DEVELOPMENT/PHENOTYPE

The Down syndrome behavioural phenotype: Taking a developmental approach

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Individuals with Down syndrome are predisposed to show a specific behavioural phenotype, or a pattern of strengths and challenges in functioning across different domains of development. It is argued that a developmental approach to researching the Down syndrome behavioural phenotype, including an examination of the dynamic process of the unfolding of the phenotype, will advance science and service for this population. Related issues including the distinction between primary and secondary phenotypic features, heterotypic continuity, and methodological implications are discussed.

In reviewing the past century of research on individuals with intellectual disability, it is possible to identify specific shifts in scientific approach that have had far-reaching impact. Debates and consensus regarding the definition of terms, the identification of the construct "adaptive behaviour", and discussions regarding quality of life have all had a profound impact on both science and service in the field of intellectual disability. For the purposes of research in Down syndrome, the introduction of the "developmental approach" to understanding intellectual disability, and the subsequent delineation of the two-group approach to studying individuals with cognitive impairments continue to impact scientific inquiry and service delivery.

In this paper, we review the contributions of the "developmental approach" to studying intellectual disability and its specific contributions to our current understanding of the Down syndrome behavioural phenotype. We then describe the current literature on the Down syndrome behavioural phenotype in the areas of cognition, language development, social-emotional functioning, personality-motivation, motor development, and psychopathology. We then consider the future directions for the developmental approach to studying Down syndrome, including questions regarding developmental continuity, the nature of change, and methodological implications in the final section of the paper.

Accomplishments of the developmental approach

The developmental approach to intellectual disability research began in the middle part of the 20th century with an examination of the rates and structures of development in children with intellectual disability compared with typically developing children[1,2]. As these developmental explorations became more nuanced, theorists began to argue for a refinement of our understanding of individuals with "intellectual disability", who likely belonged to either one of two groups. The "two-group" approach states that when an individual meets criteria for intellectual disability because of inherited genes and environmental factors, this disability is termed "environmental" or "familial"; when an individual meets criteria for intellectual disability because of an underlying genetic disorder, a disruption in prenatal development, or other related factors, the disability is termed "organic" [3].

This approach made it possible for researchers to more closely examine the underlying causes and consequences of specific types of disabilities within each group. In particular, it set in motion a line of research into the various disorders that are encompassed by the "organic" disability group. Disorders, such as Down syndrome, that are genetic in origin (but not necessarily heritable), began to receive a different type of research attention. Researchers began to examine how the genetic insult involved in various disorders predisposed children to specific types of outcomes. This scientific approach has led to what is now understood as research into "behavioural phenotypes" - or the pattern of behavioural strengths and weaknesses - associated with genetic disorders, with a large amount of attention being placed on outcomes in Down syndrome and a small number of other disorders.

Two important findings have made the discovery of the two group approach pivotal to our understanding of the nature of intellectual disability. First, there is now overwhelming evidence that different types of organic intellectual disability, in particular those disabilities of genetic origin, lead to notably different profiles of developmental performance (see REF 4). Thus, while two children with different genetic disorders such as Down syndrome and Williams syndrome may earn similar standard scores on overall measures of IQ, they are likely to show quite different profiles of performance when specific domains of development are examined. In addition to the finding that children with different disorders are likely to show distinctive developmental profiles, this line of research has highlighted the fact that many disorders associated

with intellectual disability do not impair individual domains of performance to an equal degree. There is now overwhelming evidence that children with genetic disorders are likely to show "mixed profiles", with peaks and valleys between and even within various domains of developmental performance. Rather than assuming that a child's abilities and achievement potential could be summarised with an overall identification of IQ or other singular performance measures, research into behavioural phenotypes has brought the understanding that children with various genetic disorders are predisposed to specific profiles of strength and weakness across many domains of development.

Overview of the Down syndrome behavioural phenotype

Of the 1000+ genetic disorders that have been identified to date, Down syndrome is among the most carefully researched. Descriptions of children with Down syndrome date back approximately 50 years and have been derived from both longitudinal and cross-sectional samples of children. A behavioural phenotype for Down syndrome has been described in the areas of social, cognitive, linguistic, motor, and psychopathology and will be reviewed next.

Cognitively, most children with Down syndrome fall into the mild to severe range for an intellectual disability and demonstrate a profile of relative strength and weakness [5]. Cognitive development has been observed to begin relatively typically for infants with Down syndrome and slow down in rate after the first two years, which may be related to delayed rates of brain myelination during this developmental period[6,7]. Fidler, Philofsky, Hepburn and Rogers observed deficits with the development of means-end thinking in pre-school-aged children with Down syndrome relative to children with other developmental delays[8]. Learning for children with Down syndrome between birth and 11 years old can be characterised by difficulty with the maintenance of existing skills and a persistent use of counterproductive strategies for novel problem solving tasks[9].

By the school-age and adolescent years, visuospatial processing tends to be strong (consistent with mental age) relative to verbal processing, with particular implication of difficulty focused on the working memory and verbal short-term memory [10,11,12]. Long-term memory for explicit information (i.e., words, a visual representation, etc.) has also been shown to be significantly more difficult for children with Down syndrome relative to matched controls with other forms of mental retardation[13]. A "ceiling" of cognitive development has not been observed in Down syndrome, such that research has suggested that learning continues for individuals with Down syndrome into the adolescent and adult years [14,15].

Language and communication development in Down syndrome has been well characterised in many areas. Language delays are characteristic of Down syndrome, with acceleration in language learning observable between the ages of two and four[5]. Difficulties with hearing additionally negatively impact upon language development in Down syndrome[16]. Miller reported that advances in mental age seem to be instrumental in the development of language, noting that as mental age increases, children with Down syndrome appear to make greater gains in receptive language than in expressive language skills[17]. A profile of relative strength in receptive compared to expressive language emerges in children with Down syndrome throughout the first few years of life and becomes more pronounced as children enter early middle childhood[17]. Among the specific domains within language, syntax has been a linguistic area of noted difficulty for individuals with Down syndrome[18]. While some authors have suggested that pragmatics - or the social use of language - is an area of relative linguistic strength in Down syndrome, others have noted difficulties in pragmatics, in particular with some aspects of referential communication[19,20,21].

In terms of social development, this area is generally rendered an area of relative strength for individuals with Down syndrome who are not also diagnosed with an autism spectrum disorder[22.23]. Individuals with Down syndrome have been described as, "charming," "affectionate," "outgoing," "cheerful," "happy," and "sociable" [24,25,26]. Zickler, Morrow and Bull reported that infants with Down syndrome demonstrated significantly more approach behaviours, compared to typically developing infants[27]. Early non-verbal communication and play skills are predictive of the frequency of initiations of peer play for preschool-aged children with Down syndrome[28]. In cognitively challenging laboratory situations, preschool children with Down syndrome have been noted to recruit their social strengths in engaging the examiner to avoid more challenging tasks[29].

Studies of social development in school-aged children with Down syndrome continue to support a relative strength. In one study, the majority of children with Down syndrome showed evidence of peer relationships that meet the criteria for true friendship[30]. An increased smile frequency compared to children with other types of mental retardation in school-aged children with Down syndrome certainly supports strength in social functioning[31]. Walz and Benson reported more parent-reported pro-social behaviours (i.e., sharing, staying on task, patience, participation in group activities, accepting redirection, etc.) for school-aged children with Down syndrome compared to children with other types of mental retardation[32]. Finally, school-aged and adolescent children with Down syndrome demonstrated the highest overall social competency (i.e., number and degree of participation in groups, number and closeness with friends, how well an individual can work/play alone, as well as with others) relative to children with Williams and Prader-Willi syndromes[33].

Motor functioning is another developmental area that has received research attention in children with Down syndrome. Low muscle tone is characteristic of Down syndrome, as is a lack of control of muscle stiffness, with both likely negatively impacting upon motor development [12,34]. While motor milestones tend to follow the same sequence as in typical development, most develop at delayed rates with the largest delays presenting for later developing milestones[12,35]. School-aged and adolescent individuals with Down syndrome demonstrate specific motor impairments in a number of fine and gross motor tasks (i.e., balance, posture, strength, and flexibility), as well as motor planning (i.e., praxis), although CA-level performance has been observed in specific skills including, running speed, agility, and visual-motor control[36,37,38].

Finally, an understanding of the psycho-

pathology characteristics of children with Down syndrome rounds out the known behavioural phenotype for Down syndrome to date. Generally, children with Down syndrome demonstrate approximately half the risk for demonstrating significant psychopathology compared to children with other forms of mental retardation[39]. Nonetheless, hyperactivity, aggression, stubbornness, disobedience, inattention and impulsivity have all been documented in children with Down syndrome[39,40]. Dykens and colleagues further observed that the risk of developing psychopathology for children with Down syndrome changes over time, such that psychopathology, as reported by parents, was significantly more common in adolescent children compared with early and middle childhood-aged samples[39]. By contrast, Stores, Stores, Fellows and Buckley observed a significant decline in rates of hyperactivity in children with Down syndrome from the school-aged years compared to the adolescent years[41].

Additional findings from the "developmental approach"

Advances in the characterisation of the Down syndrome behavioural phenotype have facilitated the development of contextual theories – most notably Robert Hodapp's description of "the indirect effects" of genetic disorders, and the focus on utilising phenotype-related findings in intervention and educational practice. Both of these approaches take the notion of behavioural phenotypes in genetic disorders and place them into the child's life context. Hodapp described that phenotypic predispositions not only impact the course of development in a child with a genetic disorder, they also indirectly predispose children to elicit certain perceptions and responses in family members and others in the child's immediate environment[42,43]. Findings from this line of research have identified different patterns in the degree to which families of children with different disabilities experience stress and support[42,44,45,46]. In particular, this line of research suggests that families of children with Down syndrome experience lower levels of stress when compared with other families of children with disabilities at similar levels of impairment [47-51]. They have also characterised specific parental perceptions and responses that are related in specific ways to the phenotypic profile associated with different disorders[52]. Thus, with his description of the indirect effects of genetic disorders on families and the child's immediate environment, Hodapp[42,47] showed that the phenotypic effects of a disorder such as Down syndrome extend beyond development in the child to impact the lives of those who interact with and care for the child in the larger community.

In addition to these indirect effects on parents and members of the community, it has been argued that the findings from this line of research have potential relevance for intervention and educational planning[53,54,55]. Though many questions exist regarding the practical implementation of syndrome-specific recommendations in educational settings, researchers are beginning to understand that the characterisation of the behavioural phenotype in Down syndrome and other genetic disorders can guide the decision making process in educational planning, help practitioners identify and monitor potential areas of vulnerability, and help families take a more proactive stance in shaping their child's developmental trajectory.

In Down syndrome, findings from information processing studies have the potential to shape the presentation of materials in educational settings. The strengths observed in visual processing and the deficits observed in verbal processing may necessitate that the presentation of verbally-based instruction be coupled with visual supports. The observed split between receptive and expressive language suggest that educators may need to strive to target the child's receptive language level - their true level of understanding - despite the fact that their expressive language abilities may make them appear to be lower functioning. Taking into account the personality-motivation orientation that involves an over-reliance on social strategies may lead educators to capitalise on social motivation in situations when appropriate, but limit social opportunities at times when inappropriate. These (and other) recommendations are generated from a rich understanding of the ways that Down syndrome impacts development and achievement, and can enable educators to make more informed decisions regarding their pedagogical approach.

Future directions for the developmental approach

The scientific accomplishments achieved to date within the developmental approach to intellectual disability are remarkable and have played a critical role in advancing the study of the Down syndrome behavioural phenotype. Despite these advances, there are some important limitations to the descriptions of syndrome-related outcomes that are available to date. Most of what is currently known about outcomes in Down syndrome and other disorders is based on a static, cross-sectional view of functioning where isolated areas of performance are assessed in one specific period of time. In addition, while there has been a good amount of research into infancy and early childhood in Down syndrome, very little of it has been programmatically designed to characterise developmental trajectories and capture the dynamic process of change over time in this population. With only a few exceptions (e.g. REF 28), questions regarding developmental continuity, core deficits, and developmental models have not been posed in rigorous ways. In addition, because most studies have not taken a longitudinal view, we have an impoverished understanding of how the developmental outcomes described in the section above emerge and develop throughout early childhood.

In short, what is missing from the developmental approach to studying Down syndrome has been the study of – to echo Annette Karmiloff-Smith's paper[56] – development itself. At this point, we have very little understanding of the processes of change that lead to the unfolding of the Down syndrome behavioural phenotype throughout early childhood and beyond. In her 1998 piece of the same title, Karmiloff-Smith stated that "development itself is the key to developmental disorders"[56]. It is argued here that development itself is the key to understanding the Down syndrome behavioural phenotype, and perhaps more importantly, identifying the most effective targets for intervention.

How is this approach different from current thinking in the developmental approach to studying the Down syndrome behavioural phenotype? We propose here that it is important to shift our focus from cross-sectional outcomes to the proc-

esses of change in a child's performance over time. Thelen and Smith write from a developmental systems perspective, and note that there are two themes that are critical to understanding change over time throughout development[57]. The first is that development involves "multiple, mutual, and continuous interaction of all the levels in the developing system, from the molecular to the cultural" [57:P.563]. The second theme is that development "can only be understood as nested processes that unfold over many time scales, from milliseconds to years"[57:P.563]. These two critical dimensions of development - the contextual and the process dimensions - should guide the next generation of developmental research into Down syndrome, and behavioural phenotypes in general.

The first theme relates to continuous interaction among many different aspects of the individual. Developmentalists tend to focus on describing a phenomenon in terms of invariants - stages or other fixed forms such as structures or schemes[57], and tend to describe them in isolation and devoid of the context of the rest of the functioning individual. The theme of "multiple, mutual, and continuous interaction" reminds us that if anything, these accounts of various domains of functioning are only snapshots of one aspect of a larger vibrant system. This is important because in the study of the Down syndrome behavioural phenotype, we may choose to focus our attention as researchers on a particular domain of functioning that is understood to be impaired in specific ways. However, there is evidence of a strong interrelationship between what are considered different domains throughout development. For example, cognition and social development impact one another early development in Down syndrome[58], and in typically developing children in general[59]. Thus, one challenge for the future of research into the Down syndrome behavioural phenotype is to explore the ways in which different domains of functioning - domains that appear to follow their own specific pathway of development - impact one another over time.

The second principle of development delineated by Thelen and Smith, to consider development as a "nested process" that "unfolds" over time, may be even more critical in shaping the next wave of research as well[57]. In considering cross-sectional outcomes only, we lose sight of the notion that development is an epigenetic process, a process of continued differentiation into more complex forms. We forget that there is a pathway that leads to the seemingly modularised endstate of a relative strength or weakness, and that outcomes of interest are in many ways "constructed by [a child's] own history and systemwide activity"[57: P. 569]. The phenotypic patterns that are observed in middle childhood and later development in Down syndrome are the result of the interaction of the existing components in the individual with Down syndrome over time, from the cellular to the organism- and the extraorganism-levels[60]. While the existence of a genetic insult, such as trisomy 21 or a translocation involving chromosome 21, does alter the early starting states of the developing[56], development still proceeds in the direction of greater complexity. But because of these variations in starting states, the self-organisation process creates patterns and order out of different raw materials or ingredients, with the presence of different constraints on functioning. Over time, areas of pronounced strength become apparent, and areas of pronounced weakness begin to emerge as well. In this way (to paraphrase Annette Karmiloff-Smith), the dynamic process of development *is* what constructs the phenotypic outcomes that are observed cross-sectionally in middle childhood and beyond in this population.

Example: Early instrumental and social development

An example of the opportunity offered by taking this more dynamic approach can be found in examining the interrelationship of cognitive and social development in infants, toddlers, and preschoolers with Down syndrome. Young children with Down syndrome begin to show deficits in instrumental thinking as early as the first year of life, at 9 months showing impaired contingency learning relative to typically developing infants[61]. Similar difficulties can be detected in research on the development of means-end thinking[62] where infants with Down syndrome show unusual stage transitioning patterns[63,64]. Toddlers with Down syndrome subsequently show shorter chains of continuous goal-directed mastery behaviours (e.g. fitting blocks through corresponding holes) [65]; and show less optimal strategies on instrumental thinking tasks than developmentally-matched comparison group children[8].

While delays in the development of instrumental thinking in young children with Down syndrome are detectable quite early in the first few years of life, a different pattern is observed in the area of social-emotional functioning. Competencies have been documented in early visual imitation in infants with Down syndrome [66], early looking behaviour [67,68,69], and early social vocalising[70]. Beyond infancy, toddlers and preschoolers with Down syndrome show competent nonverbal social interaction in the form of play behaviour and social initiations when compared to typically developing children[28,71]. Fidler, Most, Booth-LaForce and Kelly have also found that from 12 to 30 months, young children with Down syndrome make greater gains in their social-orientation performances than developmentally matched children with other developmental disabilities[72].

While these competencies are evident in some foundational social relatedness behaviours, there is some evidence that as the demands of social functioning become more complex in later development, social competence may not remain as robust of an area of functioning. But an early split between competent social relatedness and difficulties with instrumental thinking has an impact on development in Down syndrome beyond a simple profile of strengths and weaknesses. Fidler argued that these two early aspects of the phenotype interact in a dynamic way, leading to a characteristic personality-motivation orientation involving poorer task persistence and an overreliance on social strategies[58]. It has been well documented that, when faced with cognitive challenges, children with Down syndrome are more likely than developmentally-matched children to avoid the tasks with both positive and negative behaviours[73]. While younger children refuse to look at a task, struggle out of chairs, or show sudden crying behaviour[74], older children with Down syndrome are known to recruit social strategies (clapping hands, blowing bubbles) to engage the experimenter and distract them from the task at hand[29].

This profile of poor task persistence and an overreliance on social strategies continues to be evident throughout early development in Down syndrome[29,65,75,76]. Fidler argued that the interrelationship between deficits in the earliest building blocks of instrumental thinking and competence in social relatedness dynamically interact over time leading to a new phenomenon related to personality-motivation[58]. When faced with instrumental tasks, difficulty with generating effective strategies dynamically interacts with the favoured modality of social relating, and children with Down syndrome self-organise into a specific way of relating to the task, mixing task abandonment with off-task social behaviours. This dynamic self-organisation process is the unfolding of the phenotype.

Describing pathways

This hypothesised model of the development of the personality-motivation orientation in Down syndrome is a beginning attempt to apply the principles described by Thelen and Smith and others who view development in this more dynamic manner[57]. Yet, it offers much promise for advancing both our understanding of behavioural phenotypes and intervention in children with Down syndrome and other genetic disorders. In other neighbouring fields of research - particularly in the study of autism and autism spectrum disorder - the emergence of clinical symptoms in early childhood has been viewed as critical for developing effective interventions. As a result, researchers have combed the literature on typical development in order to identify candidate behaviours that may serve as core deficits in this disorder, which in turn has led to cutting edge developmental theorising regarding the "cascading effects" of core deficits on later development[77,78].

The advances in the neighbouring field of autism research are relevant because the level of developmental theorising and the elegance of the studies that have been executed to test competing hypotheses have advanced their field further than the field of research in children with intellectual disability and other disorders. It could be argued that while much catch-up work is needed in order to reach the level of sophistication observed in the field of autism research, many of the techniques that have been developed can be readily adapted to ask and answer questions about development in Down syndrome and other genetic disorders.

This approach to autism researchers has led to funded projects where researchers identify behavioural domains that had been discussed in the literature as potential core deficits in individuals with autism. They then collect data on children with autism (and various comparison groups) at various age intervals in order to trace the development of these domains of functioning, and to characterise the relationship between those domains and behavioural symptoms of autism. This methodical approach enabled research teams to ask questions about the uniqueness of the core deficits to autism versus other developmental disabilities, the degree to which specific symptoms predicted outcomes in middle childhood, and the nature of growth in autism using growth modelling and other methods for characterising change over time. As a result, research of this sort is making it possible for researchers to identify appropriate targets for intervention, to understand issues relating to timing of interventions, and to understand the degree to which interventions need to be specialised for children with this disorder.

This type of science is both readily adapted for and deeply needed in the field of Down syndrome research. Now that great progress has been made in characterising the nature of the Down syndrome behavioural phenotype cross-sectionally, it is possible to take the next steps and attempt to describe the pathway leading to these endstates. Adapting the developmental approach that has been taken in autism, it could be possible to identify candidate behaviours in early childhood that are the earliest manifestations of the later, more pronounced deficits. These early, subtle deficits can then serve as ideal targets for interventionists who could develop techniques that specifically target the earliest manifestations of a later deficit.

Primary versus secondary phenotypic features

Understanding development as a self-organising process can also help researchers disentangle which phenomena are more foundational aspects of the disorder, and which emerge as epiphenomena as the result of the interaction of different aspects of the developmental profile over time. It may be, for example, that there is a distinction to be made between what could be termed "primary" and "secondary" phenotypic features in Down syndrome and other genetic disorders[58]. Some features of the Down syndrome behavioural phenotype are rooted in the genetic and biological insult that is associated with trisomy 21. For example, verbal processing deficits may be directly linked to atypical brain development and a smaller planum temporal[79]. Similarly, imaging findings that report a sparing of occipital and temporal gray matter could be related to the strengths observed in visual processing[80]. Another example relates to the motor and articulatory deficits in expressive language observed in Down syndrome, which could be linked to anatomical differences in the development of the oral cavity. These aspects of the Down syndrome behavioural phenotype may be considered "primary phenotypic features", in that they are directly linked to basic features of the syndrome that arise directly from the atypically developing physiology and neurodevelopment associated with trisomy 21.

In contrast, other aspects of the Down syndrome behavioural phenotype may result more indirectly from the interaction between two or more primary phenotypic features. For example, it may be that visual processing strengths and social relatedness strengths interact in early development in the population, contributing to the "gesture advantage" that has been described in early communication in this population. Or, in the example presented above, strengths in core social relatedness and deficits in early instrumental thinking may interact to result in a personality-motivation style that involves poorer task persistence and an over-reliance on social strategies (see REF 58 for a review). These outcomes can be described as "secondary phenotypic features", as they are epiphenomena that result from the cross-domain relations among more primary aspects of the developing phenotype.

Though this distinction may ultimately break down, the further back one goes in the developmental timeline, perhaps understanding primary versus secondary phenotypic features has its true relevance in the timing and planning of intervention. In understanding how specific so-

called secondary phenotypic features arise, interventionists can choose to time interventions in such a way that minimise the chances of secondary features from becoming evident, and they can choose to target more primary features of the phenotype to avoid the downstream development of such secondary features. Of course, these recommendations are purely speculative at this point, in that intervention efficacy studies of this kind have not yet been conducted. However, from a theoretical perspective, such intervention planning offers great promise and the potential to identify factors that can optimise intervention outcomes for a population in great need of innovation in this area.

Heterotypic continuity

Another construct that may be important for researchers to incorporate into their studies of development in Down syndrome is the notion of heterotypic continuity. While homotypic continuity involves the presence of similar performance of a specific behaviour or characteristic at different timepoints, heterotypic continuity involves the association between earlier and later behavioural forms that manifest themselves in different age-appropriate ways, but reflect a similar underlying phenomenon[81]. Thus, the unfolding of a deficit in instrumental thinking may take the form of difficulty with nonverbal requesting and early means-end strategising in a toddler with Down syndrome, but it may take the form of difficulty with self-corrections on a maths task in a 4th grade child with Down syndrome. Identifying the instances of heterotypic continuity, in this example instrumental thinking and goal-directed strategising are at the root of both deficits, will be important for characterising developmental trajectories in Down syndrome.

Methodological considerations

In order to effectively address questions about change, consideration must be given to study design and methods of data analysis that are appropriate for the study of development. A shift in focus from posing questions about cross-sectional outcomes to understanding processes of change requires a simultaneous shift in the design of empirical studies and in the methods used to analyse data. Each of these areas is briefly addressed below.

Design issues

As mentioned above, cross-sectional data have been a main source of evidence for describing and theorising about development in Down syndrome. While cross-sectional data are useful for characterising the distribution of an outcome at a single point in time, they are of little use for understanding processes of change. This truism has important implications for study design if development is of primary concern.

Singer and Willett discuss design characteristics of studies of change that offer the potential to describe processes of change[82]. First, they comment on the necessity of multiple waves of data collection. One wave of data collection (i.e., a cross-sectional design) is fundamentally inadequate for capturing change. Observed variability on an outcome in an age-heterogeneous sample might yield clues about the nature of change, but suggested age effects can be confounded by cohort effects[82], and cross-sectional measures of variability tell us nothing about complex processes. In the case of cross-sectional data, we are only on solid ground when we characterise the variability in an outcome of interest. Collecting two waves of data does not advance one much further, as all that as been observed is an incremental difference from one point in time to a later point in time[83]. The size of a difference cannot tell us anything about the shape of a developmental trajectory. In other words, capturing the complex temporal dimensions of change cannot be accomplished with two waves of data collection. Therefore, to adequately describe and begin to understand how outcomes emerge and develop over time, it is essential to collect multiple waves of data.

Second, Singer and Willett argue that attention must be devoted to the number and timing of measurement occasions[82]. All else being equal, more waves of data are better than less. From a statistical standpoint, at least three waves are generally needed to characterise linear change, and four or more waves are required if we are interested in modelling nonlinear change[84]. Substantive considerations, however, are what truly must drive design. The timing of the waves must be such that multiple measurements occur during a time interval in which change is expected to occur. Periods of relatively rapid change require more closely spaced measurement occasions. Describing and examining substantive theories regarding complex (e.g., nonlinear or discontinuous) trajectories of change through childhood may typically necessitate multiple intervals of multiple measurements. Singer and Willett also note that, in order to consider the notion of a trajectory of change, the metric in which a developmental outcome is measured must be preserved and equally valid over time[82]. Thus, substantive considerations may limit the age range over which a particular outcome's trajectory can be characterised. In sum, taking a developmental approach to describing and understanding how outcomes emerge and develop throughout early childhood means carefully designing a true longitudinal study to capture complex and dynamic processes of change.

Analysis issues

Modern methods of longitudinal data analysis, and, in particular, growth modelling, offer powerful and flexible tools for modelling change over time with multiple waves of measurement. Nonetheless, methods such as growth modelling have not yet become part of the standard repertoire of tools used by those studying the development in Down syndrome. Even in those rare instances when a study has gathered multiple waves of data, it is common to find analyses and interpretation that make incomplete use of the longitudinal features of the data.

For a goal of characterising the complex nature of developmental trajectories, growth modelling is an appealing choice. Growth modelling is statistical tool for examining how an outcome changes over time. It can be used to address questions about complex temporal patterns of change within an individual, between-person differences in patterns of change, and the correlates of between-person variability in change[85]. Multiple outcomes can be modelled simultaneously, as parallel (and sequential) process growth models can be used to explore relationships between trajectories of change in different outcomes[86]. These tools have the potential to enable researchers to describe and take steps toward understand the nature

of the interrelationships between different domains of development. Growth modelling does not require that individual study participants have the same number of waves of data collection, the same data collection schedule, or equally spaced waves of data collection[82]. In this respect, the benefits methods of longitudinal data analysis are not restricted to the analysis portion of a study. Rather, the flexibility of an analysis tool such as growth modelling extends to study design. For example, waves of data collection can be scheduled as a function of theoretical and practical considerations without concern for having to rigidly design a study to accommodate a more traditional method of data analysis. In sum, the power and flexibility of modern methods of longitudinal data analysis, such as growth modelling, seem well suited to characterising the nature of the of the Down syndrome behavioural phenotype in a developmental fashion.

Conclusion

Thus, while the past several decades have brought a much richer and more refined of the nature of the behavioural phenotype associated with Down syndrome, there are many questions regarding the emergence of the behavioural phenotype in early development, and changes in the phenotype throughout development, that have been left unanswered. In designing the next generation of research in Down syndrome, studies should aim to characterise the nature of change and the self-organising processes that leads to the pattern of strengths and weaknesses in middle childhood and beyond. Innovations in the area of research design and analysis will facilitate this work, as will a deep appreciation for the dynamic process of change that lies at the heart of human development.

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