



Assessment of Neurodisability and Malnutrition in Children in Africa

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Neurodevelopmental delay, neurodisability, and malnutrition interact to contribute a significant burden of disease in global settings. Assessments which are well integrated with plans of management or advice are most likely to improve outcomes. Assessment tools used in clinical research and programming to evaluate outcomes include developmental and cognitive tools that vary in complexity, sensitivity, and validity as well as the target age of assessment. Few tools have been used to measure socioemotional outcomes and fewer to assess the disabled child with malnutrition. There is a paucity of tools used clinically which actually provide families and professionals with advice to improve outcomes. Brain imaging, electroencephalography, audiology, and visual assessment can also be used to assess the effect of malnutrition on brain structure and function. The interaction of neurodisability and malnutrition is powerful, and both need to be considered when assessing children. Without an integrated approach to assessment and management, we will not support children and families to reach their best potential outcomes.

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Introduction

There is good evidence for the interplay between neuro-disabling conditions and malnutrition. We know that malnutrition causes neurodevelopmental delay¹ and neuro-disability leads to poor growth.²⁻⁴ A large number of tools are used in research or for programming purposes to assess neurodevelopmental outcomes in children with malnutrition; however, few tools are applied clinically. In Africa, any assessments of children with neurodisabilities and malnutrition are very limited.

Research studies have focused neurodevelopmental assessment on general development, intelligence, and school readiness,⁵ with less emphasis on socioemotional regulation and wider cognition (attention and memory). There is no consensus as to which assessment tools provide the most robust evidence for assessing change. At a population level, assessment can clarify burden of disease and effectiveness of programs. Programs to improve malnutrition are most effective if they also target the neurodevelopment of children⁶ and robust assessment tools are required that measure not just growth but also development.⁶ Tools at this level need to be easy to provide training on, be reliable, and if possible, be linked to programs that can help families. Clinical tools are few

but good examples of validated tools for use in Africa include the Malawi Developmental Assessment Tool⁷ and Kilifi Developmental Inventory.⁸ These will be most beneficial if linked into programs for training health professionals, community provision of advice, and interventions for families for children with malnutrition or neurodisabilities or both.^{6,9,10}

In this review, we discuss assessment tools as well as clinical imaging tools used to assess neurodevelopmental and neurodisabling conditions in children with malnutrition. We focus on tools validated in Africa and discuss the implications of the use of these tools.

Assessment of Neurodevelopment in Children With Malnutrition

Children's neurodevelopment may be assessed using general developmental assessment tools or more precise measures to identify specific changes in brain function as a result of malnutrition. Tools include those to assess cognition (memory, executive function, and nonverbal or verbal reasoning), specific language abilities or behavioral aspects of the child such as attention or emotional regulation. It is clearly important that the relevant domains and constructs are assessed with tools that are specific and sensitive. Tools vary depending on the nature of studies (longitudinal vs cross-sectional), age of child (infancy, preschool, school age, or adolescence), timing of insult of malnutrition (antenatal, neonatal, preschool, etc) and type of malnutrition. The effects of malnutrition on the brain may differ according to the type of malnutrition, for example, chronic malnutrition (stunting, manifested as low height for age), acute malnutrition (formerly known as protein-energy malnutrition [PEM] and manifested as either kwashiorkor or wasting, low middle-upper arm circumference [MUAC] or low weight for height), or a specific micronutrient deficiency such as iron or zinc.¹¹ Some deficiencies, such as chronic malnutrition, will affect global functioning of the brain and are assessed best through general developmental assessment tools. Other deficiencies such as iron deficiency may have more effect on myelination and tools to assess processing speeds may be more useful.

In assessing the neurodevelopmental status of children with malnutrition, a thorough physical examination should be made looking for evidence of chronic disease. A neurologic examination should include assessment of tone, cranial nerve problems (particularly swallowing difficulties), head circumference, and dysmorphic features to help in understanding any underlying etiology for the child's condition.

Developmental Assessment

Developmental tools are generally used for children up to the age of 5 or 6 years with more detailed cognitive assessments being used in school-aged children. Many of these require training and are expensive to buy. They include the Griffith's Scales of Mental Development¹²⁻¹⁵ and the Bayley Scales of

Infant Development.^{16,17} Developmental screening tools such as the Denver II^{18,19} require less training and are more user-friendly but there is debate about their sensitivity or specificity or how culturally appropriate these tools are.^{20,21} Their use can lead to overreferrals of children who do not need to be treated, which is particularly difficult when resources are limited. Parental report measures such as the Ages and Stages or the Paediatric Evaluation of Development Status²²⁻²⁵ are used to detect developmental delay^{21,26-31} and are highly predictive of true problems. These tools require reading abilities unless a professional reads out the items to the parent. They have all been used in Africa (as referenced) to assess outcomes. Often these different developmental assessment tools are translated into local languages³² but not adapted or validated for a particular population.³³⁻³⁵ It is rare that there are standardized norms for these tools, and they are mainly used for research rather than for clinical purposes. In more recent years, some developmental tools such as the Malawi Developmental Assessment Tool and the Kilifi Developmental Inventory have been created or adapted specifically for African settings^{7,8,36-38} and have gone through validation and reliability processes to show good predictive validity. The WHO Gross Motor Milestones are also used but the normal parameters for attainment on these are wide.³⁹ New tools are being created that may be used for surveillance with specific messages interlinked to provide parents and caregivers with advice.⁹

Cognitive and Executive Function

Specific measures to assess cognitive function, executive function, and attention are used primarily for research. Many proponents would recommend using these specific tests rather than general developmental tools as they are more sensitive to specific nutritional deficiencies.^{35,40} These tests require training, time, and psychological support. Previously, IQ tests such as the Stanford-Binet⁴¹ or the Weschler Adult intelligence scales were used.⁴² Recently, tools that do not require language such as Raven's progressive matrices⁴³ or the Kaufman ABC⁴⁴⁻⁴⁶ have become popular, with some tools specifically adapted for African settings such as the Kilifi ABC.³⁴ Other recent studies have used computer-administered tests in the form of simple touch screen games—which also have the advantage of language independence.^{47,48} Developmental psychologists are recognizing how closely linked cognition is with emotional regulation, motor development, and motor activity.⁵ Therefore some specific simple tests of executive function have been used, particularly with infants. These include measures of self-control or delay inhibition such as the “snack delay test.”⁴⁹ Other tests of executive function in infants include “the windows test” or the A not B task.⁵⁰

Specific Areas of Development or Language

Specific language abilities have been assessed to identify particular impairments in children that may be related to malnutrition. For example, the test of verbal analogies or the Peabody Picture Vocabulary Test. Recently, the MacArthur

Bates Communication Development Inventory has been used more widely and has been shown to provide a more sensitive description of the level of language of children between 1 and 2 years of age than many developmental tools. It has been used in different cultural settings with good validity and reliability.⁵⁰⁻⁵⁵

Socioemotional Functioning

It is becoming clearer how relevant and predictive socioemotional functioning is in relation to malnutrition.⁵⁶ Carers have often described the malnourished child as apathetic with little ability to interact with others. There are few assessment tools which have been used, but one research tool which has shown good validity in some settings is the Socio Emotional Development Scale.^{57,58} Many researchers see maternal-child interaction as an important factor in childhood malnutrition. Maternal depression or mental health difficulties that lead to poor interaction may play a part in this.⁵⁹⁻⁶⁴ A clinically useful assessment of the child with malnutrition should include an assessment of maternal mental health and the interaction between child and mother or caregiver. Specific tools for this exist,^{63,65,66} but they vary in their use at a practical level as many take time and require equipment such as video facilities.

The Assessment of Nutritional Status and Functioning of the Child With Neurodisability

Assessing nutritional status in nondisabled children can be challenging; it is even more so in those with disabilities. As a result, nutritional status is often assessed poorly and

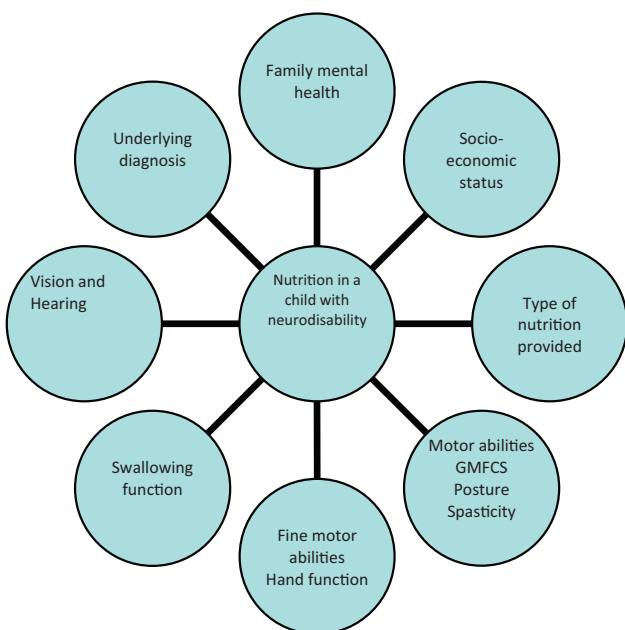


Figure 1 Interaction of multiple factors in the child with neurodisability and malnutrition.

sometimes neglected entirely. One challenge is that there are many forms of malnutrition—often coexisting in the same child—that require different types of assessment. Many of these are proxies for what really determines nutritional “health.” Assessing these children in a clinical setting reveals a number of interactions which, if addressed by the family, can make big differences to the ability to feed and to nutritional intake. The most common difficulty is low nutritional intake and studies have shown that this is often the case when little time is spent with children who have difficulties feeding⁶⁷ (Fig. 1).

Firstly, understanding the specific problems for that child is important. These include understanding the underlying diagnosis. A general examination looking for signs of nutrient deficiencies should include an examination of the skin looking for depigmentation, hyperpigmentation, and desquamation, sometimes seen in kwashiorkor, as well as hyperpigmented hyperkeratosis in zinc deficiency. Other signs to look for are general pallor and koilonychia in iron deficiency. An eye examination should include looking for conjunctival pallor and dryness, wrinkling and Bitot spots (silvery plaques of desquamated epithelial cells and mucus on the bulbar aspect)—all seen in vitamin A deficiency. Examination of the locomotor system, checking for sternal deformities, rib rosaries, and bowing of the tibia will be useful—all signs of rickets (vitamin D deficiency). Children should be assessed for medical conditions (eg, cardiac or renal disease).⁶⁸ On

	<p>GMFCS Level I Children walk at home, school, outdoors and in the community. They can climb stairs without the use of a railing. Children perform gross motor skills such as running and jumping, but speed, balance and coordination are limited</p>
	<p>GMFCS Level II Children walk in most settings and climb stairs holding onto a railing. They may experience difficulty walking long distances and balancing on uneven terrain, inclines, in crowded areas or confined spaces. Children may walk with physical assistance, a hand-held mobility device or used wheeled mobility over long distances. Children have only minimal ability to perform gross motor skills such as running and jumping.</p>
	<p>GMFCS Level III Children walk using a hand-held mobility device in most indoor settings. They may climb stairs holding onto a railing with supervision or assistance. Children use wheeled mobility when traveling long distances and may self-propel for shorter distances.</p>
	<p>GMFCS Level IV Children use methods of mobility that require physical assistance or powered mobility in most settings. They may walk for short distances at home with physical assistance or use powered mobility or a body support walker when positioned. At school, outdoors and in the community children are transported in a manual wheelchair or use powered mobility.</p>
	<p>GMFCS Level V Children are transported in a manual wheelchair in all settings. Children are limited in their ability to maintain antigravity head and trunk postures and control leg and arm movements.</p>

Figure 2 GMFCS E&R descriptors and illustrations for children between their 6th and 12th birthday.

neurologic assessment, the child's tone (stiff or floppy) would aid in advice about positioning (vital for good feeding).⁶⁹ The severity of a child's motor disability is known to be associated with feeding difficulties. Assessing the child's ability to sit, their use of assistive devices and their abilities and positioning for feeding in the home may provide further information for the assessor.⁷⁰ A classification system such as the Gross Motor Functioning Classification System (Fig. 2), a broad 5-category classification system of motor functional limitations and abilities, may help to put this in context^{71,72} (Fig. 2).

We know that anthropometric measurement is crucial in all children but it is particularly important in children with disabilities. Their underlying difficulties can make anthropometry challenging. Measurement of height and weight are not easy in children who cannot stand or sit and who have limb or spine flexion deformities. This influences the ability to undertake height-for-age (a marker of chronic malnutrition or stunting), body mass index, and weight-for-height (a marker of wasting and a key criterion for entry to therapeutic feeding programs) evaluations. In addition, we must not use appearance alone as a way of assessing acute malnutrition as this has poor sensitivity or specificity and many children would be missed and would not get needed treatment. Arm span and tibial length, as proxy measures of height, have good validity, in particular for nonambulant children, for example, those with cerebral palsy.⁷³⁻⁷⁵ Weight measurements should be encouraged but interpreted with caution. The easiest and most useful tool to assess acute malnutrition is the MUAC. MUAC avoids the need for height measurement, is cheap, quick, and easy to use, and is the assessment of choice in populations at risk of wasting.^{76,77} Head circumference may imply an underlying diagnosis and likely continued progression of the neurological condition. Children with cerebral palsy or other developmental disorders have different parameters for normal growth.⁷⁸⁻⁸⁰ Normal growth charts are often not applicable and many children do not achieve "normal" growth. Some disabilities (eg, Down syndrome and cerebral palsy) result in different growth patterns and specialized growth charts are needed to determine growth or nutrition.⁸¹ As cerebral palsy is a heterogenous and complex group, there are different charts for each of the 5 functional levels of cerebral palsy as related to the Gross Motor Functioning Classification System. These are not always easily available so for clinicians, it is more important to just have a general awareness that these children do have different growth trajectories.

Assessment of vision and hearing helps a family understand how best they can enable some children to improve their development, play, communication, and feeding. If visual impairments are not understood, it may be difficult for children to feed. If hearing impairments are present, children can have delayed communication skills and behavioral problems that affect their ability to ask for food.

The assessment of a child with a disability should include a detailed feeding history. This includes information about how they feed, how long it takes, who feeds them, what they feed with (utensils), what kind of foods they take (soft, lumpy, and thickened only), whether they choke or cough regularly, have recurrent chest infections, and whether they drool.⁴

Understanding the social situation for a family with a child with neurodisability enables work with families to improve nutrition. Often, the families of children with disabilities do not really understand their child's diagnosis. Compounding this, families may feel isolated and stigmatized and have problems with child care.⁸² Access to food is a right for children with disabilities, guaranteed under the United Nations Committee of the Rights of Disabled Persons and the United Nations Committee of the Rights of the Child. However, if parents and carers anticipate that their child will die young or will be unable to contribute to the welfare of the household as an adult, families may hesitate to provide enough food, enough nutritious food, or may withhold food altogether.⁸³ We need to understand issues surrounding quality of life and participation of those with disabilities within society—as promoted within the new International Classification of Functioning framework of disability.⁸⁴ It is important to consider the effect of the child's condition on the family and the community, and how this may affect the ability of the family to care for and nurture a child. Social support structures and the assessment of these for a family are vital for these children. Availability of services for children vary but in some settings there may be a social or disability welfare worker or a palliative care service which can provide advice and information for families.

Neuroimaging and Electrophysiological Assessment of Children With Malnutrition

Studies over many years have demonstrated that nutritional deficiency impairs central nervous system functioning at many levels.⁸⁵⁻⁹¹ Human and animal histological and imaging studies of the developing brain have shown both macrostructural and microstructural changes in the nutritionally impaired brain.^{92,93} Kwashiorkor is associated with retarded brain growth,⁹⁴ reduced cerebral cellularity,⁹⁵ reduced or delayed myelination,⁹⁶ and, in the neurophysiological field, changes in electroencephalography (EEG)^{97,98} and evoked potential tracings.⁹⁹

Neuroradiology

Neuroimaging technology is now available in some low-income settings. Imaging studies have shown that cerebral atrophy and ventricular dilatation with prominent sylvian fissures and basal cisterns are common in children with kwashiorkor.¹⁰⁰⁻¹⁰³ Some studies have shown that brain pathology, as demonstrated on magnetic resonance imaging, is reversible after nutritional rehabilitation.^{100,101,104}

EEGs and Malnutrition

EEG, has become more useful with recent advances in EEG technology, particularly through computer analysis procedures.¹⁰⁵ The first studies were conducted in West Africa in the 1950s¹⁰⁶ where abnormal EEGs in children with PEM were shown. In these children, the dominant frequency of the EEG was much lower than in normal children. Similarly, lower frequencies over all EEG bands have been shown in up to one-

third of children with kwashiorkor. Some studies have demonstrated that with treatment these abnormalities tend to disappear but may persist for several months after nutritional rehabilitation in case of severe malnutrition and in children who had PEM before 6 months of age.^{97,98} Long-term follow-up of previously marasmic children confirms that acute PEM results in marked retardation in faster EEG frequencies (α rhythm) for up to 12 years after successful nutritional treatment.^{94,107} Some studies have also related poor cognitive outcomes to the EEG changes of diminished voltage and excessively slow rhythm.¹⁰⁸

Auditory Evoked Potentials and Malnutrition

Auditory evoked potentials (AEP) are understood to be a sensitive measure of brain functions and have been used by many researchers both in human studies^{109,110} and experimental animal studies.¹¹¹ Studies evaluating electrophysiological parameters have reported diverse nervous system consisting of auditory,¹¹² visual,^{112,113} corticospinal,¹¹⁴ and somatosensory paths,¹¹⁵ as well as interhemispheric modulation.¹¹⁶ Clinical studies have shown that early malnutrition (marasmus and kwashiorkor) can produce marked alterations in the electrophysiological parameters of AEP^{117,118} and irreversible increased latencies of AEP waves 12 months after rehabilitation. This suggests deficiencies in the myelination process with decreased synaptic efficiency in the auditory system. Studies have shown brain recovery in laboratory animals when stimulated.^{119,120} Some studies report that the effects of malnutrition on AEPs are reversed by nutritional rehabilitation if associated with daily and individual

sensorimotor and environmental stimulation.¹²¹ Sensory stimulation used in a properly directed, systematic, and individualized manner showed encouraging results in AEP recovery in these children.

Future Plans

The interaction among malnutrition, developmental delay, neurodisability, and malnutrition is strong. Nutritional assessment tools have been used in low-income settings but developmental assessment or cognitive tools have not been well used in these settings. Many tools are not designed for practical identification of developmental delay or disability with linked advice and support for families. There is an obvious need to make available simple, practical neurodevelopmental monitoring or surveillance tools that can be integrated with nutritional assessments to benefit children with neurodevelopmental delays or disabilities and nutritional disorders. All acute malnutrition units should use simple developmental monitoring tools and give advice to families. Table 1 describes some simple measures to use in a busy clinic.

Sensitive and specific tools are required to assess the effect of interventions on outcomes in malnourished children. It may be that specific cognitive and language measures that identify specific brain function problems are of more practical use than overall developmental or cognitive tools. All such tools must be valid and reliable in a variety of cultural settings.^{35,36,51} Improved imaging and EEG technology has advanced the understanding of neurobiological changes in the brain as a result of malnutrition. These modalities will continue to direct

Table 1 The 5 Most Important Things to Assess in Children With Malnutrition and Those With Neurodisability

Malnutrition	Neurodevelopment or Disability
<p>1 Middle-upper arm circumference (MUAC)* In children aged 6-59 mo: < 125 mm = moderate wasting < 115 mm = severe wasting</p> <p>2 Weight for age (and weight trend) Weight for age may be lower than in nondisabled children, but all children should be growing. Loss of weight is a dangerous sign needing further assessment.</p> <p>3 Appetite test and feeding technique If a malnourished child still has appetite and is able to consume a "test" feed, he or she may be eligible for home-based treatment. Those without appetite or with significant feeding problems may need admission</p> <p>4 Oedema If bilateral pitting edema, then consider kwashiorkor</p> <p>5 HIV status In HIV-prevalent areas, this is another major factor underlying malnutrition and should be tested for and excluded</p>	<p>1 Maternal child interaction Knowing if the carer is able to interact and play with the child—encouragement of this is crucial for good feeding and development.</p> <p>2 Developmental stages *Is the child sitting by 9 mo, walking by 18 mo? *Is the child understanding and able to express himself in some way? *Is the child able to use hands to play and feed? Getting an idea of the developmental level of the child can help to providing advice to carers on stimulating the child.</p> <p>3 Feeding and swallowing abilities Some children need specific advice about what utensils and support are best used to help them to feed and swallow as well as what textures of food are helpful.</p> <p>4 Muscle tone and posture (examine undressed) If a child has increased muscle tone or low muscle tone, they may need help in positioning while they feed.</p> <p>5 Vision/hearing Ability to hear and see has profound effects on abilities to feed and interact.</p>

*Weight for height or length is also used to assess wasting severity but is a poorer predictor of mortality outcomes than MUAC—plus and is difficult to assess in some disabilities (eg, children who cannot stand or those with contractures).

research on anatomical areas most affected in different types of malnutrition.

The combined assessments of neurodisabilities and nutrition and growth are not always straightforward but provide the basis for appropriate advice and interventions to improve outcomes and quality of life for children and families. Comprehensive and integrated approaches between health, education, and social services will take this forward.

References

1. Grantham-McGregor S, Cheung YB, Cueto S, et al: Developmental potential in the first 5 years for children in developing countries. *Lancet* 369:60-70, 2007
2. Kuperminc MN, Stevenson RD: Growth and nutrition disorders in children with cerebral palsy. *Dev Disabil Res Rev* 14:137-146, 2008
3. Andrew MJ, Sullivan PB: Feeding difficulties in disabled children. *Paediatr Child Health* 20:321, 2010
4. Sullivan PB: Gastrointestinal disorders in children with neurodevelopmental disabilities. *Dev Disabil Res Rev* 14:128-136, 2008
5. Pollitt E: Developmental sequel from early nutritional deficiencies: Conclusive and probability judgements. *J Nutr* 130:350-353, 2000
6. Engle PL, Fernald LC, Alderman H, et al: Strategies for reducing inequalities and improving developmental outcomes for young children in low-income and middle-income countries. *Lancet* 378:1339-1353, 2011
7. Gladstone M, Lancaster GA, Umar E, et al: The Malawi Developmental Assessment Tool (MDAT): The creation, validation, and reliability of a tool to assess child development in rural African settings. *PLoS Med* 7: e1000273, 2010
8. Abubakar A, Holding PA, Van Baar A, et al: Monitoring psychomotor development in a resource limited setting: An evaluation of the Kilifi Developmental Inventory. *Ann Trop Paediatr* 28:217-226, 2008
9. Ertem IO, Dogan DG, Gok CG, et al: A guide for monitoring child development in low- and middle-income countries. *Pediatrics* 121: e581-e589, 2008
10. Khan NZ: Best resource use for disabled children. *World Health Forum* 19:47-52, 1998
11. Georgieff MK: Nutrition and the developing brain: Nutrient priorities and measurement. *Am J Clin Nutr* 85:614S-620S, 2007
12. Griffiths R: *The Abilities of Young Children*. Amersham: ARICD, 1984
13. Griffiths R: *The Abilities of Babies*. High Wycombe, Bucks: The Test Agency Ltd, 1986
14. Grantham-McGregor S: A review of studies of the effect of severe malnutrition on mental development. *J Nutr* 125:2233-2238, 1995
15. Luiz D, Faragher B, Barnard A, et al: Griffiths Mental Development Scales—Extended Revised (GMD5-ER): 2-8 Years. Technical Manual. Amersham: Association for Research in Child Development (ARICD), 2006
16. Bayley N: *Bayley Scales of Infant Development Manual*. Orlando: The Psychological Association. Harcourt, Brace and Company, 1993
17. Black MM, Baqui AH, Zaman K, et al: Iron and zinc supplementation promote motor development and exploratory behavior among Bangladeshi infants. *Am J Clin Nutr* 80:903-910, 2004
18. Boivin MJ, Green SD, Davies AG, et al: A preliminary evaluation of the cognitive and motor effects of pediatric HIV infection in Zairian children. *Health Psychol* 14:13-21, 1995
19. Oberhelman RA, Guerrero ES, Fernandez ML, et al: Correlations between intestinal parasitosis, physical growth and psychomotor development among infants and children from rural Nicaragua. *Am J Trop Med Hyg* 58:470-475, 1998
20. Glascoe FP: Developmental Screening. In: Parker S, Zuckerman B (eds): *Behavioral and Developmental Pediatrics*. Boston, Little, Brown and Company, 25-29, 1995
21. Glascoe FP, Martin ED, Humphrey SA: Comparative review of developmental screening tests. *Pediatrics* 86:547-554, 1990
22. Juneja M, Mohanty M, Jain R, et al: Ages and Stages Questionnaire as a screening tool for developmental delay in Indian children. *Indian Pediatr* 49:457-461, 2012
23. Kvestad I, Taneja S, Kumar T, et al: The assessment of developmental status using the Ages and Stages questionnaire-3 in nutritional research in north Indian young children. *Nutr J* 12:1-11, 2013
24. Abubakar A, Uriyo J, Stray-Pedersen B, et al: Prevalence and risk factors for poor nutritional status among children in the Kilimanjaro Region of Tanzania. *Int J Environ Res Public Health* 9:3506-3518, 2012
25. Glascoe FP: *Parents' Evaluation of Developmental Status* Nashville, TN: Ellsworth & Vandermeer Press, 1997
26. Glascoe FP: *Collaborating With Parents: Using Parents Education of Developmental Status to Detect and Address Developmental and Behavioural Problems* Nashville, TN: Ellsworth and Vandermeer Press, 1998
27. Glascoe FP: If you don't ask, parents may not tell: Noticing problems vs expressing concerns. *Arch Pediatr Adolesc Med* 160:220, 2006; [author reply 20-21]
28. Glascoe FP: Re: Parents' evaluation of developmental status. *J Paediatr Child Health* 41:615-616, 2005; [author reply 16]
29. Glascoe FP: Parents' evaluation of developmental status: How well do parents' concerns identify children with behavioral and emotional problems? *Clin Pediatr* 42:133-138, 2003
30. Glascoe FP, Altemeier WA, MacLean WE: The importance of parents' concerns about their child's development. *Am J Dis Child* 143:955-958, 1989
31. Glascoe FP, MacLean WE, Stone WL: The importance of parents' concerns about their child's behavior. *Clin Pediatr* 30:8-11, 1991; [discussion 12-4]
32. Geisinger K: Cross-cultural normative assessment: Translation and adaptation issues influencing the normative interpretation of assessment instruments. *Psychol Assess* 6:304-312, 2006
33. Carter JA, Lees JA, Murira G, et al: Issues in the development of cross-cultural assessments of speech and language for children. *Int J Lang Commun Disord* 40:385-401, 2005
34. Holding PA, Taylor HG, Kazungu SD, et al: Assessing cognitive outcomes in a rural African population: Development of a neuropsychological battery in Kilifi District, Kenya. *J Int Neuropsychol Soc* 10:246-260, 2004
35. Prado EL, Hartini S, Rahmawati A, et al: Test selection, adaptation, and evaluation: A systematic approach to assess nutritional influences on child development in developing countries. *Br J Educ Psychol* 80:31-53, 2010
36. Gladstone M, Lancaster G, Jones A, et al: Can Western developmental screening tools be modified for use in a rural Malawian setting? *Arch Dis Child* 93:23-29, 2008
37. Gladstone M, Lancaster G, Umar E, et al: Perspectives of normal child development in rural Malawi—A qualitative analysis to create a more culturally appropriate developmental assessment tool. *Child Care Health Dev* 36:346-353, 2010
38. Abubakar A, Van de Vijver FJR, Van Baar A, et al: Socioeconomic status, anthropometric status and psychomotor development of Kenyan children from resource-limited settings: A path-analytic study. *Early Hum Dev* 84:613-621, 2008
39. Group WHOMGRS. W.H.O Motor Development Study: Windows of achievement for six gross motor developmental milestones. *Acta Paediatr Suppl* 450:86-95, 2006
40. Connolly KJ, Kvalsvig JD: Infection, nutrition and cognitive performance in children. *Parasitology* 107:S187-S200, 1993
41. Stoch MB, Smythe PM: 15-Year developmental study on effects of severe undernutrition during infancy on subsequent physical growth and intellectual functioning. *Arch Dis Child* 51:327-336, 1976
42. Walker SP, Chang S, Powell CA, et al: Effects of early childhood psychosocial stimulation and nutritional supplementation on cognition and education in growth-stunted Jamaican children: Prospective cohort study. *Lancet* 366:1804-1807, 2005
43. Raven J: The Raven's progressive matrices: Change and stability over culture and time. *Cognit Psychol* 41:1-48, 2000

44. Kaufman AS, Kaufman NL: Kaufman Assessment Battery for Children Circle Pines: American Guidance Service, 1983
45. Bogale A, Stoecker BJ, Kennedy T, et al: Nutritional status and cognitive performance of mother-child pairs in Sidama, Southern Ethiopia. *Matern Child Nutr* 9:274-284, 2013
46. Bangenda D, Nassali A, Kalyesubula I, et al: Health, neurologic, and cognitive status of HIV-infected, long-surviving, and antiretroviral-naive Ugandan children. *Pediatrics* 117:729-740, 2006
47. CANTAB. Cambridge Cognition Computerised Testing. (R). <http://www.camcog.com/cantab-tests.asp>
48. Nkhoma OW, Duffy ME, Cory-Slechta DA: Early-stage primary school children attending a school in the Malawian School Feeding Program (SFP) have better reversal learning and lean muscle mass growth than those attending a non-SFP school. *J Nutr* 143:1324-1330, 2013
49. Kochanska G, Murray KT, Harlan ET: Effortful control in early childhood: Continuity and change, antecedents, and implications for social development. *Dev Psychol* 36:220-232, 2000
50. Nampijja M, Apule B, Lule S, et al: Effects of maternal worm infections and anthelmintic treatment during pregnancy on infant motor and neurocognitive functioning. *J Int Neuropsychol Soc* 18:1019-1030, 2012
51. Nampijja M, Apule B, Lule S, et al: Adaptation of Western measures of cognition for assessing 5-year-old semi-urban Ugandan children. *Br J Educ Psychol* 80:15-30, 2010
52. Rescorla L, Ratner NB, Jusczyk P, et al: Concurrent validity of the language development survey: Associations with the MacArthur-Bates communicative development inventories: Words and sentences. *Am J Speech Lang Pathol* 14:156-163, 2005
53. Skarakis-Doyle E, Campbell W, Dempsey L: Identification of children with language impairment: Investigating the classification accuracy of the MacArthur-Bates Communicative Development Inventories, Level III. *Am J Speech Lang Pathol* 18:277-288, 2009
54. Thal D, Desjardin JL, Eisenberg LS: Validity of the MacArthur-Bates Communicative Development Inventories for measuring language abilities in children with cochlear implants. *Am J Speech Lang Pathol* 16:54-64, 2007
55. Westerlund M, Berglund E, Eriksson M: Can severely language delayed 3-year-olds be identified at 18 months? Evaluation of a screening version of the MacArthur-Bates Communicative Development Inventories. *J Speech Lang Hear Res* 49:237-247, 2006
56. Walker SP, Wachs TD, Grantham-McGregor S, et al: Inequality in early childhood: Risk and protective factors for early child development. *Lancet* 378:1325-1338, 2011
57. Briggs-Gowan MJ, Carter AS: Applying the Infant-Toddler Social & Emotional Assessment (ITSEA) and Brief-ITSEA in early intervention. *Infant Ment Health J* 28:564-583, 2007
58. Kruizinga I, Jansen W, Carter AS, et al: Evaluation of an early detection tool for social-emotional and behavioral problems in toddlers: The Brief Infant Toddler Social and Emotional Assessment—A cluster randomized trial. *BMC Public Health* 11:494
59. Rahman A, Iqbal Z, Roberts C, et al: Cluster randomized trial of a parent-based intervention to support early development of children in a low-income country. *Child Care Health Dev* 35:56-62, 2009
60. Rahman A, Lovel H, Bunn J, et al: Mothers' mental health and infant growth: A case-control study from Rawalpindi, Pakistan. *Child Care Health Dev* 30:21-27, 2004
61. Rahman A, Malik A, Sikander S, et al: Cognitive behaviour therapy-based intervention by community health workers for mothers with depression and their infants in rural Pakistan: A cluster-randomised controlled trial. *Lancet* 372:902-909, 2008
62. Rahman A, Patel V, Maselko J, et al: The neglected "m" in MCH programmes—Why mental health of mothers is important for child nutrition. *Trop Med Int Health* 13:579-583, 2008
63. Cooper PJ, Tomlinson M, Swartz L, et al: Improving quality of mother-infant relationship and infant attachment in socioeconomically deprived community in South Africa: Randomised controlled trial. *Br Med J* 338:b974, 2009
64. Stewart RC, Bunn J, Vokhiwa M, et al: A prospective study of psychological distress among mothers of children admitted to a nutritional rehabilitation unit in Malawi. *Child Care Health Dev* 37:55-63, 2011
65. Aboud FE, Alemu T: Nutrition, maternal responsiveness and mental development of Ethiopian children. *Soc Sci Med* 41:725-732, 1995
66. Cooper PJ, Landman M, Tomlinson M, et al: Impact of a mother-infant intervention in an indigent peri-urban South African context: Pilot study. *Br J Psychiatry* 180:76-81, 2002
67. Yousafzai AK, Pagedar S, Wirz S, et al: Beliefs about feeding practices and nutrition for children with disabilities among families in Dharavi, Mumbai. *Int J Rehabil Res* 26:33-41, 2003
68. Freeman JV, Christian P, Khatri SK, et al: Evaluation of neonatal verbal autopsy using physician review versus algorithm-based cause-of-death assignment in rural Nepal. *Paediatr Perinat Epidemiol* 19:323-331, 2005
69. Larnert G, Ekberg O: Positioning improves the oral and pharyngeal swallowing function in children with cerebral-palsy. *Acta Paediatrica* 84:689-692, 1995
70. Adams MS, Khan NZ, Begum SA, et al: Feeding difficulties in children with cerebral palsy: Low-cost caregiver training in Dhaka, Bangladesh. *Child Care Health Dev* 38:878-888, 2012
71. Palisano RJ, Hanna SE, Rosenbaum PL, et al: Validation of a model of gross motor function for children with cerebral palsy. *Phys Ther* 80:974-985, 2000
72. Rosenbaum PL, Palisano RJ, Bartlett DJ, et al: Development of the Gross Motor Function Classification System for cerebral palsy. *Dev Med Child Neurol* 50:249-253, 2008
73. Reeves SL, Varakamin C, Henry CJ: The relationship between arm-span measurement and height with special reference to gender and ethnicity. *Eur J Clin Nutr* 50:398-400, 1996
74. Abe K, Tamaki J, Kadowaki E, et al: Use of anthropometric indicators in screening for undiagnosed vertebral fractures: A cross-sectional analysis of the Fukui Osteoporosis Cohort (FOC) study. *BMC Musculoskelet Disord* 9:157, 2008
75. Yousafzai AK, Filteau SM, Wirz SL, et al: Comparison of armspan, arm length and tibia length as predictors of actual height of disabled and nondisabled children in Dharavi, Mumbai, India. *Eur J Clin Nutr* 57:1230-1234, 2003
76. Myatt M, Khara T, Collins S: A review of methods to detect cases of severely malnourished children in the community for their admission into community-based therapeutic care programs. *Food Nutr Bull* 27:S7-S23, 2006
77. Briand A, Maire B, Fontaine O, et al: Mid-upper arm circumference and weight-for-height to identify high-risk malnourished under-five children. *Matern Child Nutr* 8:130-133, 2012
78. Day SM, Strauss DJ, Vachon PJ, et al: Growth patterns in a population of children and adolescents with cerebral palsy. *Dev Med Child Neurol* 49:167-171, 2007
79. Stevenson RD, Conaway M, Chumlea WC, et al: Growth and health in children with moderate-to-severe cerebral palsy. *Pediatrics* 118:1010, 2006
80. Van Gameren-Oosterom HBM, Van Dommelen P, Oudesluis-Murphy AM, et al: Healthy growth in children with Down syndrome. *PLoS One* 7:1-8, 2012
81. Rosenbloom ST, McGregor TL, Chen Q, et al: Specialized pediatric growth charts for electronic health record systems: The example of Down syndrome. *Annual Symposium proceedings/AMIA Symposium*. 687-691, 2010
82. Gona JK, Mung'ala-Odera V, Newton CR, et al: Caring for children with disabilities in Kilifi, Kenya: What is the carer's experience? *Child Care Health Dev* 37:175-183, 2011
83. Pinheiro, World Report on Violence Against Children, 2006, United Nations, Geneva, Switzerland. www.violencestudy.org
84. Morris C, Kurinczuk JJ, Fitzpatrick R: Child or family assessed measures of activity performance and participation for children with cerebral palsy: A structured review. *Child Care Health Dev* 31:397-407, 2005
85. Bedi KS: Lasting neuroanatomical changes following undernutrition during early life. In: Dobbing J (ed): *Early Nutrition and Later Achievement*. New York: Academic Press, 1987

86. Bedi KS, Thomas YM, Davies AA, et al: Synapse to neuron ratios of the frontal and cerebellar cortex of 30 day old and adult rats undernourished during early post natal life. *J Comp Neurol* 193:49-56, 1980
87. Cragg BG: The development of cortical synapses during starvation in the rat. *Brain* 95:143-150, 1972
88. Cravioto J, E.R. D, Birch HG: Nutrition, growth and neurointegrative development: An experimental and ecological study. *Pediatrics* 38:319-367, 1966
89. Dobbing J: Effects of experimental undernutrition on development of the nervous system. In: Scrimshaw NS, Gordon JE (eds): *Malnutrition, Learning and Behaviour*. Cambridge, Mass, MIT Press, 181-202, 1968
90. Dobbing J, Sands J: Vulnerability of developing brain. IX. The effect of nutrition, growth retardation on the timing of the brain growth spurt. *Biol Neonate* 19:363-378, 1971
91. Finger S, Stein DG: *Brain Damage and Recovery: Research and Clinical Perspectives*. New York: Academic Press, 1982
92. Quirk GJ, Mejia WR, Hesse H, Su H: Early malnutrition followed by nutritional restoration lowers the conduction velocity and excitability of the corticospinal tract. *Brain Res* 670:277-282, 1995
93. Wang L, Xu RJ: The effects of perinatal protein malnutrition on spatial learning and memory behaviour and brain-derived neurotrophic factor concentration in the brain tissue in young rats. *Asia Pac J Clin Nutr* 16:467-472, 2007
94. Stoch MB, Smythe PM: Does undernutrition during infancy inhibit brain growth and subsequent intellectual development? *Arch Dis Child* 38:546-552, 1963
95. Winick M, Rosso P: The effect of severe early malnutrition on cellular growth of human brain *Pediatr Res* 3:181, 1969
96. Fishman MA, Prensley AL, Dodge PR: Low content of cerebral lipids in infants suffering from malnutrition. *Nature* 221:552-553, 1969
97. Engel R: Abnormal brain wave patterns in Kwashiorkor. *Electroenceph Clin Neurophysiol* 8:489, 1956
98. Nelson GK: The electroencephalogram in kwashiorkor. *Electroenceph Clin Neurophysiol* 11:73, 1959
99. Flinn JM, Barnet AB, Lydick S, et al: Infant malnutrition affects cortical auditory evoked potentials. *Percept Mot Skills* 76:1359-1362, 1993
100. Akinyinka OO, Adeyinka AO, Falade AG: The computed axial tomography of the brain in protein energy malnutrition. *Ann Trop Paediatr* 15:329-333, 1995
101. Gunston G, Burkimsher D, Malan H, et al: Reversible cerebral shrinkage in kwashiorkor: An MRI study. *Arch Dis Child* 62:589-592, 1992
102. Househam KC, De Villiers JF: Computed tomography in severe protein energy malnutrition. *Arch Dis Child* 62:589-592, 1987
103. Atlabi OM, Lagunju IA, Tongo OO, et al: Cranial magnetic resonance imaging findings in kwashiorkor. *Int J Neurosci* 120:23-27, 2010
104. Stein DG, Finger S, Hart T: Brain damage and recovery: Problems and perspectives. *Behav Neural Biol* 37:185-222, 1983
105. Metcalfe DL: Electroencephalography. In: Prescott JW, Read MS, Coursin DB (eds): *Brain Function and Malnutrition. Neurophysiological Methods of Assessment*. New York, John Wiley and Sons, 119, 1995
106. Gallais PJ, Bert J, Corriol J, et al: Les rythms des noires d'Afrique (Etude des 100 premiers traces subjects normaux). *Electroenceph Clin Neurophysiol* 3:110, 1951
107. Baraitser M, Evans DE: The effect of undernutrition on brain-rhythm development. *S Afr Med J* 43:56, 1969
108. Sarrouy C, Saint-Jean M, Clausee Algeria Med: 57:584, 1953
109. Hecox K, Galambos R: Brainstem auditory responses in human infants and adults. *Arch Otolaryngol* 99:30-33, 1974
110. Shipley C, Buchwald JS, Norman R, et al: Brain stem auditory evoked response development in the kitten. *Brain Res* 182:313-326, 1980
111. Buchwald JS, Huang C: Far-field acoustic response: Origins in the cat. *Science* 189:382-384, 1975
112. Durmaz S, Karagol U, Deda G, et al: Brainstem audiotry and visual evoked potentials in children with protein energy malnutrition. *Pediatr Int* 41:615-619, 1999
113. McDonald CG, Joffe CL, Barnet AB, et al: Abnormal flash visual evoked potentials in malnourished infants: An evaluation using principal component analysis. *Clin Neurophysiol* 118:896-900, 2007
114. Karak B, Misra S, Garg RK, et al: A study of transcranial magnetic stimulation in older (> 3 years) patients of malnutrition. *Neurol India* 47:229-233, 1999
115. Hesse H, Rivera MF, de Diaz I, et al: Central somatosensory conduction time in severely growth-stunted children. *Am J Clin Nutr* 67:93-96, 1998
116. Pinto AV, Guedes RC: Direct evidence of inter-hemispheric modulation by callosal fibers: A cortical spreading depression study in well-nourished and early-malnourished adult rats. *Exp Brain Res* 186:39-46, 2008
117. Barnet AB, Weiss IP, Sotillo MV, et al: Abnormal auditory evoked potentials in early infancy malnutrition. *Science* 201:450-452, 1978
118. Bartel PR, Robson E, Conradie JM, et al: Brainstem auditory evoked potentials in severely malnourished children with kwashiorkor. *Neuropediatrics* 17:178-182, 1986
119. Bedi KS, Bhide PG: Effects of environmental diversity on brain morphology. *Early Hum Dev* 17:107-143, 1988
120. Rocinholi LF, de Oliveira LM, Colafemina JF: Malnutrition and environmental stimulation in rats: Wave latencies of the brainstem auditory evoked potentials. *Nutr Neurosci* 4:199-212, 2001
121. Lima JG: Estudo morfológico e morfométrico do corpo caloso de ratos submetidos a diferentes tipos de dietas e à estimulação sensorial ambiental. Universidade de São Paulo, 1992