

Perinatal Iron Nutrition and Child Development

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The major roles of iron

- Haemoglobin: O₂ carrier
- Energy production
- DNA & Fatty acids
- Neurotransmitters
 - brain function



Iron deficiency anaemia (IDA)

- Prevalence
 - Toddlers & preschoolers: 20-25%
 - Pregnant women : 52% in the developing world
23% in the developed countries
- Consequences:
 - fatigue
 - ↓ productivity & ↑ infection



IDA and child development

- IDA in children → poorer cognitive function
- Is the association causal?
 - Therapeutic trials: corrected IDA, deficits can persist
 - Preventative trials: no conclusive evidence of benefits
- Critical developmental window before birth?

Is fetal stage a critical period?

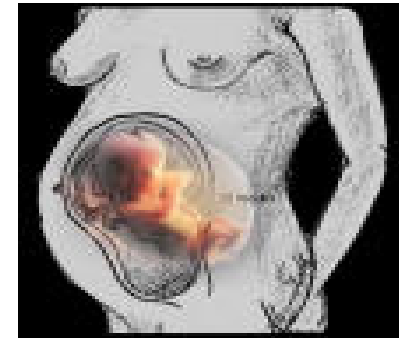
Fetal stage → rapid brain development

Rats



Offspring: *abnormal* brain structure & functions

Humans



Fetus: brain growth & functions *unknown*

Does iron nutrition during pregnancy
influence child development?

Australian Mothers' and Babies' Iron Trial (AMBIT)

AMBIT background:

- RCT (1997 – 1999): 430 women
- Iron vs placebo
- Iron dose : 20mg/d
 - Iron intake of pregnant women: ~12mg/d
 - RDI : 22-36mg/d



AMBIT Results

At the end of pregnancy:

	Iron	Placebo	MD/RR	P-value
Hb (g/l)	127±13	120 ±12	6.9	<0.001
Ferritin (ug/l)	21 ±18	14 ±10	7.1	<0.001
ID (%)	65/186 (35)	102/176 (58)	0.6	<0.001
IDA (%)	6/198 (3)	20/185 (11)	0.3	<0.05

Makrides, et al 2003

Effect size: similar to trials with iron \geq 100mg/d

The 1st AMBIT Follow Up

(During 2002 - 2004: 4 years after birth)



The 1st AMBIT Follow Up

- Aims:
 - To determine if iron supplementation in pregnancy influences child development
- 1^o outcome: IQ (Stanford – Binet)

Stanford Binet Intelligence test

- Overall cognitive ability – composite IQ
- Short-term memory
- Verbal
- Visual abstract
- Quantitative reasoning



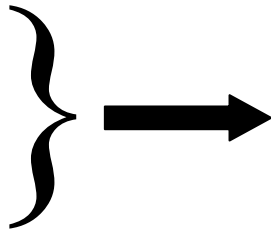
The 1st AMBIT Follow Up

- Aims:
 - To determine if iron supplementation in pregnancy influences child development
- 1^o outcome: IQ (Stanford – Binet)
- 2^o outcome: behaviour (SDQ)

Behaviour: SDQ

- Brief screening measure to assess behavioural problems

1. Peer
2. Emotion
3. Conduct
4. Hyperactive
5. Prosocial



Total difficulties score



Abnormal: total score ≥ 17

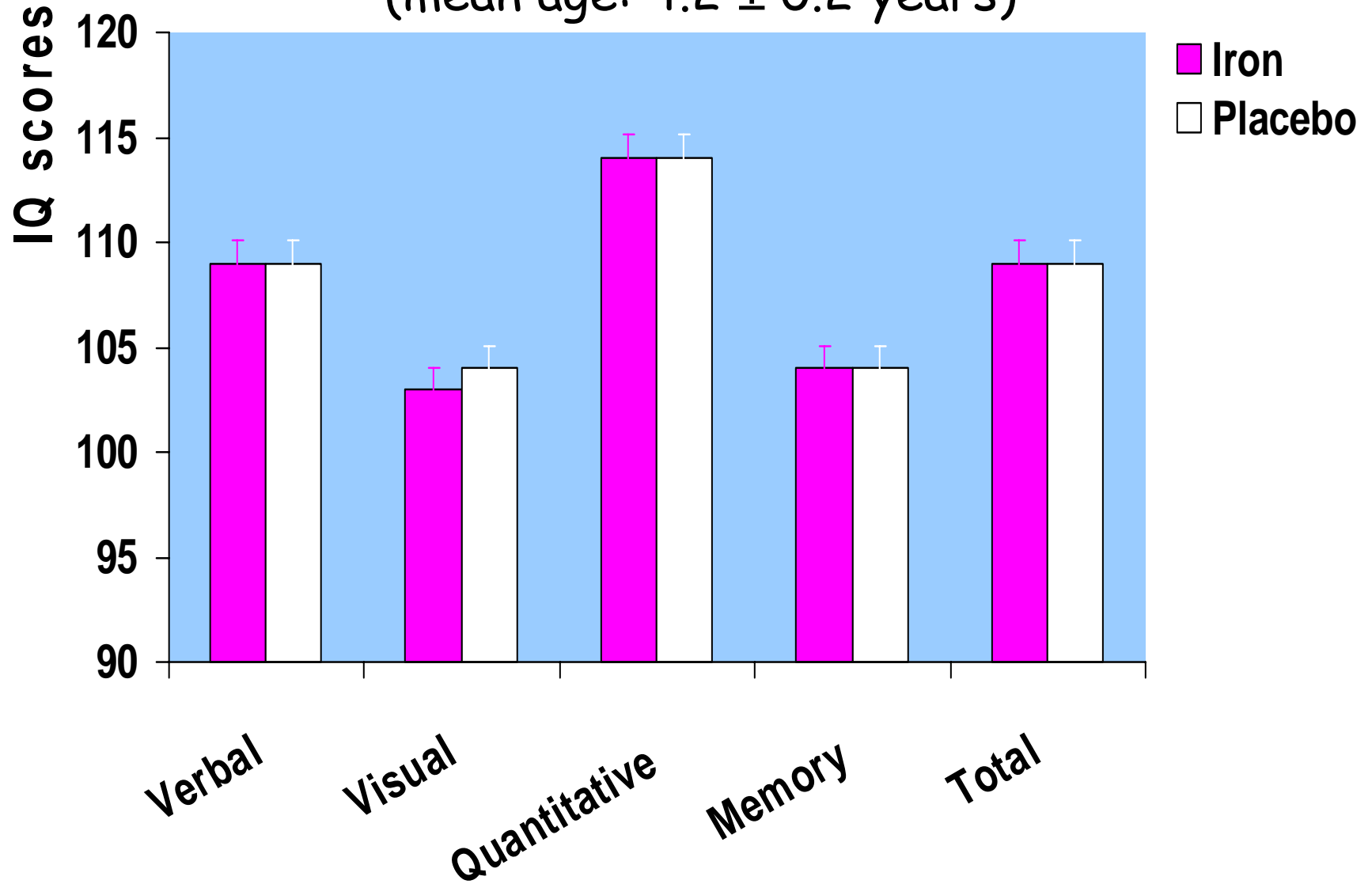
High risk: score in the top 10%

- Validated in Australia
- Self reported form (parent / teacher version)

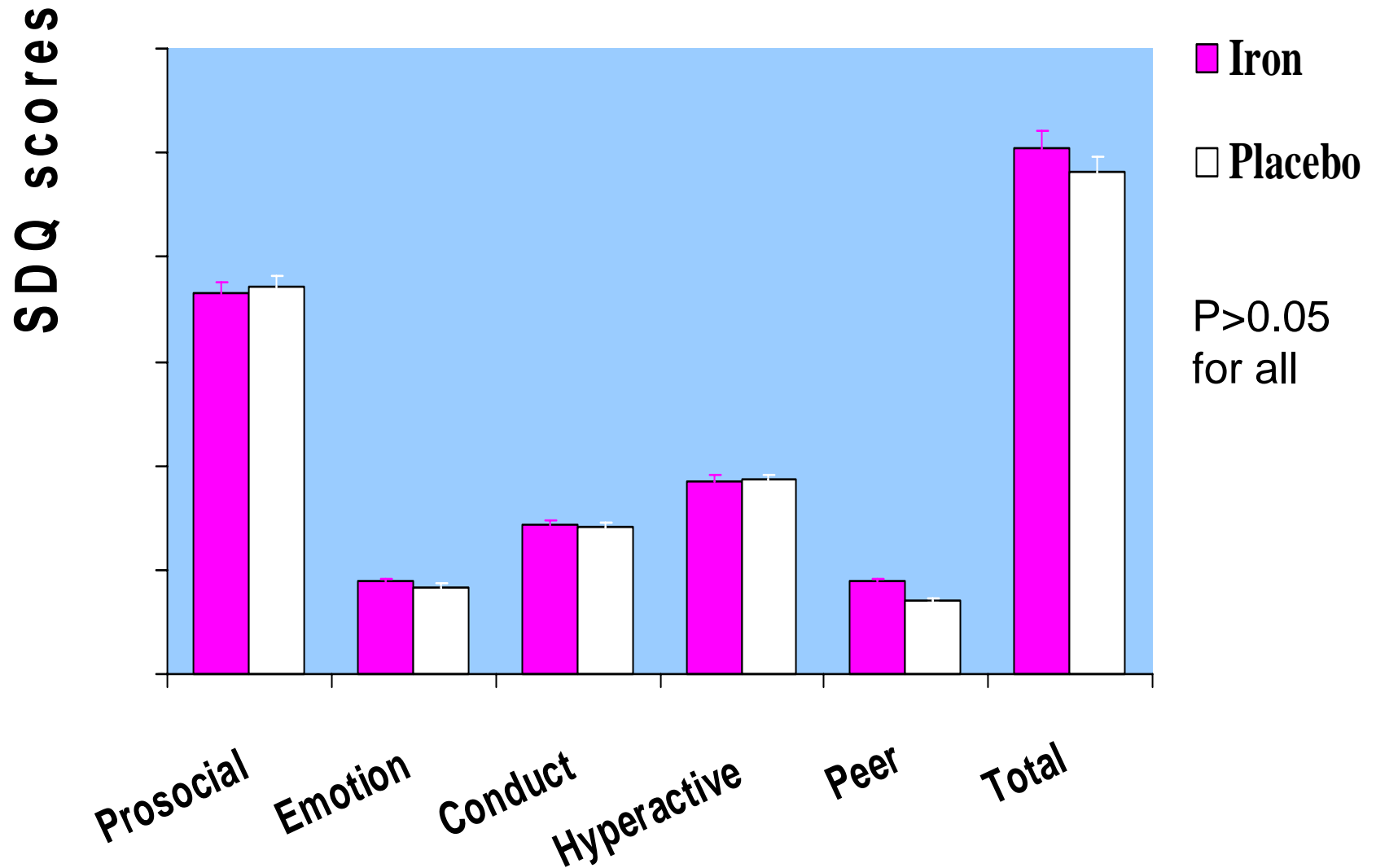
Results: 1st Ambit follow up

IQ of the children

(mean age: 4.2 ± 0.2 years)



Behaviour scores (parent rated)



Abnormal behaviour: parent-rated score

SDQ score	Iron (n=151)	Placebo (n=149)	P
Abnormal	24 (16%)	12 (8%)	0.037
High risk	24 (16%)	11 (7%)	0.021

- ? Chance (small incidence, secondary outcome)
- ? True negative effect of prenatal iron exposure

Neonatal iron exposure & later development

- Animal data
 - Excessive iron exposure in neonatal period → later behavioural problems (Fredriksson et al., 1999)
- Cohort study in SGA children (Tamura et al., 2002)
 - Cord ferritin concentration & IQ at 5 yrs: U-shaped
 - Ferritin in both low & high quartiles → lower IQ
 - High cord ferritin concentration:
 - ? False elevation due to infection
 - ? Negative effect of high fetal iron

2nd AMBIT Follow-up

(Conducted in 2006: 6 - 8 years after birth)

- Aim: assess behaviour at school age
- Behaviour assessment:
 - SDQ: both parent & teacher



Results: 2nd Ambit follow up

Parent-rated Behaviour

- No differences in:
 - Total difficulties
 - Any subscales
 - % of abnormal behavioural scores

Teacher-rated behaviour

SDQ score	Iron (n=112)	Placebo (n=113)	P
Total difficulty	10 (8%)	13 (10%)	0.52
Peer problem	11 (8%)	3 (2%)	0.03

- ? Chance (small incidence & limited sample size)
- Same direction as 1st follow up
- Differences in parent & teacher rating
- ? True negative effect of prenatal iron exposure

Summary & Implications for clinical practice

- Iron supplementation in pregnancy has no benefit in child development
- Possibility of adverse effect on childhood behaviour cannot be excluded
- Selective iron supplements during pregnancy rather than routine iron supplementation



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