

TREATING THE CHILD WITH ADHD

-

***DO PSYCHOLOGICAL INTERVENTIONS
WORK?***

DON'T SHOOT THE MESSENGER!

Edmund Sonuga-Barke March 2016
Financial Disclosures (last 3 years)

	Lecturer	Consultancy	Research Grant	Royalties
Medice	X			
Janssen-Cilag	X			
Shire	X	X	X	
Neurotech solutions		X		
New Forest Parenting Package				X
MRC, ESRC, NIHR, Wellcome Trust			X	
KU Leuven, Aarhus University U of Copenhagen		X		

DO NON-PHARMA ADHD TREATMENTS WORK? DEPENDS WHAT YOU MEAN! DEPENDS WHO YOU ASK!

- Do they control core ADHD symptoms?
- Do parents think things have improved?
- Do they reduce other common co-occurring problems?
- Do they improve everyday functioning?
- Do they change parent's attitudes/behaviours to child?
- Do they promote parental wellbeing?
- Do they strengthen family functioning?
- Do they increase QoL in the long run?

OVERVIEW

- Why is a stringent systematic assessment of non-pharma interventions needed?
- EAGG methodology and strategy.
- Initial Findings - Do non-pharmacological interventions reduce ADHD symptoms? (Sonuga-Barke et al., 2013).
- Update and extensions for psychological interventions.
 - Behavioural Interventions (Daley et al., 2014).
 - Cognitive Training (Cortese et al., 2015).
 - Neurofeedback (Cortese et al., 2016).
- Early intervention – a way forward?

NEED FOR THE RECENT EAGG REVIEWS

- Medication - front-line treatment - effective but limited
 - normalization – rare
 - key functional outcomes untouched
 - long term effects - uncertain
 - side effects – frequent
 - resistance from parents and clinicians
 - societal concern about the increasing prescribing rates.
- Effective non-pharmacological treatments are essential.
- European ADHD Guidelines Group has produced influential treatment guidelines in the past.
- About five years ago we decided to extend these guidelines to non-pharmacological treatments.
- We had loads of expertise and thought we knew the literature back to front – easy then!

THE EUROPEAN ADHD GUIDELINES GROUP

KNOWLEDGABLE AND PASSIONATE ABOUT ADHD TREATMENT

Sergeant (Netherlands: Chair); Banaschewski (Germany); Brandeis (Switzerland/Germany); Buitelaar (Netherlands); Coghill (UK); Cortese (US/Italy); Danckaerts (Belgium); Daley (UK); Dittman (Germany); Doepfner (Germany); Ferrin (UK/Spain); Fallisard (France); Hollis (UK); Konofal (France); Lecendreux (France); Rothenberger (Germany); Santosh (UK); Sayal (UK); Sonuga-Barke (UK/Belgium); Simonoff (UK); Stevenson (UK); Steinhausen (Switzerland/Denmark); Stringaris (UK); Thompson (UK); Van der Oord (Belgium); Wong (Hong Kong/UK); Zuddas (Italy); Santosh (UK); Holtman (Germany); Taylor (UK).

INDEPENDENT EVIDENCE AS THE ANTEDOTE FOR INTRINSIC BIAS IN CLINICAL SCIENCE AND PRACTICE

- Naturally, parents hold strong views about what's best for their child when mental health problems arise - shaped by personal values.
- Clinicians' decisions are not immune from such values but evidence based approaches attempt to temper their impact.
- Scientists provide the evidence - but their research choices are also prone to, often unconscious, biases.
- Trials to generate, and meta-analyses to review, evidence can, inadvertently, become vehicles for promoting favoured therapies while giving a spurious sense of objectivity.

A MIX OF VIEWS AND A BALANCE OF POTENTIAL COMPETING INTERESTS

A majority of EAGG members have some declared competing financial interests in relation to (i) work for pharmaceutical companies (research, consultancy, advisory boards and travel bursaries), (ii) producers of dietary supplements (research, consultancy and advisory board memberships) and (iii) the development and commercial exploitation of non-pharmaceutical therapies such as parent training, cognitive training and neurofeedback (research, consultancy, training and spin out companies).

A STRINGENT SYSTEMATIC REVIEW OF THE EVIDENCE WAS NEEDED

- What we found was that NPTs are recommended on the basis of systematic reviews and meta-analyses.
- Given this we initially considered a light touch – review of reviews - to generate our evidence.
- However – when we looked closely we found the existing reviews unsatisfactory in a number of ways –
 - Methodological issues
 - non-RCT designs - lack of blinding of outcomes
 - Trial inclusion criteria
 - non-ADHD patients - non-ADHD outcomes

On balance we did not feel the reviews were of sufficient quality to recommend NPT for ADHD.

Unfortunately some heavy lifting was needed.

INDEPENDENT EVIDENCE AS THE ANTEDOTE FOR INTRINSIC BIAS IN CLINICAL SCIENCE AND PRACTICE

- Naturally, parents hold strong views about what's best for their child when mental health problems arise - shaped by personal values.
- Clinicians' decisions are not immune from such values but evidence based approaches attempt to temper their impact.
- Scientists provide the evidence - but their research choices are also prone to, often unconscious, biases.
- Trials to generate, and meta-analyses to review, evidence can, inadvertently, become vehicles for promoting favoured therapies while giving a spurious sense of objectivity.
- Stringent, transparent and reliable evaluations cut through biases to provide a bias free estimate of the value of a treatment.

EAGG METHODOLOGY

INCLUSION CRITERIA

- RCT (including non-blinded and cross over trials)
- Peer reviewed
- ADHD diagnosis (or meeting validated cut-off).
- 3 to 18 years
- Comorbidity – Common comorbidities OK but not rarer comorbidities specifically selected for study (e.g. groups selected to have both ADHD and Autism).
- ADHD outcome.
- Suitable control (placebo/attention-active/wait list/TAU).
 - *Meds can be included in TAU except where non-pharma is planned as an add on to meds.*

OUTCOMES

- The primary outcome was ADHD symptom change (standard mean different).
- The issue of blinding addressed by comparing two outcomes.
 - *MPROX* – *The ADHD assessment most proximal to the intervention setting.*
 - Typically parent ratings except for school-based interventions.
 - Usually the primary outcome so most available.
 - *P-BLIND* – *Only ADHD outcomes where the rater was likely to be unaware of treatment allocation.*
 - *any ADHD outcome of placebo controlled trials*
 - *teacher ratings on home delivered treatments*
 - *where there was more than one option the most blinded was chosen. (i.e., teacher ratings on placebo controlled trials).*

INITIAL ESTIMATES

SONUGA-BARKE ET AL., 2013

NON-PHARMACOLOGICAL TREATMENTS REVIEWED

PSYCHOLOGICAL INTERVENTIONS

- a) Behavioural interventions*
- b) Neurofeedback*
- c) Cognitive training*

DIETARY INTERVENTIONS

- d) Restrictive elimination diets.*
- e) Artificial food colour exclusion.*
- f) Free fatty acid supplements.*
- g) Other supplements*

NON-PHARMACOLOGICAL TREATMENTS REVIEWED

PSYCHOLOGICAL INTERVENTIONS

- a) Behavioural interventions*
- b) Neurofeedback*
- c) Cognitive training*

DIETARY INTERVENTIONS

- d) Restrictive elimination diets.*
- e) Artificial food colour exclusion.*
- f) Free fatty acid supplements.*
- g) Other supplements*

BEHAVIOURAL PARENT TRAINING

- Based on reinforcement and social learning models.
- Delivered 1-2-1 or in groups/at home or at the clinic - varies in duration/intensity.
- Trains parents and/or teachers in ways to modify their child's behaviour by manipulating behavioural antecedence and consequences and modeling appropriate behaviours.
- Antecedents - Restructures child's social and physical environment to ensure clear rules and expectations - communicated clearly and improves parent-child relationship quality.
- Consequences – Positively reinforces appropriate behaviours and negatively reinforces inappropriate behaviours.
- Often implemented alongside social, organisational and academic skills training at home and at school.

PARENT TRAINING – BIG BUSINESS?

**managing
the
fiant
child**
DE TO PARENT TRAINING

SSSELL A. BARKLEY

BUT ARE POSITIVE EFFECTS OF BPT ON CORE ADHD SYMPTOMS EXPECTABLE?

BPT DEVELOPED FOR CONDUCT PROBLEMS ASSUMED TO EMERGE FROM COERCIVE PARENT-CHILD INTERACTIONS WHICH CAN BE REMEDIED BY PARENTS' ALTERED RESPONSE TO CHILDRENS' BEHAVIOUR.

IS THIS A REASONABLE EXPECTATION FOR ADHD?

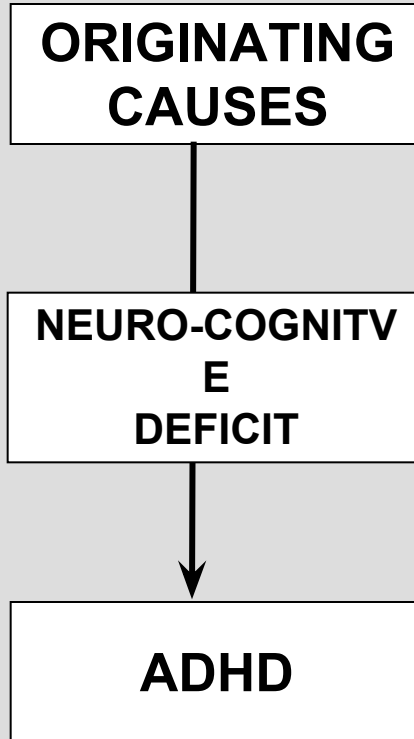
ARE THERE OTHER MORE EXPECTABLE POSITIVE BENEFITS OF BPT?

***PARENTING BEHAVIOUR?
CHILD CONDUCT PROBLEMS?***

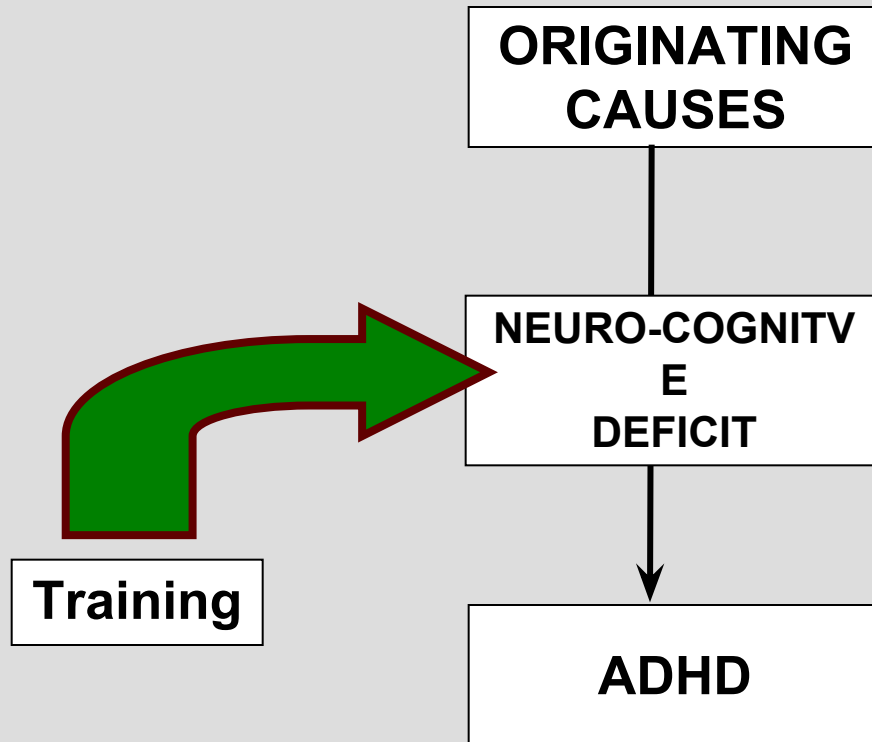
**If we want to target ADHD symptoms
do we need a radically different
approach to treatment?**

**A translational model holds out the
promise that psycho-therapeutic
innovation can be built on scientific
discoveries about ADHD
pathogenesis.**

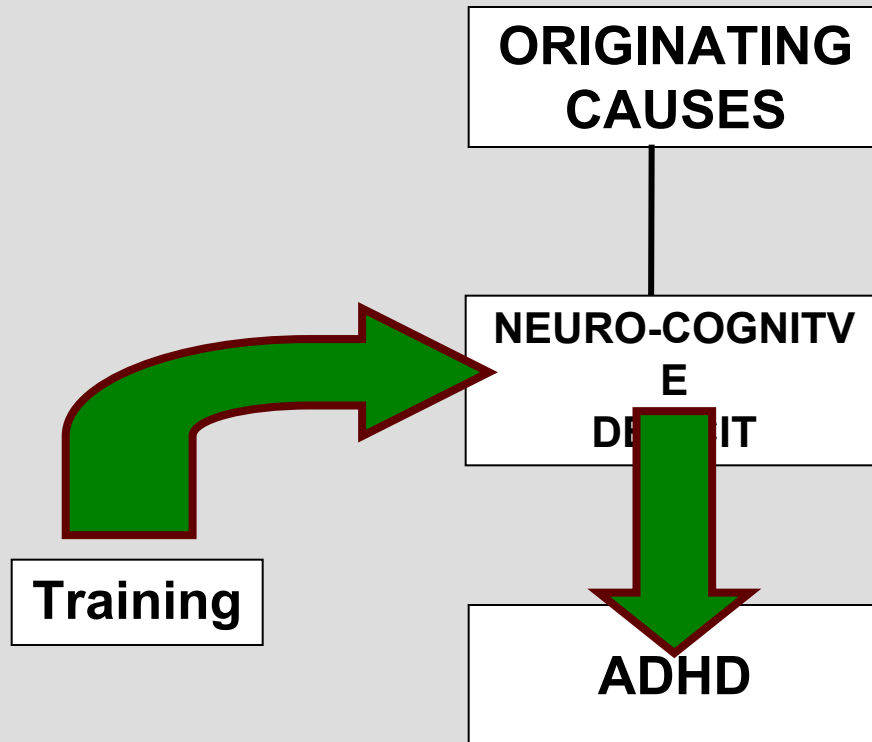
COGNITIVE MEDIATORS OF CAUSAL PATHWAYS BECOME TARGETS FOR REMEDIATION



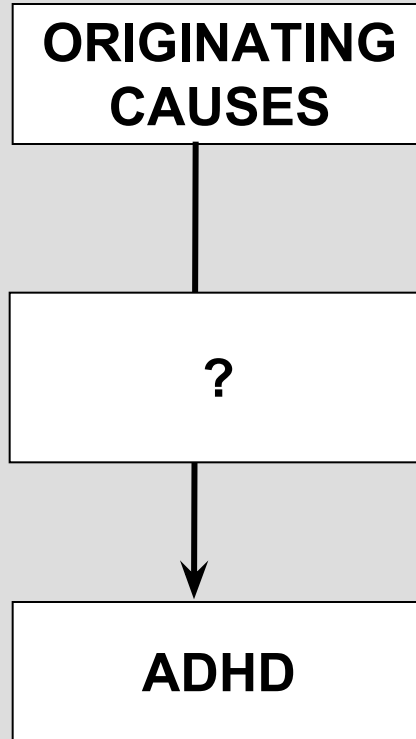
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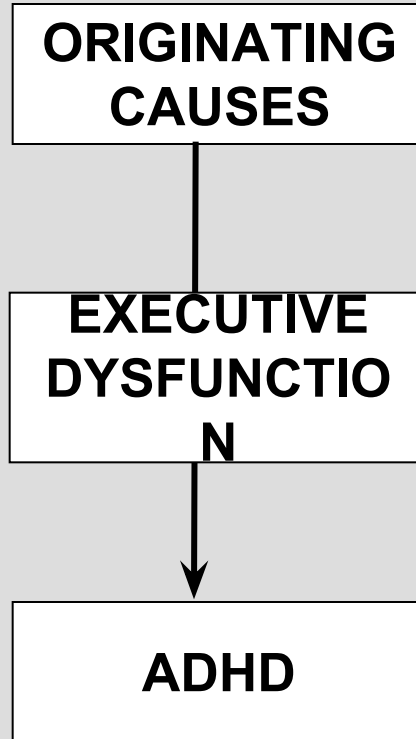
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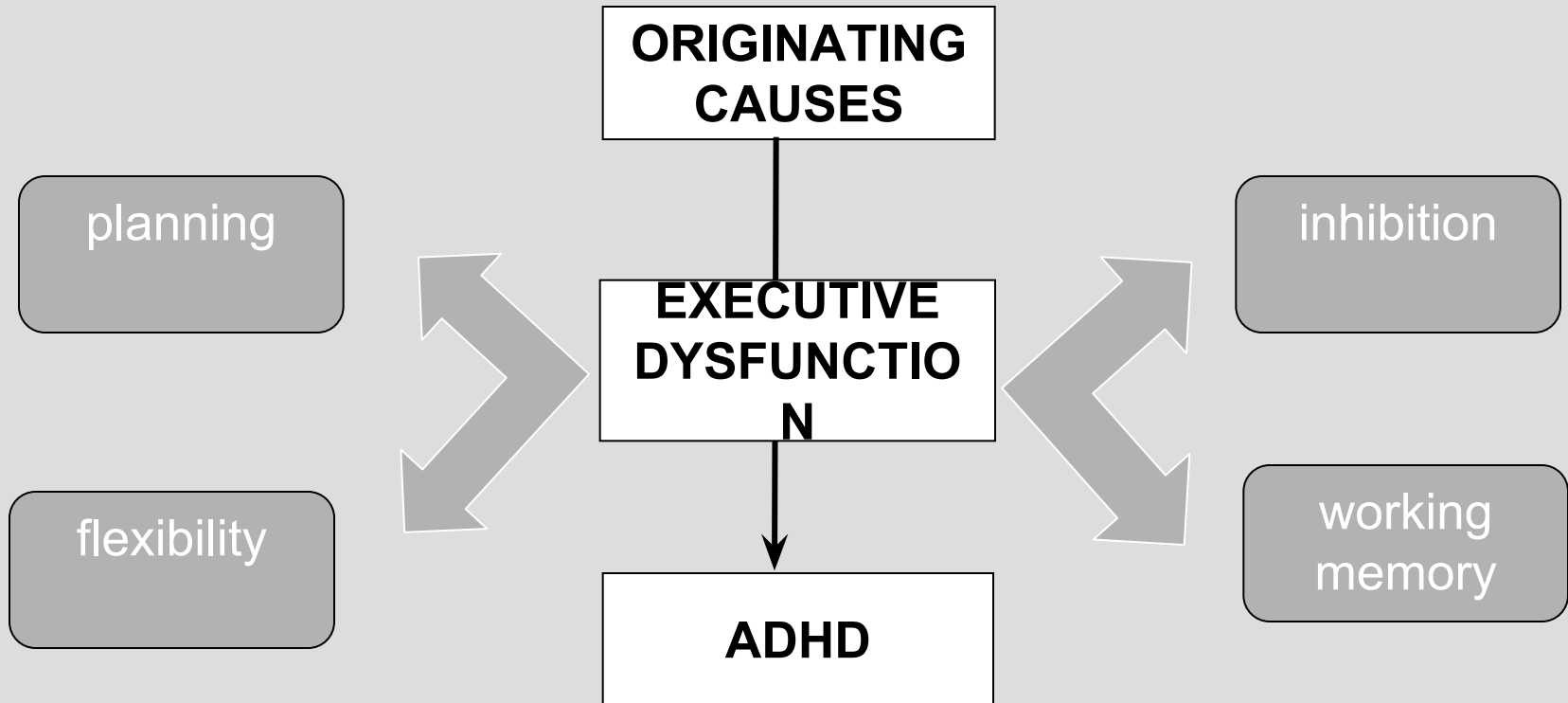
**FOUNDATIONAL QUESTION
WHAT COGNITIVE DEFICITS MEDIATE ADHD CAUSAL
PATHWAYS?**



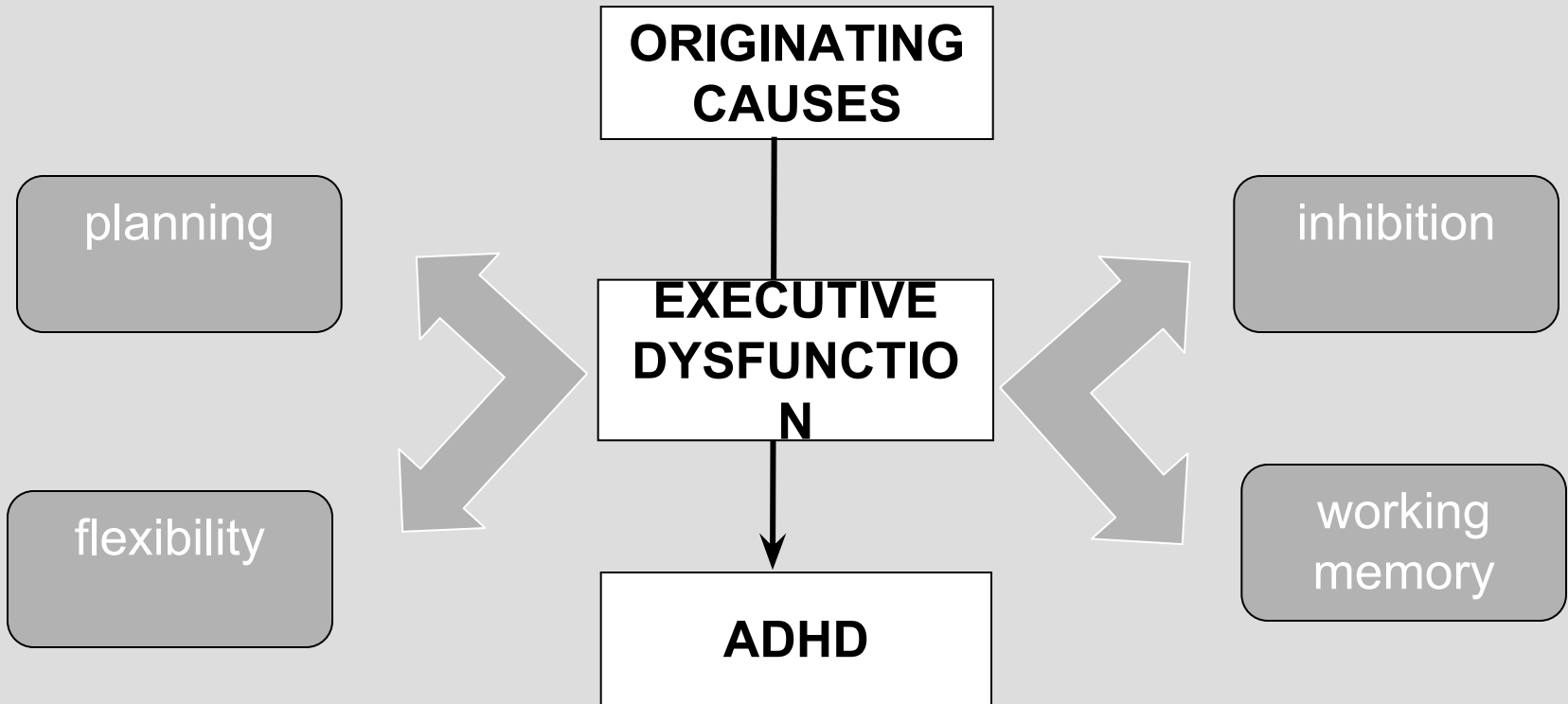
THE BARKLEY HYPOTHESIS



THE BARKLEY HYPOTHESIS



THE BARKLEY HYPOTHESIS



**THIS MODEL IS CONSISTENT WITH MUCH
NEUROSCIENCE DATA**

***ADHD IS ASSOCIATED WITH A BROAD RANGE OF EF
DEFICITS***

**FROM STRATEGY TO TACTICS
RESPONDING TO THE NEUROPSYCHOLOGICAL
IMPAIRMENT IN ADHD**



“SCALPEL”

OR

“SHOTGUN”

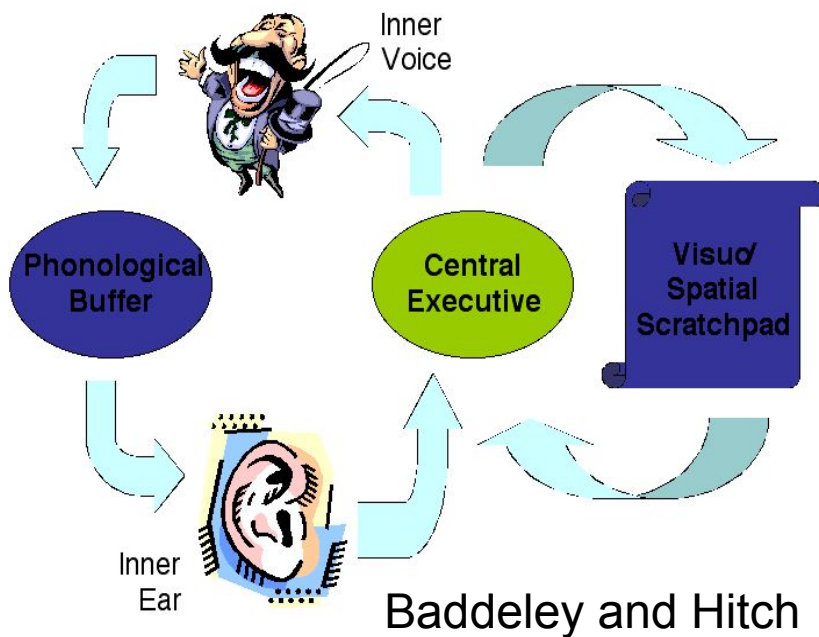


THE WORKING MEMORY TRAINING “SCALPEL”



WORKING MEMORY TRAINING FOR ADHD – A PRECISION APPROACH TO COGNITIVE TRAINING

“A mental workbench” (Klingberg, 2009)
“Dynamic brain process that helps us create and maintain internal representations” (Tannock, 2010)



Goldman-Rakic

**ROBO MEMORY BE COGMED IS THE MOST WIDELY
USED AND THOROUGHLY EVALUATED COGNITIVE
TRAINING APPROACH**

**THE PIONEERING WORK BY TORDEL KLINGBERG AND HIS TEAM AT
THE KAROLINSKA**



THE MULTI-SYSTEMS TRAINING “SHOTGUN”



THE WORKS OF BRAIN: A GAMIFIED MULTI- PROCESS TRAINING



Note: Tiles on the right light up in a random sequence; the child has to reproduce the order of the tiles; with every correct reproduced trial, the child sees more of the reward that can be earned in the game (here painting the house of the parents of the main character Brian).

NEUROFEEDBACK

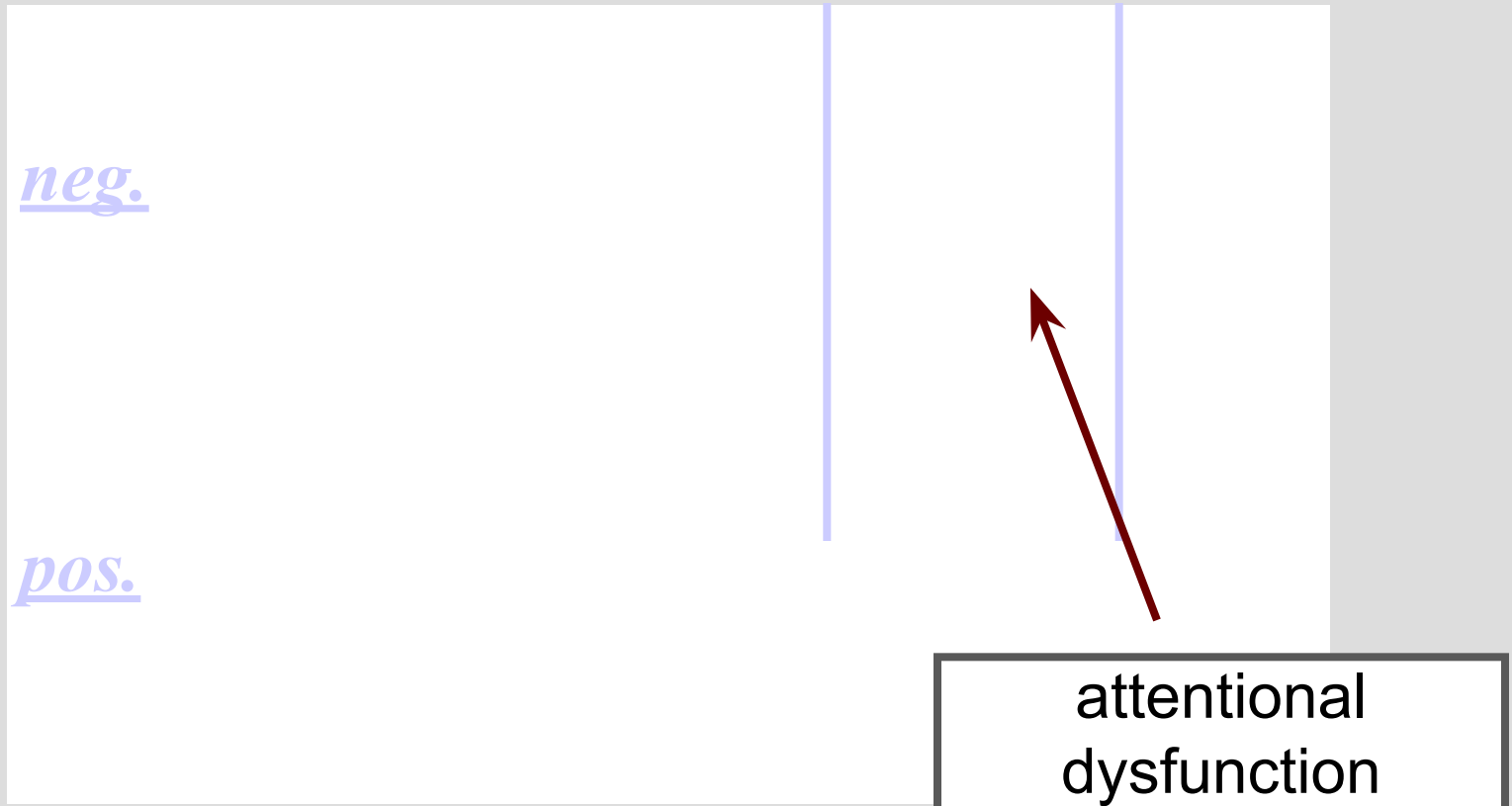
Rationale: Patients can self regulate brain activity to alter aberrant patterns using reinforcement procedures.

Intervention: EEG measures of interest are converted into visual or acoustic signals and automatically feedback in real time to the patient using computers.

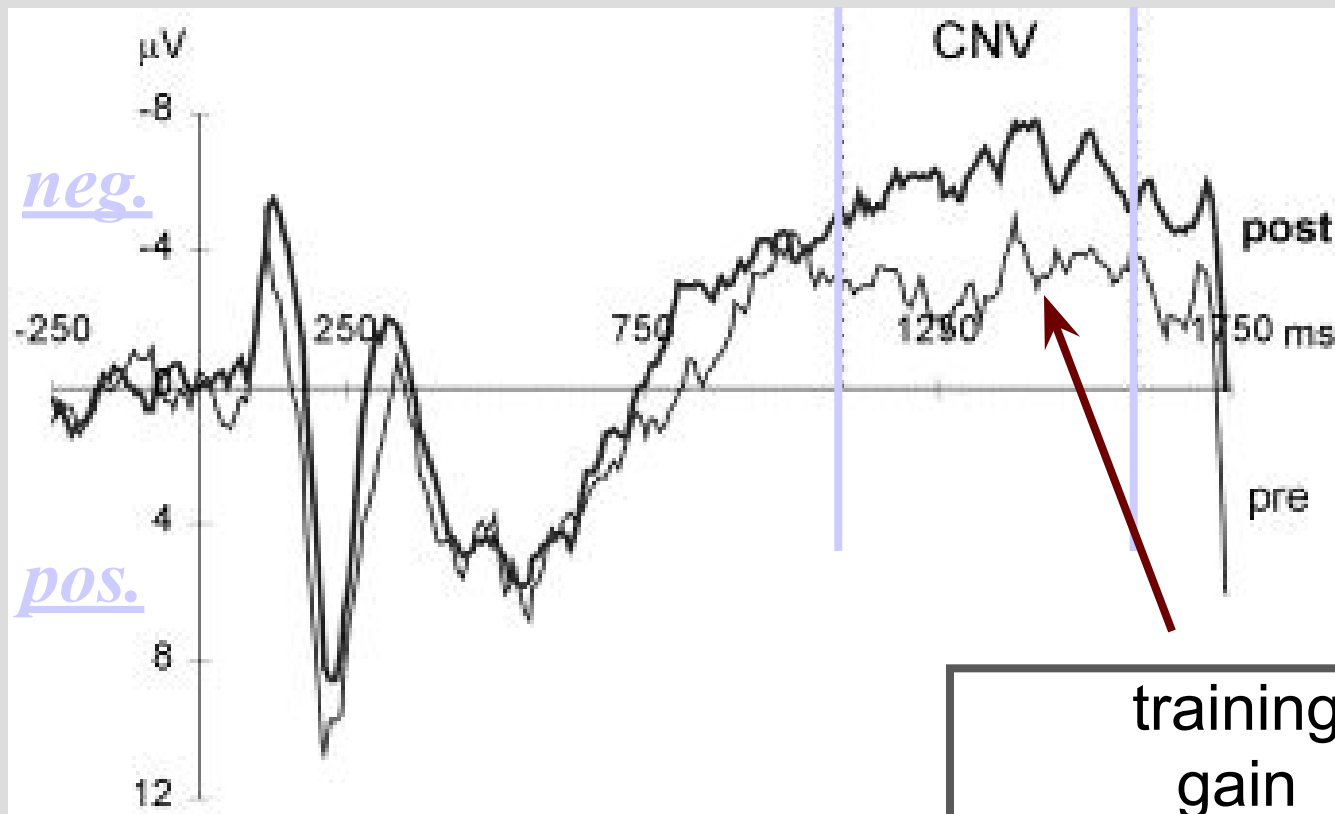
Two general approaches.

- (i) **EEG frequency band training** - alter the balance between slow and fast EEG.
- (ii) **Slow cortical potentials training** - regulates cortical excitation thresholds by focusing on activity elicited by external cues (so called evoked potentials).

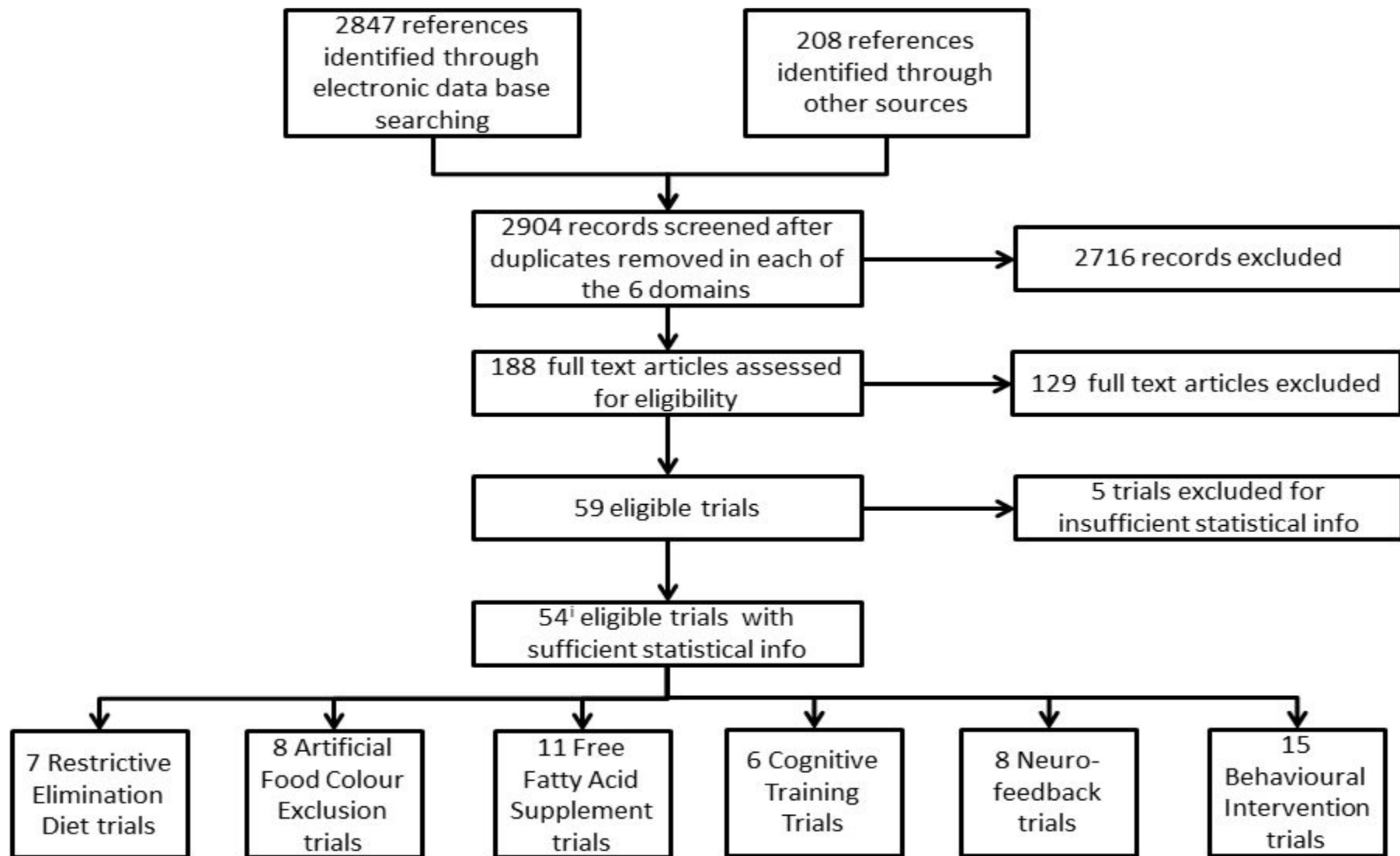
NORMALISATION OF EVENT-RELATED POTENTIALS



NORMALISATION OF EVENT-RELATED POTENTIALS

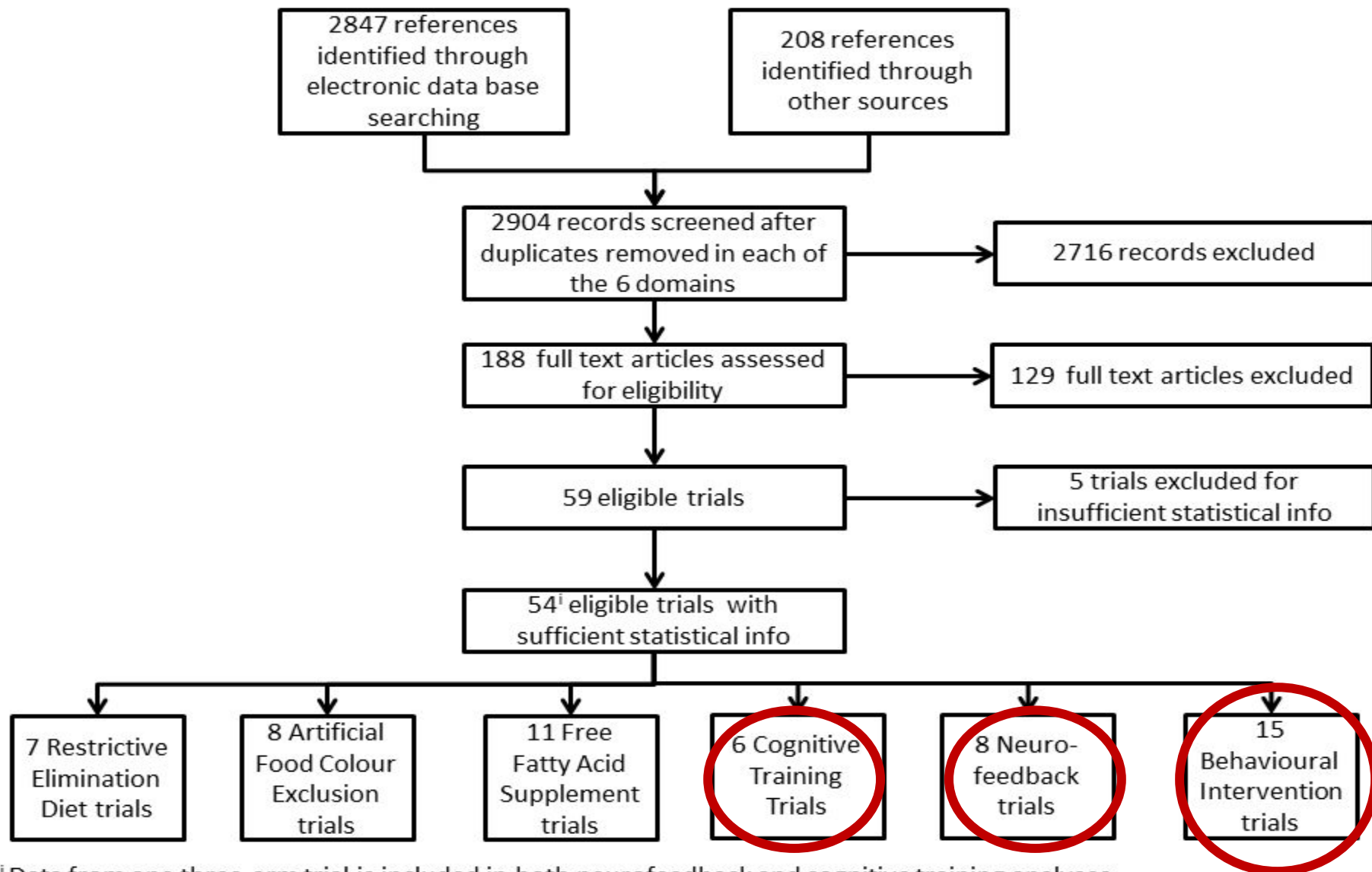


RECORDS SCREENED/TRIALS INCLUDED



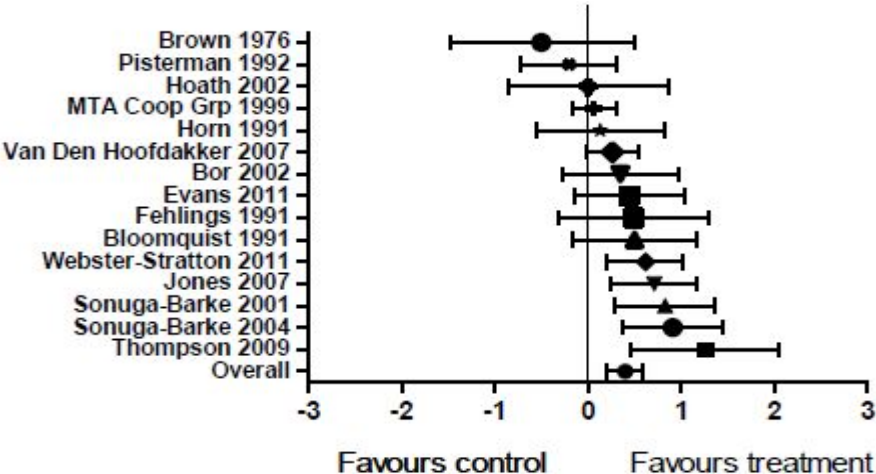
ⁱ Data from one three-arm trial is included in both neurofeedback and cognitive training analyses

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BEHAVIOURAL INTERVENTIONS

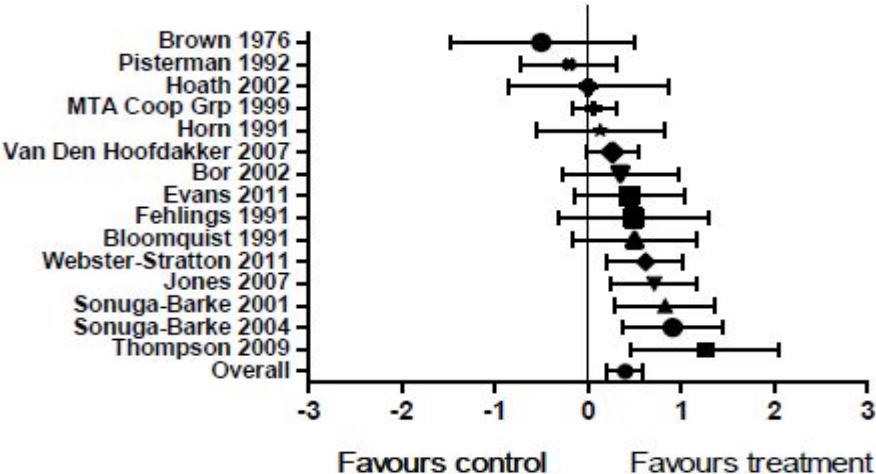


Overall SMD (95% CI) = 0.40 (0.20, 0.60)
Test for overall effect: $Z = 2.99$, $p = 0.003$

M-PROX

ES = 0.40*

BEHAVIOURAL INTERVENTIONS



Overall SMD (95% CI) = 0.40 (0.20, 0.60)
Test for overall effect: $Z = 2.99$, $p = 0.0004$

M-PROX

ES = 0.40*

P-BLIND

ES = 0.02

COGNITIVE TRAINING

M-PROX

ES = 0.64*

P-BLIND

ES = 0.24

NEUROFEEDBACK

M-PROX

ES = 0.59*

P-BLIND

ES = 0.29

ADHD – COMPARISON ACROSS TREATMENTS

N=7

INITIAL CONCLUSION

There were significant effects but only for MPROX.

“Better evidence for efficacy from blinded assessments is required for behavioral interventions, neurofeedback, cognitive training,before they can be supported as treatments for core ADHD symptoms.” (Sonuga-Barke et al., 2013).

We also recognised that psychological interventions may be valuable in remediating other areas of dysfunction and this need to be assessed.

THE REACTION – Chronis-Tuscano, et al (2013)

- Restricting analysis to RCTs
- Focus on core ADHD symptoms only
- Inclusion of interventions known non-effective
- PBLIND effect simply a lack of generalisation to school
- Inclusion of only published trials
- Medication effects – *reliant soley on information in reports.*
- Is it not enough just to change parents perceptions?
- Lack evidence of efficacy or evidence of lack of efficacy?
- Should we not hold medication up to the same standard? – *yes!*

“Properly powered, RCTs with blinded, ecologically valid outcome measures are urgently needed, especially in the psychological treatment domain.” (Sonuga-Barke et al., 2013)

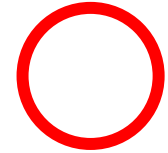
UPDATES AND EXTENSIONS BEHAVIOURAL INTERVENTIONS

Added Domains

- Parent: parent mental health; parent self concept; positive negative parenting
- Child: conduct problems; academic and social skills

THE EUROPEAN ADHD GUIDELINES GROUP

KNOWLEDGABLE AND PASSIONATE ABOUT ADHD TREATMENT

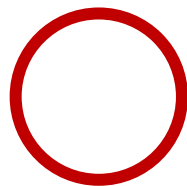


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RECORDS SCREENED/TRIALS INCLUDED



RECORDS SCREENED/TRIALS INCLUDED



CHILD OUTCOMES – SUMMARY (SMD)

Vertical line

Dashed vertical line

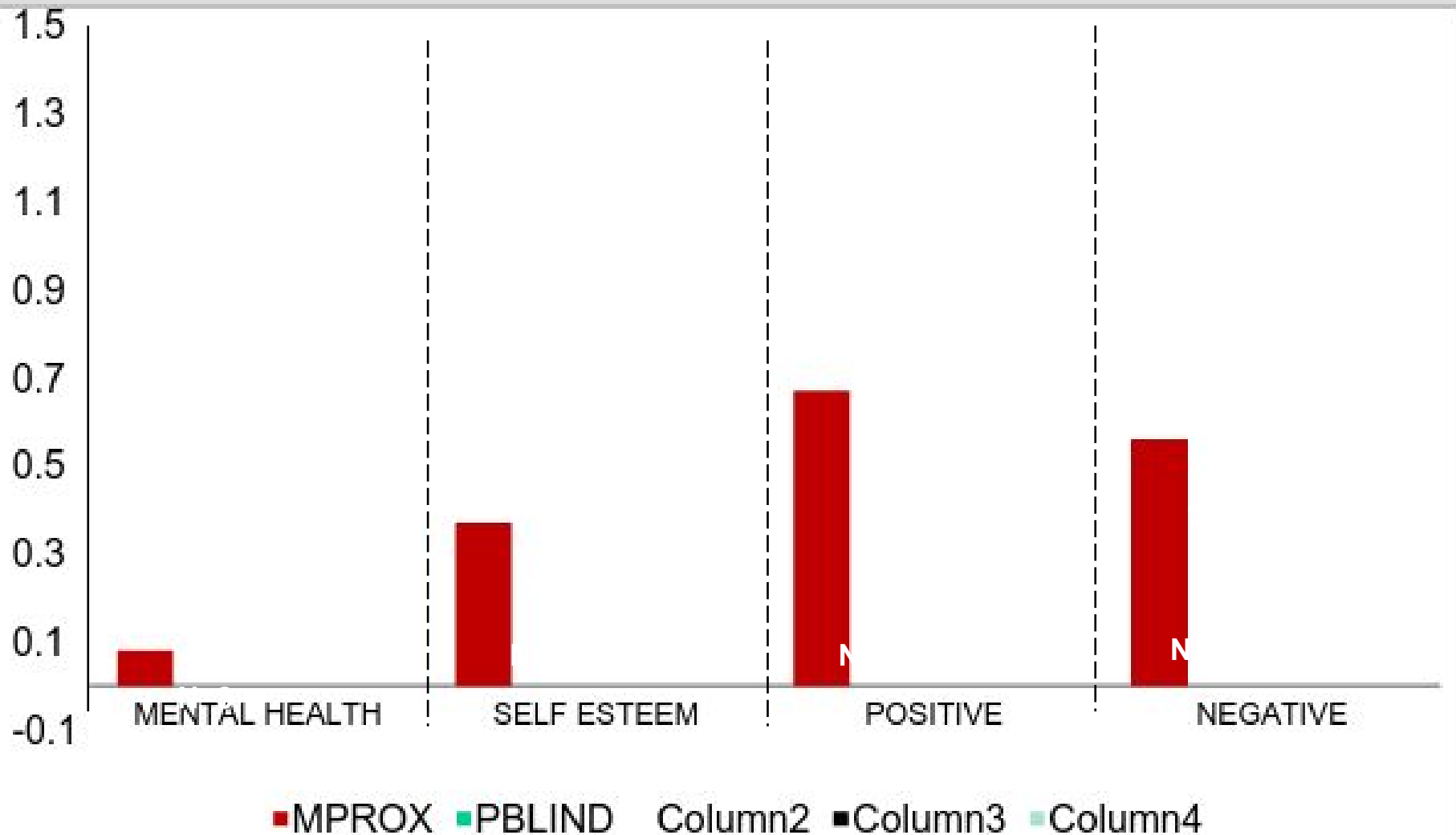
Dashed vertical line

Dashed vertical line

CHILD OUTCOMES – SUMMARY (SMD)

N=7

PARENT OUTCOMES – SUMMARY (SMD)



PARENT OUTCOMES – SUMMARY (SMD)

Vertical line

Dashed vertical line

Dashed vertical line

Dashed vertical line

Cognitive Training for Attention-Deficit/Hyperactivity Disorder: Meta-Analysis of Clinical and Neuropsychological Outcomes From Randomized Controlled Trials

UPDATES AND EXTENSIONS

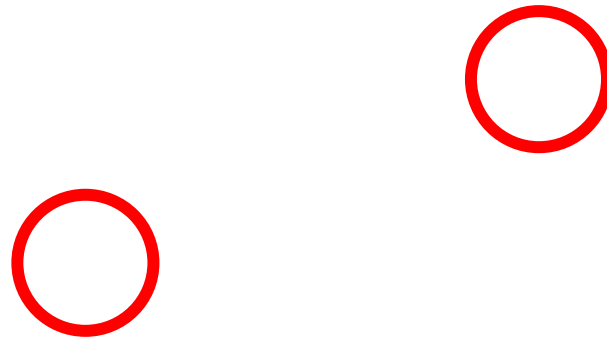
COGNITIVE TRAINING

Added Domains

- Neuropsychology: working memory, inhibition & attention
- Academic: Reading and Maths

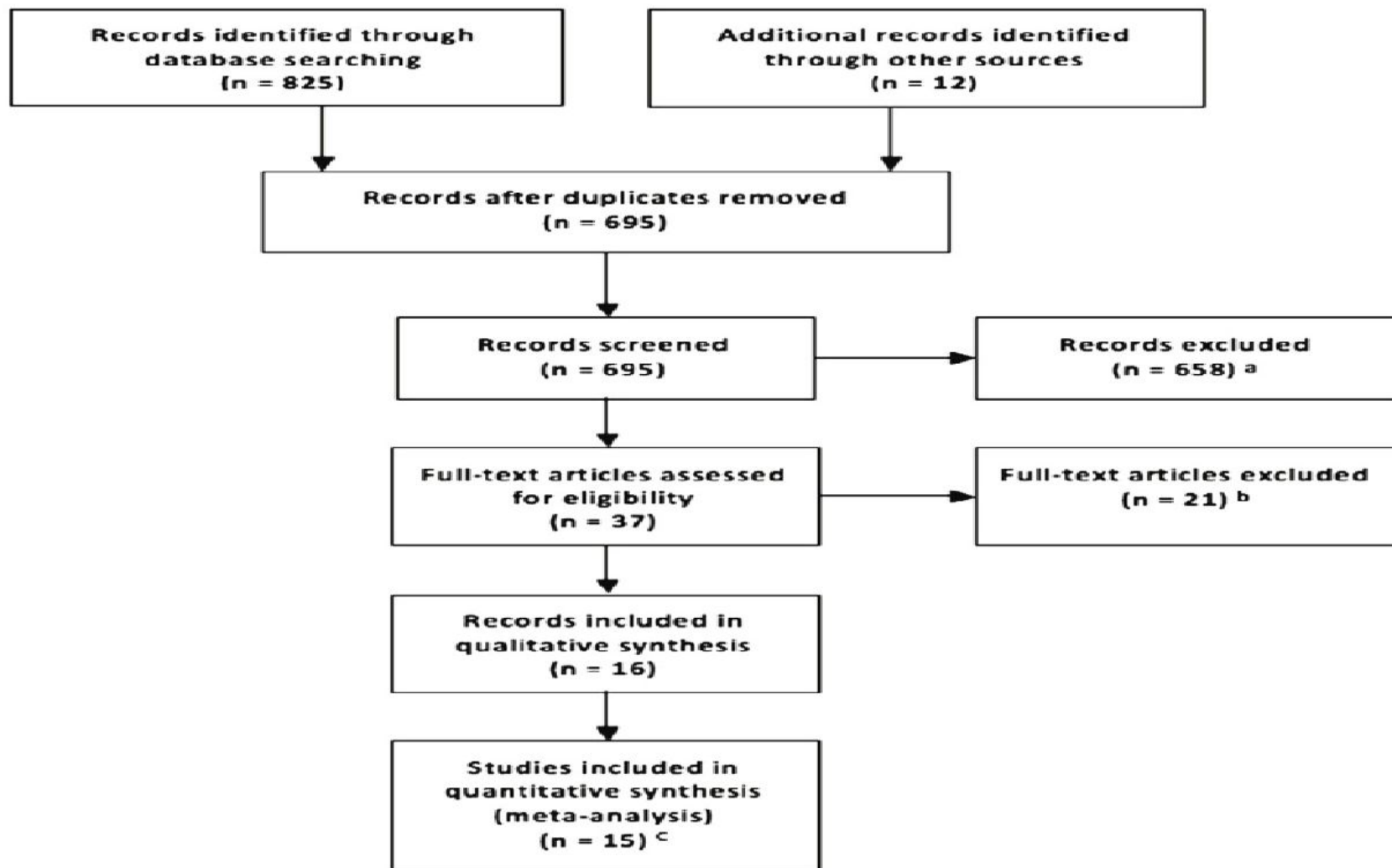
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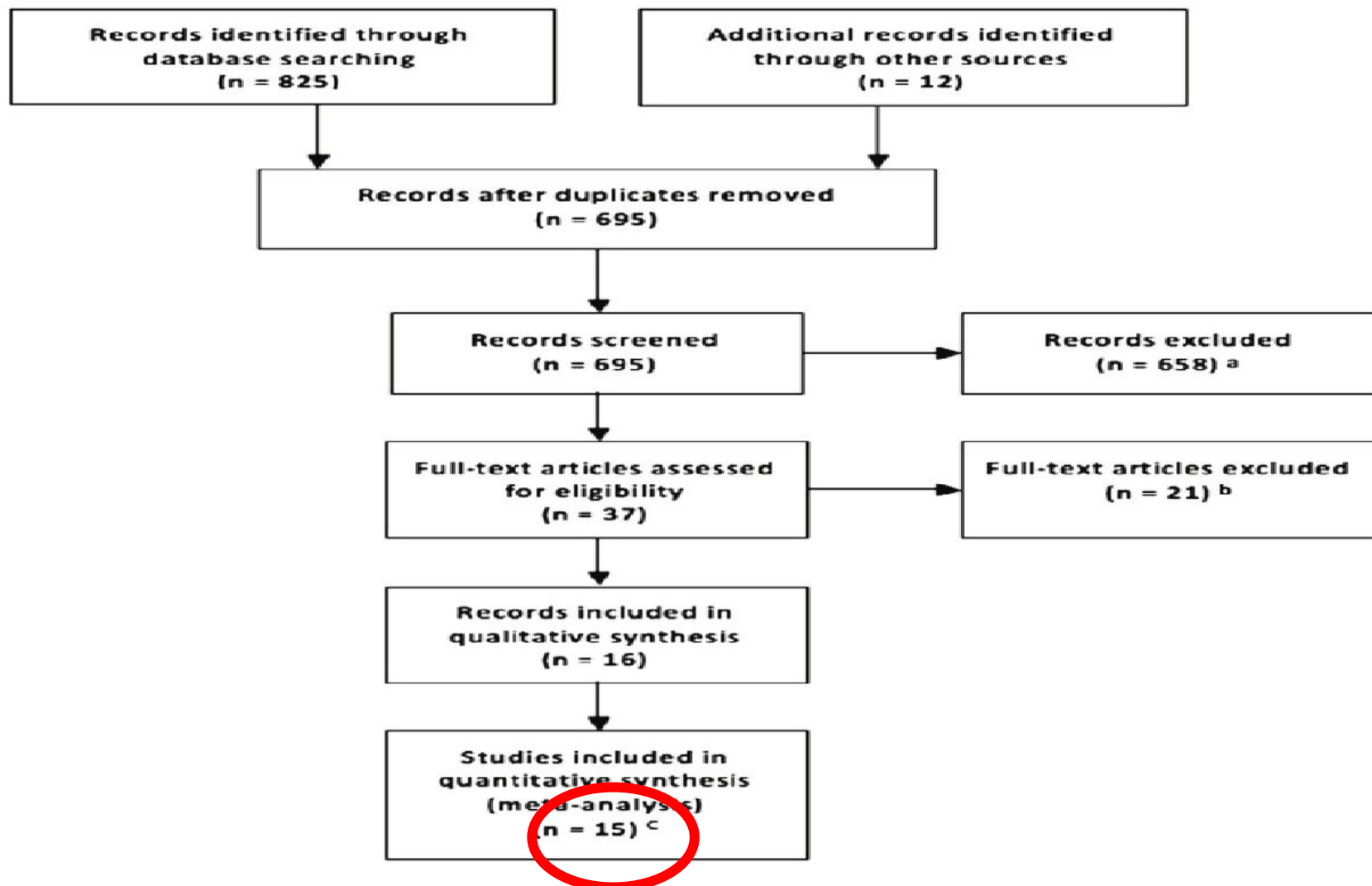


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RECORDS SCREENED/TRIALS INCLUDED



RECORDS SCREENED/TRIALS INCLUDED



ADHD SYMPTOMS (SMD)

N=6

no analysis
possible for
PBLIND

no analysis
possible for
PBLIND

ADHD SYMPTOMS (SMD)

Effects mainly driven by changes in
inattention

N=6

no analysis
possible for
PBLIND

no analysis
possible for
PBLIND

NEUROPSYCHOLOGICAL OUTCOMES (SMD)

no analysis
possible for
WMT

N=5

no analysis
possible for
WMT

THE SUPERIORITY OF MULTIPROCESS TRAINING



UPDATES AND EXTENSIONS

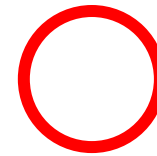
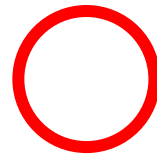
NEUROFEEDBACK

Added Domains

- Symptoms of inattention and hyperactivity/impulsivity.
- Neuropsychology: inhibition & attention

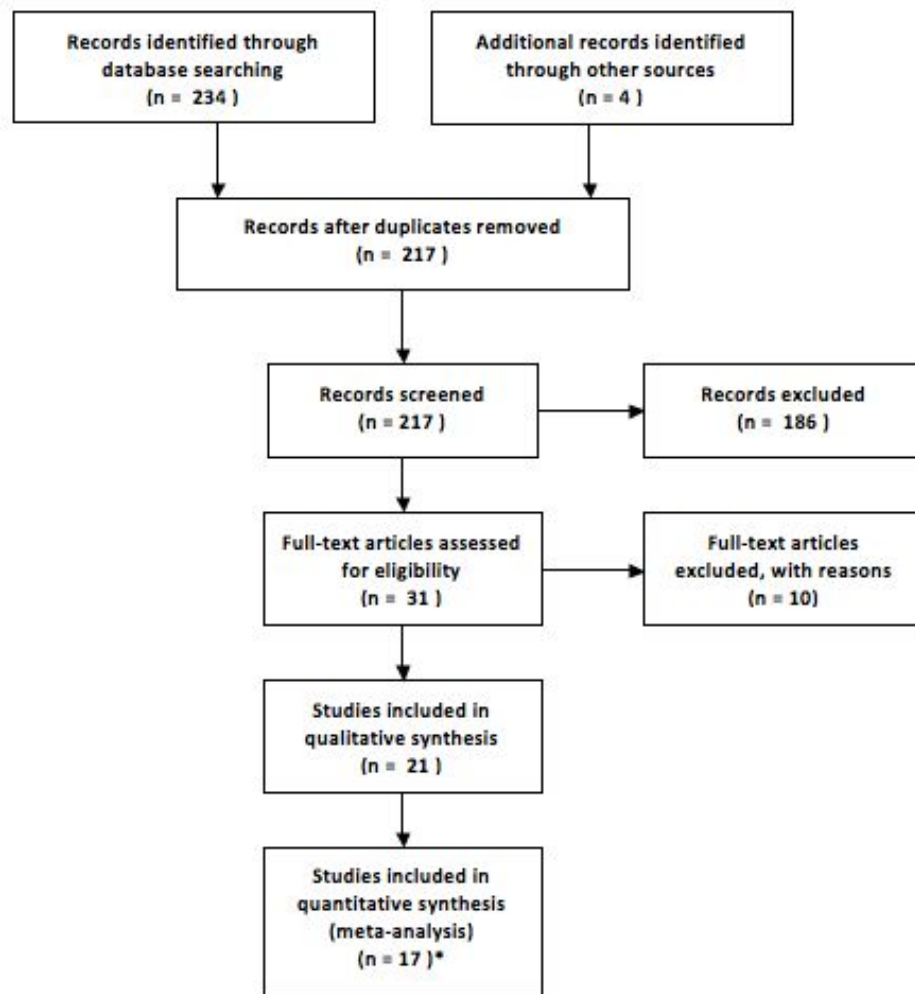
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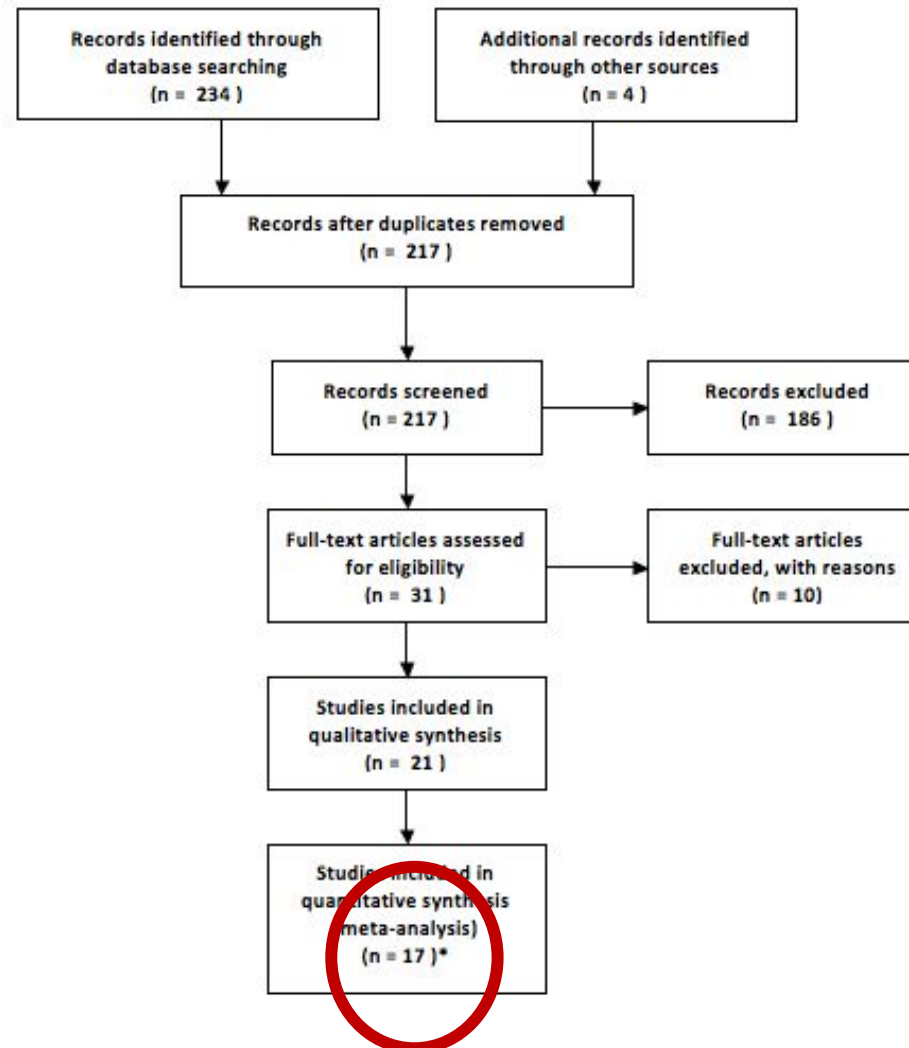


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RECORDS SCREENED/TRIALS INCLUDED



RECORDS SCREENED/TRIALS INCLUDED



ADHD SYMPTOMS (SMD)

N=8

ADHD SYMPTOMS (SMD)

**No evidence of effects on
neuropsychological deficits**

N=8

INITIAL VERSUS UPDATED SMDS *MPROX*

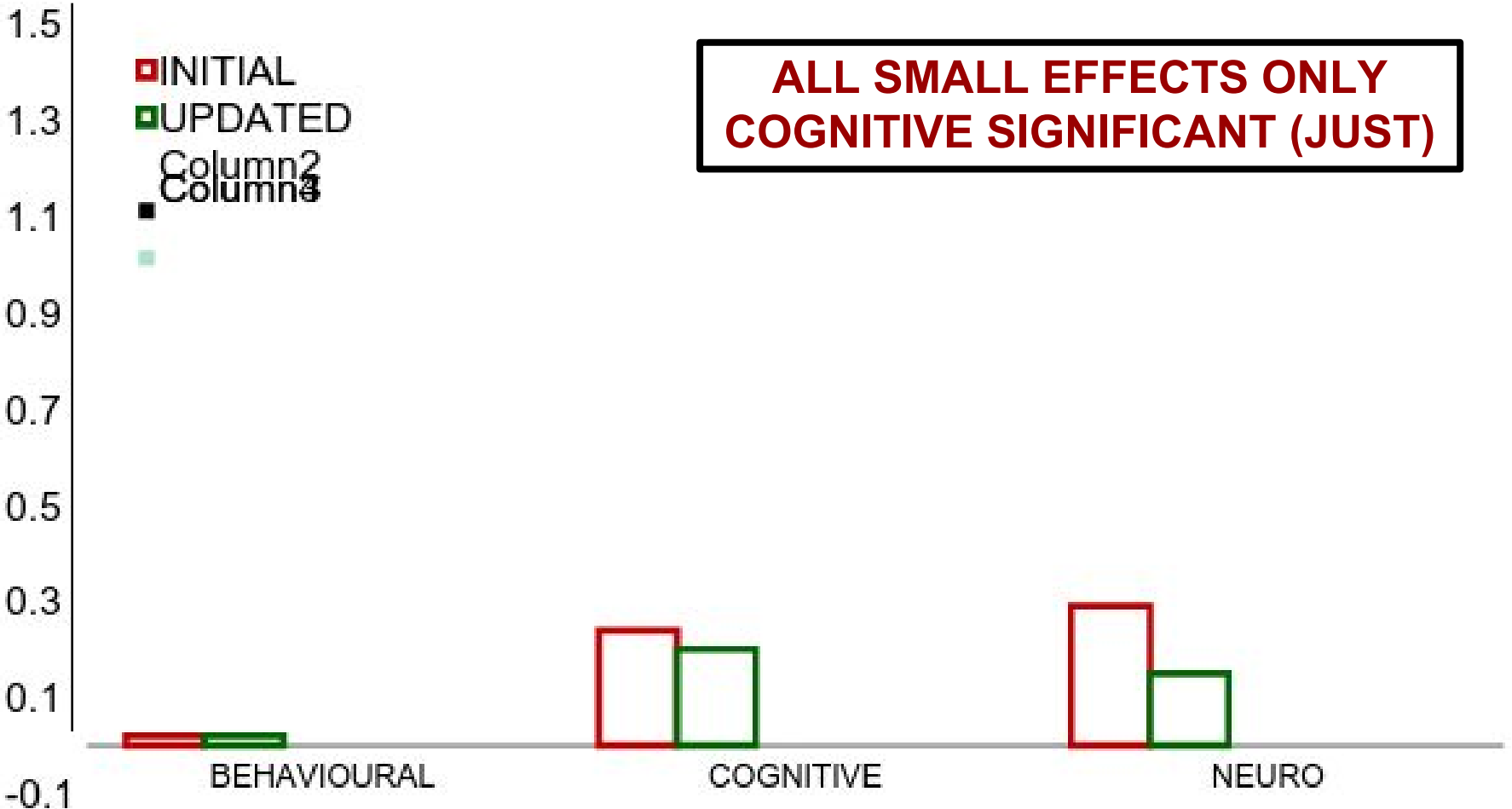


INITIAL VERSUS UPDATED SMDS

MPROX

**EQUAL EFFECTS FOR ALL BUT
LIKELY TO BE AFFECTED BY
PARENTAL BIAS**

INITIAL VERSUS UPDATED SMDS *PBLIND*



DO NON-PHARMA ADHD TREATMENTS WORK? DEPENDS WHAT YOU MEAN! DEPENDS WHO YOU ASK!

- Do they control core ADHD symptoms?
- Do parent's think things have improved?
- Do they reduce other common comorbidities?
- Do they improve everyday functioning?
- Do they change parent's attitudes/behaviours to child?
- Do they promote parental wellbeing?
- Do they strengthen family functioning?
- Do they improve QoL for the child/family in the long run?

THE CASE FOR EARLY INTERVENTION IN ADHD

**AS WELL AS *TREATING* PRESCHOOL ADHD
EARLY INTERVENTION STRATEGIES COULD BE
USEFUL IN ..**

**PREVENTING - EMERGENCE OF ADHD FROM
PRODROMAL FORMS...**

**LIMIT - ESCALATION TO MORE COMPLEX
/SEVERE FORMS**

**REDUCE ITS IMPACT ON THE CHILD, THEIR
FAMILY AND SOCIETY**

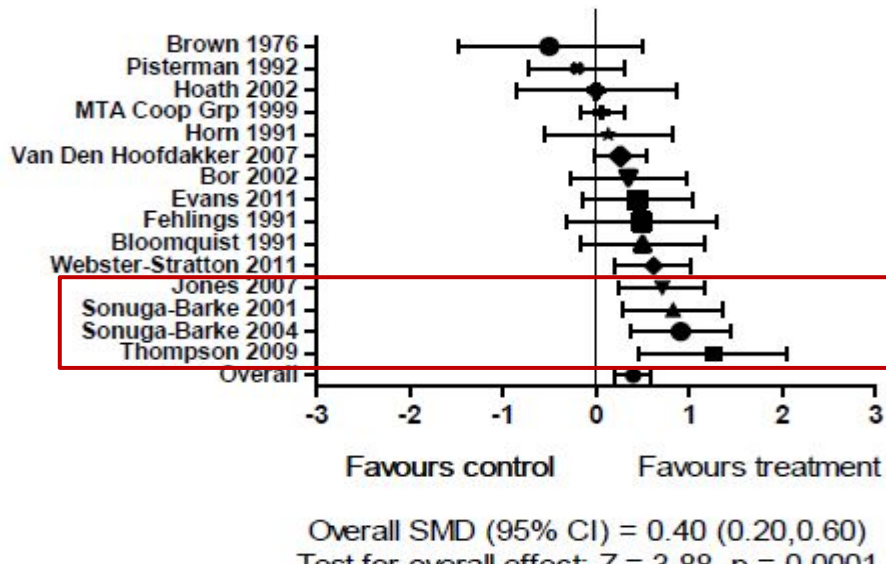
**..REDUCING THE NEED FOR THE LONG TERM USE
MEDICATION.**

WHY SHOULD EARLY INTERVENTION WORK BETTER?

- Evidence for efficacy of later non-pharma interventions limited.
- Early intervention is expected to be more effective because
- Its exploits plasticity
 - Child's brain more open to environmental influence?
 - Child's behavioural habits less engrained?
- It is in a clinical window of opportunity
 - Parent less set and rigid – more open to change?
 - Less comorbidity – easier access to core problems.

**WHAT IS THE EVIDENCE FOR
EFFECTS OF BEHAVIOURAL
INTERVENTIONS IN THE PRESCHOOL
YEARS?**

BPT



M-PROX

ES = 0.40*

P-BLIND

ES = 0.02

JUST PRESCHOOLERS (<5 YEARS)

FULL SAMPLE

PRESCHOOL

N=7

JUST PRESCHOOLERS (<5 YEARS)

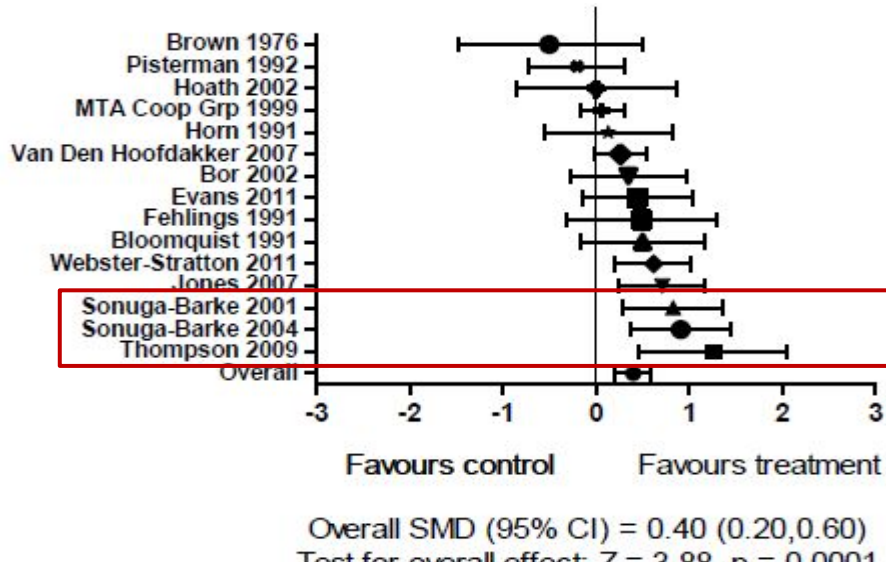
FULL SAMPLE

PRESCHOOL

N=7

**CAN WE LEARN FROM THE MOST PROMISING
APPROACHES?**

BPT



M-PROX

ES = 0.40*

P-BLIND

ES = 0.02

**NEW FOREST PARENTING PROGRAMME –
COMBINING BEHAVIOURAL AND COGNITIVE
ELEMENTS IN SPECIALISED PARENT
TRAINING.**

NEW FOREST PARENTING PROGRAMME
THOMPSON & LAVER-BRADBURY

NEW FOREST PARENTING PROGRAMME
THOMPSON & LAVER-BRADBURY



DISTINCTIVE ELEMENTS

- Individual home based intervention.
- Improve parent's acceptance of ADHD.
- Model mother-child interaction to improve relationship.
- Focus on teachable moments through the use of diaries.
- Target **constructive parenting** and the effectiveness of parents as facilitators of their child's development - enhance home as a context for learning self-control/behavioral regulation.
- Teach parents to change their child's (training/practice), to **address areas of neuro-psychological weakness**.

**IS NFPP SUPERIOR TO GENERIC BPT FOR
THE TREATMENT OF PRESCHOOL ADHD?**

***NFPP VERSUS HELPING THE
NON-COMPLIANT CHILD***

**IS NFPP SUPERIOR TO GENERIC BPT FOR
THE TREATMENT OF PRESCHOOL ADHD?**

***NFPP VERSUS HELPING THE
NON-COMPLIANT CHILD***

STUDY DESIGN

- Children randomized to NFPP, HNC or WL in 2:2:1 ratio
- Assessment at PRE, POST, F-UP (Oct-Nov next school year);
- Outcome domains
 - ADHD
 - parent, teacher Conners:
 - lab tasks of on-task behavior and ability to delay
 - Conduct problems
 - Parent and teacher ratings (NYBRS)
 - Parent functioning
 - Parenting practices, parental stress, quality of P-C interactions
- Same, experienced and well trained, therapists provided both treatments

SAMPLE CHARACTERISTICS (N=164)

Groups: NFPP (n = 67); HNC (n = 63); WL (n = 34)

Age: 3.6 yrs

Male: 73.8%

IQ: 101.8

Race: 69.2% white; 16.4% black; 8.8% 25.6% Asian

Subtype: 50.6% Combined; 33.5% H/IMP; 15.2% INAT.

Comorbidity: ODD (41.5%); ANX (6.7%);

Employment: 67.7% mothers, 82.7% fathers employed

Marital Status: 77.6% married.

ADHD (MPROX – PARENT CONNERS)

SMD=.99

SMD = 1.18

BASELINE

POST TREATMENT

NEXT YEAR

ADHD (PBLIND TEACHER-CONNERS)

SMD=.30

SMD =.14

BASELINE

POST TREATMENT

NEXT YEAR

CONDUCT (MPROX - PARENT – NYPRS DEFIANCE)

SMD=.73

SMD=.67

BASELINE

POST TREATMENT

NEXT YEAR

CONDUCT (PBLIND - TEACHER – NYPRS DEFIANCE)

SMD=.39

SMD=.05

BASELINE

POST TREATMENT

NEXT YEAR

WHITHER COGNITIVE TRAINING IN ADHD?

HALPERIN & HEALEY'S TEAMS

Green Games – Working Memory

2) What's Under There?

1) Shopping



3) Copy Me

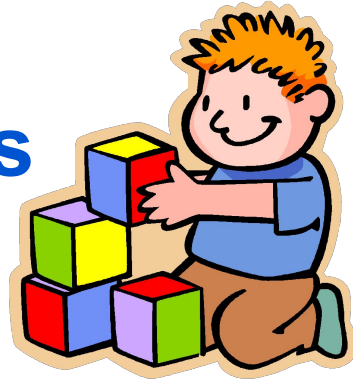


4) Memory Game

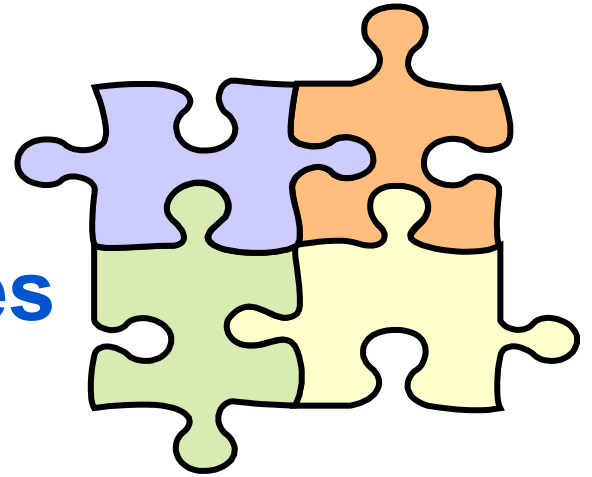
5) Remember the Treasure

Yellow Games – Visual-Spatial/Pattern Recognition and Organization

1) Blocks



2) Puzzles



3) Beads

4) Track It

Blue Games – Inhibitory Control

1) Freeze Dance

2) Puppet Says



3) Red Yellow Green

4) Taboo

SUMMARY

- Therapeutic innovation to improve non-pharma treatment remains a major challenge for ADHD translational science.
- Effects of psychological interventions similar across treatment domains
 - small effects on unblinded outcomes.
 - no effects on blinded outcomes.
- Behavioural interventions improve parenting and may be valuable for the treatment of comorbid conduct problems.
- Cognitive Training may remediate neuropsychological impairment.
- Early interventions approaches combining parent training and cognitive training targeting multiple domains offer promise.
- Whether psychological intervention improve outcomes over the long-, rather than short-term have not been tested.