

Systematic review of cognitive development across childhood in Down syndrome: implications for treatment interventions

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Abstract

Background There is conjecture regarding the profile of cognitive development over time in children with Down syndrome (DS). Characterising this profile would be valuable for the planning and assessment of intervention studies.

Method A systematic search of the literature from 1990 to the present was conducted to identify longitudinal data on cognitive trajectories in children with DS.

Results Thirteen studies were identified: six assessed overall cognitive performance and seven assessed specific cognitive domains. Studies assessing IQ reported a decline across time. Studies assessing change in cognitive domains were, for the most part, not interpretable because of large age ranges in samples obscuring age-specific data.

Conclusion The current literature has only begun to describe typical cognitive developmental trajectories in children with DS; additional research is needed to clarify this topic.

Keywords cognitive development, Down syndrome, intellectual disability, longitudinal

Introduction

Impaired cognitive function is a central feature of Down syndrome (DS). Attempts to enhance cognitive functioning in individuals with DS have emphasised increased educational and training input and/or improved socialisation, especially in childhood and adolescence (Connolly *et al.* 1993; Ryba *et al.* 2005). Over the last decade substantial advances have been made in understanding the genetics of cognitive performance and cognitive dysfunction in syndromic and non-syndromic intellectual disability (ID; Plomin 2006; Ropers 2008; Kramer & van Bokhoven 2009). In syndromic ID, specific molecular mechanisms have been identified that might contribute to impaired cognition and raise the possibility that treatments targeting such mechanisms may be developed that could enhance cognitive performance in individuals with DS (Glue & Patterson 2009; Kishnani *et al.* 2010; Surmeli & Ertem 2010). In addition, theoretical advances and a developmental approach to ID have led to the characterisation of a cognitive phenotype for DS (Karmiloff-Smith 1998; Silverman 2007; Fidler

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et al. 2009). It has been suggested that understanding the trajectory of cognitive development in children with DS may lead to the design of more effective interventions (Fidler *et al.* 2007).

Of critical methodological importance, then, is against a background of age-related change, how can enhancement of cognitive function, through behavioural or drug treatments, be identified in intervention research? Conceptually, this might be assessed as differences in cognitive development trajectories between treatment and control groups (Ramey & Ramey 1998; Glue & Patterson 2009). In practical terms, however, such assessments are likely to be considerably more complex, given the multiple cognitive domains involved, the observation that these domains are variably affected (Dykens 1995), and that within this single syndrome, there may be wide variability in individual performance for a cognitive domain (Miller *et al.* 1995; Tsao & Kindelberger 2009).

Issues to consider when measuring change in cognitive functioning in Down syndrome

Children with DS have a distinctive cognitive phenotype (for reviews, see Chapman & Hesketh 2000; Silverman 2007; Fidler *et al.* 2009) characterised by a particular pattern of deficits, as well as a pattern of relative strengths, when compared to children developing typically and children with other types of cognitive impairment (Dykens 1995; Powell *et al.* 1997; Abbeduto *et al.* 2001; Vicari *et al.* 2002; Vicari & Carlesimo 2006). Broadly speaking, children with DS appear to have a particular profile of memory and information-processing abilities, including reduced working memory capacity (Vicari *et al.* 1995), intact implicit memory but reduced long-term memory for explicit information (Jarrold *et al.* 2009), and poorer verbal processing and auditory short-term memory skills in relation to non-verbal mental age and relative strengths in visuospatial processing and non-verbal memory (Chapman *et al.* 1991; Chapman & Hesketh 2001; Jarrold & Baddeley 2001). Further, children with DS tend to be slower to acquire new skills and appear to have greater difficulty with stability of acquisition, that is, skills demonstrated on one testing occasion may be absent on a later occasion (Fidler & Nadel 2007). In addition, children with DS exhibit greater

weaknesses in the language domain than would be predicted by mental age whereas non-verbal reasoning is a relative strength (Chapman & Hesketh 2001; Chapman 2003; Abbeduto *et al.* 2007). Within the language domain, children with DS show relative strength in receptive compared with expressive language (Chapman 1997). Further, syntax comprehension falls behind vocabulary comprehension with greater deficits appearing in syntactic expression (Abbeduto *et al.* 2007).

Characterisation of a cognitive phenotype is constrained by a number of factors, including individual variation within a group; measuring cognitive abilities with tools that are an imperfect measure of the underlying processes (Pennington *et al.* 2003); and performance confounded by other factors, such as motivation (Gilmore & Cuskelly 2009). Moreover, the process of development itself leads to probabilistic expression of genetic variation and a cognitive profile that may be different across developmental periods (Silverman 2007). This latter point emphasises the importance of detailing a cognitive profile across time. Do performance trajectories have a consistent (linear) profile or are changes intermittent with periods of acceleration, deceleration and plateau (Gibson 1966; Fowler 1988; Wishart 1996; Hasan & Messer 1997; Crombie & Gunn 1998; Dykens *et al.* 2006)?

Methodologically, cross-sectional data can be used to describe the status of the cognitive phenotype at a single time point and to compare this developmental status with other groups; however, longitudinal data are optimal for the identification of the dynamic process of cognitive change and description of a trajectory of development (Thomas *et al.* 2009; see Table 1 for methodological considerations. Also, see Thomas *et al.* 2009 for a method of characterising developmental trajectories using cross-sectional data). Longitudinal data allow for observation of the unfolding process of development and tracking whether cognitive change in DS is delayed but parallel to typically developing children or whether it is atypical (e.g. with acquisition of skills occurring in a protracted step like pattern). Longitudinal data, ideally with multiple waves of measurement, allow for observation of such developmental trajectories (i.e. linear vs. periods of

Table 1 Cognitive change across childhood: methodological considerations

Methodology	Allows for observation of:
Cross-sectional	<ul style="list-style-type: none"> • Performance at one point in time • Between-group comparison, e.g. of age-related performance if different ages are sampled
Longitudinal	<ul style="list-style-type: none"> • Predictors of performance at one point in time • Performance across time • Within-group analysis of the dynamic process of development: <ul style="list-style-type: none"> • the shape of the trajectory, e.g. linear versus stepwise • effect of change in one domain on another domain • predictors of change • Change in relationship between domains • Non-linear change
Domain-specific measurement (vs. measurement of DQ/IQ)	<ul style="list-style-type: none"> • Allows assessment of complex phenotypes
Analysis of individual growth curves	<ul style="list-style-type: none"> • Subtle changes in one domain that may be masked by no or inverse change in other domains • Variations in growth patterns in different individuals • Clustering of subgroups

acceleration, deceleration or plateau, Fidler *et al.* 2009, see Table 1 for benefits of longitudinal data vs. cross-sectional).

Ideally, longitudinal assessment of development in DS should specify development within specific domains rather than just an overall measure of IQ. This helps identify which primary deficits may lead to secondary deficits, identify predictors of performance, clarify individual differences in development and understand heterotypic (different deficits at different time points) versus homotypic deficits (the same deficit displayed in different but developmentally concordant ways). If only overall IQ is measured, increasing ability in one domain may be masked by a plateau or decrease in ability in another domain. Moreover, measurement of multiple domains allows for assessment of change not only in domains but in the relationship between domains, that is, change may proceed at a different rate in different domains (Fidler *et al.* 2009).

Additionally, the cognitive starting point needs to be taken into consideration when measuring change. First, children with DS are known to vary widely in level of cognitive functioning (Tsao & Kindelberger 2009). Longitudinal data allow for modelling of growth trajectories and examination of the path of development for individuals. Analysis of individual data rather than group means considers variations in individual performance, which may

otherwise mask effects (Tsao & Kindelberger 2009). Second, it can be hypothesised that the cognitive starting point is likely to be predictive of the final outcome, that is, a more severe deficit may result in less growth over time. However, such a hypothesis assumes a linear growth curve and requires testing.

Summary and present review

In sum, for adequate intervention planning and assessment of cognitive enhancement, three factors must be considered. First, DS has a unique cognitive phenotype and therefore careful attention must be given to measurement of particular domains. Second, this phenotype may unfold in a unique manner across time, which is best tracked by longitudinal data. Third, to adequately measure whether an intervention aimed at enhancing cognition in DS is effective (whether that intervention is drug treatment or educational), a clear understanding of typical age-related changes in cognitive functioning across multiple domains needs to be obtained. In this way, the effects of treatment versus the effects of age-related developmental changes can be differentiated. Considering the above issues, the objective of this structured review was to examine the published literature on longitudinal data of cognitive development in DS to identify age-related changes in cognitive performance.

Method

A search was performed to identify all longitudinal studies that assessed cognitive functioning in children with DS published between 1990 and November 2011. Longitudinal studies prior to 1990 were not included primarily because of identified methodological issues (see Carr 1992, for a review) and to reduce the effect of cohort differences likely to be inherent in earlier studies. These include the shift in the care of DS children from institution to home, improved medical care, including hearing and vision testing, provision of early intervention programmes, mainstream education, and opportunities for vocational training and involvement (Crombie & Gunn 1998; Chapman & Hesketh 2000), all of which may have implications for performance on cognitive tests.

Studies were identified and obtained through electronic searches using MEDLINE (1990–2010), PubMed and PsycInfo. The following Boolean phrases were used when searching electronic databases ‘Down syndrome OR Down’s syndrome OR Trisomy 21’ AND ‘cognitive development OR cognition OR intellectual development OR intelligence OR language OR memory OR information processing OR visuo-spatial OR verbal OR non-verbal’. Additionally, reference lists of identified articles and review articles were consulted to identify any longitudinal studies not already identified through electronic searching.

Within the electronic database, the search was limited to English-language, peer-reviewed journals, published from 1990 onwards, and children and adolescents. Articles identified by electronic searching were then read to ensure they met the following criteria:

- 1 Data reported for at least one quantitative measure of cognitive functioning assessed at two time points.
- 2 At least one of the time periods assessed subjects when they were aged 5 years to 18 years in order to capture cognitive change through childhood and adolescence. Studies were still selected if they included participants that were younger at the start of the study or older than this at the end of the study. The goal of the review was to characterise change in childhood, although overlap with infancy and late adolescence was accepted in order to

include all studies that could contribute to this goal.

Articles meeting criteria were then read with the goal of recording all available data pertaining to sample characteristics including sample size, age range and mean, gender, timing of assessment periods, cognitive domains tested, performance on cognitive tests including raw and standardised scores if available, analysis of performance on cognitive tests related to time or age, and control group. Summary statistics (means, percent change, and coefficients of variability) were calculated for comparable study data.

Results

A total of 13 articles met the inclusion criteria. Studies were most typically excluded because they did not provide data for more than two time points or because they did not provide assessment data for cognitive functioning. Six studies (Brown *et al.* 1990; Carr 1992; Connolly *et al.* 1993; Crombie & Gunn 1998; Sigman & Ruskin 1999; Hauser-Cram *et al.* 2001) assessed IQ only and seven studies (Laws *et al.* 1995; Cupples & Iacono 2000; Kay-Raining Bird *et al.* 2000; Byrne *et al.* 2002; Chapman *et al.* 2002; Hick *et al.* 2005; Couzens *et al.* 2011) assessed domain-specific performance. Sample size ranged from 10 to 130 participants (mean = 52.2).

Findings of studies measuring DQ/IQ

Six studies assessed DQ/IQ and are shown in Table 2. Two studies (Brown *et al.* 1990; Carr 1992) reported DQ/IQ as a group mean for homogeneously aged samples over regular intervals. Brown *et al.* (1990) reported results in the form of a linear regression line for participants at age 5 to 55 years at 5-year intervals; actual data were collected (but not reported) at 3-year intervals for children beginning prior to 1 year of age and at 10-year intervals for adults up to 59 years. Carr (1992) assessed participants five times during infancy then at 4, 11 and 21 years.

Connolly *et al.* (1993) reported aggregate IQ scores for similarly aged participants at three time points over 11 years. Sigman & Ruskin (1999) assessed IQ and reported group means for hetero-

Table 2 Summary of findings for studies assessing overall cognitive performance in childhood and adolescence in children with Down syndrome

	Brown <i>et al.</i> (1990)	Carr (1992)	Connolly <i>et al.</i> (1993)	Crombie & Gunn (1998)	Hauser-Cram <i>et al.</i> (2001)	Sigman & Ruskin (1999)
Sample size	130	54	10	69	60	93
Age at testing waves	Range: <1–59 years, reported in 5-year intervals	4, 11 and 21 years	X (SD) = 4.5 (0.8), 8.9 (1.0), 15.7 (1.3) years	11, 12, 14 years	3 and 10 years	X (SD) = 2.8 (1.17), 10.9 (3.58) years
Decline in DQ/IQ	Yes	Yes	Yes	Yes	Yes	Yes

DQ, developmental quotient; IQ, intelligence quotient.

geneously aged participants (mean age at intake = 2 years, 8 months, SD = 1.17; mean age at follow-up = 10 years, 9 months, SD = 3.58). Hauser-Cram *et al.* (2001) reported a growth curve analysis of mental age from age 3 to age 10, for which the rate of change for the children with DS was 0.52 (SE = 0.32) with reference to a group of children with developmental delay.

As shown in Table 2, all studies reported a decline in IQ over time. The duration of the studies varied, as did the number of assessment waves. All but one of the studies covered the early childhood period through to 10 years of age, three studies continued to follow participants throughout adolescence, and one study tracked children throughout early adolescence only. For studies that reported scores for children of comparable ages, two studies (Brown *et al.* 1990; Carr 1992) found that IQ declined across time: from an IQ of 50 (approximately) at age 4–5 to an IQ of 35 (approximately) at age 10–11 years. Sigman & Ruskin (1999) also noted a decline in IQ for participants with DS over the course of the study; however, they did not report data. These authors reported that 40% of the sample had an IQ higher than 70 at intake, but none of the group had an IQ higher than 70 by middle childhood. Crombie & Gunn (1998) reported mental age, as assessed by the Stanford-Binet at 11, 12 and 14 years of age. When mental age was converted to IQ (mental age/chronological age \times 100), there was a slight decline in IQ at each of the three time points.

Two studies (Carr 1992; Sigman & Ruskin 1999) assessed the predictive validity of IQ in early child-

hood (i.e. whether IQ is relatively stable, with those participants who have lower DQ/IQs at a young age being the same individuals who have lower IQs at an older age). There was a consistent relationship between early DQ/IQ and later IQ (Pearson's $r = 0.41$ – 0.83); low-functioning children continued to be low-functioning. However, the strength of this association varied across the two studies and across time periods.

Two studies (Sigman & Ruskin 1999; Hauser-Cram *et al.* 2001) included groups of children with ID other than DS. Hauser-Cram *et al.* (2001) performed a complex modelling analysis and reported that compared with children with developmental delay and motor impairment, behavioural and parental variables influenced the trajectory of IQ scores over time to a lesser degree for children with DS. Sigman & Ruskin (1999) reported that children with DS demonstrated a different profile of change in IQ scores over time (almost all declined) compared with children with autism or developmental delay (approximately one half of each group showed increased IQ scores). Further, children with DS became more homogenous in terms of IQ, as shown by a decreasing standard deviation, whereas children with autism or developmental delay became less homogenous as shown by an increasing standard deviation across the assessment period.

Findings of studies measuring domain-specific performance

Seven studies (see Table 3) presented results for specific cognitive domains; all assessed language or

Table 3 Summary of characteristics and findings of studies assessing specific cognitive domains in children with Down syndrome

	Byrne <i>et al.</i> (2002)	Couzens <i>et al.</i> (2011)	Chapman <i>et al.</i> (2002)	Cupples & Iacono (2000)	Hick <i>et al.</i> (2005)	Kay-Raining Bird <i>et al.</i> (2000)	Laws <i>et al.</i> (1995)
Sample size	24	147*	31	22	12	12	14
Length of study (years)	2	17	6	<1–1	1	4.5	4
Raw scores	√	√		√	√	√	√
Age-equivalent scores	√	√	√	√		√	
Control group	√				√		
Assessed language	√	√	√	√	√	√	√
Assessed visuospatial		√	√		√		√
Assessed memory	√	√	√	√	√	√	√
Analysis of individual data		√	√				
Number of tests with increase in raw scores/total number of tests in study	9/9†	6/6	5/6†	3/11†‡	4/5§	3/6† 3/3§	5/5†

* Participants were part of more than one sample and assessed at a varying number of time points.

† Increase was statistically significant ($P > 0.05$).

‡ Eight of the tasks were non-standardised tasks that assessed phonological awareness and an increase was only shown in two of these tasks.

§ The increase in performance was not assessed for significance.

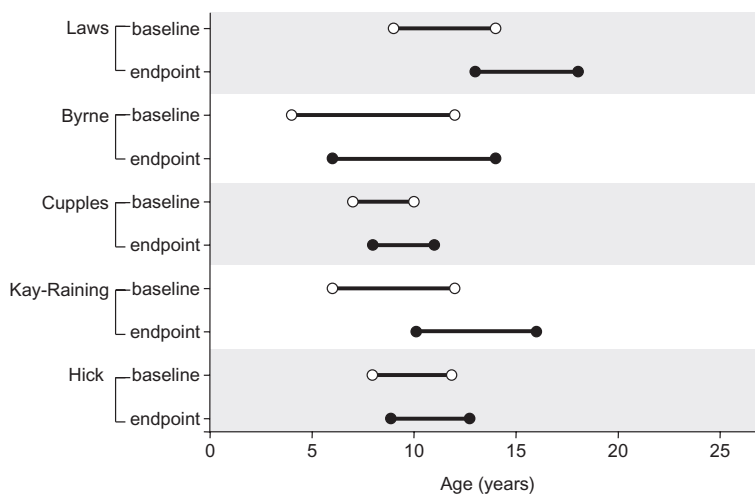


Figure 1 High degree of overlap in subjects' ages for studies using aggregate performance scores in longitudinal assessment: baseline and endpoint data.

reading, all studies assessed memory, and three assessed visuospatial skills. Compared with studies assessing changes in DQ/IQ (Table 2), sample sizes for studies reporting performance on specific cognitive domains were smaller than those reporting overall IQ. All studies except Chapman *et al.* (2002) and Couzens *et al.* (2011) analysed results as an aggregate (i.e. group means). All studies included a sample of children that covered a range of ages; as

demonstrated in Fig. 1, the age difference between the youngest and oldest participants ranged from 15 months to 8 years. Samples included participants ranging in age from 2 years at the beginning of one study to 26 years at the end of another study. Chapman *et al.* (2002) included participants with an age range of 15 years but analysed individual data using a modelling approach. Another study analysed data as group means and also

Table 4 Comparison of results from cognitive measures used in more than one study in children with Down syndrome

Assessment of language	n	Raw score % change/year	Standardised score change/year (year;month)	Study
Test of the Reception of Grammar (TROG)	7	19.3 (readers)		Laws <i>et al.</i> (1995)
	7	8.41 (non-readers)		Laws <i>et al.</i> (1995)
	24	17.0	0;3	Byrne <i>et al.</i> (2002)
British Picture Vocabulary Scale (BPVS)	7	14.4 (readers)		Laws <i>et al.</i> (1995)
	7	6.2 (non-readers)		Laws <i>et al.</i> (1995)
	24	11.3	0;6	Byrne <i>et al.</i> (2002)
	12	14.5		Hick <i>et al.</i> (2005)
Woodcock Reading Mastery Tests – Revised (WRMT-R): word ID	22	44.8	0;4	Cupples & Iacono (2000)
	12	16.6	0;2	Kay-Raining Bird <i>et al.</i> (2000)
WRMT-R: word attack	22	75.0	0;2	Cupples & Iacono (2000)
	12	23.8	0;0	Kay-Raining Bird <i>et al.</i> (2000)
Mean length of utterance (MLU)	31	7.0		Chapman <i>et al.</i> (2002)
	12	0.7		Kay-Raining Bird <i>et al.</i> (2000)
Peabody Picture Vocabulary Test (PPVT)	31		0;2	Chapman <i>et al.</i> (2002)
	12		0;3	Kay-Raining Bird <i>et al.</i> (2000)
Assessment of memory				
Digit span (longest)	22	4.2		Cupples & Iacono (2000)
Digit span (longest, ITPA)	12	5.7		Kay-Raining Bird <i>et al.</i> (2000)
Digit span (ITPA)	31		0;0	Chapman <i>et al.</i> (2002)
Digit span (ITPA)	12	7.9		Kay-Raining Bird <i>et al.</i> (2000)
Digit span (BAS)	24	11.9	0;4	Byrne <i>et al.</i> (2002)
Digit span (BAS)	12	–6.2		Hick <i>et al.</i> (2005)

Standardised scores = age-equivalent or grade-equivalent scores; ITPA, Illinois Test of Psycholinguistic Ability; BAS, British Ability Scales.

reported individual data (Kay-Raining Bird *et al.* 2000).

In studies assessing domain-specific cognitive performance (see Table 3), there was an increase in raw scores on most of the tests over time, as measured by retesting at intervals between 7 months to 12 years. Tests assessing phonological skill and short-term memory were less likely to increase than tests assessing receptive language and word recognition. Four studies also reported age-equivalent scores. Although age-equivalent scores gradually increased over the period of the study time, the increases were at a substantially slower rate than the increasing chronological age of the children (see Table 4). However, as shown in Fig. 1, the high degree of overlap in children's ages at baseline and at endpoint (because of the

wide range of ages included in the sample) makes it difficult to draw specific conclusions about the nature of the change in children's performance across different ages. That is, although gradual increases in raw scores were demonstrated it was not possible to determine whether these changes proceeded in a linear fashion or whether the gradient of change may have been different at different ages.

Findings of studies assessing domains with equivalent testing tools

Six measures assessing performance in the language and reading domain were used by more than one study, thereby allowing comparison of results (see Table 4). Digit span assessment was used to

measure auditory short-term memory in five studies. Two studies used the Illinois Test of Psycholinguistic Ability and two studies used the British Ability Scales. There was no overlap in the tests used to assess the visuospatial domain.

For both memory and language tasks, changes in standardised scores indicated slow or, less commonly, no, gains over time, with rates of change on most tests less than half of that expected from typically developing children (Table 4). Auditory short-term memory as assessed by digit span appeared less likely to increase than did language skills based on raw score data; however, the ranges of standardised scores were similar for both sets of assessments. Within the language assessments, yearly changes in raw scores were greater in readers than in non-readers. For the digit span task, there was no significant change in performance in two studies (Cupples & Iacono 2000; Chapman *et al.* 2002); a decrease was shown in one study (Hick *et al.* 2005), increases were observed on two measures that were not assessed for significance in one study (Kay-Raining Bird *et al.* 2000), and a significant increase was shown in one study (Byrne *et al.* 2002).

Due to data being reported as a mean from cohorts with mixed ages, it was not possible to report on age-specific performance. Although description of cognitive trajectories is impeded by lack of age-specific data, for studies that assessed children over more than two time periods, examination of age-equivalent scores at each period suggested that change may have proceeded at different rates at different ages in some domains (Kay-Raining Bird *et al.* 2000; Byrne *et al.* 2002). Specifically, over 2 years Byrne *et al.* (2002) reported no annual increase in age-equivalent scores on a vocabulary assessment (British Picture Vocabulary Scale) from baseline to year 1 but an increase of 11 months from year 1 to year 2, for children ranging in age from 4 to 12 years. Kay-Raining Bird *et al.* (2000) reported an increase of 8 months on the Peabody Picture Vocabulary Test over the first 3 years but a decrease of 2 months over the final 18 months of testing for children ranging in age from 6.2 to 11.6 years. Although these data suggest that change is greater or lesser at certain time periods, the wide spread of ages makes interpretation difficult.

Data variability was noted to be substantial, with coefficients of variation >40% in over 75% of studies at baseline, and over half of all studies at endpoint. This is consistent with other literature that has reported wide variation in test performance (Silverman 2007). The decrease in variability is consistent with the declining standard deviation reported by Sigman & Ruskin (1999); both findings suggest that there may be a narrowing in the range of performance abilities over time for children with DS.

Findings of studies performing non-aggregate data analysis

Chapman *et al.* (2002) used hierarchical linear modelling to model individual change in performance on measures of syntactic comprehension (Test of Auditory Comprehension of Language – Revised) and syntactic expression (mean length of utterances). Data were reported for four time periods over 6 years with 31 participants aged between 5 to 20 years. Chapman *et al.* (2002) reported that change in syntax comprehension was best predicted by age at the start of the study, with younger participants showing a greater increase in learning and older participants beginning to show a decrease in learning. For predicted slope of change, participants aged 7.5 years showed the most positive slope, the slope was positive but less steep at 12.5 years, and for those aged 17.5 years the predicted slope was negative (Fig. 2). This pattern was different to the pattern for change in syntax expression, which was not affected by age but continued to increase for those of all ages.

Couzens *et al.* (2011) used combined data from longitudinal and cross-sectional research to model age-related change on domains of the Stanford-Binet (fourth edition). Individual and group trajectories were analysed. The reported findings support analysis of domain scores rather than overall, full-scale IQ scores. In particular, group analysis of performance on the Pattern Analysis subtest (a test of fluid intelligence) showed a trajectory that developed at a steeper rate than the other subtests and at a rate comparable to normative development, whereas for all participants Memory for Sentences (a test of auditory short-term memory) was well below age-equivalent performance. In addition, analysis of individual data showed substantial varia-

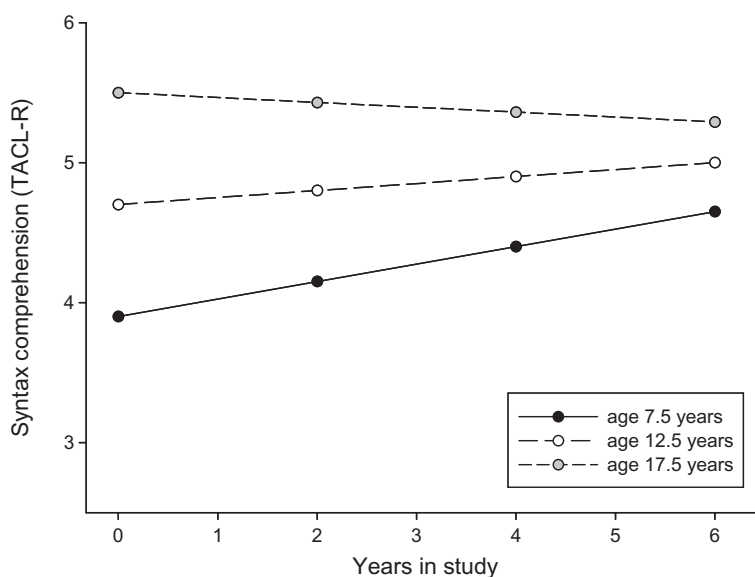


Figure 2 Best model of syntactic comprehension: Predicted performance for ages 7.5, 12.5 and 17.5 (reproduced from Chapman *et al.* 2002, with kind permission of the Editor, *J Speech Lang Hear Res*). TACL-R, Test of Auditory Comprehension of Language – Revised.

tion among participants in performance on several of the subtests but not on Memory for Sentences. Individual variation in performance on the Vocabulary subtest was seen in a variation of scores at 4 years and different rates of growth; however, a ‘soft ceiling’ was observed such that few children advanced beyond Item 14. Finally, this study illustrates the value of longitudinal data, for example, there was minimal variation in performance on Pattern Analysis at 4 years; however, there were significant differences in rate of development over time. A key limitation of this study is that cross-sectional and longitudinal data were included, which may confound analysis

Discussion

Despite the scientific and clinical importance of understanding the pattern of cognitive development over time in children with DS, only 13 longitudinal studies were identified since 1990 that met search criteria. Six of the studies used global cognitive measurements (IQ/DQ) rather than assessments of specific cognitive domains. Almost all of the studies contained methodological issues that confounded data interpretation, in particular the studies assessing domain-specific performance reported results for participants spanning a wide age range. Two

studies (Chapman *et al.* 2002; Couzens *et al.* 2011) avoided confounding of results across different ages and also analysed domain-specific results. Preliminary conclusions can be drawn from Couzens *et al.* (2011), including the value of domain-specific analysis with individuals demonstrating difficulty with the task assessing phonological memory but an initially steep trajectory with ongoing improvement on Pattern Analysis, evidence towards wide individual variation in performance, and the hypothesis that a ‘soft ceiling’ may exist for performance on some tasks with few individuals achieving beyond the boundary. However, the combined cross-sectional and longitudinal data limit the strength of these conclusions. Chapman *et al.*’s (2002) finding that language development over time in different domains is differentially affected by age is important, but requires confirmation.

IQ/DQ is a composite measure of intelligence, and was assessed in six studies (Brown *et al.* 1990; Carr 1992; Crombie & Gunn 1998; Sigman & Ruskin 1999; Hauser-Cram *et al.* 2001). All studies showed declining IQ/DQ scores over time, with some evidence that decline in IQ was more likely for children with DS than for children with other types of disability. Evidence for a decline is consistent with earlier studies (Carr 1992), and confirms the observation that cognitive development in children with DS proceeds at a slower rate than for

typically developing children, leading to a progressively widening disparity in age-related performance (Glue & Patterson 2009).

Although providing some information, using IQ/DQ as a measure of cognitive ability has limited value in describing a cognitive trajectory, as this composite score is derived from assessments in a number of cognitive/performance domains (Chapman & Hesketh 2000). Such limitations were revealed by Couzens *et al.* (2011), who reported sub-domain test performance as well as overall IQ, and were also illustrated by studies in this review that tested specific cognitive domains and that showed an uneven profile of development across domains for children with DS. For example, the pattern of development across different age groups varied according to expressive or receptive language domain (Chapman *et al.* 2002).

For the studies that examined cognitive change over time in specific domains, the main issue identified by this review was that data were presented as group means which included children and adolescents with a wide range of ages (Fig. 1). Such widely spread age ranges made it impossible to determine if there were different trends at different ages, and confounded assessment of age-related developmental trajectories. Inconsistent changes across assessment waves in two studies (Kay-Raining Bird *et al.* 2000; Byrne *et al.* 2002) support the hypothesis that change may occur at different rates for different ages; however, because these changes were based on heterogeneous group means it was not possible to determine at what specific age slowing or acceleration may have occurred.

Two exceptions to the issue of heterogeneously aged samples in the analysis were Chapman *et al.* (2002) and Couzens *et al.* (2011). Chapman *et al.* (2002) presented individual data for participants over 6 years, and identified significant effects of age on some, but not other, cognitive domains. In their study, differences were reported in the growth trajectories of expressive language (this continued to improve irrespective of age) versus receptive language (this increased in early childhood, flattened somewhat in late childhood and adolescence, and then began to plateau or decline in mid to late adolescence; Fig. 2). The potential significance of this finding is that there may be ages at which interventions to enhance specific cognitive domains may be

less or more effective, and also participants' ages will impact on the perceived effectiveness of the intervention (e.g. an intervention study conducted in late adolescence may be considered effective if no decline in receptive language is found). Likewise, Couzens *et al.*'s (2011) report that some individuals show a steeper trajectory of development on Pattern Analysis is important because identification of factors associated with a faster rate of development may be useful for designing interventions for those who proceed at a slower rate. Additional studies to confirm this set of findings will be important.

Another finding was that, in general, minimal progress was observed on digit span tests. This is consistent with cross-sectional studies that show children with DS have particular difficulty with this task (Jarrold *et al.* 2009). A reasonable hypothesis may be that less progress should be expected on a digit span task, that is slow development in line with the cognitive starting point. However, it may also be that children with DS do not show the same synchrony of development as typically developing children; a flat trajectory may be indicative of a syndromic deficit, perhaps with an organic aetiology (Jarrold *et al.* 2001; Couzens *et al.* 2011).

This review identifies a number of methodological issues that must be considered in new research initiatives in this area. Ideally, ages of subjects should be relatively homogenous, unless the study is specifically designed to analyse change in cognitive domains over time with baseline age as a covariate. One implication of controlling for age is that studies need to have adequate sample sizes to account for this variability, and this, as with homogeneously aged samples, has additional implications on study feasibility, namely accessing samples of sufficient size.

Even with enrolment of similarly aged children, analysis of group data may be problematic if there is wide individual variation in performance. Wide variation in the performance of children with DS has been commonly noted (Silverman 2007; Thomas *et al.* 2009; Tsao & Kindelberger 2009), was reported by Couzens *et al.* (2011), and observed in the present analysis as shown by large coefficients of variation in most studies on most tests. In small sample sizes, wide variability in performance limits conclusions about typical development in children with DS. Moreover, it may be that there are subgroups of children with differing abilities

within the one group of children with DS. For example, Laws *et al.* (1995) compared the performance of readers versus non-readers and reported significantly different results between groups. In addition, there was some evidence that variation may decrease over time, which adds to the importance of including a control group in intervention studies.

A strength of most of the studies under review relates to measurement of performance. For the most part, standardised testing tools were used and age-equivalent or grade-equivalent scores were reported when possible. Use of standardised tests and age and standardised scores allowed for comparison between several studies, comparison over time on subsequent versions of the same test, and assessment of meaningful change. Raw scores were also reported and often used in data analysis. Use of standardised scores is preferred but can be problematic if children do not score above baseline, making standardised scores an insensitive measure of change (Strauss 2001). This suggests the importance of selecting tests that have a sufficiently low baseline for the population (Thomas *et al.* 2009). In addition, we note that specific standardised neuropsychological tests that have a sufficiently low baseline to eradicate floor effects would allow for more precise testing of deficits (Edgin *et al.* 2010).

In summary, conclusions about cognitive trajectories in children and adolescents with DS cannot be clearly defined based on published data. Not only is this important from both a clinical and a scientific perspective, but methodologically this has important implications for development of treatments. Currently, if one were to test an intervention to enhance cognitive development in children and adolescents with DS, it would be difficult to assert that specific changes in cognition are the result of the intervention and not the result of age-related developmental changes in cognition. Further, although existing literature indicates some consistent findings (e.g. IQ declines over time), these findings have not been delineated for specific ages, which may mean that measuring the effect of an intervention needs evaluation over an extended time period (e.g. years). This may raise concerns about carrying out interventions whose benefits are not known until years later.

The present review identifies the paucity of research and the limitations of our knowledge around cognitive development in DS and also outlines some of the implications this has for assessing the success or benefits of cognition-enhancing interventions in DS. In absence of data tracking typical development in children with DS, any studies assessing interventions in children with DS must have an adequate control group (see Chapman & Hesketh 2000 for a discussion of this). Ideally, in intervention trials, control and intervention groups would consist of children with DS, and would be matched for age and performance on the endpoint measures used. Further, future studies should continue to use standardised testing tools, should report age-equivalent scores, and use analytical techniques that allow for construction of growth curves or that account for individual baseline differences.

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