A Randomised Controlled Trial of DHA-Rich Fish Oil Supplementation During Pregnancy and Subsequent Development of Language in Early Childhood

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ABSTRACT

There is no more important period in human development than conception through early childhood in maximizing developmental potential. It is during the last trimester of pregnancy when brain development accelerates (1, 2) and where accumulation of docosahexaenoic acid (DHA) in neural tissues occurs most rapidly (1, 3). Dietary intake and maternal stores of DHA during pregnancy and lactation have important implications for the developing brain. Uncertainty surrounding the ability of Westernised diets to fulfill requirements of DHA during pregnancy has raised concern for the developmental outcome of children raised in this dietary context (4).

Some children in Australia have very limited language ability, impacting both the individual and society. Intervention for language development during the early years should be a primary focus for research. The role that DHA might play presents as a compelling area of investigation undertaken in this thesis.

This thesis contains a literature review, including a systematic review and meta-analysis, and also proposes a theoretical framework from which to understand the potential variation in language development as a function not only of DHA but also of interacting biological and social variables (Chapter 1). The methods used in the current study are detailed (Chapter 2). Within a randomised controlled trial design (Chapter 3) the current study investigates whether DHA supplementation during the prenatal period has an
effect on language development at 4 years of age. Interactions between DHA and other individually contributing factors posed by the bio-ecological model (Chapter 4) and relationships between markers of DHA and language development (Chapter 5) are examined. A model proposed to provide a broader or more comprehensive conceptualization of the role of DHA within the larger system of influences on language development was tested (Chapter 6).

The current study found no significant effect of DHA supplementation during pregnancy on children’s language development at 4 years of age as measured by the primary outcome of the current study: mean Core Language Scores, assessed using the second edition of the Clinical Evaluation of Language Fundamentals Preschool. There were no significant interactions between treatment group and child sex, maternal age, in utero exposure to maternal cigarette smoking or alcohol consumption, or maternal depression. There was, however, a significant interaction for maternal education. There was also no significant relationship between markers of DHA status and language development for the whole group, and no significant difference in language development between those with cord blood DHA in the 25th and 75th percentile. There were, however, both significant positive and negative relationships between the number of fish meals and DHA foods (respectively) the child consumed in the month prior to the 4-year assessment and language development at 4 years of age. Findings from structural equation modelling analyses provided no support for understanding the relationship between DHA and children’s language
development through focusing on the relationships proposed by the bio-ecological model.

Overall, findings suggest that prenatal DHA supplementation does not benefit children’s language development. Longer-term follow-up of early DHA supplementation is required to determine whether delayed effects emerge.
DECLARATION

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

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Nicola Gawlik

21 June 2016
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Finally, it is with my deepest gratitude and love that I dedicate this thesis to my grandparents who have been a constant source of knowledge and inspiration. And also for the myriad of ways in which, throughout my life, they have actively supported me in my determination to find and realize my potential, and to make a positive contribution to our world.
**GLOSSARY**

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<tr>
<td>AA</td>
<td>Arachidonic Acid</td>
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<tr>
<td>AEDC</td>
<td>Australian Early Development Census</td>
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<td>AEDI</td>
<td>Australian Early Development Index</td>
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<td>AI</td>
<td>Adequate Intake/s</td>
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<td>ALA</td>
<td>Alpha linolenic Acid</td>
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<td>ASQ</td>
<td>Ages and Stages Questionnaire</td>
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<td>Bayley-II</td>
<td>Bayley Scales of Infant Development, Second Edition</td>
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<td>Bayley-III</td>
<td>Bayley Scales of Infant Development, Third Edition</td>
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<tr>
<td>BRIEF-P</td>
<td>Behaviour Rating Inventory of Executive Function–Preschool</td>
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<td>BW</td>
<td>Birth Weight</td>
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<tr>
<td>C</td>
<td>Capsule</td>
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<tr>
<td>CA</td>
<td>Corrected Age</td>
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<td>CBCL</td>
<td>Child Behaviour Checklist</td>
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<tr>
<td>CELF P-2</td>
<td>Clinical Evaluation of Language Fundamentals Preschool, Second Edition</td>
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<tr>
<td>CFI</td>
<td>Comparative Fit Index</td>
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<tr>
<td>CI</td>
<td>Confidence Interval</td>
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<tr>
<td>CLAMS</td>
<td>Clinical Linguistic and Auditory Milestone Scale</td>
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<tr>
<td>CLS</td>
<td>Core Language Score</td>
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<tr>
<td>CNS</td>
<td>Central Nervous System</td>
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<td>Ctrl</td>
<td>Control</td>
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<td>d</td>
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<td>DAS-II</td>
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<td>Docosahexaenoic Acid</td>
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<tr>
<td>Diff</td>
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<td>DNBC</td>
<td>Danish National Birth Cohort</td>
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<td>DNS</td>
<td>Day Night Stroop</td>
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<td>DOMInO</td>
<td>DHA to Optimise Mother Infant Outcomes</td>
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<td>DPA</td>
<td>Docosapentaenoic Acid</td>
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<tr>
<td>Egg-DTG</td>
<td>Egg-Derived Triglyceride</td>
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<td>ELVS</td>
<td>Early Language in Victoria Study</td>
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<td>Egg Phospholipid</td>
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<td>EPA</td>
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<td>EV</td>
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<td>F</td>
<td>Formula</td>
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<td>Fatty Acid/s</td>
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<td>FAD GF</td>
<td>Family Assessment Device – General Functioning subscale</td>
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<td>FAS</td>
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<td>FASD</td>
<td>Fetal Alcohol Spectrum Disorders</td>
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<td>FMC</td>
<td>Flinders Medical Centre</td>
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<td>Fish Oil</td>
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<td>g</td>
<td>Grams</td>
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<td>GA</td>
<td>Gestational Age</td>
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<td>Griffiths Mental Development Scales</td>
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<td>GP</td>
<td>General Practitioner</td>
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PPVT-III Peabody Picture Vocabulary Test, Third Edition
Preg Pregnancy
RBC Red Blood Cell
RCT Randomised controlled trial/s
RLE Recent Life Events
SD Standard Deviation
SDQ Strengths and Difficulties Questionnaire
SS Sentence Structure
SSRI Selective Serotonin Reuptake Inhibitor
TLI Tucker and Lewis Index
Trt Treatment
UK United Kingdom
USA United States of America
Veg Vegetable
VIQ Verbal IQ
VLBW Very Low Birth Weight
WASI Wechsler Abbreviated Scale of Intelligence
WCH Women’s and Children’s Hospital
WIAT-II Wechsler Individual Achievement Test, Second Edition
WISC-III Wechsler Intelligence Scale for Children, Third Edition
Wk Week/s
WMD Weighted Mean Difference
WPPSI-R Wechsler Preschool and Primary Scale of Intelligence – Revised
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<td>Wechsler Preschool and Primary Scale of Intelligence, Third Edition</td>
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<td>WS</td>
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