspective of different treatment stratergies for tics in children and adolescents with tourette syndrome: - a systematic review and qualitative analysis: Health Technol Assess Jan 20 (4), 1-450

3) Roesnner,V,. Et al., European clinical guidelines for Tourette syndrome and other tic disorders—version 2.0. Part III: pharmacological treatment. European Child & Adolescent Psychiatry (2022) 31:425–441 https://doi.org/10.1007/s00787-021-01899-z

4) Elbe, D, 2020, Switching from Clonidine Immediate-Release to Guanfacine Extended-Release (J Can Acad Child Adolesc Psychiatry). 2020 May; 29(2): 121–123. Published online 2020 May 1.

5)Stahl, S.M, and Mignon, L., (2010), *Antipsychotics: Treating psychosis, Mania and Depression*. [2nd Edition],Cambridge University Press, New York.

6) *Taylor, D. M., Barnes, T. R. E., & Young, A. H. (2021). The Maudsley prescribing guidelines in psychiatry (14th ed.). John Wiley & Sons.]*