MENTAL RETARDATION AND DEVELOPMENTAL DISABILITIES
RESEARCH REVIEWS *13: 262–271 (2007)*

Education and Children with Down Syndrome: Neuroscience, Development, and Intervention

Deborah J. Fidler[1]* and Lynn Nadel[2]

[1]Human Development and Family Studies, Colorado State University, Fort Collins, Colorado

[2]Department of Psychology, University of Arizona, Tucson, Arizona

Of the recent advances in education-related research in Down syndrome, the characterization of the Down syndrome behavioral phenotype has become a potentially critical tool for shaping education and intervention in this population. This article briefly reviews the literature on brain–behavior connections in Down syndrome and identifies aspects of the Down syndrome behavioral phenotype that are potentially relevant to educators. Potential challenges to etiologically informed educational planning are discussed.
MRDD Research Reviews 2007;13:262–271.

Key Words: Down syndrome; behavioral phenotypes; education; intervention

As the most common chromosomal abnormality associated with intellectual disability, Down syndrome has been the focus of more behavioral and educational research than most other genetic disorders. These efforts have led to notable milestones in the advancement of education in Down syndrome, including cases in the literature of young adults with Down syndrome attending university courses [Hamill, 2003; Casale-Giannola and Wilson Kamens, 2006] and achievements in the area of educating children and adolescents in inclusive environments [Buckley et al., 2006]. The past five years alone have brought innovations that include teacher training interventions to shape attitudes toward inclusion in Down syndrome [Campbell et al., 2003], a refined understanding of effective inclusive practice in Down syndrome [Wolpert, 2001], and new instructional approaches involving computer technology [Lloyd et al., 2006; Ortega-Tudela and Gomez-Ariza, 2006].

However, the innovation that has the potential to have the greatest impact on educational practice in Down syndrome is the characterization of the Down syndrome "behavioral phenotype," or the pattern of behavioral outcomes associated with this disorder throughout development. Research into the phenotypic outcomes associated with Down syndrome has led to a better understanding of the learning profile associated with this disorder, and has offered new information regarding the possible brain–behavior pathways leading to these outcomes. Over the past few decades, researchers have uncovered characteristic patterns of functioning in the areas of cognition, language development, social–emotional functioning, and personality-motivation [see Dykens et al., 2000; Rondal and Buckley, 2001; Fidler, 2005]. Though many questions regarding development in this population remain unanswered, researchers have gained a clearer understanding of the developmental trajectory associated with Down syndrome, and how this chromosomal abnormality impacts development in a dynamic and multisystemic way.

Amidst these advances in delineating the Down syndrome behavioral phenotype, there remains a wide gap between these research findings and the development of innovative practice [Hodapp and Fidler, 1999; Fidler et al., 2007]. While it has been argued that etiology-based information could be of importance for education in Down syndrome [Hodapp and Fidler, 1999; Freeman and Hodapp, 2000; Fidler, 2005], the use of these connections has not nearly met its full potential. It is true that relative to other disorders, greater research emphasis has been placed on identifying educational strategies that might improve outcomes in Down syndrome. Some of these recent approaches are informed by and specifically target aspects of the Down syndrome behavioral phenotype [Laws et al., 1996; Kennedy and Flynn, 2003; Iarocci et al., 2006; van Bysterveldt et al., 2006], and others do not [Garcia and Conte, 2004; Park et al., 2005; Trent et al., 2005]. Those existing syndrome-based recommendations may be potentially quite useful, but lack empirical validation [Alton, 1998; Fidler, 2005].

Though the gap between research findings and targeted practice in Down syndrome remains wide, there is evidence that educators and practitioners themselves recognize the importance of scientific progress in this area. Wolpert [2001] asked educators of children with Down syndrome in inclusive settings to identify factors that might improve the outcomes in the classroom. Among their answers was "... more informa-

*Correspondence to: Deborah J. Fidler, Human Development and Family Studies, Colorado State University, 502 W. Lake Street, Fort Collins, CO 80523-1570.
E-mail: deborah.fidler@colostate.edu
Received 10 August 2007; Accepted 13 August 2007
Published online in Wiley InterScience (www.interscience.wiley.com).
DOI: 10.1002/mrdd.20166

tion on learning characteristics of children with Down syndrome" (p. 33). Similarly, parents seem to endorse etiology-specific modifications to their child's educational planning [Fidler et al., 2003]. As part of an effort to address the gap between research and practice in this area, this article will first review the current literature on the pathway from brain to behavior in Down syndrome. We then identify examples of phenotypic outcomes that may have educational relevance, with particular attention to the development of cognition and information processing in Down syndrome. Additional areas that may have educational relevance, including language development, social–emotional development, and personality-motivation, are briefly summarized. We conclude with a brief discussion of the potential challenges involved in shaping educational instruction in etiologically relevant ways. Although we start our review with discussion of neurobiology, we believe these kinds of data will be most relevant to the development of animal models, which then can be used to validate biological approaches to mitigation of the syndrome's impact on cognitive function. More important for educational practice will be an understanding of the phenotypic result of these neurobiological sequellae of trisomy 21, and we will accordingly focus on such behavioral approaches below.

THE NEUROBIOLOGY OF DOWN SYNDROME

The brain of an individual with Down syndrome at or shortly before birth is in many respects indistinguishable from the brain of a normal individual [Brooksbank et al., 1989; Wisniewski and Schmidt-Sidor 1989; Flórez et al., 1990; Schmidt-Sidor et al., 1990; Bar-Peled et al., 1991; Pazos et al., 1994]. Normal values have been reported for brain and skull shape, brain weight, proportion of specific cerebral lobes, size of cerebellum and brain stem, and the emergence of most neurotransmitter systems. There is evidence, however, that some changes begin to emerge as early as 22 weeks gestational age [e.g., Schmidt-Sidor et al., 1990; Golden and Hyman, 1994; Wisniewski and Kida, 1994; Engidawork and Lubec, 2003] and it is clear that by the age of 6 months a number of important differences are already obvious. Some of these differences are expressed in terms of the proportion of individuals with Down syndrome who show abnormal values, rather than in terms of a uniform abnormality in all instances. This is important as it highlights the variability in this population sharing the genotypic feature of trisomy 21.

While there is a postnatal delay in myelination [Wisniewski, 1990], it is worth noting that in all cases myelination is within normal range at birth, while in 75% of the cases it is within normal range throughout early development. Neuropathological differences after 3–5 months of age include a shortening of the fronto-occipital length of the brain that appears to result from a reduction in growth of the frontal lobes, a narrowing of the superior temporal gyrus (observed in about 35% of cases), a diminished size of the brain stem and cerebellum (observed in most cases), and a 20–50% reduction in the number of cortical granular neurons [see Crome et al., 1966; Benda, 1971; Blackwood and Corsellis, 1976]. In sum, the overall picture at birth or shortly thereafter shows that individuals with Down syndrome tend to fall towards the bottom of the normal range (or outside it) on most measures.

Investigations of neural function, as opposed to structure, in early infancy suggest some abnormalities: there is evidence of either delayed or aberrant auditory system development [Jiang et al., 1990], which might contribute to the widespread hearing disorders observed in Down syndrome. Obviously, such a disorder, if organic, could be related to subsequent difficulties seen in the learning of language. Hill Karrer et al. [1998] have reported delayed development of cerebral inhibition using visual event-related potentials (ERP) in a visual recognition memory paradigm.

There have been few studies of brain function in adolescents and young adults with Down syndrome and the existing data are somewhat equivocal. Pinter et al. [2001] used high-resolution MRI methods to analyze brain structure in 16 children (mean age 11.3 years) with Down syndrome. After correcting for overall brain volume, hippocampal, but not amygdala, volume reductions were seen in this group. This result confirms some earlier work using lower resolution MRI methods [Jernigan et al., 1993]. Kates et al. [2002] looked at a group of 12 children with Down syndrome (all males, mean age 5.94 years) and compared them with children with fragile-X, developmental language delay, or typical development. The children with Down syndrome had smaller brain volumes than any of the others, with previously unreported reductions in parietal cortex as well as the oft-reported reductions in the temporal lobe. Pinter et al. [2001], on the other hand, note the relative preservation of parietal cortex.

Overall, study of neuropathology points to problems in certain regions of the cortex, including most prominently the temporal lobe and the hippocampal formation [Wisniewski et al., 1986], the prefrontal cortex, and the cerebellum. This conclusion meshes well with what has been learned from the development of mouse models of the syndrome [e.g., Kleschevnikov et al., 2004]. These models have generally demonstrated selective impairments in the anatomy, physiology, pharmacology, and behavior, which are associated with the hippocampal formation, the prefrontal cortex, and the cerebellum.

These neurobiological findings in Down syndrome can inform education in several ways. First, as only modest abnormalities are detectable at birth, the role of development is critical in building into the pronounced profile of strengths and weaknesses observed in this population. This offers educators an important window of opportunity for intervention in the first few years of life, a point that will be revisited later. Second, the atypical development of specific brain structures suggests that some areas of functioning may become more impaired than others throughout development. In addition, early in development, many of the differences observed are expressed in terms of the proportion of individuals with Down syndrome who show abnormal values, rather than in terms of a uniform abnormality in all instances. This is in line with the probabilistic approach to understanding outcomes in individuals with genetic disorders [Dykens, 1995], where children may be at risk for certain neurobiological features, but not all children will show those specific abnormalities. These three themes are educationally relevant and will be explored in greater depth in the following sections. Additional links between brain and behavior will be noted throughout the next section where relevant findings have been reported.

REVIEW OF EDUCATIONALLY-RELEVANT LITERATURE ON DEVELOPMENT IN DOWN SYNDROME

In this section, we explore the current literature on development in Down syndrome and highlight some of

the main findings that are potentially relevant to educators and interventionists. Before we examine the phenotypic profile associated with Down syndrome, there are two important issues that should be noted. First, these findings are part of a probabilistic approach to understanding the link between syndrome and outcome in behavioral phenotype research [Dykens, 1995]. Within this approach, it is understood that there is a higher probability that children with Down syndrome will show any of these specific outcomes relative to other children who do not have Down syndrome; however, not every child with Down syndrome will exhibit each of these phenotypic features [Dykens, 1995]. Thus, educators might use this information to adopt a "ready stance" regarding areas of potential strength and weakness in children with Down syndrome, but might expect that children will likely vary in the degree to which they express any one of these predisposed outcomes.

Second, researchers are currently exploring the question of whether there is a subgroup of individuals with Down syndrome who meet criteria for autism spectrum disorders. Some studies suggest that a small percentage of individuals with Down syndrome have behavioral profiles consistent with autism [Collacott et al., 1992; Ghaziuddin et al., 1992; Kent et al., 1999; Paly and Hurley, 2002; Hepburn et al., in press]. These findings are not based on studies that have employed epidemiological methods for estimating the prevalence of comoribidity in this population, so they should be taken with a note of caution. However, it is possible that Down syndrome with children who have comorbid autism may show a different behavioral profile than their counterparts with Down syndrome who do not have autism, and may require a different educational approach [Hepburn et al., in press].

COGNITION IN DOWN SYNDROME

Early Cognition

In line with the neurobiological findings described earlier, infants with Down syndrome show relatively normal abilities in learning and memory. This does not mean that either they, or indeed normally developing infants, have the full adult range of learning and memory abilities at birth. In fact this is not the case because some parts of the brain mature postnatally and the forms of learning and memory dependent on them are not available until some time after birth. The medial temporal lobe, and particularly, the hippocampus, as well as parts of the prefrontal cortex and cerebellum, are included in this category. The fact that these late-developing structures are apparently particularly at risk in Down syndrome is probably of considerable importance [see Nadel, 1986].

In an early series of studies, Ohr and Fagen [1991, 1993] reported that 3-month-old infants with Down syndrome were entirely normal in learning about the contingencies between their own movements (leg kicking) and reinforcement, including initial learning, acquisition speed, and retention. In a later report, Ohr and Fagen [1994] showed that 9-month-old infants with Down syndrome were impaired, as a group, in learning about the contingency between arm movements and reinforcement. However, they noted that some infants with Down syndrome were able to learn. They concluded that there is a relative decline in conditionability in infants with Down syndrome compared to normally developing infants after 6 months. Mangan [1992] tested control infants and infants with Down syndrome on a variety of spatial tasks, one of which, a place-learning task, was designed especially to assess the state of function of the hippocampal system. The pattern of results was consistent with diffuse, but mild, neuropathology combined with much more extensive pathology localized to the hippocampus.

Children with Down syndrome have typically been shown to acquire basic object concept more slowly than normal [see, e.g., Rast and Meltzoff, 1995] but with extensive training they can acquire it at more-or-less the same time as normally developing infants [Wishart, 1993]. However, a different kind of problem emerges in this task situation: instability of acquisition. Although the typical subject with Down syndrome solved various levels of the tasks used to assess the object concept at ages not very far from the norm, performance after acquisition could be highly variable and apparently beset by motivational difficulties. These problems, if representative of the learning style of children with Down syndrome, are extremely important in thinking about effective intervention. The results of Wishart's studies using standard intelligence test batteries suggest that they are indeed representative. Test–retest reliability was very low because successes gained in one test might not appear upon retest, as soon as 2 weeks later. New skills show up, only to disappear shortly thereafter. One could speculate that evidence of such "rapid forgetting" is consistent with damage in the hippocampal formation but considerably more data are required before this conclusion can be accepted. These developmental differences may have important implications for educators. For example, if the learning process involves more observable regressions for children with Down syndrome than for other children, it might be important for teachers and interventionists to account for these differences with more frequent reviews of materials, and it may be important to monitor the stability with which a child with Down syndrome has acquired a skill.

Information Processing

The learning and memory problems that begin to emerge in late infancy become considerably more noticeable as the infant grows to childhood and adolescence. These effects vary as a function of the type of memory being assessed. Explicit memory involves things like facts and events that subjects consciously recollect, whereas implicit memory can be demonstrated indirectly, without conscious recollection. This distinction has been shown to be important in understanding organic amnesia, since most amnesics are profoundly impaired on explicit memory tasks but can be relatively normal on implicit tasks. One common kind of implicit memory test looks at skills or procedures, such as mirror-tracing; another common implicit memory test involves "priming," where prior exposure to a word or picture can influence subsequent performance on word-stem or partial-picture completion tasks even though the subjects might not recall having seen the relevant items before.

Carlesimo et al. [1997] examined the performance of children with Down syndrome in the area of "implicit" (procedural) and "explicit" (episodic) memory paradigms, including word-stem completion, list learning, and prose recall. Robust priming effects were seen in the Down syndrome group, comparable to those observed in controls, indicating that implicit memory was intact. However, deficits were observed in both explicit memory tasks. Performance on these kinds of explicit memory paradigms has been linked to functions

of the hippocampal system; hence, the defects suggest differential impairment in hippocampal function and thereby converge with the data from study of spatial cognition. This selective impairment of explicit, but not implicit, memory was also reported in Vicari [2001].

A great deal of research attention has been focused on deficits in the processing of verbal information in Down syndrome, and how these deficits contribute to poor language and learning outcomes [Byrne et al., 1995; Hesketh and Chapman, 1998; Laws, 1998]. Most commonly, the verbal working memory deficit in Down syndrome is measured by performance on an auditory digit span task. Poor auditory digit span performance findings in Down syndrome were first reported several decades ago [Bilvosky and Share, 1965; Rempel, 1974].

More recently, a series of studies by Hulme and Mackenzie [1992] described the development of poor verbal working memory in children with Down syndrome in great detail. They found that children in the Down syndrome group scored lower than the typical MA-matched controls on auditory digit span, and mental age and verbal working memory tasks were more correlated in the typically developing children than in the Down syndrome group. Similar deficits in verbal working memory are also observable when letters are substituted for numbers in the paradigm [Varnhagen et al., 1987]. This deficit is also not subject to changes when experimental design is manipulated in order to reduce unrelated demands on individuals with Down syndrome [Marcell and Weeks, 1988; Marcell et al., 1988; Laws, 1998].

Deficits in verbal working memory may relate to neuroanatomical characteristics associated with Down syndrome, including a proportionately smaller planum temporale, which is referred to as the auditory association cortex [Frangou et al., 1997]. It is important to note, however, that the relationship between the planum temporale volume deficit and cognitive-linguistic functioning in Down syndrome remains unclear [Frangou et al., 1997].

Though there is a great deal of evidence of verbal working memory deficits in Down syndrome, it is important to note that the main evidence for this dysfunction comes from studies that measure the processing of acoustically-presented information only. Auditory digit span, auditory sentence recall, and other commonly used techniques auditory nonword repetition all involve the processing of acoustic, rather than speech-based visually presented information. Thus, one might argue that the verbal working memory difficulty in Down syndrome has only been demonstrated in the maintenance of auditorally presented information, rather than the processing of all types of verbal information. The processing of speech-based visual information in Down syndrome has not yet been shown to be equally impaired, and importantly, may not be.

In contrast with their performance on verbal processing tasks, individuals with Down syndrome show relative strengths in visuospatial memory, and show a profile of higher visuospatial processing than verbal processing [Silverstein et al., 1982; Thase et al., 1984; Pueschel et al., 1987; Wang and Bellugi, 1994; Jarrold et al., 1999; Klein and Mervis, 1999]. The Corsi span, a block tapping memory task, is most often used as the test of visuospatial processing. In terms of raw scores, most individuals without Down syndrome (both with developmental delay and typically developing) tend to show higher raw auditory digit span recall scores than Corsi span recall scores. However, individuals with Down syndrome seem to perform equally well on these tests, or even show an advantage for Corsi span recall [Haxby, 1989; Azari et al., 1994; Wang and Bellugi, 1994; Vicari et al., 1995; Jarrold and Baddeley, 1997], especially when participants were not required to include order in their responses. These results have also been demonstrated with tasks other than the Corsi and auditory digit span [Pueschel et al., 1987; Hodapp et al., 1992; Bower and Hayes, 1994; Klein and Mervis, 1999]. The visuospatial working memory advantage is also demonstrated when identical stimulus information is simply presented either visually versus auditorally [Varnhagen et al., 1987].

Neuroanatomical correlates for this relative strength in Down syndrome visuospatial processing have been posited. Pinter et al. [2001] reported what they call "striking preservation" of parietal and occipital cortical gray matter in an MRI study of 5–23-year olds with Down syndrome. Studies have shown the importance of both parietal and occipital lobe functioning for some aspects of visuospatial processing [Black and Bernard, 1984; Jonides et al., 1993].

An information processing profile that includes strengths in visual processing and implicit memory, and deficits in verbal processing and explicit memory could potentially inform educational approaches to working with children with Down syndrome. Instruction that is verbally based—and especially auditorally mediated—might pose a greater challenge to children with Down syndrome than instruction that is presented with visual supports. Minor and subtle teaching modifications can be made to address this issue, without any noticeable disruption to a larger classroom environment. In addition, instruction that involves explicit memory, such as logic problems, may be presented with greater sensitivity given that this is an area of challenge as well. Awareness of this area of deficit might allow an educator to make informed decisions regarding prompts, wait time, and supports for a child who may have particular difficulty with this type of information processing.

Reading

The cognitive underpinnings of reading are of particular relevance for education in Down syndrome. Despite the impairments observed in other areas of cognition, many individuals with Down syndrome are able to show competence in some aspects of reading development. In particular, word identification appears to be an area of relative strength within reading skills in this population, while word attack and reading comprehension appear to be more impaired [Byrne et al., 1995; Cupples and Iacono, 2000; Kay-Raining Bird et al., 2000]. Strengths in word identification have been linked to relative strengths in visual processing [Fidler et al., 2005b], while deficits in word attack skills have been linked to difficulties with verbal processing skills in Down syndrome [Boudreau, 2002].

There is some controversy regarding the implications of this profile for reading instruction in Down syndrome [see Hodapp and Freeman, 2003 for a summary], with some arguing that visually-based approaches might be warranted [Buckley and Bird, 2002], and others emphasizing the role of phonological processing in reading in this population, despite impairments [Cupples and Iaocono, 2002]. Regardless of this debate, there is evidence that children with Down syndrome recruit both their visual and verbal processing skills when reading, particularly when identifying words [Cupples and Iacono, 2000; Fidler et al., 2005b].

BRAIN–BEHAVIOR CONNECTIONS

In a series of recent studies, Pennington, Nadel and colleagues have tested several different groups of individuals with Down syndrome on a range of tasks designed to directly assess the function of specific brain systems. This "cognitive neuropsychological" approach often uses tasks first developed in animal models, where the critical underlying brain circuits can be identified and carefully studied in invasive experiments. The team started with a focus on three brain systems identified by the neuropathological data, much of which was discussed above: the hippocampal system, the prefrontal cortex, and the cerebellum. They developed a set of tasks that could, collectively, tell us something about how these brain systems are faring. In the first set of studies, Pennington et al. [2003] found evidence of specific hippocampal dysfunction in our sample of 28 adolescents, using mental age matched controls.

Little evidence of prefrontal dysfunction was observed in a battery of nonverbal tasks. Subsequent pilot work, however, suggested that verbal tasks might yield a different result, and indeed that is what is being observed (Moon et al., unpublished data). Using verbal tasks to explore the prefrontal cortex, Moon et al. found in the young (aged 5–11) and old (aged 30–41) groups strong signs of dysfunction in both the hippocampal and prefrontal systems. Deficits were observed in a range of tasks although verbal mediation was necessary to bring out the prefrontal effect. Taken as a whole, these studies show that particular problems emerge in the memory domains served by the hippocampal system and the prefrontal system. The latter impairment appears to be linked to the use of verbal test materials. The impairment in hippocampal function could in principle reflect problems in any of the structures of the hippocampal region; a recent study of two neuropsychological paradigms dependent on parahippocampal and perirhinal regions (delayed nonmatching to sample and visual paired comparison), however, suggests that these areas are functioning appropriately, and that the impairment is more likely to reflect improper development of the hippocampus itself [Dawson et al., 2001].

The prefrontal cortex, as noted already, plays an important role in a wide range of functions, including episodic/explicit memory and working memory. As noted earlier, explicit memory is impaired in individuals with Down syndrome. There has been extensive research on working memory in this population, and clear deficits have been observed in a number of studies [Varnhagen et al., 1987; Marcell and Weeks, 1988; Laws, 1998; Jarrold et al., 1999]. However, this impairment seems to be limited to verbal information, as impairments are minimal in visuospatial domains. The deficit appears to be neither a motor nor articulatory problem [Kanno and Ikeda, 2002] and may relate to the so-called phonological loop [Jarrold and Baddeley, 2001; Laws, 2002].

OTHER AREAS OF EDUCATIONAL RELEVANCE

In addition to cognitive development and information processing, there are other areas of development in Down syndrome that may be relevant to decisions made by educators. Brief descriptions of findings in the area of language development, social–emotional functioning, and personality-motivation are presented in this section.

Language Development

Individuals with Down syndrome generally show a profile of stronger receptive language skills and weaker expressive language skills. This profile seems to emerge in early childhood and become more pronounced as children progress into middle childhood and beyond [Miller, 1999]. Expressive language deficits are often manifested in terms of morphosyntactic delays [Chapman et al., 1998; Eadie et al., 2002] and difficulties with speech intelligibility [Miller et al., 1999; Stoel-Gammon, 2003; Kumin, 2006]. And while receptive language is stronger than expressive language in most individuals with Down syndrome, some areas such as receptive syntax, are more compromised than others [Abbeduto et al., 2003]. In contrast, some areas of pragmatic functioning seem to be an area of relative strength in individuals with Down syndrome [Johnston and Stansfield, 1997; Laws and Bishop, 2004].

This language profile is potentially relevant for educational planning in several ways. First, because many children with Down syndrome have stronger receptive than expressive language skills, they often understand much more language than they can produce. To an uninformed educator who is not aware of the discrepancy between expressive and receptive language, it might be natural to address the child with input language and instruction at the level of their expressive language. But such an approach would likely involve a marked underestimation of the child's academic and receptive abilities. When considering how best to present class material, it may be important for educators to identify and target the receptive language level of a child with Down syndrome so as to appropriately challenge them and engage them at their true level of understanding [Roberts et al., 2007].

In addition, it may be useful for educators to be aware that difficulties with expressive language—and speech intelligibility in particular—may be frustrating for children with Down syndrome in classroom contexts. Morphosyntactic difficulties demand extra motivation from children with Down syndrome to produce lengthier utterances [Miller and Leddy, 1999], and intelligibility problems may lead to situations where a child must repeat herself in order to be understood. Thus, educators may want to consider both the social and motivational consequences of expressive language difficulties. It may be beneficial to identify ways to minimize the potential for negative experiences, while allowing the child with Down syndrome to benefit from the opportunity to build their speech, language, and communication skills.

Social–Emotional Functioning

The majority of individuals with Down syndrome show strengths in various aspects of social–emotional functioning, exhibiting behaviors that suggest evidence of intact social relatedness and some measure of social competence in early childhood [Fidler et al., 2006]. In the first few years of life, markers of primary intersubjectivity, the earliest forms of dyadic social relating based on emotional displays and reciprocal signaling, are identified as emerging in a delayed, but competent manner in this population [see Fidler, 2006 for a review]. In particular, young children with Down syndrome show evidence of primary intersubjective development in the form of increased eye gaze and vocalizations directed to other people [Gunn et al., 1982; Crown et al., 1992; Legerstee et al., 1992; Kasari et al., 1995], increased direction of positive facial displays in the form of smiles [Kasari and Freeman, 1990; Fidler et al., 2005a].

In addition, there is also support for the notion that many aspects of secondary intersubjectivity, the ability to engage with a social partner in a triadic fashion, also emerge with competence, albeit in a delayed fashion. Several studies suggest that children with Down syndrome show either MA-appropriate or even increased levels of joint attention relative to other children without Down syndrome [Mundy et al., 1988; Kasari et al., 1995; Fidler et al., 2005c]. Toddlers and preschoolers with Down syndrome also show competent triadic relating in the forms of play acts, turn taking, invitations, and object shows [Mundy et al., 1988; Sigman and Ruskin, 1999].

In the context of these strengths in the development of social relatedness and other social–emotional skills, there is evidence that children with Down syndrome may show difficulties when cognitive demands in social decision making increase. While socialization skills remain a relative strength in middle childhood [Dykens et al., 1994], and many children with Down syndrome appear to be able to form reciprocal friendships with peers [Freeman and Kasari, 2002], there is mixed evidence regarding whether individuals with Down syndrome show impairments in the ability perform more complex social cognition tasks [Baron-Cohen et al., 1985; Baron-Cohen, 1989; Yirmiya et al., 1996; Zelazo et al., 1996; Abbeduto et al., 2001]. Williams and Wishart [in press] identify other factors that may contribute to the difficulty that individuals with Down syndrome have on social–cognitive tasks, including executive function or memory difficulties. Nevertheless, it may be that despite competence in the area of social relatedness, as the demands and complexities of social situations increase in middle childhood and beyond, individuals with Down syndrome may show difficulties with social adaptation and selecting appropriate social strategies, especially as they enter adolescence and face changes in emotional functioning and mood [Dykens et al., 2002; Fidler et al., 2005a].

This social profile is relevant for educational planning in several ways. First, these strengths may make it possible for children with Down syndrome to learn through social techniques such as modeling, peer collaboration, social groups [Lloveras and Fornells, 1998; Rogoff, 2003]. Though there is a surprising lack of empirical exploration of the efficacy of these techniques in children with Down syndrome, it could be hypothesized that such techniques would capitalize on social motivation may be a useful reinforcer for children with Down syndrome. However, it is important to consider that the strong social motivation observed in this population may serve as a distractor as well [Wishart, 1996; Fidler, 2006; see discussion below]. There is also some evidence that, because of strengths in early social relatedness in this population, affective cues put forth by a teacher or interventionist can impact learning and motivation in a particularly pronounced way [Park et al., 2005]. It may also be important for educators to be mindful of potential changes in mood and social engagement as children with Down syndrome transition into adolescence, and perhaps adopt modified strategies as these behavioral changes become evident [Dykens et al., 2002].

Personality-Motivation

Another aspect of the behavioral profile in Down syndrome that may be educationally relevant relates to motivational orientation and task persistence [Gunn and Cuskelly, 1991]. In laboratory settings, when presented with tasks such as puzzles and other nonsocial/nonverbal tasks, children with Down syndrome have been shown to abandon the task sooner than other children at similar developmental levels, and to adopt strategies that divert attention away from the task [Landry and Chapieski, 1990; Pitcairn and Wishart, 1994; Ruskin et al., 1994; Vlachou and Farrell, 2000; Kasari and Freeman, 2001]. This, coupled with the strengths in aspects of social initiation described in the previous section, can lead to a style that involves an over-reliance on social strategies, especially in contexts that require instrumental thinking [Kasari and Freeman, 2001]. It may be that the interaction between emerging difficulties with instrumental thinking and strengths in social relatedness lead to a personality-motivation orientation that ultimately impacts the ability of a child with Down syndrome to learn effectively [Wishart, 1996; Fidler, 2006].

A style that leads children to remove themselves from challenging situations in favor of social interaction may deprive children with Down syndrome of important opportunities to challenge themselves and gain new skills through active engagement with the environment that surrounds them. Awareness of this profile may be important for educators when selecting techniques for involving individuals with Down syndrome in classroom settings. It may be important for educators to identify situations when the child with Down syndrome may be recruiting social strategies when engaging with the task at hand is more appropriate [Fidler, 2006]. Educators might also manage behavior using social consequences as reinforcement, not as a distracter during tasks that might pose a cognitive challenge [Fidler, 2006].

CHALLENGES IN LINKING RESEARCH TO PRACTICE

Are Behavioral Phenotypes Modifiable?

Though many aspects of the behavioral phenotype in Down syndrome are potentially relevant for educators, there are several challenges that must be addressed as researchers aim to translate research findings into educational practice. The first challenge relates to the notion of genes and modifiability. There is a danger in discussing the notion of behavioral outcomes associated with genetic disorders in that genetic effects can connote fixed, nonmodifiable pathways. What we now know about the mechanisms by which genes give rise to phenotypes, particularly behavioral phenotypes, indicates that we need not worry about this danger. First, from a neurodevelopmental perspective, at every step of the way, opportunities exist to modulate the translational process. In addition, all learning and education is rooted in the notion that neurophysiological changes can be observed in response to environmental input, leading the brain to undergo various types of reorganization [Nelson, 2000]. Nelson notes that it is commonly understood that, "... the success of early childhood intervention strategies rests to a great degree on the relative plasticity of the human brain (p. 222)," and this applies to children with and without genetic disorders alike.

In addition, potential evidence of the modifiability of the Down syndrome phenotypic profile has been reported in a long-term study of British inclusion in this population. Buckley et al. [2006] report that the practice of including children with Down syndrome in mainstream classrooms in England has had an impact on the phenotypic profile in older children and adolescents with Down syndrome. They note that previous studies showed that children with Down syndrome who

attended school in special education settings demonstrated a profile of strengths in socialization and daily living skills, but deficits in adaptive communication abilities [Dykens et al., 1994; Fidler et al., 2006]. However, in their sample of children with Down syndrome who underwent schooling in inclusive settings, they found that the marked deficits in adaptive communication were not observable [Buckley et al., 2006]. They argue that the social challenges associated with being educated in an inclusive setting modified the phenotypic profile and narrowed the gap between areas of strength and challenge. The authors of this study note that this warrants replication, but if supported, there this would be a critical means of modifying the profile of strengths and weaknesses associated with Down syndrome.

When considering whether educational approaches can modify phenotypic profiles, it is also important to note that the pattern of strengths and weaknesses associated with genetic disorders does not simply appear in a pronounced fashion in middle childhood. There is a developmental process that leads to the more pronounced end states of relative strengths and weaknesses in any genetic disorder. This is important to recognize because there may be opportunities to target early emerging phenotypic characteristics in very young children, before dissociations in profile become pronounced [see Karmiloff-Smith, 1997, 1998; Fidler, 2005, 2006]. Fidler [2005] argued that for some aspects of the Down syndrome behavioral phenotype, it may be possible to identify early developmental precursors to later more pronounced outcomes. If these early developmental precursors can be identified and targeted with empirically validated intervention techniques, this too may be another means for altering the developmental pathway and the phenotypic profile associated with Down syndrome.

What Constitutes Empirical Support for Etiology-Specific Education/Intervention?

Another challenge in the attempt to bridge research and practice in this area relates to the empirical validation of techniques aimed at addressing phenotype-specific dimensions. There is a small, but growing literature that describes the efficacy of educational techniques such as computer-based learning (Lloyd et al., 2006; Ortega-Tudela and Gomez-Ariza, 2006], instructional approaches to reading and its component skills [Laws et al., 1996; Moni and Jobling, 2001; Cupples and Iacono, 2002; Kennedy and Flynn, 2003; van Bysterveldt et al., 2006], and math skills [Irwin, 1991; Nye and Buckley, 2006; Ortega-Tudela and Gomez-Ariza, 2006] for children with Down syndrome. While more studies of this kind are warranted, only a few of these studies show educational benefits when using one specific technique over another Cupples and Iacono, 2002].

The question remains whether this type of empirical validation is sufficient to warrant a syndrome-specific approach to educational planning. Some might argue that the efficacy of these techniques have little to do with the phenotypic profile associated with Down syndrome—rather they simply show that one technique is superior to another regardless of the population to which it is applied. By extension, it could be argued that in order to justify a syndrome-specific set of recommendations for educational practice, there must be a set of techniques that work differentially across populations. That is, there must be techniques identified that are effective for children with Down syndrome, but not effective for children who do not have Down syndrome or the developmental profile associated with Down syndrome [see Fidler et al., 2007 for a discussion]. At present, there are relatively few examples in the literature that demonstrate such differential effects [Fey et al., 2006; Yoder and Warren, 2002]. Those that do exist suggest that the personality-motivational orientation associated with Down syndrome may be particularly important to consider when selecting educational and intervention techniques [Yoder and Warren, 2002; see Fidler et al., 2007 for a discussion of this issue].

Is Syndrome-Specific Education Feasible?

A third challenge to the idea of linking phenotype research into practice relates to issues of classroom management and the training of teachers. While future research may show the benefits of etiology-specific instructional approaches, it could be argued that specific techniques for different children in the classroom would be too unwieldy and would require too great of a personnel demand. It could also be argued that the training of teachers in etiology-specific instructional approaches would make teacher education programs too lengthy of a process, requiring a mastery of approaches that target any number of the many syndromes and behavioral disorders present in the student population.

While adopting an etiology-specific approach in the classroom will undoubtedly place additional demands on educators, some potential approaches involve less of a diversion of resources from the larger classroom culture than others. Techniques to be developed in the future can be imbedded in naturalistic ways, and might only involve subtle adjustments in teacher decision making and presentation of material. For example, supplementing instruction with supports that rely on a favored information processing modality might not be detectable to the larger classroom, and in some instances could potentially enhance instruction for children in the classroom without disabilities. In addition, while some additional training might be involved for teachers, these can come in the form of continuing educational trainings, or useful informational materials (websites, booklets) that need not burden a teacher in training. While the details of implementation would need to be addressed in a real-world process, it is likely that the implementation of some syndrome-specific instructional approaches, if they receive empirical validation, might not necessarily pose a prohibitively large challenge to educators.

Future Directions

Despite the many advances that have been made in the study of brain and behavioral development in Down syndrome, there is still a great deal of progress to be made both in the basic study of development in Down syndrome and in the application of these findings to practice. In terms of the potential contributions of the neurobiological approach, future work uncovering the neurobiological causes of the cognitive, language, and behavioral impairments associated with Down syndrome will ultimately lead to creation of an ever-more precise animal model of Down syndrome. A more precise animal model of Down syndrome could make it possible to develop biological interventions that might ultimately impact development in this population. Thus, advances in this area will rely on the close collaboration of behavioral scientists who are carefully delineating the nature of the Down syndrome behavioral phenotype, neurobiologists who are able to map these phenotypic outcomes onto brain anatomy and brain

physiology in this population, and animal model researchers who can use this information to develop an ever more precise model of the disorder. This process will be aided by the neuropsychological approach, which offers the promise of identifying exactly those areas of disproportionate cognitive impairment that might guide the mapping from behavior to brain functioning.

Given the probabilistic nature of phenotypic outcomes in genetic disorders, these approaches may also make it possible to more deeply understand the nature of within syndrome variability in the population of individuals with Down syndrome. As researchers collaborate to uncover the pathway from gene to brain to behavior, it may be possible to identify with greater precision the sources of within-syndrome variability in outcomes of interest, and it may be possible to address the needs of children who show variations around the phenotypic profile that is associated with the larger group of individuals with Down syndrome. These advances offer the hope of even more targeted educational planning and the possibility of addressing the variability in outcomes that is classically associated with this population.

Another important future direction for research in Down syndrome relates to the importance of detecting emerging phenotypes in early childhood [Fidler, 2005]. This type of research transforms the view of outcomes in Down syndrome from a static, cross-sectional approach into a dynamic, longitudinal approach to studying this population. In taking this more dynamic view, it may be possible to identify the more subtle developmental precursors to more pronounced outcomes in later childhood and adolescence. These early precursors may serve as potentially useful targets for early intervention in this population. Rather than waiting to intervene once a split profile of strengths and weaknesses has become pronounced, educators and interventionist may be able to target these early precursors in their more subtle forms, which may set development on a more optimal pathway.

Finally, as the research community sorts through the various controversies related to syndrome-specific educational approaches, continued advances have still been made in the education of individuals with Down syndrome. These efforts continue to challenge the outmoded notions that children with genetic disorders such as Down syndrome have limited educational potential. Though the goal of bridging research and practice in the study of development in Down syndrome faces challenges-especially the difficulty of collaboration among scientists across neighboring fields-it is a goal that promises greater returns than simply educating children with Down syndrome according to their severity of impairment (mild, moderate, severe, profound intellectual disability) and ignoring the complex profile associated with the disorder. It is likely that our best hope for improving outcomes in genetic disorders such as Down syndrome lies in our ability to use all of the scientific information that is available, with developmentalists, education scientists, and brain experts collaborating to generate the most effective and innovative practice approaches possible. ■

REFERENCES

Abbeduto L, Murphy MM, Cawthon SW, et al. 2003. Receptive language skills of adolescents and young adults with Down or fragile X syndrome. Am J Ment Retard 108: 149–160.

Abbeduto L, Pavetto M, Kesin E, et al. 2001. The linguistic and cognitive profile of Down syndrome: evidence from a comparison with fragile X syndrome. Down Syndrome: Res Pract 7:9–15.

Alton S. 1998. Differentiation not discrimination: delivering the curriculum for children with Down's syndrome in mainstream schools. Support Learn 13:167–173.

Azari NP, Horwitz B, Pettigrew KD, et al. 1994. Abnormal pattern of cerebral glucose metabolic rates involving language areas in young adults with Down syndrome. Brain Lang 46:1–20.

Baron-Cohen S. 1989. The autistic child's theory of mind: a case of specific developmental delay. J Child Psychol Psychiatry 30:285–297.

Baron-Cohen S, Leslie A, Frith U. 1985. Does the autistic child have a "theory of mind"? Cognition 21:37–46.

Bar-Peled O, Israeli M, Ben-hur H, et al. 1991. Developmental patterns of muscarinic receptors in normal and Down's syndrome fetal brain—an autoradiographic study. Neurosci Lett 133:154–158.

Benda CE. 1971.Mongolism. In: Minckler J, editor. Pathology of the nervous system, Vol. 2. New York: McGraw-Hill. p. 1867.

Bilvosky D, Share J. 1965. The Illinois Test of Psycholinguistic ability and Down's Syndrome: an exploratory study. Am J Ment Defic 70:78–82.

Black FW, Bernard BA. 1984. Constructional apraxia as a function of lesion locus and size in patients with focal brain damage. Cortex 20:111–120.

Blackwood W, Corsellis JAN. 1976. Greenfield's neuropathology. Chicago: Yearbook Medical. p 420–421.

Boudreau, D. 2002. Literacy skills in children and adolescents with Down syndrome. Read Writ Interdiscipl J 15:497–525.

Bower A, Hayes A. 1994. Short-term memory deficits and Down's syndrome: a comparative study. Down Syndrome: Res Pract 2:47–50.

Brooksbank BWL, Walker D, Balazs R, et al. 1989. Neuronal maturation in the foetal brain in Down syndrome. Early Hum Dev 18:237–246.

Buckley S, Bird G. 2002. Cognitive development and education: perspectives on Down syndrome from a twenty-year research programme. In: Cuskelly M, Jobling A, Buckley S, editors. Down syndrome across the lifespan. London England: Whurr Publishers. p 66–80.

Buckley S, Bird G, Sacks B. 2006. Evidence that we can change the profile from a study of inclusive education. Down Syndrome: Res Pract 9:51–53.

Byrne A, Buckley S, MacDonald J, et al. 1995. Investigating the literacy, language, and memory skills of children with Down's syndrome. Down's Syndrome: Res Pract 3:53– 58.

Campbell J, Gilmore L, Cuskelly M. 2003. Changing student teachers' attitudes towards disability and inclusion. J Intellect Dev Disabil 28:369–379.

Carlesimo GA, Marotta L, Vicari S. 1997. Long-term memory in mental retardation: evidence for a specific impairment in subjects with Down's syndrome. Neuropsychologia 35:71–79.

Casale-Giannola D, Wilson Kamens M. 2006. Inclusion at a university: experiences of a young woman with Down syndrome. Ment Retard 44:344–352.

Chapman R, Seung H, Schwartz S, et al. 1998. Language skills of children and adolescents with Down syndrome: II. Production deficits. J Speech Lang Hear Res 41:861–873.

Collacott RA, Cooper SA, McGrother A. 1992. Differential rates of psychiatric disorders in adults with Down's syndrome compared to other mentally handicapped adults. Br J Psychiatry 161:671–674.

Crome L, Cowie V, Slater, E. 1966. A statistical note on cerebellar and brain-stem weight in Mongolism. J Ment Defic 10:69–72.

Crown CL, Feldstein S, Jasnow MD, et al. 1992. Down's syndrome and infant gaze: gaze behavior of Down's syndrome and nondelayed infants in interactions with their mothers. Eur J Child Adoles Psychiatry: Acta Paedopsychiatr 55:51–55.

Cupples L, Iacono T. 2000. Phonological awareness and oral reading skill in children with Down syndrome. J Speech Lang Hear Res 43:595–608.

Cupples L, Iacono T. 2002. The efficacy of 'whole word' versus 'analytic' reading instruction for children with Down Syndrome. Read Writ 15:549–574.

Dawson G, Osterling J, Rinaldi J, Carver L, McPartland J. 2001. Brief Report: Recognition memory and stimulus-reward associations: indirect support for the role of ventromedial prefrontal dysfunction in autism. J Autism Dev Disord 31:337–341.

Dykens E, Shah B, Beck T, et al. 2002. Maladaptive behavior in children and adolescents with Down's syndrome. J Intellect Disabil Res 46:484–492.

Dykens EM. 1995. Measuring behavioral phenotypes: provocations from the "New Genetics". Am J Ment Retard 99:522–532.

Dykens EM, Hodapp RM, Evans DW. 1994. Profiles and development of adaptive behavior in children with Down syndrome. Am J Ment Retard 98:580–587.

Dykens EM, Hodapp RM, Finucane B. 2000. Genetics and mental retardation syndromes. Baltimore: Paul H. Brookes Publishing.
Eadie PA, Fey ME, Douglas JM, et al. 2002. Profiles of grammatical morphology and sentence imitation in children with specific language impairment and Down syndrome. J Speech Lang Hear Res 45:720–732.
Engidawork E, Lubec G. 2003. Molecular changes in fetal Down syndrome brain. J Neurochem 84:895–904.
Fey ME, Warren SF, Brady N, et al. 2006. Early effects of responsivity education/prelinguistic milieu teaching for children with developmental delays and their parents. J Speech Lang Hear Res 49:526–547.
Fidler DJ. 2005. The emerging Down syndrome behavioral phenotype in early childhood: implications for practice. Infants Young Child 18:86–103.
Fidler DJ. 2006.The emergence of a syndrome-specific personality-motivation profile in young children with Down syndrome. In: Rondal JA, Perera J, editors. Down syndrome neurobehavioral specificity. Wiley.
Fidler DJ, Barrett KC, Most DE. 2005a. Age related differences in smiling and personality in Down syndrome. J Dev Phys Disabil 17: 263–280.
Fidler DJ, Hepburn S, Rogers S. 2006. Early learning and adaptive behavior in toddlers with Down syndrome: evidence for an emerging behavioral phenotype? Down Syndrome: Res Pract 10:37–44.
Fidler DJ, Lawson J, Hodapp RM. 2003. What do parents want? an analysis of education-related comments made by parents of children with different genetic mental retardation syndromes. J Intellect Dev Disabil 28: 196–204.
Fidler DJ, Most DE, Guiberson MM. 2005b. Neuropsychological correlates of word identification in Down syndrome. Res Dev Disabil 26:487–501.
Fidler DJ, Philofsky A, Hepburn S. 2007. Language phenotypes and intervention planning: bridging research and practice. Ment Retard Dev Disabil Res Rev 13:47–57.
Fidler DJ, Philofsky A, Hepburn S, et al. 2005c. Nonverbal requesting and problem-solving by toddlers with Down syndrome. Am J Ment Retard 110:312–322.
Flórez J, Del Arco C, Gonzalez A, et al. 1990. Autoradiographic studies of neurotransmitter receptors in the brain of newborn infants with Down syndrome. Am J Med Genet Suppl 7:301–305.
Frangou S, Aylward E, Warren A, et al. 1997. Small planum temporale volume in Down's syndrome: a volumetric MRI study. Am J Psychiatry 154:1424–1429.
Freeman SFN, Hodapp RM. 2000. Educating children with Down syndrome: linking behavioral characteristics to promising intervention strategies. Down Syndrome Quart 5:1–9.
Freeman SFN, Kasari C. 2002. Characteristics and qualities of the play dates of children with Down syndrome: emerging or true friendships. Am J Ment Retard 107:16–31.
Garcia SM, Conte EV. 2004. Improvement of cognitive functions in children with Down syndrome through the Bright Start Program. J Cogn Educ Psychol 4:65–86.
Gathercole SE, Adams AM. 1995. Phonological working memory and speech production in preschool children. J Speech Hear Res 38: 403–414.
Ghaziuddin M, Tsai L, Ghaziuddin N. 1992. Autism in Down's syndrome: presentation and diagnosis. J Intellect Disabil Res 36:449–456.
Golden JA, Hyman BT. 1994. Development of the superior temporal neocortex is anomalous in trisomy 21. J Neuropathol Exp Neurol 53:513–520.
Gunn P, Cuskelly M. 1991. Down syndrome temperament: the stereotype at middle childhood and adolescence. Int J Disabil Dev Educ 38:59–70.
Gunn P, Berry P, Andrews RJ. 1982. Looking behavior of Down syndrome infants. Am J Ment Defic 87:344–347.
Hamill L. 2003. Going to college: the experiences of a young woman with Down syndrome. Ment Retard 41:340–353.
Haxby JV. 1989. Neuropsychological evaluation of adults with Down's syndrome: patterns of selective impairment in non-demented old adults. J Ment Defic Res 33:193–210.
Hepburn S, Fidler DJ, Rogers S. in press. Autism symptoms in toddlers with Down syndrome. J Appl Res Intellect Disabil.
Hesketh LJ, Chapman RS. 1998. Verb use by individuals with Down syndrome. Am J Ment Retard 103:288–304.
Hill Karrer J, Karrer R, Bloom D, Chaney L, Davis R. 1998. Event-related brain potentials during an extended visual recognition memory task depict delayed development of cerebral inhibitory processes among 6-month-old infants with Down syndrome. Int J Psychophysiol 29:167–200.
Hodapp RM, Fidler DJ. 1999. Special education and genetics: connections for the 21st century. J Spec Educ 33:130–137.
Hodapp RM, Freeman SFN. 2003. Advances in educational strategies for children with Down syndrome. Curr Opin Psychiatry 16:511–516.
Hodapp RM, Leckman JF, Dykens EM, et al. 1992. K-ABC profiles in children with fragile X syndrome, Down syndrome, and nonspecific mental retardation. Am J Ment Retard 97:39–46.
Hulme C, Mackenzie S. 1992. Working memory and severe learning difficulties. Hove: Lawrence Erlbaum.
Iarocci G, Virji-Babul N, Reebye P. 2006. The Learn at Play Program (LAPP): merging family, developmental research, early intervention, and policy goals for children with Down syndrome. J Policy Pract Intellec Disabil 3:11–21.
Irwin KC. 1991. Teaching children with Down syndrome to add by counting-on. Educ Treat Child 14:128–141.
Jarrold C, Baddeley AD. 1997. Short-term memory for verbal and visuospatial information in Down's syndrome. Cogn Neuropschiatry 2:101–122.
Jarrold C, Baddeley AD. 2001. Short-term memory in Down syndrome: applying the working memory model. Down Syndrome Res Pract 7:17–23.
Jarrold C, Baddeley AD, Hewes AK. 1999. Genetically dissociated components of working memory: evidence from Down's and Williams syndrome. Neuropsychologia 37:637–651.
Jernigan TL, Bellugi U, Sowell E, Doherty S, Hesselink JR. 1993. Cerebral morphological distinctions between Williams and Down syndrome. Arch Neurol 50:186–191.
Jiang ZD, Wu YY, Liu XY. 1990. Early development of brainstem auditory evoked potentials in Down's syndrome. Early Hum Dev 23:41–51.
Johnston F, Stansfield J. 1997. Expressive pragmatics skills in pre-school children with and without Down's syndrome: parental perceptions. J Intellec Disabil Res 41: 19–29.
Jonides J, Smith EE, Koeppe RA, et al. 1993. Spatial working memory in humans as revealed by PET. Nature 363:623–625.
Kanno K, Ikeda Y. 2002. Word-length effect in verbal short term memory in individuals with Down's syndrome. J Intellec Disabil Res 46:613–618.
Karmiloff-Smith A. 1997. Crucial differences between developmental cognitive neuroscience and adult neuropsychology. Dev Neuropsychol 13:513–524.
Karmiloff-Smith A. 1998. Development itself is the key to understanding developmental disorders. Trends Cogn Sci 2:389–398.
Kasari C, Freeman SFN. 2001. Task-related social behavior in children with Down syndrome. Am J Ment Retard 106:253–264.
Kasari C, Freeman S, Mundy P, et al. 1995. Attention regulation by children with Down syndrome: coordinated joint attention and social referencing looks. Am J Ment Retard 100:128–136.
Kasari C, Mundy P, Yirmiya N, et al. 1990. Affect and attention in children with Down syndrome. Am J Ment Retard 95:55–67.
Kates WR, Folley BS, Lanham DC, et al. 2002. Cerebral growth in fragile X syndrome: review and comparison with Down syndrome. Microsc Res Tech 57:159–167.
Kay-Raining Bird E, Cleave PL, McConnell L. 2000. Reading and phonological awareness in children with Down syndrome. Am J Speech-Lang Pathol 9:319–330.
Kennedy EJ, Flynn MC. 2003. Training, phonological awareness in children with Down syndrome. Res Dev Disabil 24:44–57.
Kent L, Evans J, Paul M, et al. 1999. Comorbidity of autistic spectrum disorders in children with Down syndrome. Dev Med Child Neurol 41:153–158.
Klein BP, Mervis CB. 1999. Contrasting patterns of cognitive abilities of 9- and 10- year-olds with Williams syndrome or Down syndrome. Dev Neuropsychol 16:177–196.
Kleschevnikov AM, Belichenko PV, Villar AJ, et al. 2004. Hippocampal long-term potentiation suppressed by increased inhibition in the Ts65Dn mouse, a genetic model of Down syndrome. J Neurosci 24:8153–8160.
Kumin L. 2006. Speech intelligibility and childhood verbal apraxia in children with Down syndrome. Down Syndrome: Res Pract 10: 10–22.
Landry SH, Chapieski ML. 1990. Joint attention and infant toy exploration: effects of Down syndrome and prematurity. Child Dev 60: 103–118.
Laws G. 1998. The use of nonword repetition as a test of phonological memory in children with Down syndrome. J Child Psychol Psychiatry 39:1119–1130.
Laws G. 2002. Working memory in children and adolescents with Down syndrome: evidence from a colour memory experiment. J Child Psychol Psychiatry 43:353–364.
Laws G, Bishop DVM. 2004. Verbal deficits in Down's syndrome and specific language impairment: a comparison. Int J Lang Commun Disord 39:423–451.
Laws G, MacDonald J, Buckley S. 1996. The effects of a short training in the use of a rehearsal strategy on memory for words and pictures in children with Down syndrome. Down Syndrome: Res Pract 4:70–78.

Legerstee M, Bowman TG, Fels S. 1992. People and objects affect the quality of vocalizations in infants with Down syndrome. Early Dev Parenting 1:149–156.
Lloveras RB, Fornells MG. 1998. The group: an instrument of intervention for the global delve of the child with Down syndrome in the process of social inclusion. Down Syndrome: Res Pract 5:88–92.
Lloyd J, Moni KB, Jobling A. 2006. Breaking the hype cycle: using the computer effectively with learners with intellectual disabilities. Down Syndrome: Res Pract 9:68–74.
Mangan PA. 1992. Spatial memory abilities and abnormal development of the hippocampal formation in Down syndrome. Unpublished doctoral dissertation, University of Arizona, Tucson.
Marcell MM, Weeks SL. 1988. Short-term memory difficulties and Down's syndrome. J Ment Defic Res 32:153–162.
Marcell MM, Harvey CF, Cothran LP. 1988. An attempt to improve auditory short-term memory in Down's syndrome individuals through reducing distractions. Res Dev Disabil 9:405–417.
Miller JF. 1999. Profiles of language development in children with Down syndrome. In: Miller J, Leddy M, Leavitt LA, editors. Improving the communication of people with Down syndrome. Baltimore: Brookes Publishing. p 11–40.
Miller JF, Leddy M. 1999. Verbal fluency, speech intelligibility, and communicative effectiveness. In: Miller JF, Leddy M, Leavitt LA, editors. Improving the communication of people with Down syndrome. Baltimore: Brookes Publishing. p 81–91.
Miller J, Leddy M, Leavitt LA, editors. 1999. Improving the communication of people with Down syndrome. Baltimore: Brookes Publishing.
Moni KB, Jobling A. 2001. Reading-related literacy learning of young adults with Down syndrome: findings from a three year teaching and research program. Int J Disabil Dev Educ 48:377–394.
Mundy P, Sigman M, Kasari C, et al. 1988. Nonverbal communication skills in Down syndrome children. Child Dev 59:235–249.
Nadel L. 1986. Down syndrome in neurobiological perspective. In: Epstein CJ, editor. The neurobiology of Down syndrome. New York: Raven Press. p 239–251.
Nelson C. 2000. The neurobiological bases of early intervention. In: Shokoff JP, Meisels J, editors. Handbook of early childhood intervention. New York: Cambridge University Press. p 204–227.
Nye J, Buckley S. 2006. Evaluating the Numicon system of teaching number to children with Down syndrome. Down Syndrome: Res Pract 11:97–104.
Ohr PS, Fagen JW. 1991. Conditioning and long-old infants with Down syndrome. Am J Ment Retard 96:151–162.
Ohr PS, Fagen JW. 1993. Temperament, conditioning, old infants with Down syndrome. J Appl Dev Psychol 14:175–190.
Ohr PS, Fagen JW. 1994. Contingency learning Down syndrome. Am J Ment Retard 99: 74–84.
Ortega-Tudela JM, Gomez-Ariza CJ. 2006. Computer-assisted teaching and mathematical learning in Down syndrome children. J Comput Assist Learn 22:298–307.
Paly RJ, Hurley AD. 2002. Down syndrome and autistic disorder. Ment Health Aspects Dev Disabil 5:64–65.
Park S, Singer GH, Gibson M. 2005. The functional effect of teacher positive and neutral affect on task performance of students with significant disabilities. J Positive Behav Interv 7:237–246.
Pazos A, Del Olmo E, Diaz A, et al. 1994. Serotonergic (5-HhT1A and 5-HhT1D) and muscarinic cholinergic receptors in DS brains: an autoradiographic analysis. Poster presented at International Down syndrome Research Conference, Charleston, South Carolina, April 1994.
Pennington BF, Moon J, Edgin J, et al. 2003. The neuropsychology of Down syndrome: evidence for hippocampal dysfunction. Child Dev 74:75–93.
Pinter JD, Eliez S, Schmitt E, et al. 2001. Neuroanatomy of Down's syndrome: a high-resolution MRI study. Am J Psychiatry 158: 1659–1665.
Pitcairn TK, Wishart JG. 1994. Reactions of young children with Down's syndrome to an impossible task. Br J Dev Psychol 12:485–489.
Pueschel SR, Gallagher PL, Zartler AS, et al. 1987. Cognitive and learning profiles in children with Down syndrome. Res Dev Disabil 8:21–37.
Rast M, Meltzoff AN. 1995. Memory and representation in young children with Down syndrome: exploring deferred imitation and object permanence. Dev Psychopathol 7: 393–407.
Rempel ED. 1974. Psycholinguistic abilities of Down's syndrome children. In: Proceedings of the Annual Meeting of the American Association on Mental Deficiency, Toronto.
Roberts J, Price J, Malkin C. 2007. Language and communication development in Down syndrome. Ment Retard Dev Disabil Res Rev 13:26–35.
Rogoff B. 2003. The cultural nature of human development. Oxford: Oxford University Press.
Rondal J, Buckley S. 2001. Speech and language intervention in Down syndrome. New York: Wiley.
Ruskin EM, Kasari C, Mundy P, et al. 1994. Attention to people and toys during social and object mastery in children with Down syndrome. Am J Ment Retard 99:103–111.
Schmidt-Sidor B, Wisniewski K, Shepard Th, et al. 1990. Brain growth in Down syndrome subjects 15 to 22 weeks of gestational age and birth to 60 months. Clin Neuropathol 9:181–190.
Sigman M, Ruskin E. 1999. Continuity and change in the social competence of children with autism, Down syndrome, and developmental delays. Monogr Soc Res Child Dev 64:v–114.
Silverstein AB, Legutki G, Friedman SL, et al. 1982. Performance of Down syndrome individuals on the Stanford–Binet Intelligence Scale. Am J Ment Retard 86:548–551.
Stoel-Gammon C. 2003. Speech acquisition and approaches to intervention. In: Rondal J, Buckley S, editors. Speech and language intervention in Down syndrome. London: Whurr. p 49–62.
Thase ME, Tigner R, Smeltzer DJ, et al. 1984. Age-related neuropsychological deficits in Down's syndrome. Biol Psychiatry 19: 571–585.
Trent JA, Kaiser AP, Wolery M. 2005. The use of responsive interaction strategies by siblings. Top Early Child Spec Educ 25:107–118.
van Bysterveldt AK, Gillon GT, Moran C. 2006. Enhancing phonological awareness and letter knowledge in preschool children with Down syndrome. Int J Disabil Dev Educ 53:301–329.
Varnhagen CK, Das JP, Varnhagen S. 1987. Auditory and visual memory span: cognitive processing by TMR individuals with Down syndrome or other etiologies. Am J Ment Defic 91:398–405.
Vicari S. 2001. Implicit versus explicit memory function in children with Down and Williams syndrome. Down Syndrome: Res Pract 7:35–40.
Vicari S, Carlesimo A, Caltagirone C. 1995. Short-term memory in persons with intellectual disabilities and Down's syndrome. J Intellect Disabil Res 39:532–537.
Vlachou M, Farrell P. 2000. Object mastery motivation in pre-school children with and without disabilities. Educ Psychol 20:167–176.
Wang PP, Bellugi U. 1994. Evidence from two genetic syndromes for a dissociation between verbal and visuo-spatial short-term memory. J Clin Exp Neuropsychol 16:317–322.
Williams K, Wishart J. in press. Social cognition in children with Down syndrome. Ment Retard Dev Disabil Res Rev.
Wishart J. 1993. The development of learning difficulties in children with Down syndrome. J Intellec Disabil Res 37:389–403.
Wishart JG. 1996. Avoidant learning styles and cognitive development in young children. In: Stratford B, Gunn P, editors. New approaches to Down syndrome. London: Cassell. p 157–172.
Wisniewski K., Schmidt-Sidor B. 1989. Postnatal delay of myelin formation in brains from Down syndrome infants and children. Clin Neuropathol 8:55–62.
Wisniewski K. 1990. Down syndrome children often have brain with maturation delay, retardation of growth, and cortical dysgenesis. Am J Med Genet Suppl 7:274–281.
Wisniewski K, Kida E. 1994. Abnormal neurogenesis and synaptogenesis in Down syndrome. Dev Brain Dysfunct 7:289–301.
Wisniewski K, Laure-Kamionowska M, Connell FF, et al. 1986. Neuronal density and synaptogenesis in the postnatal stage of brain maturation in Down syndrome. In: Epstein CJ, editor. The neurobiology of Down syndrome. New York: Raven Press. p 29–44.
Wolpert G. 2001. What general educators have to say about successfully including students with Down syndrome in their classes. J Res Child Educ 16:28–38.
Yirmiya N, Solomonica-Levi D, Shulman C, et al. 1996. Theory of mind abilities in individual with autism, Down syndrome, and retardation of unknown etiology: The role of age and intelligence. J Child Psychol Psychiatry 37:1003–1014.
Yoder P, Warren S. 2002. Effects of prelinguistic milieu teaching and parent responsivity education on dyads involving children with intellectual disabilities. J Speech Lang Hear Res 45:1158–1174.
Zelazo PD, Burack JA, Benedetto E, et al. 1996. Theory of mind and rule use in individuals with Down syndrome: a test of the uniqueness and specificity claims. J Child Psychol Psychiatry 37:479–484.