A description of the Griffiths III scores in a cohort of HIV-exposed and HIV-unexposed South African children at 9 months of age

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Background. The Griffiths Mental Developmental Scales (GMDS) is a developmental tool commonly used in South Africa (SA). The most recent version, the GMDS III (Griffiths III) was standardised in the UK and the Republic of Ireland and published in 2016.
Objectives. To describe neurodevelopmental scores using the Griffiths III, demographics and confounding variables, in children aged 8 - 10 months, living in an urban setting in Cape Town, SA. To compare the scores between children who were HIV-exposed and -uninfected (CHEU) and children who were HIV-unexposed and -uninfected (CHUU).
Method. We conducted a retrospective cross-sectional data analysis of 85 infants with completed Griffiths III assessments at 8 to 10 months of age. This is a substudy of a prospective, longitudinal descriptive study describing neuroimaging and neurodevelopmental outcomes in 31 CHUU and 54 CHEU.
Results. Across all Griffiths III subscales, SA infants tested between average and very superior ranges in raw and quotient scores and between 63rd and 76th percentiles. They outperformed the UK normative sample. Caregivers of CHUUs highest level of education was significantly higher than caregivers of CHEU (p=0.002). CHUU scored higher on the eye and hand coordination scale compared with CHEU (p=0.02).
Conclusion. Due to favourable developmental scores achieved by South African children in comparison to the standardised sample, the revision of the Griffiths Scales to the Griffiths III is likely to have clinical use in SA infants.
Keywords. Griffiths III; South Africa; neurodevelopment; HIV-exposed; infants.

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Due to the advancement in management of early childhood illnesses, the increased coverage of vaccination programmes and an improvement in neonatal services, there has been a marked decline in under five mortality rates in low to middle income countries in recent years.[1-3] Within these high-risk groups, it is estimated that there are 200 million children living with developmental delay/disabilities globally.[2,4] In communities with high rates of HIV, factors contributing to developmental delay are compounded. Due to programmes for preventing vertical transmission of HIV, there are many children who are HIV-exposed and -uninfected (CHEU). There are an estimated 4 million CHEU in South Africa (SA) and this number is increasing annually.[5] Despite being HIV-uninfected, many CHEU continue to demonstrate reduced growth[6,7] and neurodevelopmental delay,[8-10] especially in the domains of expressive speech and gross motor function.[6]

Early detection of deviation from expected development improves the likelihood of early, holistic intervention and should improve outcomes.[1,2,4,11,12] Developmental assessment tools are used to assess a child's developmental trajectory in one or more areas of development.[13]

The Griffiths Mental Developmental Scales (GMDS) are comprehensive developmental assessment tools commonly used in SA. The scales are used to: (*i*) assess if a child is developing appropriately for their age; (*ii*) assess if there is a delay in a child's development within a specific domain which could be linked to a specific developmental disorder; and (*iii*) track and monitor a child's development to assist in planning for interventions and management of a child.[11,13-15] In a previous construct validity study[14] looking at the performance of a group of SA children tested on the previous version of the GMDS and compared with the British standardisation sample group, there was a positive correlation coefficient between the two groups. This indicated that the scales measured a construct that was consistent across cultures.[14]

Owing to the 'Flynn effect', which is the cognitive gain of a child over time, influenced by current social climate, the Griffiths original scales needed to be revised to maintain relevance.[11,14]

The most recent version is the GMDS III (Griffiths III), which was published by the Association for Research in Childhood Development (ARICD) in 2016. It was developed with the assistance of researchers from Nelson Mandela Metropolitan University in Gqeberha, SA. Items were specifically chosen to be culturally fair among globally diverse cultural groups. The Griffiths III was standardised in the UK and the Republic of Ireland on 426 children. This diagnostic tool assesses five domains of development; it provides a developmental profile of strengths and weaknesses across each domain and provides an indication of a child's global development (developmental quotient).[11] The domains assessed are: (*i*) foundations of learning subscale – assesses aspects of cognition, executive function, visual and auditory short- and long-term memory, and visual sequencing; (*ii*) language and communication subscale – assesses expressive and receptive language and syntactic, pragmatic, and semantic language; (*iii*) eye and hand coordination subscale – assesses fine motor and visual perceptual skills; (*iv*) personal-social-emotional subscale – assesses adaptive skills, facial expressions and measures empathy, the capacity for self-evaluation and moral reasoning; and (*v*) gross motor subscale – assesses whole-body control and movement, posture, and balance.[11,13] The global score provides an overall measure of a child's development.

Advantages of the most recent version include that it reflects the latest research in the field of neurodevelopment and new norms will address the 'Flynn effect'. It is now a continuous scale from 0 to 6 years, which addresses the previous challenge of transitioning from the 0- to 2-year-old scales to 2 - 8 years scales for longitudinal profiles. This improvement streamlines tool administration. Other advantages include that the materials can be cleaned, and the content is up to date and fun for the children.[13]

Although there are currently no data on the use of the GMDS III in SA children, a study by Mutapi *et al.*[16] showed that the Griffiths III was both sensitive in assessing the development of children as well as useful in monitoring treatment effect in a group of Zimbabwean children with schistosome infections.[16] We share our experience on the GMDS III in SA children.

The primary aim of the study was to describe the neurodevelopmental scores using the GMDS III, as well as the demographics and confounding variables, in a cohort of Xhosa speaking children at 8-10 months of age, living in an urban setting in Cape Town, South Africa. The exploratory aim is to compare CHEU and CHUU.

Methods

This is a sub-study using data from a prospective, longitudinal descriptive study entitled 'Neonatal imaging as an early marker of neurodevelopment and predictor of cognitive performance in infants who were exposed to HIV and antiretroviral therapy (ART) *in utero* and postnatally'.[12,17] This sub-study is a retrospective cross-sectional data analysis of 85 infants with completed GMDS III assessments at their 9-month study visit (8 - 10 months of age). Of these infants, 31 were CHUU and 54 were CHEU.

All infants of HIV-positive mothers were exposed to maternal ART – either from the time of conception or from 12 weeks' gestational age. These infants had negative HIV-1 PCR test results at their 3-, 6-, 12- and 19-month visits; none of the infants seroconverted. As per Western Cape Health Services guidelines: breastfeeding was recommended instead of formula feeding for HIV-exposed infants; infants born to low-risk HIV-infected mothers received daily nevirapine for 6 weeks regardless of feeding choice; infants born from mothers with a viral load >1 000 copies/mL received nevirapine for at least 12 weeks (if breastfed) and zidovudine for 6 weeks; and HIV-negative mothers had repeated HIV testing at their 20-week and 32- to 34-week antenatal visits, as well as every 3 months post delivery while breastfeeding.

Infants with any of the following parameters were excluded from the parent and present study: born <37 or >42 weeks' gestational age; birthweight <2 500 g; positive HIV-1 PCR test results; severe congenital malformations or chromosomal abnormalities; neonatal asphyxia; sepsis; persistent neonatal hypoglycaemia; and severe neonatal jaundice.

The GMDS III was performed at the 9-month study visit between January 2019 and November 2020. Assessments were conducted by a GMDS III -trained research assistant in isiXhosa (unless the participants' mother/caregiver particularly requested English or Afrikaans) and were supervised by a GMDS III -certified developmental paediatrician or educational psychologist. The GMDS III instructions and some social questions were translated into isiXhosa and recorded. These recordings were used for all participants, to ensure all tests were carried out using the same translations. Both the research assistant and the supervisor scored each child, these scores were then compared and discussed after the assessment. The tests were also video recorded for quality assurance purposes. Tests were performed when the infants were not tired, hungry, or unwell – they were either first given something to eat or a space to sleep or brought back on another day if they were unsettled.

The variables considered include the following: home language; test language; sex of the infant; age at the time of testing; growth parameters (used as a representation of nutritional status), daytime care setting at the time of the assessment; the maternal highest level of education; HIV exposure; breast, formula or mixed feeding; vision and hearing; behaviour of the child during testing; raw, quotient and percentile scores of the GMDS III subscales.

A case report form and the GMDS III scoring card was used to record the clinical data for each infant participant. Test age was calculated from the gestational age. A ceiling and basal score of 6 items was used. The raw scores obtained in each subscale, were used (with norm tables in the GMDS III manual) as a refence point from which developmental quotient and percentile scores were determined. The Interpretive Descriptive Classification table also in the GMDS III manual, which provides descriptive categories, was used to interpret normative information.[11,15]

In addition to the GMDS III, visual screening was performed using 'hundreds-and-thousands' and small silver balls (silver dragées), which are tiny cake decorations. Formal hearing screening was not conducted, but any child that was not responding to examiners' interactions or that scored low on the language subset, was referred to audiology for a formal assessment. Parent study data was captured on a RedCap database and extracted as a Microsoft Excel (Microsoft Corp., USA) spreadsheet for this sub-study.

Statistics

Descriptive statistics (mean and standard deviations (SDs) for continuous data, and proportions for categorical data) were used to represent GMDS III scores and demographic data. For the exploratory aim comparing CHEU and CHUU, independent sample *t*-tests compared GMDS III scores and continuous demographic and confounder variables between groups. Chi squared tests were used to test the association between categorical demographic and confounder variables between groups (CHEU and CHUU). Data were analysed using SPSS (version 26; IBM Corp., USA), with the threshold for statistical significance set at p=0.05.

Ethics

Ethics approval for the parent study was obtained from Stellenbosch University (ref. no. N16/10/04) and for this sub study from The University of the Witwatersrand (ref. no. R14/49). Caregivers were provided with feedback and a formal report of their child's scores on the assessment. If necessary, advice on stimulation in the weaker developmental domains was given. If significant developmental delay was noted, participants were referred as per standard care for Western Cape health services.

Results

More than half (54.1%) of infants were male and 45.9% were female (Table 1). The mean (SD) gestational age of the group (at birth) was 39.5 (1.3) weeks. The mean birth growth parameters were as follows: weight 3 289.5 g (WAZ (weight-for-age *Z*-score) boys 0; WAZ girls above 0); length 50.1 cm (LAZ (length-for-age *Z*-score) boys 0; LAZ girls just above 0) and head circumference 34.0 cm (HCAZ (head-circumference-for-age *Z*-score) boys just below 0; HCAZ girls 0).[18] There was no significant difference in gestational age and birth growth parameters between the CHUU and CHEU (Table 2).

The mean (SD) age at the examination was 9.2 (0.2) months. The mean growth parameters at time of examination were as follows: weight 9.5 kg (WAZ boys above 0; WAZ girls above 0); length 71.4 cm (LAZ boys 0; LAZ girls just above 0) and head circumference 46.1 cm (HCAZ boys +1; HCAZ girls above +1).[18] There was no significant difference in growth parameters at the time of examination between CHUU and CHEU.

Three participants had mild behavioural problems during testing. Two participants were quieter and more reserved than expected. The third child did not engage well and at follow-up at 19 months of

Table 1. Descriptive statistics for demographic and confounder variables, and the analyses for between-group comparisons.

	Whole sample (*N*=85), *n* (%)*	CHUU (*n*=31), *n* (%)*	CHEU (*n*=54), *n* (%)*	*p*-value†
Gestational age at birth (weeks)	39.5 (1.3)	39.6 (1.3)	39.4 (1.4)	0.668
Birthweight (g)	3 289.5 (427.6), range 2 500.0 - 4 345.0	3 329.0 (448.5)	3 266.8 (417.7)	0.522
Birth length (cm)	50.1 (2.8), range 45 - 52.5	50.4 (3.5)	49.9 (2.4)	0.445
Birth head circumference (cm)	34.0 (1.5), range 31 - 39	34.4 (1.3)	33.9 (1.6)	0.132
Age at examination (months)	9.2 (0.2)	9.2 (0.3)	9.2 (0.2)	0.706
Maternal education (years)	11.4 (1.0)	11.6 (0.8)	11.2 (1.1)	0.127
Weight at examination (kg)	9.5 (1.3), range 6.2 - 13.5	9.7 (1.3)	9.3 (1.4)	0.239
Length at examination (cm)	71.4 (2.8), range 64 - 79	71.9 (2.7)	71.2 (2.9)	0.264
Head circumference at examination (cm)	46.1 (1.6), range 43 - 50.5	46.5 (1.5)	45.9 (1.6)	0.132
Sex				0.744
Male	46 (54.1)	18 (58.1)	28 (51.9)	
Female	39(45.9)	13 (41.9)	26 (48.1)	
Feeding				0.079
EBF	16 (18.8)	6 (19.4)	10 (18.5)	1.00
EFF	49 (57.6)	14 (45.2)	35 (64.8)	0.100
MF (formula and breast)	19 (22.4)	11 (35.5)	8 (14.8)	0.059
Did not answer	1 (1.2)	0	1 (1.9)	-
Behaviour during testing				1.00‡
No problem	82 (96.5)	30 (96.8)	52 (96.3)	
Mild problem	3 (3.5)	1 (3.2)	2 (3.7)	
Current Care				0.271‡
Home	63 (74.1)	26 (83.9)	37 (68.5)	
Créche	9 (10.6)	1 (3.2)	8 (14.8)	
Day mother	11 (12.9)	3 (9.7)	8 (14.8)	
Other	2 (2.4)	1 (3.2)	1 (1.9)	
Caregiver				1.00‡
Mother	83 (97.6)	30 (96.8)	53 (98.1)	
Grandmother	2 (2.4)	1 (3.2)	1 (1.9)	
Caregiver's highest level of education				0.002‡
<Grade 10	6 (7.1)	3 (9.7)	3 (5.6)	0.664
Grade 10	35 (41.2)	5 (16.1)	30 (55.6)	<0.001
Grade 12	35 (41.2)	17 (54.8)	18 (33.3)	0.068
Technikon/College	8 (9.4)	5 (16.1)	3 (5.6)	0.134
University	1 (1.2)	1 (3.2)	0	0.365

EBF = exclusively breastfed; EFF = exclusively formula fed; MF = mixed feeding (formula and breastmilk).
*Unless otherwise specified.
†Unexposed v. exposed.
‡Fisher's exact test.

age,)this participant met the Diagnostic and Statistical Manual for Mental Disorders (DSM-V) criteria for autism spectrum disorder.

The only significant finding between groups when evaluating demographic and confounding variables in the cohort, was that caregivers of CHUUs attained higher levels of education compared with caregivers of CHEU (p=0.002); and a significantly higher proportion of CHEU had caregivers with a Grade 10 level of education compared with CHUU (56% v. 16%; p<0.001) (Table 3)

General development, quotient and percentile scores were not provided for the UK sample.

The GMDS III manual does not account for the discrepancy in descriptive classification between the raw score mean (SD) and quotient (SD).[15]

The only significant finding between groups when evaluating GMDS III scores was that CHUU had a significantly higher quotient score on the Eye and Hand Coordination Subscale compared with CHEU (p=0.023).

Discussion

Demographics

As no significant gender differences were found when standardising the GMDS III, gender did not have to be considered when delineating norm groups.[11] As a result, when performing statistical analysis of the SA group, participants were not grouped according to gender.

To obtain an accurate overview of the nutritional status of the study population, World Health Organization *Z*-score growth charts were used (WAZ, LAZ, HCAZ).[18] When the average measurements of the group were plotted for growth parameters (boys and girls), most plots fell on and around the 0 *Z*-score. The data points that deviated from this pattern included above the +1 HCAZ for girls at time of examination and +1 HCAZ for boys at the time of examination, neither of which were significant. These findings infer that the sample used had a good nutritional status.

There were no statistical differences within the study population between types of feeding; behaviour during testing; care setting or primary caregiver. If significant differences had been found, these factors may have skewed developmental outcomes of this study.[2,4,6,11]

GMDS III scores

Across all five of the GMDS III subscales and general development, the SA group tested between the average and very superior ranges in mean raw scores and mean quotient scores, and between the 63rd and 76th percentiles.

When compared with scores in year 1 provided by the ARICD, across all the domains, SA infants (n=85) outperformed the UK sample (n=86).[11] This is despite CHEU children having been included in the SA sample. These findings differed from the findings of Amod *et al.*[19] in 2007 'Use of the 1996 Griffiths Mental Developmental Scales for Infants', in which SA infants performed better in only 2 subscales (eye and hand coordination and performance), whereas British infants scored significantly better on personal-social subscales.[19]

Infant numbers were well matched between the SA (n=85) and UK (n=86) groups. The UK group considered the medical history and geographical location of the child, as well as maternal level of education in selecting their sample.

The differences in the sampling of the groups include:

- The UK sample considered children in year 1 and had a mean (SD) age of 6.45 (3.47) months, while the SA sample had a mean (SD) age of 9.2 (0.2) months.
- The medical exclusion criteria for the UK sample selection were not detailed in the Griffiths Manual, while the SA sample had stringent exclusion criteria based on susceptibility for neurological insults.
- The UK sampled children from a wide geographical area including both urban and rural areas in England, Republic and Northern Ireland, Scotland and Wales, whereas the SA sample included a small geographical sample of children living in an urban setting in Cape Town, South Africa.
- The UK sample used the Index of Multiple Deprivation Tool when considering maternal education, whereas the SA sample evaluated maternal highest level of education achieved.
- Testing of the SA sample was limited to four testers including one developmental paediatrician, two educational psychologists and one research assistant, while the UK sample had nineteen testers.[11]

CHUU and CHEU comparison

Demographics

Maternal education is a positive contributing factor towards a child's development.[4] Caregivers of CHUU's highest level of education was significantly higher than caregivers of CHEU (p=0.002); 74.1% of caregivers of CHUU had a grade 12 or higher level of education compared with 38.9% of caregivers of CHEU. In previous studies, it has been noted that the difference in developmental outcomes of CHEU compared with CHUU in resource-poor countries with lower levels of maternal education is worse than in resource-rich countries.[20]

Griffiths III scores

There was only one significant difference between groups: CHUU had a significantly higher quotient score on the eye and hand coordination scale compared with CHEU (p=0.023). This finding is despite not having any concerns regarding vision from screening done on the study group and may be associated with the higher maternal level of education found in the CHUU group. In previous studies comparing neurodevelopmental outcomes in CHUU and CHEU children, results have been inconsistent. Some have shown no difference in developmental outcomes between these groups[20-22] and others have shown subtle speech and language delay,[20] motor delay[23] and motor and expressive language delay in the CHEU group.[24] In a recent meta-analysis by Wedderburn *et al.*[6] in 2022, although the effects are subtle, there was found to be a language and gross motor deficit in CHEU compared with CHUU.[6] The clinical significance of this is that language delay can affect scholastic performance and gross motor delay can influence other domains of development. No previous studies have identified eye and hand coordination delay. For our comparisons, the groups sizes may have been too small. Significant language and communication deficits may also only become evident after 12 months of age.[6]

Study limitations

Limitations of this study are that only the 8- to 10-month age group was tested which leaves space for a descriptive analysis of SA children aged 1 to 6 years using the GMDS III to be undertaken. Only children in an urban setting were sampled. The small sample size in groups may have prevented identification of differences between groups. Other factors that were not considered are maternal mental health and caregiver intelligence quotient, which may have played a role in these findings.

Conclusion

Based on our findings of a group of isiXhosa-speaking children from an urban setting in Cape Town, achieving favourable developmental scores when using the revised GMDS III, the test is likely to be

Table 2. Raw mean (SD), quotient (SD) and percentile scores and descriptive classification for the groups: South African (SA) children at 9 months (*n*=85) and UK children in year one (*n*=86)[11,16]

Subscale	Sample of children	Raw score, mean (SD)	Category	Quotient, mean (SD)	Category	Percentile
Foundations of learning	SA	13.4 (1.9)	Above average	109.6 (12.6)	Average	67.6 (22.7)
	UK	10.2 (5.9)	Average			
Language and communication	SA	13.4 (2.2)	Above Average	106.9 (10.1)	Average	63.9 (19.8)
	UK	9.5 (5.6)	Average			
Hand and eye coordination	SA	14.7 (1.7)	Superior	106.6 (9.4)	Average	63.4 (18.6)
	UK	10.9 (6.2)	Average			
Personal, social and emotional	SA	16.1 (2.1)	Very Superior	111.9 (8.6)	Above average	74.1 (14.8)
	UK	10.7 (6.5)	Average			
Gross motor	SA	17.0 (2.3)	Very Superior	115.7 (13.6)	Above average	76.7 (22.3)
	UK	11.1 (6.4)	Average			
General development	SA	14.9 (1.4)	Superior	111.7 (8.7)	Above average	73.9 (15.8)

Table 3. Griffiths III scores for CHUU and CHEU

	Whole sample (*N*=85)	CHUU (*n*=31)	CHEU (*n*=54)	*p*-value*
Age at test (months), mean (SD)	9.2 (0.2)	9.2 (0.3)	9.2 (0.2)	0.706
Foundations of learning				
Raw score	13.4 (1.9)	13.5 (2.1)	13.2 (1.8)	0.471
Quotient	109.6 (12.6)	111.7 (14.5)	108.4 (11.3)	0.247
Percentile	67.6 (22.7)	70.5 (24.7)	66.0 (21.5)	0.381
Language and communication				
Raw score	13.4 (2.2)	13.8 (2.3)	13.1 (2.1)	0.156
Quotient	106.9 (10.1)	109.6 (11.3)	105.4 (9.2)	0.064
Percentile	63.9 (19.8)	68.4 (20.0)	61.3 (19.4)	0.110
Eye and hand coordination				
Raw score	14.7 (1.7)	15.1 (2.0)	14.4 (1.5)	0.082
Quotient	106.6 (9.4)	109.6 (11.5)	104.9 (7.5)	0.023†
Percentile	63.4 (18.6)	68.0 (20.8)	60.8 (16.9)	0.084
Personal, social, and emotional				
Raw score	16.1 (2.1)	15.9 (2.0)	16.2 (2.1)	0.606
Quotient	111.9 (8.6)	111.9 (9.1)	112.0 (8.4)	0.962
Percentile	74.1 (14.8)	73.7 (15.5)	74.3 (14.5)	0.865
Gross motor				
Raw score	17.0 (2.3)	17.2 (2.3)	16.8 (2.3)	0.463
Quotient	115.7 (13.6)	117.9 (13.9)	114.5 (13.4)	0.271
Percentile	76.7 (22.3)	79.6 (21.8)	75.0 (22.6)	0.354
General development				
Raw score	14.9 (1.4)	15.1 (1.5)	14.8 (1.3)	0.322
Quotient	111.7 (8.7)	113.6 (10.7)	110.5 (7.2)	0.112
Percentile	73.9 (15.8)	76.1 (18.5)	72.7 (14.1)	0.347

CHEU = children who were HIV-exposed and -uninfected; CHUU = children who were HIV-unexposed and -uninfected.
*Unexposed v. exposed.
†Statistically significant.

clinically useful in the SA context, despite cultural differences to the population on which it was standardised. However, when interpreting scores for clinical reasons in children from similar SA populations in the 8- to 10-month age group, practitioners should be mindful of the higher scores achieved in this study. There is scope for more research to be conducted using the GMDS III on SA children from diverse geographical areas (rural and urban) and in different age groups, particularly from 0 to 8 months and 10 to 72 months.

When developmental scores were compared between CHUU and CHEU in the present study, the GMDS III detected a difference between groups in the Eye and Hand coordination subscale – CHUU children achieving significantly higher quotient scores. No previous studies have found this neurodevelopmental outcome between these groups.

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Data availability. The datasets generated and analysed during the current study are available from the corresponding author on reasonable request. Additionally, the data can be accessed via the [name of the repository] at [link to the repository], under the accession number [accession number]. Any restrictions or additional information regarding data access can be discussed with the corresponding author.

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