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Gross Motor Function Measure (GMFM-66) trajectories in children recovering after severe acquired brain injury

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What this paper adds

- The GMFM-66 is an informative measure of the outcome of motor rehabilitation for children with Acquired Brain Injury (ABI).
- Aetiology of ABI is an important determinant of gross motor outcome with children with hypoxic-ischaemic injury resulting in poorer gross motor recoveries than other forms of acquired brain injury.
- In this study rate of recovery correlated with age: younger children made slower recoveries.
- The shape of recovery trajectories may give insights into the biology of recovery.
Abstract

**Objectives:** To explore the appropriateness of using the interval-scale version of the Gross Motor Function Measure (GMFM-66) in paediatric acquired brain injury (ABI); and to characterise GMFM-66 recovery trajectories and factors that affect them

**Design:** Observational study of gross motor recovery trajectories during rehabilitation using repeated GMFM-66 observations

**Setting:** A single specialist paediatric inpatient rehabilitation centre

**Participants:** Cohort of children rehabilitating after severe ABI of various causes.

**Results:** 287 GMFM observations were made on 74 children. Differences in item difficulty estimates between this sample and the cerebral palsy (CP) population in which the GMFM-66 was initially developed are not detectable at this sample size. Changes in GMFM over time show lag-exponential forms. Children sustaining hypoxic-ischaemic injuries made the slowest and least complete recoveries. Older children made faster gross motor recoveries after controlling for aetiology. The time at which gross motor ability began to rise coincided approximately with admission to the rehabilitation facility.

**Conclusions:** Aetiology is strongly associated with gross motor recovery after ABI. Younger age at injury was associated with slower recovery. Comparable item difficulty scores in this sample and in the CP population suggest comparable sequences of gross motor ability (re)acquisition.
Abbreviations

ABI       Acquired Brain Injury
GMFM     Gross Motor Function Measure
IQR       Inter-quartile range
TBI       Traumatic Brain Injury
**Introduction**

Acquired Brain Injury (ABI) – sustained postnatally after a period of typical development – is an important cause of paediatric neurodisability. Although the incidence of ABI of traumatic origin (Traumatic Brain Injury, TBI) is decreasing in well-resourced countries(1) as a result of improved car safety and environmental modifications to reduce traffic speed in residential areas, its importance as a global health problem is growing rapidly with increasing urbanisation(2). The incidence of all-cause ABI is also increasing as survival after critical illness improves. In one study 26% of previously healthy children surviving to discharge from paediatric intensive care had acquired neurological morbidity(3).

Restoration of motor function is an important focus of early rehabilitation. A degree of recovery of function is often seen in the early post-injury period, although the extent to which this can be attributed to the rehabilitation delivered is disputed(4). Understanding patterns of expected motor recovery is necessary for the identification of children making better or worse than expected recoveries, which in turn is a pre-requisite for rehabilitation research and for the setting of realistic activity goals(5,6).

The Gross Motor Function Measure (GMFM) is the established standard for assessment of gross motor function in children with cerebral palsy (CP) (7,8). It has been recommended as an outcome measure after paediatric ABI(9) although experience of its
use in this context is limited. Linder-Lucht et al.(10) validated the GMFM-88 for children with TBI using video analysis as a gold standard and concluded that the GMFM was sensitive to change (see also Beretta et al.(11)). Kuhtz-Buschbeck et al.(12) found that GMFM scores correlated with kinematic measures derived from gait analysis in a sample of 5-15 year olds rehabilitating from severe TBI. There has been no examination to date of the GMFM in ABI of causes other than TBI.

The GMFM-66 is a development of the original 88-item instrument using a subset of items demonstrated to have Rasch properties(8). The original 88-item GMFM, describing performance in five domains (lying and rolling; crawling and kneeling; sitting; standing; and walking, running and jumping), becomes a 66-item measure describing performance in a single domain of gross motor ability. The likelihood of children completing items in this subset fits a model in which all items are assumed to reflect a single latent trait of gross motor ability, with the probability of task completion reflecting the child’s inherent ability and an intrinsic-difficulty score for each item. An important benefit of Rasch-proprietyied scores is that they can be treated as continuous data and subjected to time-course analysis.

As (re)habilitation services increasingly see children with morbidity acquired after a period of typical development it is important that they understand how the needs and care of these children may differ from those of the children with neurodisability of developmental onset with which they may be more familiar. The original GMFM-66 item-difficulty scores were derived from a population-based sample of children with
CP(13). Although in general terms the biology of recovery after injury is believed to be similar to that of physiological development(14), children rehabilitating after ABI may have had many years of typical motor skill acquisition prior to injury. One might hypothesise that relearning of previously acquired skills might be easier than their first learning. Comparison of the published GMFM-66 item-difficulty scores with scores derived in an ABI population would provide useful insight into the biology of gross motor recovery after ABI, for example identifying whether any skills are more or less readily regained by this population than they would be acquired by children with CP.

The aims of this study were therefore (i) to examine the Rasch scaling of GMFM data derived from a sample of children rehabilitating after ABI of multiple causes, as a prelude (ii) to examining observed GMFM recovery trajectories and factors that influence them.
Methods

The study sample comprised consecutive admissions to a large residential paediatric rehabilitation facility (The Children’s Trust), of children requiring intensive multidisciplinary inpatient rehabilitation after severe ABI of various causes. The aetiology of the children’s ABI was categorised as either traumatic brain injury (TBI: e.g. involvement in a severe road traffic accident); hypoxic injury (e.g. due to strangulation or near-drowning); or ‘other’ mechanism of acquired injury.

The full 88-item version of the criterion-referenced Gross Motor Function Measure (GMFM-88) was administered soon after admission and periodically at therapists’ discretion, typically every few weeks. GMFM item responses are scored from 0 (does not attempt/initiate item) through 3 (completes item) with criteria for intermediate scores of 1 or 2 defined for each item in the GMFM manual(8).

Appropriateness of calculating GMFM-66 scores in the ABI sample

The original derivation of the GMFM-66 in children with CP(15) used BigSteps software(16), which uses the Joint Maximum Likelihood (JML) algorithm(17). However, the JML algorithm does not produce a likelihood statistic suitable for robust comparison of the item difficulty estimates in the ABI population. Thus the original raw data from the Avery CP population study(15) were reanalysed using the MML algorithm in
OpenMx(18). Item difficulty scores using OpenMx are expressed as standardised
residuals (z-scores) rather than on the 0-100 scale conventionally used for the GMFM-66.

In Avery et al’s paper(15) each child contributed one GMFM assessment. In this ABI
sample children contributed multiple GMFM assessments. To fit item parameters against
all assessments would violate assumptions of conditional independence because
measurements within individuals are more correlated than between individuals, however
there were too few children in the ABI sample to derive de novo item difficulty scores
using a single randomly selected assessment from each child. We therefore had to use the
existing item difficulties derived from the CP population sample(15). To assess the
appropriateness of doing this we conducted a likelihood ratio test between two models:
(i) item parameters fixed to those derived from the original GMFM-66 validation
population sample(15) alone and (ii) items difficulties fit against this CP sample pooled
with one randomly selected GMFM measurement from each ABI child. A power analysis
was also performed to determine how many ABI participants would be needed to have a
good chance of finding that the CP-derived item parameters are not optimal for ABI
participants. In this power calculation sample size was increased by resampling with
replacement (bootstrap) and replicated 200 times.

Timecourse

Having failed to reject the null hypothesis that it is appropriate to use the standard
GMFM-66 in the ABI population (see Results), individual children’s GMFM-66 scores at
each time point were calculated using Gross Motor Ability Estimator software(8) and GMFM-66 trajectories inspected. Possible effects of age, gender and ABI aetiology on recovery timecourses were examined in a mixed effects using the *lme* package(19) in R(20). Inspection of individual trajectories (Figure 3) suggested that an asymptotic growth function could be assumed where for the jth observation in child i:

\[ GMFM_{i,j} = A_i \left(1 - e^{\lambda_i(t_{i,j} - O_i)}\right) \]

This describes the gross motor recovery (expressed as a GMFM-66 score) as a function of days after injury (t) and three parameters estimated for each child: A, the asymptotic, ultimate gross motor recovery seen late after injury; O, an offset parameter, the post-injury day on which gross motor recovery commences; and a rate constant λ. The rate constant is related to the half-life of the recovery (the time to get from 0 to 50%, 50% to 75%, etc of final recovery) by the equation half-life = \(\log_2 2/\lambda\). In the mixed effects model A was bounded between the maximum GMFM observation for each child and 100 (the maximum possible GMFM score) and O was bounded between zero and the first observation for each child. The child-specific rate constant \(\lambda_i\) was modelled as log-linear in age, injury type (as a factor with baseline aetiology = ABI) and gender (baseline = female), i.e.

\[
\log(\lambda_i) = \beta_0 + \beta_M \cdot \text{Male} + \beta_a \cdot \text{age} + \beta_H \cdot \text{HYPOXIC} + \beta_T \cdot \text{TBI} + U_i
\]

where \(U_i\) is a child-specific random effect assumed to be normally distributed with mean zero and \(\beta_0, \beta_M, \beta_a, \beta_H\) and \(\beta_T\) are parameters to be estimated.
**Ethics**

The project was reviewed by The Children’s Trust Research Scrutiny Panel and deemed to be service evaluation not requiring external ethical approval.
Results

The raw data comprised 287 GMFM-88 observations in 74 children (45 males) with ages at injury ranging from 0.3-17.3 years (median 11.3; interquartile range (IQR) 6.6-15.0 years). 32% had sustained traumatic brain injuries (TBI); 15% had sustained hypoxic-ischaemic brain injuries; and 53% had sustained acquired brain injury by other mechanisms. The timing of the first GMFM assessment ranged from 55 to 2102 days post-injury in a highly skewed distribution (median 160; IQR 105-242 days; 90th centile 395 days). The children with hypoxic injury were significantly younger at injury (median 5.3 years, IQR 1.2-9.9) than the children in the TBI (median 11.9, IQR 9.5-16.0) or other ABI (median 11.7, IQR 8.2-14.4) groups \(F_{2,24}=4.13, p<0.05\).

The sample of children with CP used for comparison was the original population-based sample used to validate the GMFM-66(8,15)

Comparison of item-difficulty estimates

The correlation between the published item difficulty scores in the CP population\(^{(15)}\) (derived using JML in BigSteps) and MML-based estimates from the same data (derived using OpenMx) was 0.997 as would be expected given the similarity of these algorithms. The study of multiple comparisons of models with item parameters fixed to those derived from the CP sample versus those derived from the CP and single measurements from each ABI child (see Methods) failed to identify any statistically significant difference between the models, although the power simulation suggested that the study was
underpowered to identify such a difference. We estimate 120 children would be required
to have an 80% chance of detecting a difference in GMFM-66 parameters between the
CP and ABI groups and 130 children to have a 95% chance.

Figure 1 shows the distribution of gross motor ability measurements in this ABI sample
in more detail. An excess of measurements from children with very poor gross motor
ability (more than 3 standard deviations below the mean; \( z < -3 \)) is evident.

**Timecourse analysis**

Each child had between 1 and 20 GMFM assessments. Inspection of trajectories suggests
a clear association with injury type, with the slowest and poorest gross motor recoveries
seen in the hypoxic injury group (Figure 2). (Examination of the conditional-

independence assumption of item-response theory using local dependence indices(21)
showed that >45% of the items in the original CP dataset show statistically significant
local dependence at the \( \alpha = .01 \) level. This greater than expected inter-item correlation –
which may reflect the many examples of both right- and left-sided performance items for
the same task in the GMFM - precludes estimation of standard errors for the trajectory
plots).

All observations on all children were used in model fitting. To illustrate the results,
Figure 3 shows the trajectories of the 31 children with four or more GMFM observations.
Ten cases (146, 159, 176, 186, 252, 257, 264, 271, 285, 301) of which five had sustained hypoxic injuries exhibited flat trajectories shown as dashed lines in Figure 3. The results of the random effects model are shown in Table 1. This confirms that recoveries after hypoxic injuries are very much slower than “other ABI” injuries; and provides some evidence that in this sample traumatic brain injuries (TBI) were also slower. Recalling that this is a log-linear model, an estimated value of -1.206 for $\beta_H$ equates to an $e^{1.206}$ or 3.34-fold increase in half-life for hypoxic injuries relative to “other ABI” injuries. There was no evidence of an effect of gender on rate of recovery but there was a highly significant age effect with evidence that older children made faster recoveries independent of aetiology with half life multiplying by a factor of $e^{-0.165}$ or 0.85 (i.e reducing by 15%) per year age at injury. Although asymptotes showed a very skewed distribution, analysis of variance did not identify effects of injury aetiology on the ultimate extent of recovery.

**Discussion**

This study provides data on gross motor recovery trajectories in a sample of children rehabilitating after severe ABI. We confirm other studies(22) that hypoxic injuries are associated with much slower and poorer recoveries. However Figure 3 has important messages for clinical practice, demonstrating that in other types of ABI gross motor recovery can commence after delays of many weeks, and continue for many months after injury. It is noteworthy that some recoveries (notably 92, 129 and 290) whilst slow (with
individual half lives of 200 to nearly 500 days) appeared on course to make reasonable ultimate motor recoveries with projected asymptotes >80. We have previously demonstrated the greater statistical power of mixed effects recovery-modelling techniques to detect potential treatment effects(23). Other advantages include distinguishing speed from ultimate extent of recovery and (in contrast with conventional repeated-measure statistics) the fact that the data set does not need to be balanced (i.e., it is not necessary for each participant to have exactly the same number of measurements made at precisely the same times).

To perform these analyses we have needed to convert GMFM-88 profiles to the unidimensional continuous GMFM-66 score. Although our sample size has not permitted a formal validation of the GMFM-66 in this ABI sample we have been able to estimate sample size required to have a high probability of finding a difference between these groups, although it would be important that any new ABI-specific measurement model was derived in a population-based sample. Unless and until evidence to the contrary is adduced, it seems reasonable to assume CP-derived parameter estimates are appropriate for ABI samples. Others have demonstrated the GMFM’s sensitivity to change in a TBI population(10,11,24).

There is a clear benefit to rehabilitation research in having a validated activity-level outcome measure that can be used to evaluate and compare rehabilitation interventions aiming to restore function. Once the recovery trajectories that should be expected under given circumstances are better understood, audit of recoveries achieved will be possible.
Documentation of observed recovery trajectories allows informed discussion with parents of likely recoveries (e.g. in the context of hypoxic injury) (6) and the setting of realistic activity goals, in a manner analogous to the benefits of understanding gross motor growth trajectories in children with CP(25).

In addition to the important advantages of a gross motor score with interval-scale properties, one additional benefit of establishing the use of the GMFM-66 in ABI addresses important limitations of the GMFM-88 that were very evident during this study. The full 88-item version of the GMFM is time-consuming and fatiguing, which can be a particular issue in the ABI population where the challenge arises of distinguishing inability from unwillingness to attempt a task (i.e. “can’t do” from “won’t do”). A Rasch-propertied instrument such as the GMFM-66 can be administered using many fewer items once a child’s approximate ability level on the latent-trait scale has been defined by a few “range-finding” items, and will be robust to missing data in items distant from that ability level. These results suggest that recently-developed even shorter variants of the GMFM(7) may in due course also prove useful in this population.

The study does have significant limitations. Unlike the population-based sample of children with CP in the original GMFM-66 derivation study this is a highly selected sample of children with very severe ABI admitted to an inpatient residential rehabilitation service because of major motor difficulties persisting for months after injury (60% met Gross Motor Function Classification System (GMFCS) level V criteria on admission). It is likely for example that the picture of poor recoveries after hypoxic injury is biased by
the absence of some children who made reasonable early recoveries from less severe insults and who were therefore not referred. Nevertheless even in this selected, severely impaired sample hypoxic and traumatic injury show very different trajectories.

The assumption of an asymptotic growth function is empiric (i.e. there is no current understanding of the biology of recovery that leads us to predict this shape). In a previous study modelling recoveries after TBI as reflected by the WeeFIM® instrument(6) a related but different equation was chosen. The justification for the function choice here depends on acceptance of the reasonableness of the individual curve fits of Figure 3.

This hypothesised growth function does however raise interesting theoretical questions as to why it might be (as this model assumes) that rate of recovery is proportional to remaining recovery capacity (i.e. the remaining gap between current and final recovery)(26).

This study does not provide direct evidence for the effectiveness of admission to the rehabilitation facility on the recovery trajectory: this would require data on the entirety of the recovery trajectory including the period before and after admission. It is interesting to note however (data not shown) that there is a strong linear correlation between individual children’s estimated offset \((O)\) parameters and admission to the rehabilitation facility. In other words, where it was seen the “take-off” in gross motor recovery trajectory coincided approximately with admission. This could reflect a rehabilitation effect, or alternatively that admission was only arranged when a child was deemed “rehabilitation
ready” by showing some early signs of recovery. Serial GMFM assessments from the onset of injury would allow one to explore this hypothesis.

These findings may have other implications for our understanding of the biology of recovery after brain injury. The individual items of an instrument that has Rasch properties are assumed to be reflecting a single latent trait (in this case, gross motor function). Item difficulties reflect the probability of their being completed successfully and thus their ordering reflects the ordering in which one should expect skills to be achieved as ability increases. In the CP population ability increases as the combined effects of natural development and therapy. In the ABI population ability increases as an effect of recovery and rehabilitation (natural development is less relevant over the shorter periods under consideration), however in contrast to the CP population these children are generally regaining skills they had already learned. There are theoretical reasons to believe this may be easier than the initial learning process(27). Although we could not demonstrate any bias toward lower item difficulty scores in this selected ABI population, such considerations may explain the age-at-injury effect seen in this sample, with older children making faster recoveries. Age-at-injury effects on recovery after ABI are hotly debated(28). In this study the effect was independent of aetiology however the finding should still be interpreted with caution (there still may be significant confounds such as age-dependent differences in injury mechanism within the broadly defined aetiology groups resulting in different injury severities) and needs replicating.
This study provides a further example of the value of the GMFM-66 in describing rehabilitation after ABI and in beginning to understand factors determining recovery, including the role of rehabilitative therapy.

Acknowledgements

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Legends to Figures

Figure 1

Distribution of individual measurements of gross motor ability in the ABI sample (left panel) compared to the population sample used to derive the GMFM-66 in children with CP(8) (right panel). Note that OpenMx-derived ability estimates are shown, expressed as z-scores rather than the conventional 0-100 scale of the GMFM-66. In the ABI sample (left panel) children contribute multiple gross motor score estimations (287 measurements from 74 children).

Figure 2

Raw GMFM-66 data for the children with >3 data points (n=31), grouped by aetiology of acquired brain injury (traumatic, hypoxic and other ABI) showing trajectories over time. Horizontal axis shows days since the ABI event.

Figure 3

Individual children’s recovery trajectories. Each plot represents one child (labelled by case number in bold) with GMFM-66 score (from 0-100) on the vertical axis. Note that the limits of the horizontal axis (days post injury) are different for each plot to optimally display that child’s trajectory.
Solid lines show individually fitted curves of the form $y = \text{asymptote}(1-e^{-\lambda(t-\text{offset})})$. Dashed lines show the estimated asymptote for children showing flat line trajectories during the period of available data. Standard errors cannot be displayed (see text).

Table 1

Results of linear mixed effects model. Table shows the estimates of the fixed effects of the model showing the coefficients of hypothesised independent effects of gender, age, aetiology and time on GMFM.
Figures

Figure 1

Figure 2
Figure 3
### Table 1

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Standard deviation of child-specific random effect = 0.828
Standard deviation of pure error term=0.583
References


