Effects of early childhood malnutrition on later cognitive development, a review of the literature

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ABSTRACT
Introduction: Childhood malnutrition causes the mortality of millions of children under five and affects the health and development of millions of other children. In particular, cognitive development may be negatively affected by early childhood malnutrition.

Background: Early childhood is a critical period for both nutrition and cognitive development. Malnourished children are more likely to experience educational failure and a reduction in adult productivity. Malnutrition and its effects on cognitive development can be prevented by nutritional and early childhood development interventions. This review aims to explore whether malnutrition has negative effects on cognitive development and if these effects can be reversed.

Methods: A comprehensive literature review was conducted. Criteria were set to establish the viability of studies according to sampling, statistical robustness, length of the study and the appropriateness of the measures used.

Results: Early childhood malnutrition has negative effects on cognitive development in childhood and adolescence but can be partially or fully reversed by appropriate interventions.

Conclusion: To prevent these adverse effects, the interventions need to focus first and foremost on children aged 0-2 years old; this can be more cost effective. Parents should be included in the interventions, and cultural and environmental contexts should be considered.

Keywords: Negative effects of stunting, cognitive development, the first two years of life, literature review, childhood malnutrition and adulthood productivity

چکیده
مقدمه: سویفتی دوران طفولت عمکر و میر میلیونها طفل زیر پنجه و سال در جهان میباشد. برخاله صحت، رشد و اگشFORMATION فلق دیگری نیز مهم‌تر می‌باشد. به‌خصوص سویفتی مراحل ابتدايی دوران طفولت، میتوانند اثرات منفی باید رشد ذهنی و فکری اطفال داشته باشند.

پس منظر: دوره مهم و حیاتی برای تغذیه و رشد فکری و همچنین مراحل ابتدايی دوره طفولت میباشد. اطفال مصاب به سویفتی معمولاً در طول مطالعه تلاشی نمی‌کنند. در ضمن در بررسی‌های دستیاردها و میزان مؤلفه کمتری را نشان می‌دهند. این نتایج خوب و مداخله مناسب در مراحل ابتدايی دوره طفولت، تا حدی میتوانند سویفتی و اثرات منفی آن را باید در رشد ذهنی و فکری اطفال تغییر و قبلاً نامیدند. این تحقیق به‌هدف بررسی اینکه آیا سویفتی اثرات منفی برای بالای رشد ذهنی و فکری اطفال دارد یا خیر؟ آیا میتوان این اثرات منفی را تغییر داد؟ اجرای گردید.

میتود: مرور و بررسی جامع و دقیق مطالعات و تحقیقاتی که کلی در مورد صورت گرفته بود، انجام پذیرفت. براساس آن میزان تحقیق تعیین و شناسایی گردید. مطالعه برای انجام تحقیق معتبر می‌باشد. نمایه‌گر، ارقام و آمار دقیق و تحلیل توافق، تست و دقت شمارش ارقام ایجاد گردید.

نتایج: سویفتی مراحل ابتدايی دوران طفولت اثرات منفی برای بالای رشد ذهنی و فکری اطفال تغییر و نوجوانان دارد. این اثرات منفی با مداخلات مناسب میتواند به طور قسمی یا کاملاً از بین برده شود.
Introduction

Globally, over a third of deaths in children under five are attributable to undernutrition, recognized as a severe public health issue (World Health Organization [WHO], 2013). In addition to its devastating impact on child mortality, undernutrition has a long-term damaging effect on intellectual and psychological development, (Grantham-McGregor et al., 2007).

Development in the first years of life involves very rapid brain and cognitive development affected by the nature of an environment, which may impact negatively or positively on the rest of a child’s life (Laus, Vales, Costa, & Almeida, 2011).

Malnutrition is the clinically inadequate or excess intake of protein, energy, and micronutrients (WHO, 2015). According to this definition, inadequate or excess intake of micronutrients also causes malnutrition and iron is one of the most important elements among micronutrients.

Cognitive development as defined in this review includes analytical skills, mental problem solving, early mathematical and memory skills (Naudeau, 2011). The early years of development include conception to age six or seven years old, but 0-2 years old is the most critical period, because uniquely during this period neurological studies have shown that synapses, connections or pathways between neurons in the nervous system develop rapidly, forming the basis of lifetime cognitive functioning (Naudeau, 2011Khan et al., 2015). Therefore, a child’s first years of life are a unique window for proper early childhood nutrition (Illig & California State Library, 1998). Children from poor and disadvantaged societies are at the greatest risk of being deprived in this critical period of life. Investment in childhood development is an important and cost-effective way to empower children to grow into capable, responsible and skilled citizens (Jolly, 2007) potentially improving adult health, productivity, education, reducing violence, and promote environmental sensitivity (Jolly, 2007). Despite being exposed to greater malnutrition and preventable diseases (Irwin, Siddiqi, & Hertzman, 2007), children from the poorest community are least likely to have access to Early Childhood Development programs.

The goal of this review was to establish whether evidence shows that “early childhood malnutrition affects subsequent cognitive development?”

The objectives are to:

- Ascertain from existing research the state of knowledge regarding the relationship between malnutrition and cognitive development;
- Examine whether studies show that there is a critical stage during which malnutrition has the most impact on the child’s cognitive development
- Establish whether there is evidence of later catch up

Establish whether the research shows that the impact is more marked those who had greater exposure to malnutrition (a dose response effect)

Methodology

To have an appropriate review, first the inclusion and exclusion criteria were set.

Inclusion. Quantitative research; studies concerning children aged 0-3.5 years; studies exploring the effects of malnutrition on cognitive development; studies presented in English language; studies conducted within the past 25 years

Exclusion. Non quantitative research; non research evidence; studies of children over 3.5 years old; studies exploring the relationship of nutrition with other aspects of development; studies exploring the relationship between cognitive development and other issues than nutrition; studies focusing on problems such as low birth weight, prematurity, congenital problems; studies associated with overweight or obesity; unpublished literature; papers not in English...

The Bournemouth University (BU) search portal was used for the literature search. This provides access to a range of databases, including Cinhal Science Direct and Medline Complete. The advanced search option
was utilized, using features such as Boolean operators, and date and language limiters (Aveyard, 2014). The search included: malnutrition, child development, growth, cognition, child nutrition and infant development. There is limited research in this field; therefore the search timespan was from 1990 to 2013. The search was conducted twice, to ensure nothing was missed adding the term longitudinal in the second search.

To increase the comprehensiveness of this review, two additional methods were used:

1. Reference chaining. The relevant papers were retrieved by searching the reference list and assessing the abstract of papers.
2. Key author’s studies. Papers were searched for Grantham-McGregor’s studies, as one of the key authors in this field. These studies were explored together with studies from the electronic search.

The literature search identified 558 hits, from the 3 methods 167 papers were duplicates; 133 papers not relevant; 181 papers did not match the inclusion criteria; the exclusion of these reduced the number to 43 relevant papers, of these 28 papers were excluded as they did not directly answer the study question; 15 papers remained. On reading the full texts of 15 articles, four were found to be review papers, not primary research leaving a total of 11 papers comprising 10 longitudinal and one case-control study. Studies’ selected spanned from 1994 to 2013, including data from Vietnam, Peru, Philippines, Mauritius, Ghana, Ethiopia, Jamaica, and Costa Rica. Most of the studies included were based on a secondary analysis of large scale population cohort studies in countries where a high proportion of children have been exposed to malnutrition at an earlier date. See Figure 1 below for the numbers of papers and studies. The papers were reviewed for quality using the Critical Appraisal Skills Program (CASP), high quality tools designed at the public health research unit of the University of Oxford (Aveyard, 2014). The findings from across the studies were synthesized using a process of narrative synthesis.

Approval was obtained from the Bournemouth University Research Evaluation Committee (BUREC) consideration was also given to ethical issues when evaluating the quality of the research papers.

The papers which met the criteria were collated and tabulated with: authors’ name; sample size; date, aim, type; main findings; ethical considerations; strengths and limitations. The majority were longitudinal studies, so details of timing of the participants and assessments were included, see Table 1 below. A coding system and themes were developed to assess the strength of evidence. Key themes were noted, recorded, and universal themes and differences noted. Finally the results were written up.

Results
Relationship between malnutrition and cognitive development
All the papers provided evidence of the negative effects of malnutrition on subsequent cognitive development. A key finding was that malnutrition aged 0-2 has an adverse effect on cognitive development. Ten of the papers were longitudinal; the exception (Drewett & Wolke, 2001) only studied the children’s development at 2 years, but found a significant effect on cognitive development in comparison with a control group.

The 10 longitudinal papers examined the outcomes from 4 to 17, some following the children on up to 4 occasions (Raine, Liu, Venables, & Mednick, 2004; Grantham-McGregor, Powell, Walker, Chang, & Fletcher, 1994; Park et al., 2011; Lukowski et al., 2010). These studies provided the opportunity to study the detailed progress of the children’s trajectory over time, showing a significant difference between the children who suffered malnutrition and matched controls in cognitive outcomes as shown in Table 1 below.

Evidence of a critical stage during which malnutrition has most effect on the child’s cognitive development
Seven of the eleven papers first studied the children at age 2, but for three studies (Watanabe, Flores, Fujiwara, & Tran, 2005; Park et al., 2011; Raine et al., 2004) the children were already 3 – 3.5 years and in one study two groups were compared following a famine, one aged 0-2 and one aged 4-6 (Ampaabeng & Tan, 2013). Eight of the 11 papers found that 0-2 years of life was a critical period for the association between nutritional status and cognitive development. The first two years of life had more adverse effects on cognitive development than later stunting, and it was these two years that were most strongly associated with cognitive impairment in later childhood (Ampaabeng & Tan, 2013; Berkman, Lescano, Gilman, Lopez, & Black 2002; Crookston et al., 2010; Grantham-McGregor et al., 1994;
Lukowski et al., 2010; Mendez & Adair, 1999; Park et al., 2011; Watanabe et al., 2005). One paper did not discuss 0-2 years old as a critical period (Park et al., 2011).

This review evidence strongly points to a critical, sensitive period age 0-2 years for nutrition and cognitive development.

What is the evidence of catch up? The children’s outcomes were followed up between 2-17 years. Six of the 11 papers reported on the children’s degree of catch-up in-cognitive gains when their nutritional status was improved.

The three main findings about catch-up were:

Severity. The severity of stunting before or at two years of age was a key predictor of catch-up; those less stunted were more likely to experience catch-up growth. Children with severe stunting at age two years appeared to sustain cognitive deficits at age 11, even when they had recovered from early stunting (Mendez & Adair, 1999). Children who had severe vs. moderate malnutrition had much lower scores in cognitive testing and were less likely to experience catch up growth (Berkman et al., 2002).

Timing. The timing of stunting was also relevant to catch up. Children who had severe stunting in the second year of life had the most substantial impairment in cognitive function, while children who had severe stunting in late childhood achieved catch up growth (Berkman et al., 2002; Crookston et al., 2010; Mendez & Adair, 1999). Berkman et al. also found the persistence of malnutrition during infancy and later childhood affects the degree of catch-up growth Persistence was not discussed in other included papers.

Socio-economic, environmental and genetic influences. Other influences apart from nutritional status examined included pre-schooling, schooling, maternal height, grandparents present, age of mother, maternal education, urban vs rural location, family size, socioeconomic condition (Ampaabeng & Tan, 2013; Crookston et al., 2010; Mendez & Adair, 1999; Park et al., 2011). In addition, Watanabe et al. (2005) suggests the importance of Early Childhood Development interventions. Adverse socio-economic and family situations contributed to outcome, but were not consistently explored.

Dose-response: Is there evidence in these studies of a link between the degree of malnutrition and cognitive development?

Seven of the eleven papers found a dose-response between malnutrition and cognitive or behavioral outcomes. Three of them were between the severity of malnutrition and cognitive development (Berkman et al., 2002; Grantham-McGregor et al., 1994; Watanabe et al., 2005) between the severity of famine and cognitive development (Ampaabeng & Tan, 2013). The remaining three papers showed different dose-response: between severity of malnutrition and externalizing behavior, (Raine et al., 2004); between age at the first onset and the severity of stunting (Mendez & Adair, 1999 Crookston et al. (2010).

The overall evidence was, therefore, that whilst catch up is possible, it relates to the severity of malnutrition, and to the timing and duration of the impact of malnutrition measured by the stunting of development.

Discussion

Evidence in this review suggests that 0-2 years old is a sensitive period for nutritional status and cognitive development. This finding is supported by other research studies outside the remit of this review (Dewey & Adu-Afarwuah, 2008; Martorell et al., 2010). Dewey and Adu-Afarwuah’s study assessed the impact of complementary feeding of children of 6–24 months in developing countries. Martorell et al. (2010) studied weight gain in the first two years of life as a predictor of schooling outcomes. They also found that 0-2 years of age was the most critical age when intervention was crucial.

The evidence in this review also confirmed that catch up is possible but is dependent upon the severity, timing and duration of stunting. It shows that 0-2 is a sensitive time to maximize the effect of supplementation programs for malnourished children (Grantham-McGregor & Baker-Hemmingham, 2005). Stein et al. (2008)’s study shows more benefits in reading comprehension and reasoning at the age of 25-42 in participants who received supplementation within 0-24 months than the participants who were supplemented later.

The findings of this review about dose-response between the severity of malnutrition and cognitive development are consistent with previous studies. Children hospitalized for severe malnutrition showed long lasting cognitive deficits in childhood in
comparison with their siblings (Grantham-McGregor & Baker-Henningham, 2005). Laus et al. (2011), who completed an extensive review also found that the effect of malnutrition depends on its severity, its duration and its timing.

This review has also highlighted the confounding factors such as socioeconomic issues, parents’ education, schooling and socio-economic status, considered in many but not all previous studies. Due to lack of consistency across the studies, it is difficult to identify the most important factors. Stein et al. (2008) considered the household socioeconomic status and the parental characteristics parental schooling, age as parents and the quality of schooling, this was also considered by Martorell et al. (2010). Genetic factors were not assessed in any of the reviewed papers, none, for instance, had any measure of parental IQ (intelligence quotient) whereas there is widespread agreement that genes also play a role in cognitive ability (Illig & California State Library, 1998).

The opportunity to study the impact of malnutrition on cognitive development is limited by the opportunity to capitalize on natural experiments; researchers need the opportunity to access large data samples in areas of severe food shortages. The sample sizes in the studies presented were generally large and provided statistical robustness to demonstrate the findings and the majority were able to follow up the samples (see Table 1 below). The researchers used standardized measures of malnutrition, but the measures of cognitive ability ranged from brief verbal ability tests to neurocognitive, spatial and memory tests (Lukowski et al., 2010) depending of the age of the children and detail of the study.

Few studies examined mechanisms between malnutrition and cognitive development. This is despite the evidence of the impact of malnutrition on the developing brain, that sub nutrition inhibits brain growth and development (Lui, Raine, Venable, Dalais & Mednick, 2003). Mechanisms include iron deficiency anemia, however, Berkman et al.’s (2002) study did not report on the effect of iron deficiency anemia, despite 25% of children under four in the study suffering from this condition.

Conclusion
The conclusions from this review are that age 0-2 years is a sensitive period for nutritional status affecting cognitive development. This review suggests that the nutritional interventions should be focused first and foremost on this period, and then continues for older children. If poor nutritional status persists, later catch up is possible, but the preference would be to prevent early childhood malnutrition in the first place.

This review has highlighted that whilst malnutrition in early childhood strongly influences cognitive development, further research into the mechanisms such as iron deficiency anemia would be beneficial. Despite the evident negative impact of malnutrition on children’s development this area is not widely researched, nor are there adequate strategies in place to prevent what could be an avoidable outcome. Appropriate early interventions to improve nutrition, involving parents and adapted to the local cultural and environmental context are needed.

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References


<table>
<thead>
<tr>
<th>Author/date/country</th>
<th>Aim of study</th>
<th>Type of study</th>
<th>Sample size</th>
<th>Recruitment time</th>
<th>Effects assessment</th>
<th>Main finding</th>
<th>Strength of study</th>
<th>Limitation of study</th>
<th>Ethical consideration</th>
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<tbody>
<tr>
<td>Watanabe et al., 2005 Vietnam</td>
<td>To assess whether an early childhood development intervention had effects on cognitive development</td>
<td>Longitudinal</td>
<td>313</td>
<td>0 - 36 months</td>
<td>4 - 5 years old</td>
<td>Early childhood interventions increase the potential for cognitive development</td>
<td>Standardized and pre validated tests, Data analysis done by standardized models. 95% CI.</td>
<td>The implementer was involved with the study so bias could be possible</td>
<td>Done</td>
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<tr>
<td>Crookston et al., 2010 Peru</td>
<td>To assess the children with catch-up has lower cognitive ability than those who did not have stunting</td>
<td>Longitudinal</td>
<td>1674</td>
<td>6 - 18 months</td>
<td>4.5 - 6 years old</td>
<td>Children with catch-up have cognitive ability similar to the children who had no stunting.</td>
<td>CI was 95%. A reliable system was established through the study.</td>
<td>Frequency and the duration of stunting were not measured. The finding is different from those who had a different definition.</td>
<td>Done</td>
</tr>
<tr>
<td>Park et al., 2011 International</td>
<td>To assess the association between nutritional status and motor/cognitive development</td>
<td>Longitudinal</td>
<td>58</td>
<td>&lt;3.5 years old</td>
<td>3, 6, 12 months after initial assessment</td>
<td>Poor nutrition was associated with higher rates of cognitive and motor developmental delays.</td>
<td>A good reliability and validity as all the tests used in the study were standardized and pre-validated.</td>
<td>Children with good motor development were not taken to the clinic and it would affect the result</td>
<td>Done + informed consent</td>
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<td>Mendez and Adair, 1999 Filipins</td>
<td>To assess stunting is associated with poor cognitive development in late childhood</td>
<td>Longitudinal</td>
<td>2131</td>
<td>0 - 2 years old</td>
<td>8 - 11 years old</td>
<td>There is a direct effect of early stunting on cognitive development later in childhood.</td>
<td>Standardized models and tests and a reliable system to minimize bias with 95% CI.</td>
<td>The inherited ability, the quality of care and stimulation was not studied.</td>
<td>No ethics, no consent</td>
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<tr>
<td>Crookston et al., 2011 Peru</td>
<td>To compare the impact of early and late stunting on cognitive ability</td>
<td>Longitudinal</td>
<td>1674</td>
<td>6 - 18 months</td>
<td>4.5 - 6 years old</td>
<td>The concurrent stunting is more important in predicting the cognition than early stunting.</td>
<td>95 % CI. Every test and questionnaire was modified and piloted locally. Standardized and previously used tests</td>
<td>Children received anthropometric assessment in the early 6-18 month shown growth restriction after assessment</td>
<td>Done + informed consent</td>
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<tr>
<td>Łukowski et al., 2010, Costa Rica</td>
<td>To assess the behavioral difficulties in young adults who had chronic, severe iron deficiency as infants</td>
<td>Longitudinal</td>
<td>33/81</td>
<td>12 - 23 months</td>
<td>5 years, 11-14 and 19 years old</td>
<td>Adults with chronic, severe iron deficiency in infancy had difficulty in their behavior</td>
<td>A range of appropriate methods and tests were used</td>
<td>Small sample size and unknown iron status in prenatal period</td>
<td>No ethics but parental consent</td>
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<tr>
<td>Study Authors</td>
<td>Study Objective</td>
<td>Study Design</td>
<td>Sample Size</td>
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<td>Raine et al., 2004 Mauritius</td>
<td>To test malnutrition at age 3 predisposes to antisocial behavior at age 8, 11 and 17.</td>
<td>Longitudinal</td>
<td>353/120 6</td>
<td>3 years old, 3, 8, 11, 17 years old</td>
<td>Malnutrition at age 3 is associated with externalizing behavior problems at age 8, 11 and 17.</td>
<td>Standardized tests and data analysis three different instruments were used for three different ages.</td>
<td>Malnutrition was assessed only at age 3; it was not assessed after age 3 or before it.</td>
<td>Done</td>
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<tr>
<td>Amoaabeng and Tan, 2013 Ghana</td>
<td>To assess the long-term cognitive outcomes of famine in children</td>
<td>Longitudinal</td>
<td>557</td>
<td>0 - 8 (0 - 2) (3 - 8) years old, 9 years and above</td>
<td>The negative effects of famine (malnutrition) on cognitive development persist into adolescence.</td>
<td>Different tests result consistent with each other. The data were checked for validity</td>
<td>The small sample size has affected the estimation of the advance version of the tests.</td>
<td>No ethics, no consent</td>
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<td>Drewett and Wolke, 2001 Ethiopia</td>
<td>To test the first months of life as a sensitive period for effects of malnutrition on cognitive development</td>
<td>Case-control</td>
<td>27/70/100</td>
<td>0 - 24 months, 2 years old</td>
<td>Early malnutrition does not have adverse effects on cognitive development in the second year of life.</td>
<td>The standard test used and the interviewer was trained and were assessed/supervised.</td>
<td>Not a proper conclusion, the early and late malnutrition was not differentiated properly.</td>
<td>Done</td>
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<tr>
<td>Grantham-McGregor et al., 1994, Jamaica</td>
<td>To investigate the benefit of intervention on severe malnourished children</td>
<td>Longitudinal/ case-control</td>
<td>17/18 cases/19 control</td>
<td>6 - 24 months, 7, 8, 9, 14 years old</td>
<td>Severely malnourished children maintained their developmental delays in 14 years old than their peers.</td>
<td>Standardized and pre-validated tests were used. A reliable system was established</td>
<td>One test did not consistent others.</td>
<td>Done</td>
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<tr>
<td>Berkman et al., 2002, Peru</td>
<td>To examine the effect of stunting, diarrheal diseases, and parasites on cognitive functions</td>
<td>Longitudinal</td>
<td>239</td>
<td>1 - 2 years old, 9 years old,</td>
<td>Severely stunted children in the first two years of life had the most significant cognitive impairment</td>
<td>A good internal validity and 95% of CI</td>
<td>Iron deficiency was not tested while 25% of children in this community had anemia.</td>
<td>Done</td>
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