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Author(s): Adele Diamond

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Close Interrelation of Motor Development and Cognitive Development and of the Cerebellum and Prefrontal Cortex

Adele Diamond

Motor development and cognitive development may be fundamentally interrelated. Contrary to popular notions that motor development begins and ends early, whereas cognitive development begins and ends later, both motor and cognitive development display equally protracted developmental timetables. When cognitive development is perturbed, as in a neurodevelopmental disorder, motor development is often adversely affected. While it has long been known that the striatum functions as part of a circuit with dorsolateral prefrontal cortex, it is suggested here that the same is true for the cerebellum and that the cerebellum may be important for cognitive as well as motor functions. Like prefrontal cortex, the cerebellum reaches maturity late. Many cognitive tasks that require prefrontal cortex also require the cerebellum. To make these points, evidence is summarized of the close co-activation of the neocerebellum and dorsolateral prefrontal cortex in functional neuroimaging, of similarities in the cognitive sequelae of damage to dorsolateral prefrontal cortex and the neocerebellum, of motor deficits in "cognitive" developmental disorders, and of abnormalities in the cerebellum and in prefrontal cortex in the same developmental disorders.

INTRODUCTION

In general, motor development and cognitive development have been studied separately. They have generally been viewed as independent phenomena, although occurring in the same organism over the same time period. Indeed, cognitive development, as befits its exalted status, has generally been viewed as the last aspect of development to fully mature. Developmental psychologists have tended to forget that motor development is equally protracted. Fine motor control, bimanual coordination, and visuomotor skills are not fully developed until adolescence, just as the most complex cognitive operations such as accurately representing transformations, flexibly manipulating information held in mind, and simultaneously taking into account multiple facets of a problem show developmental improvements into adolescence.

Motor development and cognitive development may be much more interrelated than has been previously appreciated. Indeed, they may be fundamentally intertwined.

Similarly, until very recently, prefrontal cortex and the neocerebellum were not thought to participate in similar functions.¹ Dorsolateral prefrontal cortex is

thought to be critical for the most complex cognitive abilities, whereas the cerebellum has been considered critical primarily for motor skills. In keeping with the lofty status of dorsolateral prefrontal cortex, its protracted developmental timetable and dramatic expansion during primate evolution have been emphasized. The fact that the neocerebellum, which also has undergone dramatic expansion during primate evolution, is late-maturing as well has received less attention, although there has been evidence for over 55 years (see Dow, 1942) that phylogenetic development of the neocerebellum and of prefrontal cortex have proceeded in parallel.

It is suggested here that the cerebellum is important not only for motor functions but also for cognitive functions. Indeed, the cerebellum is important for the very same cognitive functions for which dorsolateral prefrontal cortex is critical. Most cognitive tasks that require dorsolateral prefrontal cortex also require the neocerebellum.

genetically newer regions of the cerebellum. These regions mature later during ontogeny than other cerebellar regions and are interconnected with the cerebral cortex. The neocerebellum includes the posterior lobe of the lateral hemispheres of cerebellar cortex (lobules HVI through HVIII, Larsell & Jansen, 1972), lobules VI and VII of the vermis in the medial portion of cerebellar cortex, and one of the deep cerebellar nuclei (the dentate nucleus). Like the rest of the neocerebellum, the dentate nucleus has increased in size in parallel with prefrontal cortex.

¹ The region of prefrontal cortex on which this paper focuses is the "dorsolateral prefrontal cortex," i.e., Areas 46 and 9. In the human brain, dorsolateral prefrontal cortex extends above and below the superior frontal sulcus, past the medial frontal sulcus to the inferior frontal sulcus. It is bordered posteriorly by Area 8 and anteriorly by Area 10. The portion of the cerebellum on which this paper focuses is the "neocerebellum," i.e., the phylo-

EVIDENCE FROM NEUROIMAGING OF THE CLOSE INTERRELATION OF DORSOLATERAL PREFRONTAL CORTEX AND THE NEOCEREBELLUM

Functional neuroimaging studies consistently find that when a cognitive task increases activation in dorsolateral prefrontal cortex it also increases activation in the contralateral cerebellum. When one sees decreased dorsolateral prefrontal cortex activation (e.g., when a task has been practiced and requires less concentration) one also sees a concomitant decrease in cerebellar activation. Activation in these two regions is strikingly correlated and closely coupled.

This co-activation of dorsolateral prefrontal cortex and the contralateral neocerebellum has been found with the "verb generation" task (Raichle et al., 1994), where on each trial participants are given a noun and asked to quickly generate a related verb. Co-activation has been found on the "verbal fluency" task (Schlosser et al., 1998), where participants are given one minute to say as many different words as they can think of that begin with a specified letter (F, then A, and finally S). It has also been found with the "Wisconsin card sorting" test (Berman et al., 1995; Nagahama et al., 1996). The Wisconsin card sorting test is a classic test of the functions of prefrontal cortex. Participants are given cards that can be sorted by color, shape, or name and must deduce the correct sorting criterion. After several consecutively correct sorts, the experimenter, without warning, changes the correct sorting criterion. Indeed, co-activation of dorsolateral prefrontal cortex and the cerebellum has been repeatedly found with several nonmotor, working memory tasks (Awh et al., 1996; Desmond et al., 1995; Desmond, Gabrieli, Wagner, Ginier, & Glover, 1997; deZubicaray et al., 1998; Grasby et al., 1994; Jonides et al., 1997; Paulesu et al., 1995; Paulesu, Frith, & Frackowiak, 1993).

Moreover, similar aspects of tasks activate the neocerebellum and dorsolateral prefrontal cortex. For example, increasing the memory load increases activation in both regions (e.g., Braver et al., 1997; Desmond et al., 1997; Diamond et al., 1999; Rypma, Prabhakaran, Desmond, Glover, & Gabrieli, 1999). The cerebellum and prefrontal cortex participate as critical parts of a neural circuit that is important when (1) a cognitive task is difficult as opposed to easy, (2) a cognitive task is new as opposed to familiar and practiced, (3) conditions of the cognitive task change, as opposed to when they remain stable and predictable, (4) a quick response is required, as opposed to longer response latencies being acceptable, and (5) one must concentrate instead of being able to operate on "automatic pilot."

EVIDENCE FROM BRAIN-DAMAGED PATIENTS OF THE CLOSE ASSOCIATION BETWEEN DORSOLATERAL PREFRONTAL CORTEX AND THE NEOCEREBELLUM

Lesions of prefrontal cortex can cause hypometabolism in the contralateral cerebellum (Fulham, Brooks, Hallett, & DiChiro, 1992; Muira et al., 1994; Tanaka et al., 1992). Similarly, cerebellar damage can cause frontal hypometabolism (Boni et al., 1992).

Cerebellar patients (especially if their damage is in the posterior lobe in the lateral hemisphere of the cerebellum and/or lobules VI and VII of the cerebellar vermis) often fail cognitive tasks linked to prefrontal cortex, such as "verbal fluency" (Appollonio, Grafman, Schwartz, Massaquoi, & Hallett, 1993; Schmahman & Sherman, 1998), verb generation (Fiez et al., 1996), planning tasks (Botez, Botez, Elie, & Attig, 1989; Grafman et al., 1992; Leiner, Leiner, & Dow, 1986; Schmahman & Sherman, 1998), tasks requiring the learning and memory of arbitrary associations (Bracke-Tolkmitt et al., 1989), set-shifting tasks (Schmahman & Sherman, 1998), working memory tasks (Fiez et al., 1996; Schmahman & Sherman, 1998), and source memory tasks (Ciranni, Dodson, & Shimamura, 1998). Indeed, there is even a case of a frontal-looking aphasia caused by a focal hypometabolism in the right cerebellum (Marien et al., 1996). The match between tasks affected by cerebellar damage and those affected by prefrontal damage is by no means exact, of course; for example, cerebellar patients are not impaired on the Wisconsin card sorting test (Bracke-Tolkmitt et al., 1989; Daum et al., 1993; Fiez, Petersen, Cheney, & Raichle, 1992).

Projections from dorsolateral prefrontal cortex reach the neocerebellum (Leiner, Leiner, & Dow, 1989; Middleton & Strick, 1997; Schmahmann & Pandya, 1995) and projections from the neocerebellum reach dorsolateral prefrontal cortex (Middleton & Strick, 1994; Sasaki, Jinnai, Gemba, Hashimoto, & Mizumo, 1979; Yamamoto, Yoshida, Yoshikawa, Kishimoto, & Oka, 1992). The cross-talk between the neocerebellum and dorsolateral prefrontal cortex is greatly increased in higher primates, especially humans.

HOW MIGHT THE CEREBELLUM AID IN COGNITIVE PERFORMANCE?

The cerebellum is quite remarkable anatomically. It has an exquisite lattice structure that is strikingly precise and regular, and the human cerebellum has more neurons than all the rest of the nervous system combined (Andersen, Korbo, & Pakkenberg, 1992). Two types of cells found in the cerebellar cortex are gran-

ule cells and Purkinje cells. Granule cells are tiny and numerous (up to 7 million per cubic centimeter in the layer below the Purkinje cells). Purkinje cells are large and have elaborate dendritic trees.

One source of input to the cerebellum is called the "climbing fibers." It consists of axons from the inferior olivary nucleus (inferior olive). Each Purkinje cell receives input from only one climbing fiber, but each climbing fiber may synapse on 10 Purkinje cells. Climbing fibers also terminate on granule cells. The granule cells in turn send out branching axons that give rise to the "parallel fibers." These rows of parallel fibers travel in a plane perpendicular to the parallel rows of Purkinje cells (hence the lattice structure). Each parallel fiber synapses on the dendrites of multiple Purkinje cells, and each Purkinje cell receives input from as many as 200,000 parallel fibers, the highest convergence ratio in the nervous system. A message conveyed by a single parallel fiber is relayed to successive Purkinje cells at precise, minutely different temporal intervals.

Cerebellar cortex can be thought of as being constructed of modules perpendicular to the cortical surface and parallel to each other (Ito, 1984; Leiner, Leiner, & Dow, 1991). The basic circuitry of each module is similar to that of every other cerebellar module (Bloedel, 1992), but each has its own unique set of inputs and outputs. Rather than evolve entirely new structures to subserve cognitive functions, it would make sense if nature built upon what was already there. Thus, it would make sense if evolution built upon the exquisitely precise and intricate cerebellar modules, recruiting existing ones, or adding additional ones, to help serve cognitive functions.

There is no question that the neocerebellum is involved in motor learning (Glickstein & Yeo, 1990; Houk, Buckingham, & Barto, 1996; Ito, 1984). Since all forms of learning share many requirements, it is not unreasonable that the neocerebellum might participate in other forms of learning as well. In motor learning, cerebellar neurons are most active during the early stages of learning a task (Flament, Ellermann, Ugurbil, & Ebner, 1994; Friston, Frith, Passingham, Liddle, & Frankowiak, 1992; van Mier et al., 1994) or when conditions change. For example, Purkinje cell firing is significantly greater when a participant moves a handle against a novel load than against a known load (Gilbert & Thach, 1977). Similarly, prism adaptation (i.e., reaching with the novel visual input provided by prisms) is impaired in patients with cerebellar damage (Weiner, Hallett, & Funkenstein, 1983).

Once a motor task is no longer novel, cerebellar firing decreases. Neuroimaging studies (cited in the first section above) are finding that on cognitive tasks, too, the cerebellum is most active when the task is novel or

when conditions change, and cerebellar participation decreases as the task becomes familiar or practiced. Evidently, it is when you must pay close attention and concentrate, when you must learn something new for cognitive or motor performance, that the cerebellum is recruited most heavily.

There are several hypotheses for why this is so. Based on the architecture and circuitry of the cerebellum, Marr (1969) and Albus (1971) proposed that the cerebellum functions as a modifiable pattern detector, which could be used in the learning of motor skills. It is easy to see how such a system might be useful in the acquisition of cognitive skills as well. Fiez and colleagues (1992) suggest that the cerebellum may play a role in error detection or in the ability to learn from errors. The cerebellar patient on whom they report seemed oblivious to his errors and showed an abnormal lack of improvement with practice. In a similar vein, Ghez (1991) has talked about the cerebellum's involvement in comparing intention and performance. Thach (1998) speculates that the cerebellum may provide the mechanism for combining response elements into larger groupings, so that a coordinated response is elicited in a contextually-appropriate way. Leiner and colleagues (1991) and Schmahmann (1996) propose that the cerebellum may serve to enable other parts of the brain to perform their functions more efficiently or optimally.

Certainly there are many reports that performance is slower and more variable, inaccurate, and effortful in the absence of cerebellar input. This is true whether one is talking about cognitive functions, such as shifting attention (Courchesne et al., 1994), or motor functions (Holmes, 1939). Courchesne et al. (1994) propose that the neocerebellum aids cognitive performance by learning to precisely predict the occurrence of anticipated stimuli and by improving sensitivity so that those stimuli can be perceived even in the presence of noise. Thus, for example, in the superior colliculus neuronal firing to a visual stimulus is enhanced when the stimulus is preceded by stimulation of the neocerebellum and, in the presence of background luminance sufficient to reduce collicular responding to noise, stimulation of the cerebellum enables collicular responding to demonstrate consistent visual target detection (Crispino & Bullock, 1984).

Finally, Ivry and Keele (Ivry, 1993; Ivry & Keele, 1989; Keele & Ivry, 1990) have a well-developed theory that the lateral hemispheres of the cerebellum perform critical timing functions important for motor, sensory, and cognitive tasks. For example, certain modules of the cerebellum are critical for learning and/or retention of the classically conditioned eye-blink response (Clark, McCormick, Lavond, & Thompson, 1984; Woodruff-Pak, Logan, & Thompson, 1990).

Ivry and Keele hypothesize that the reason for this is that the lateral cerebellum is critical for measuring the time interval between the warning stimulus (a tone) and the noxious stimulus (an air puff), and in using that temporal calculation so that the eye blinks at exactly the right moment. Precise timing is critical here for if the eye blinks too late it fails to protect the eye, and if it occurs too early, the blink ends before the airpuff is presented and again fails to protect the eye. Acquisition of the conditioned eyeblink response depends crucially upon the cerebellar cortex and the interpositus nucleus (Chen, Bao, Lockard, & Kim, 1996; Chen, Bao, & Thompson, 1999; Kim & Thompson, 1997; Thompson, 1990; Thompson et al., 1997; Yeo & Hardiman, 1992). This has been demonstrated in humans by PET (Logan & Grafton, 1995) and by work with patients with cerebellar damage or atrophy (Daum et al., 1993; Solomon, Stowe, & Pendlebury, 1989; Topka, Valls-Sole, Massaquoi, & Hallett, 1993).

That infants show robust conditioning even in the first couple months of life (e.g., Fagen & Rovee-Collier, 1982; Rovee-Collier, 1990, 1997), might lead one to wonder if the role of the cerebellum in the classically conditioned eyeblink response is inconsistent with evidence that the neocerebellum does not reach full maturity until at least puberty. It is not inconsistent for several reasons. First, infants are not very good at acquiring the classically conditioned eyeblink response (Ivkovich, Collins, Eckerman, Krasnegor, & Stanton, 1999; Lipsitt, 1990). Second, even if the neocerebellum does subserve functions that aid conditioning during infancy, that would still be consistent with the neocerebellum not reaching full maturity for another 10 years or so. A brain system that is not fully developed can subserve certain functions early in development and more sophisticated functions later in development when it is more mature (e.g., Diamond, Prevor, Callender, & Druin, 1997). Third, there is no evidence that the forms of conditioning that are robust in early infancy (e.g., the conjugately reinforced footkick response to cause an appealing mobile to move) depend upon the cerebellum, much less the neocerebellum. It has been demonstrated that the cerebellum is critical for aversive conditioning of reflexive responses to noxious stimuli (the eyeblink response to an airpuff to the eye and the leg flexion response to footshock), but the cerebellum is not involved in all forms of conditioning. A case in point is autonomic conditioning (electrodermal responses to an impending airpuff to the eye or heart rate conditioning to impending shock), which does not require the cerebellum (e.g., Daum & Schugens, 1996; Daum et al., 1993; Lavond, Lincoln, McCormick, & Thompson, 1984).

EVIDENCE FROM DEVELOPMENTAL DISORDERS, A: MOTOR PROBLEMS FOUND IN CHILDREN WITH "COGNITIVE" DISORDERS

Motor coordination problems are common in children with Attention Deficit Hyperactivity Disorder (ADHD), although the cognitive deficits associated with this disorder have received far more attention. At least half of all ADHD children have poor motor coordination and fit the diagnosis for developmental coordination disorder (Barkley, DuPaul, & McMurray, 1990; Denckla & Rudel, 1978; Gillberg, 1995; Hartsough & Lambert, 1985; Hellgren, Gillberg, Gillberg, & Enerskog, 1993; Kadesjo & Gillberg, 1998; Piek, Pitcher, & Hay, 1999; Stewart, Pitts, Craig, & Dieruf, 1966; Szatmari, Offord, & Boyle, 1989). ADHD children tend to have motor problems associated with cerebellar dysfunction (e.g., problems with balance, with rapid alternating movements, and with consistently producing movements of the correct distance or correct timing) as well as motor problems with less specific bases (e.g., poor handwriting). Four studies report finding the cerebellum to be smaller in ADHD boys than in normal controls (Berquin et al., 1998; Castellanos 1997; Castellanos et al., 1996; Mostofsky et al., 1998). Rapoport (personal communication) reports that, in their MRI study of over 200 children, the largest difference in the brains of ADHD and non-ADHD children is the smaller cerebellum in ADHD children. For example, Kadesjo and Gillberg found that roughly 50% of the ADHD children in their Swedish sample also met the diagnosis for developmental coordination disorder, and 50% of the children with developmental coordination disorder met the diagnosis for ADHD.

Movement deficits are also evident in children with dyslexia or specific language disorder, although of course the deficits that have been focused upon in these children are in the linguistic domain. Children who are dyslexic, like children who are clumsy, have difficulties with continuous tapping tasks compared to same-aged peers (Geuze & Kalverboer, 1994; Wolff, Michel, Ovrut, & Drake, 1990). Wolff and colleagues note in particular a problem with timing precision on bimanual tasks that require the integration of asynchronous responses. Timing precision is a function that has been attributed to the cerebellum (e.g., Ivry, Keele, & Diener, 1988; Keele & Ivry, 1990). Hill and colleagues report that children with specific language disorder show a deficit in the production of familiar hand postures similar to that seen in children with developmental coordination disorder (Hill, Bishop, & Nimmo-Smith, 1998).

Many investigators have also reported movement disturbances in children who are autistic (for a review see Leary & Hill, 1996). For example, even among high functioning autistic individuals and those with a more benign variant of autism (Asperger's syndrome), Manjiviona and Prior (1995) found that 67% and 50% respectively showed a clinically significant level of motor impairment. Hughes (1996) found young people with autism to have problems in executing goal-directed motor acts even in very simple situations. Slavoff and Bonvillian (1997) report that all of the autistic children they tested scored below age norms on the Peabody Developmental Motor Scales. Page and Boucher (1998) studied 25 autistic children and found that 55% had manual impairments and 18% had additional gross motor impairments.

To be sure, motor impairments are not the most prominent characteristic of ADHD, dyslexia, specific language disorder, or autism. The point is simply that along with the prominent cognitive deficits apparent in these disorders many children appear to have concomitant motor problems, and the suggestion is that perhaps the cognitive and motor systems are not as totally separate as has traditionally been thought.

To be sure, as well, cognitive and motor strengths or weaknesses do not always co-vary. For example, not all ADHD children have motor impairments and not all children with a disorder of motor coordination have cognitive impairments. One of many possible reasons for the diversity in outcomes is the marked segregation and specificity of inputs and outputs within the cerebellum. Even within a single cerebellar nucleus, different subregions of dorsolateral prefrontal cortex (Areas 46 and 9) project to, and receive projections from, different subregions of the nucleus. For example, the most ventral portions of the dentate nucleus of the cerebellum project to Area 46 whereas projections to Area 9 arise rostrocaudally in the middle third of the dentate nucleus (Middleton & Strick, 1997). Other cerebellar modules do not project to dorsolateral prefrontal cortex at all. Because of the different neural systems in which different modules of the cerebellum participate, it is easy to see how dysfunctions that have slightly different regional extents within the cerebellum might produce very different outcomes.

EVIDENCE FROM DEVELOPMENTAL DISORDERS, B: ABNORMALITIES FOUND IN THE CEREBELLUM AND IN PREFRONTAL CORTEX IN THE SAME DISORDER

Ciesielski, Harris, Hart, and Pabst (1997) and Lesnik, Ciesielski, Hart, and Sanders (1998) report that the cerebellum (especially the posterior lobe) and pre-

frontal cortex are more susceptible than other brain regions to damage from intrathecal chemotherapy for leukemia during early childhood. These investigators attribute this vulnerability to the protracted period of postnatal maturation of the neocerebellum and prefrontal cortex.

Several studies report finding the cerebellum, especially posteriorly, to be smaller in boys with ADHD than in typically developing boys of the same age (Berquin et al., 1998; Castellanos et al., 1996; Mostofsky, Reiss, Lockhart, & Denckla, 1998). Similarly, several studies report finding significant reductions in the size of frontal cortex: Casey et al. (1997), Castellanos et al. (1996), and Filipek et al. (1997) all report volumetric analyses of structural magnetic resonance (MR) scans showing a significant size reduction in frontal cortex in ADHD children compared to healthy controls. Hynd, Semrud-Clikeman, Lorys, Novey, and Eliopoulos (1990) found an absence in ADHD children of the right-greater-than-left frontal asymmetry found in normally developing children.

Functional neuroimaging studies show unusual prefrontal cortex activity in persons with ADHD. Reduced prefrontal activity has been reported in both children and adults with ADHD (in children: Amen, Paldi, & Thisted, 1993, using SPECT [blood flow]; in adults: Zametkin et al., 1990, using PET [cerebral glucose utilization]). Elevated prefrontal activity in ADHD children has also been reported (Vaidya et al., 1998, using functional magnetic resonance imaging (fMRI) [blood oxygen uptake]). Thus far, I have seen no studies of cerebellar activation in ADHD individuals.

In vivo evidence of a reduced cerebellum in autistic individuals has been reported by two independent groups of researchers (Courchesne, Hesselink, Jernigan, & Yeung-Courchesne, 1987; Courchesne, Yeung-Courchesne, Press, Hesselink, & Jernigan, 1988; Gaffney, Kuperman, Tsai, & Minchin, 1987; Gaffney, Kuperman, Tsai, Minchin, & Hassanein, 1988). Others, too, have reported cerebellar hypoplasia in autistic individuals (Bauman & Kemper, 1985; Murakami, Courchesne, Press, Yeung-Courchesne, & Hesselink, 1989). Indeed, in a review of numerous studies, Courchesne (1991) found consistent evidence of pathology in the neocerebellum, especially the posterior lobe and lobules VI and VII of the vermis, in autistic individuals. It should be noted, however, that not all studies have found cerebellar abnormalities or dysfunction in autistic children (Ekman et al., 1991; Minshew, Luna, & Sweeney, 1999).

Zilbovicius et al. (1995) report delayed maturation of frontal cortex in autistic children. They investigated the metabolic maturation of frontal cortex us-

ing regional cerebral blood flow. They found hypoperfusion in frontal cortex in autistic children 3 to 4 years of age, similar to the pattern of perfusion seen in much younger normal children. Chugani et al. (1997) report asymmetries of serotonin synthesis in frontal cortex, the thalamus, and the dentate nucleus of the cerebellum in autistic boys. They found decreased serotonin synthesis in frontal cortex and the thalamus and increased serotonin synthesis in the contralateral cerebellum.

This last finding reminds us that prefrontal cortex and the neocerebellum are interconnected parts of a neural system and that a dysfunction in one component of the system can affect the other components. Hua and Houk (1997) have proposed a model whereby the cerebellum aids in the development of premotor cortex. One could imagine a similar model of how dysfunction in the subregions of the cerebellum connected with prefrontal cortex might impair the proper development of prefrontal cortex. A final possible reason for why abnormalities in both the neocerebellum and prefrontal cortex might occur in the same disorders is that, because both prefrontal cortex and the neocerebellum have an extended period of maturation, insults too late in development to affect the maturation of other neural structures can have profound consequences for both prefrontal and cerebellar development.

THE IMPORTANCE OF THE CAUDATE NUCLEUS FOR COGNITIVE, AS WELL AS MOTOR, FUNCTIONS

Although this review has focused on the cerebellum as a neuroanatomical structure important for movement that appears (1) to function in a circuit with prefrontal cortex, (2) to play a role in cognitive functions, and (3) to be affected in children with cognitive neurodevelopmental disorders, a similar argument could be made with reference to the caudate nucleus. The caudate nucleus is a C-shaped structure that roughly parallels the lateral ventricle. It is considered part of the collection of structures known as the striatum, which in turn is part of the neural system known as the basal ganglia. The basal ganglia, and the caudate specifically, is important for movement control, such as selecting the proper movement, the appropriate muscles to perform a movement, or the appropriate force with which to execute the movement (e.g., DeLong & Georgopoulos, 1981; Groves, 1983; Stelmach & Worringham, 1988). For example, reduced dopamine in the caudate, and in the basal ganglia more generally, as occurs in Parkinson's disease, is often associated with akinesia (difficulty initiating movements and

a poverty of spontaneous movement) and hypertonia (muscle rigidity), whereas loss of cell bodies in the caudate, characteristic of Huntington's chorea, is associated with hyperkinesia (excessive movement, often in jerky bursts and performed involuntarily) and hypotonia (decreased muscle tone) (e.g., Albin, Young, & Penney, 1989; Bowen, 1976; Halliday et al., 1998).

The caudate is the major output structure of dorsolateral prefrontal cortex (e.g., Selemon & Goldman-Rakic, 1985, 1988). Prefrontal cortex and the caudate nucleus are critical elements in a neural circuit (see, e.g., Alexander, DeLong, & Strick, 1986). Damage to the caudate, as in Parkinson's disease, often produces cognitive deficits similar to those found after prefrontal damage (Lees & Smith, 1983; Owen et al., 1992; Pantelis et al., 1997; Taylor, Saint-Cyr, & Lang, 1987; Taylor, Saint-Cyr, Lang, & Kenny, 1986; for reviews, see Lang, Paul, Robbins, & Marsden, 1993; Taylor, Saint-Cyr, & Lang, 1990). It should be noted, however, that some of the cognitive deficits associated with Parkinson's disease and with prefrontal pathology appear to be dissociable (Owen et al., 1993; Robbins et al., 1994). In addition to the neuroanatomical abnormalities found in frontal cortex and the cerebellum in ADHD children, studies report size reductions and reduced left-right asymmetry in the caudate nucleus in ADHD children (Castellanos et al., 1996; Filipek et al., 1997; Hynd et al., 1993). In addition, four functional neuroimaging studies report reduced caudate activity in ADHD children performing a cognitive task compared to age-matched controls (Lou, Henriksen, & Bruhn, 1990; Lou, Henriksen, Bruhn, Borner, & Nielsen, 1989; Teicher, Ito, Glod, & Barber, 1996; Vaidya et al., 1998).

Hence, the caudate nucleus, like the cerebellum, appears to participate in neural systems important for motor and for cognitive functions. The caudate's roles in both functions, and the critical role of dopamine in both functions and in the functions of both prefrontal cortex and the caudate nucleus (on *dopamine and prefrontal cortex*, see, e.g., Diamond, 1996; Goldman-Rakic, Lidow, Smiley, & Williams, 1992; Lewis, Foote, Goldstein, & Morrison, 1988; Williams & Goldman-Rakic, 1995; on *dopamine and the caudate*, see, e.g., Aosaki, Graybiel, & Kimura, 1994; Graybiel, 1990; Kostowski, 1972), provide additional reasons why cognitive development and motor development may be more intertwined than has been previously appreciated.

MOTOR FUNCTIONS OF FRONTAL CORTEX

Dorsolateral prefrontal cortex subserves cognitive functions such as enabling us to hold information in mind so that we can remember what it is we are sup-

posed to do, to work with the information held in mind to organize and reorganize it, to resist distraction and stay on task, to resist the temptation to respond too early, and to inhibit one action that might perhaps be our first inclination when another behavior is more appropriate. All of these cognitive functions are clearly important for skilled motor performance. Thus, it makes sense that not only may the cerebellum and striatum play a role in cognition, but dorsolateral prefrontal cortex may contribute to motor performance. Dorsolateral prefrontal cortex has extensive interconnections with regions of frontal cortex more directly involved in motor functions such as premotor cortex and the supplementary motor area (SMA) (on *premotor cortex*, see Barbas & Pandya, 1987; Dum & Strick, 1991; Kunzle, 1978; on *SMA*, see Tanji, 1994; Wiesendanger, 1981). Premotor cortex is important for functions such as the planning of, preparation for, and sensory guidance of movement (e.g., Goldberg, 1987; Humphrey, 1979; Passingham, 1985, 1988; Wise, 1985). SMA is important for functions such as bimanual coordination and the generation and execution of motor sequences (e.g., Brinkman, 1984; Dick, Benecke, Rothwell, Day, & Marsden, 1986; Gaymard, Pierrot-Deseilligny, & Rivaud, 1990; Goldberg, 1985; Orgogozo & Larsen, 1979; Roland, Larsen, Larsen, & Skinhoj, 1980; Romo & Schultz, 1992). Premotor cortex and the SMA in turn have strong interconnections with motor cortex, which is also a region within frontal cortex. Hence, dorsolateral prefrontal cortex is positioned to be in close communication not only with subcortical regions important for motor function but with cortical centers important for movement as well.

CONCLUSIONS

It has been suggested here that motor development and cognitive development may be more interrelated than has been previously appreciated. When there are perturbations, genetic or environmental, that affect the motor system (as in developmental coordination disorder) or cognition (as in ADHD) it is often the case that both motor and cognitive functions are affected, not just one or the other. The caudate nucleus and the neurotransmitter, dopamine, play roles in neural systems subserving cognitive and motor functions. Developmental psychologists tend to focus on the protracted developmental progression in cognitive achievements, often forgetting that motor development is equally protracted. Similarly, the protracted period of prefrontal maturation is often emphasized, whereas the protracted period of cerebellar maturation has received less attention. Study after study using functional neuroimaging has found close co-activation

of the neocerebellum and dorsolateral prefrontal cortex during performance of cognitive tasks. When prefrontal activation is increased on a task, cerebellar activation is increased in the contralateral hemisphere, and when prefrontal activation is decreased, cerebellar activation is decreased in the contralateral hemisphere, although motor demands remain constant. It appears that the cerebellum may not only subserve motor function, but may play a role in cognition as well. Conversely, prefrontal cortex, through its connections with cortical and subcortical centers important for movement control, may play a role in motor function, not simply in cognition.

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ADDRESS AND AFFILIATION

Corresponding author: Adele Diamond, Center for Developmental Cognitive Neuroscience, Eunice Kennedy Shriver Center, 200 Trapelo Road, Waltham, MA 02452; e-mail: adiamond@shriver.org.

REFERENCES

- Albin, R. L., Young, A. B., & Penney, J. B. (1989). The functional anatomy of basal ganglia disorders. *Trends in Neuroscience*, *12*, 366–375.
- Albus, J. S. (1971). Afferent areas in the cerebellum connected with the limbs. *Brain*, *66*, 289–315.
- Alexander, G. E., DeLong, M. R., & Strick, P. L. (1986). Parallel organization of functionally segregated circuits linking basal ganglia and cortex. *Annual Review of Neuroscience*, *9*, 357–381.
- Amen, D. G., Paldi, F., & Thisted, R. A. (1993). Brain SPECT imaging. *Journal of American Academy of Child and Adolescent Psychiatry*, *32*, 1080–1081.
- Andersen, B. B., Korbo, L., & Pakkenberg, B. (1992). A quantitative study of the human cerebellum with unbiased stereological techniques. *Journal of Comparative Neurology*, *326*, 549–560.
- Aosaki, T., Graybiel, A. M., & Kimura, M. (1994). Effect of the nigrostriatal dopamine system on acquired neural responses in the striatum of behaving monkeys. *Science*, *265*, 412–415.
- Appollonio, I. M., Grafman, J., Schwartz, V., Massaquoi, S., & Hallett, M. (1993). Memory in patients with cerebellar degeneration. *Neurology*, *43*, 1536–1544.
- Awh, E., Jonides, J., Smith, E. E., Schumacher, E. H., Koeppe, R. A., & Katz, S. (1996). Dissociation of storage and rehearsal in verbal working memory: Evidence from positron emission tomography. *Psychological Science*, *7*, 25–31.

- Barbas, H., & Pandya, D. N. (1987). Architecture and frontal cortical connections of the premotor cortex (area 6) in the rhesus monkey. *Journal of Comparative Neurology*, 256, 211–228.
- Barkley, R. A., DuPaul, G. J., & McMurray, M. B. (1990). A comprehensive evaluation of attention deficit disorder with and without hyperactivity. *Journal of Consulting and Clinical Psychology*, 58, 775–789.
- Bauman, M., & Kemper, T. L. (1985). Histoanatomic observations of the brain in early infantile autism. *Neurology*, 35, 866–874.
- Berman, K. F., Ostrem, J. L., Randoulph, C., Gold, J., Goldberg, T. E., Coppola, R., Carson, R. E., Herscovitch, P., & Weinberger, D. R. (1995). Physiological activation of a cortical network during performance of the Wisconsin Card Sorting Test: A positron emission tomography study. *Neuropsychologia*, 33, 1027–1046.
- Berquin, P. C., Gidd, J. N., Jacobsen, L. K., Burger, S. D., Krain, A. L., Rapoport, J. L., & Castellanos, F. X. (1998). Cerebellum in attention-deficit hyperactivity disorder: A morphometric MRI study. *Neurology*, 50, 1087–1093.
- Bloedel, J. R. (1992). Functional heterogeneity with structural homogeneity: How does the cerebellum operate? *Behavioral and Brain Sciences*, 15, 666–678.
- Boni, S., Valle, G., Cioffi, R. P., Bonetti, M. G., Perrone, E., Tofani, A., & Maini, C. L. (1992). Crossed cerebello-cerebral diaschisis: A SPECT study. *Nuclear Medical Communication*, 13, 824–831.
- Botez, M. I., Botez, T., Elie, R., & Attig, E. (1989). Role of the cerebellum in complex human behavior. *Italian Journal of Neurological Sciences*, 10, 291–300.
- Bowen, F. P. (1976). Behavioral alterations in patients with basal ganglia lesions. In M. D. Yahr (Ed.), *The basal ganglia* (pp. 169–180). New York: Raven Press.
- Bracke-Tolkmitt, R., Linden, A., Canavan, A. G. M., Rockstroh, B., Scholz, E., Wessel, K., & Diener, H.-C. (1989). The cerebellum contributes to mental skills. *Behavioral Neuroscience*, 103, 442–446.
- Braver, T. S., Cohen, J. D., Nystrom, L. E., Jonides, J., Smith, E. E., & Noll, D. C. (1997). A parametric study of prefrontal cortex involvement in human working memory. *Neuroimage*, 5, 49–62.
- Brinkman, C. (1984). Supplementary motor area of the monkey's cerebral cortex: Short- and long-term deficits after unilateral ablation and the effects of subsequent callosal section. *Journal of Neuroscience*, 4, 918–929.
- Casey, B. J., Castellanos, F. X., Giedd, J. N., Marsh, W. L., Hamburger, S. D., Schubert, A. B., Vauss, Y. C., Vaituzis, A. C., Dickstein, D. P., Sarfatti, S. E., & Rapoport, J. L. (1997). Implication of right frontostriatal circuitry in response inhibition and attention deficit/hyperactivity disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, 36, 374–383.
- Castellanos, F. X. (1997). Toward a pathophysiology of attention-deficit/hyperactivity disorder. *Clinical Pediatrics*, 36, 381–393.
- Castellanos, F. X., Giedd, J. N., Marsh, W. L., Hamburger, S. D., Vaituzis, A. C., Dickstein, D. P., Sarfatti, S. E., Vauss, Y. C., Snell, J. W., Lange, N., Kaysen, D., Krain, A. L., Ritchie, G. F., Rajapakse, J. C., & Rapoport, J. L. (1996). Quantitative brain magnetic resonance imaging in attention-deficit/hyperactivity disorder. *Archives of General Psychiatry*, 53, 607–616.
- Chen, L., Bao, S., Lockard, J. M., & Kim, J. J. (1996). Impaired classical eyeblink conditioning in cerebellar-lesioned and purkinje cell degeneration (pcd) mutant mice. *Journal of Neuroscience*, 16, 2829–2838.
- Chen, L., Bao, S., & Thompson, R. F. (1999). Bilateral lesions of the interpositus nucleus completely prevent eyeblink conditioning in Purkinje cell-degeneration mutant mice. *Behavioral Neuroscience*, 113, 204–210.
- Chugani, D. C., Muzic, O., Rothermel, R., Behen, M., Chakraborty, P., Mangner, T., daSilva, E. A., & Chugani, H. T. (1997). Altered serotonin synthesis in the dento-thalamocortical pathway in autistic boys. *Annals of Neurology*, 42, 666–669.
- Ciesielski, K. T., Harris, R. J., Hart, B. L., & Pabst, H. F. (1997). Cerebellar hypoplasia and frontal lobe cognitive deficits in disorders of early childhood. *Neuropsychologia*, 35, 643–655.
- Ciranni, M. A., Dodson, C. S., & Shimamura, A. P. (1998). Impaired source memory in cerebellar patients. *Society for Neuroscience Abstracts*, 24, 2115.
- Clark, G. A., McCormick, D. A., Lavond, D. G., & Thompson, R. F. (1984). Effects of lesions of cerebellar nuclei on conditioned behavioral and hippocampal neuronal responses. *Brain Research*, 291, 125–136.
- Courchesne, E. (1991). Neuroanatomic imaging in autism. *Pediatrics*, 87, 781–790.
- Courchesne, E., Hesselink, J. R., Jernigan, T. L., & Yeung-Courchesne, R. (1987). Abnormal neuroanatomy in a nonretarded person with autism: Unusual findings with magnetic resonance imaging. *Archives of Neurology*, 44, 335–341.
- Courchesne, E., Townsend, J. P., Akshoomoff, N. A., Saitoh, O., Yeung-Courchesne, R., Lincoln, A., James, H., Haas, R. H., Schreibman, L., & Lau, L. (1994). Impairment in shifting attention in autistic and cerebellar patients. *Behavioral Neuroscience*, 108, 848–865.
- Courchesne, E., Yeung-Courchesne, R., Press, G. A., Hesselink, J. R., & Jernigan, T. L. (1988). Hypoplasia of cerebellar vermal lobules VI and VII in autism. *The New England Journal of Medicine*, 318, 1349–1354.
- Crispino, L., & Bullock, T. H. (1984). Cerebellum mediates modality-specific modulation of sensory responses of the midbrain and forebrain in rat. *Proceedings of the National Academy of Sciences (USA)*, 81, 2917–2920.
- Daum, I., Ackermann, H., Schugens, M. M., Reimold, C., Dichgans, J., & Bribmuer, N. (1993). The cerebellum and cognitive functions in humans. *Behavioral Neuroscience*, 107, 411–419.
- Daum, I., & Schugens, M. M. (1996). On the cerebellum and classical conditioning. *Current Directions in Psychological Science*, 5, 58–61.
- Daum, I., Schugens, M. M., Ackermann, H., Lutzenberger, W., Dichgans, J., & Birbaumer, N. (1993). Classical conditioning after cerebellar lesions in humans. *Behavioral Neuroscience*, 107, 748–756.

- DeLong, M. R., & Georgopoulos, A. P. (1981). Motor functions of the basal ganglia. In V. B. Brooks (Ed.), *Handbook of physiology, Section 1: The nervous system: Vol. 2. Motor control, part 2* (pp. 1017–1061). Bethesda, MD: American Physiological Society.
- Denckla, M. B., & Rudel, R. G. (1978). Anomalies of motor development in hyperactive boys. *Annals of Neurology, 3*, 231–233.
- Desmond, J. E., Gabrieli, J. D. E., Ginier, B. I., Demb, J. B., Wagner, A. D., Enzmann, D. R., & Glover, G. H. (1995). A functional MRI (fMRI) study of cerebellum during motor and working memory tasks. *Society for Neuroscience Abstracts, 21*, 1210.
- Desmond, J. E., Gabrieli, J. D. E., Wagner, A. D., Ginier, B. I., & Glover, G. H. (1997). Lobular patterns of cerebellar activation in verbal working memory and finger tapping tasks as revealed by functional MRI. *Journal of Neuroscience, 17*, 9675–9685.
- deZubicaray, G. I., Williams, S. C., Wilson, S. J., Rose, S. E., Brammer, M. J., Bullmore, E. T., Simmons, A., Chalk, J. B., Semple, J., Brown, A. P., Smith, G. A., Ashton, R., & Doddrill, D. M. (1998). Prefrontal cortex involvement in selective letter generation: A functional magnetic resonance imaging study. *Cortex, 34*, 389–401.
- Diamond, A. (1996). Evidence for the importance of dopamine for prefrontal cortex functions early in life. *Philosophical Transactions of the Royal Society (London) Series B, 351*, 1483–1494.
- Diamond, A., O'Craven, K. M., Davidson, M., Cruess, L., Bergida, R., & Savoy, R. L. (1999). *Further fMRI-based studies of memory and inhibition in prefrontal cortex of adults*. Paper presented at the annual meeting of the Cognitive Neuroscience Society, Washington, DC.
- Diamond, A., Prevor, M., Callender, G., & Druin, D. P. (1997). Prefrontal cortex cognitive deficits in children treated early and continuously for PKU. *Monographs of the Society for Research in Child Development, 62*(4, Serial No. 252).
- Dick, J. P. R., Benecke, R., Rothwell, J. C., Day, B. L., & Marsden, C. D. (1986). Simple and complex movements in a patient with infarction of the right supplementary motor cortex. *Movement Disorders, 1*, 255–266.
- Dow, R. S. (1942). The evolution and anatomy of the cerebellum. *Biological Reviews of the Cambridge Philosophical Society, 17*, 179–220.
- Dum, R. P., & Strick, P. L. (1991). The origin of corticospinal projections from the premotor areas in the frontal lobe. *Journal of Neuroscience, 11*, 667–689.
- Ekman, G., deChateau, P., Marions, O., Sellden, H., Wahlund, L. O., Wetterberg, L. (1991). Low field magnetic resonance imaging of the central nervous system in 15 children with autistic disorder. *Acta Paediatrica Scandinavica, 80*, 243–247.
- Fagen, J. W., & Rovee-Collier, C. K. (1982). A conditioning analysis of infant memory. In R. L. Isaacson & N. Spear (Eds.), *The expression of knowledge* (pp. 67–111). New York: Plenum Press.
- Fiez, J. A., Petersen, S. E., Cheney, M. K., & Raichle, M. E. (1992). Impaired non-motor learning and error detection associated with cerebellar damage. *Brain, 115*, 155–178.
- Fiez, J. A., Raife, E. A., Balota, D. A., Schwarz, J. P., Raichle, M. E., & Petersen, S. E. (1996). A positron emission tomography study of the short-term maintenance of verbal information. *Journal of Neuroscience, 16*, 808–822.
- Filipek, P. A., Semrud-Clikeman, M., Steingard, R. J., Renshaw, P. F., Kennedy, D. N., & Beiderman, J. (1997). Volumetric MRI analysis comparing subjects having attention-deficit hyperactivity disorder with normal controls. *Neurology, 48*, 589–601.
- Flament, D., Ellermann, J., Ugurbil, K., & Ebner, T. J. (1994). Functional magnetic resonance imaging (fMRI) of cerebellar activation while learning to correct for visuomotor errors. *Society for Neuroscience Abstracts, 20*, 20.
- Friston, K. J., Frith, C. D., Passingham, R. E., Liddle, P. F., & Frankowiak, R. S. J. (1992). Motor practice and neurophysiological adaptation in the cerebellum: A positron tomography study. *Proceedings of the Royal Society London, 248*, 223–228.
- Fulham, M. J., Brooks, R. A., Hallett, M., & Di Chiro, G. (1992). Cerebellar diaschisis revisited: pontine hypometabolism and dentate sparing. *Neurology, 42*, 2267–2273.
- Gaffney, G. R., Kuperman, S., Tsai, L. Y., & Minchin, S. (1987). Cerebellar structure in autism. *American Journal of Diseases in Children, 141*, 1330–1332.
- Gaffney, G. R., Kuperman, S., Tsai, L. Y., Minchin, S., & Hasanein, K. M. (1988). Midsagittal magnetic resonance imaging of autism. *British Journal of Psychiatry, 24*, 578–586.
- Gaymard, B., Pierrot-Deseilligny, C., & Rivaud, S. (1990). Impairment of sequences of memory-guided saccades after supplementary motor area lesions. *Annals of Neurology, 28*, 622–625.
- Geuze, R. H., & Kalverboer, A. F. (1994). Tapping a rhythm: A problem of timing for children who are clumsy and dyslexic? *Adapted Physical Activity Quarterly, 11*, 203–213.
- Ghez, C. (1991). The cerebellum. In E. R. Kandel, J. H. Schwartz, & T. M. Jessell (Eds.), *Principles of neural science* (pp. 626–646). Norwalk, CT: Appleton & Lange.
- Gilbert, P. F., & Thatch, W. T. (1977). Purkinje cell activity during motor learning. *Brain Research, 128*, 309–328.
- Glickstein, M., & Yeo, C. (1990). The cerebellum and motor learning. *Journal of Cognitive Neuroscience, 2*, 69–80.
- Goldberg, G. (1985). Supplementary motor area structure and function: Review and hypotheses. *Behavioral and Brain Sciences, 8*, 567–616.
- Goldberg, G. (1987). From intent to action: Evolution and function of the premotor systems of the frontal lobe. In E. Perecman (Ed.), *The frontal lobes revisited* (pp. 273–306). New York: The IRBN Press.
- Goldman-Rakic, P. S., Lidow, M. S., Smiley, J. F., & Williams, M. S. (1992). The anatomy of dopamine in monkey and human prefrontal cortex. *Journal of Neural Transmission Supplement, 36*, 163–177.
- Grafman, J., Litvan, I., Massaquoi, S., Stewart, M., Sirigu, A., & Hallett, M. (1992). Cognitive planning deficit in patients with cerebellar atrophy. *Neurology, 42*, 1493–1496.
- Grasby, P. M., Frith, C. D., Friston, K. J., Simpson, J., Fletcher, P. C., Frackowiak, R. S., & Dolan, R. J. (1994). A graded task approach to the functional mapping of brain

- areas implicated in auditory verbal memory. *Brain*, 117, 1271–1282.
- Graybiel, A. M. (1990). Neurotransmitters and neuromodulators in the basal ganglia. *Trends in Neuroscience*, 13, 244–254.
- Groves, P. M. (1983). A theory of the functional organization of the neostriatum and the neostriatal control of voluntary movement. *Brain Research Reviews*, 5, 109–132.
- Halliday, G. M., McRitchie, D. A., Macdonald, V., Double, K. L., Trent, R. J., & McCusker, E. (1998). Regional specificity of brain atrophy in Huntington's disease. *Experimental Neuropsychology*, 154, 663–672.
- Halsband, U., & Freund, H.-J. (1990). Premotor cortex and conditional motor learning in man. *Brain*, 113, 207–222.
- Hartsough, C. S., & Lambert, N. M. (1985). Medical factors in hyperactive and normal children: Prenatal developmental and health history findings. *American Journal of Orthopsychiatry*, 55, 190–201.
- Hellgren, L., Gillberg, C., Gillberg, I. C., & Enerskog, I. (1993). Children with deficits in attention, motor control, and perception (DAMP) almost grown up. General health at age 16 years. *Developmental Medicine and Child Neurology*, 35, 881–892.
- Hill, E. L. (1998). A dyspraxic deficit in specific language impairment and developmental coordination disorder? Evidence from hand and arm movements. *Developmental Medicine and Child Neurology*, 40, 388–395.
- Hill, E. L., Bishop, D. V. M., & Nimmo-Smith, I. (1998). Representational gestures in developmental co-ordination disorder and specific language impairment: Error types and the reliability of ratings. *Human Movement Science*, 17, 655–678.
- Holmes, G. (1939). The cerebellum of man. *Brain*, 62, 1–30.
- Houk, J. C., Buckingham, J. T., & Barto, A. G. (1996). Models of the cerebellum and motor learning. *Behavioral and Brain Sciences*, 19, 368–383.
- Hua, S. E., & Houk, J. C. (1997). Cerebellar guidance of premotor network development and sensorimotor learning. *Learning and Memory*, 4, 63–76.
- Hughes, C. (1996). Brief report: Planning problems in autism at the level of motor control. *Journal of Autism and Developmental Disorders*, 26, 99–107.
- Humphrey, D. R. (1979). On the cortical control of visually directed reaching: Contributions by nonprecentral motor areas. In R. E. Talbot & D. R. Humphrey (Eds.), *Posture and movement* (pp. 51–112). New York: Raven Press.
- Hynd, G. W., Hern, K. L., Novey, E. S., Eliopoulos, D., Marshall, R., Gonzalez, J. J., & Voeller, K. K. (1993). Attention deficit-hyperactivity disorder and asymmetry of the caudate nucleus. *Journal of Child Neurology*, 8, 339–347.
- Hynd, G. W., Semrud-Clikeman, M., Lorys, A. R., Novey, E. S., & Eliopoulos, D. (1990). Brain morphology in developmental dyslexia and attention deficit disorder/hyperactivity. *Archives of Neurology*, 47, 919–926.
- Ito, M. (1984). *The cerebellum and neural control*. New York: Raven Press.
- Ivkovich, D., Collins, K. L., Eckerman, C. O., Krasnegor, N. A., & Stanton, M. E. (1999). Classical delay eyeblink conditioning in 4- and 5-month-old human infants. *Psychological Science*, 10, 4–8.
- Ivry, R. B. (1993). Cerebellar involvement in the explicit representation of temporal information. In P. Tallal, A. M. Galaburda, R. R. Llinas, & C. von Euler (Eds.), *Temporal information processing in the nervous system: Special reference to dyslexia and dysphasia* (pp. 214–230). New York: New York Academy of Sciences.
- Ivry, R. B., & Keele, S. W. (1989). Timing functions of the cerebellum. *Journal of Cognitive Neuroscience*, 1, 136–152.
- Ivry, R. B., Keele, S. W., & Diener, H. C. (1988). Dissociation of the lateral and medial temporal cerebellum in movement timing and movement execution. *Experimental Brain Research*, 73, 167–180.
- Jonides, J., Schumacher, E. H., Smith, E. E., Lauber, E. J., Awh, E., Misnoshima, S., & Koeppe, R. A. (1997). Verbal memory load affects regional brain activation as measured by PET. *Journal of Cognitive Neuroscience*, 9, 462–475.
- Kadesjo, B., & Gillberg, C. (1998). Attention deficits and clumsiness in Swedish 7-year-old children. *Developmental Medicine and Child Neurology*, 40, 796–804.
- Keele, S. W., & Ivry, R. (1990). Does the cerebellum provide a common computation for diverse tasks? A timing hypothesis. *Annals of the New York Academy of Sciences*, 608, 179–211.
- Kim, J. J., & Thompson, R. F. (1997). Cerebellar circuits and synaptic mechanisms involved in classical eyeblink conditioning. *Trends in Neuroscience*, 20, 177–181.
- Kostowski, W. (1972). Certain aspects of physiological role of dopamine as synaptic transmitter in the striatum. *Acta Physiologica Polonica*, 23, 567–583.
- Kunzle, H. (1978). An autoradiographic analysis of the efferent connections from premotor and adjacent prefrontal regions (Areas 6 and 9) in Macaca fascicularis. *Brain, Behavior, and Evolution*, 15, 185–234.
- Lang, K. W., Paul, G. M., Robbins, T. W., & Marsden, C. D. (1993). L-dopa and frontal cognitive function in Parkinson's disease. *Advances in Neurology*, 60, 475–478.
- Larsell, O., & Jansen, J. (1972). *The comparative anatomy and histology of the cerebellum* (Vol. 3). Minneapolis: University of Minnesota Press.
- Lavond, D. G., Lincoln, J. C., McCormick, D. A., & Thompson, R. F. (1984). Effect of bilateral lesions of the dentate and interpositus cerebellar nuclei on conditioning of heart rate and nictitating membrane eyelid responses in the rabbit. *Brain Research*, 305, 323–330.
- Leary, M. R., & Hill, D. A. (1996). Moving on: Autism and movement disturbance. *Mental Retardation*, 34, 39–53.
- Lees, A. J., & Smith, E. (1983). Cognitive deficits in the early stages of Parkinson's disease. *Brain*, 106, 257–270.
- Leiner, H. C., Leiner, A. L., & Dow, R. S. (1986). Does the cerebellum contribute to mental skills? *Behavioral Neuroscience*, 100, 443–454.
- Leiner, H. C., Leiner, A. L., & Dow, R. S. (1989). Reappraising the cerebellum: What does the hindbrain contribute to the forebrain? *Behavioral Neuroscience*, 103, 998–1008.
- Leiner, H. C., Leiner, A. L., & Dow, R. S. (1991). The human cerebro-cerebellar system: Its computing, cognitive, and language skills. *Behavioral Brain Research*, 44, 113–128.

- Lesnik, P. G., Ciesielski, K. T., Hart, B. L., & Sanders, J. A. (1998). Evidence for cerebellar-frontal subsystem changes in children treated with intrathecal chemotherapy for leukemia: enhanced data analysis using an effect size model. *Archives of Neurology*, *55*, 1561–1568.
- Lewis, D. A., Foote, S. L., Goldstein, M., & Morrison, J. H. (1988). The dopaminergic innervation of monkey prefrontal cortex: A tyrosine hydroxylase immunohistochemical study. *Brain Research*, *449*, 225–243.
- Lipsitt, L. P. (1990). Learning processes in the human newborn: Sensitization, habituation, and classical conditioning. In A. Diamond (Ed.), *The development and neural bases of higher cognitive functions* (Vol. 608, pp. 113–127). New York: Annals of the New York Academy of Sciences.
- Logan, C. G., & Grafton, S. T. (1995). Functional anatomy of human eyeblink conditioning determined with regional cerebral glucose metabolism and positron emission tomography. *Proceedings of the National Academy of Sciences, USA*, *92*, 7500–7504.
- Lou, H. C., Henriksen, L., & Bruhn, P. (1990). Focal cerebral dysfunction in developmental learning disabilities. *Lancet*, *335*, 8–11.
- Lou, H. C., Henriksen, L., Bruhn, P., Borner, H., & Nielsen, J. B. (1989). Striatal dysfunction in attention deficit and hyperkinetic disorder. *Archives of Neurology*, *46*, 48–52.
- Manjiviona, J., & Prior, M. (1995). Comparison of Asperger syndrome and high-functioning autistic children on a test of motor impairment. *Journal of Autism and Developmental Disorders*, *25*, 23–39.
- Marien, P., Saerens, J., Nanhoe, R., Moens, E., Nagels, G., Pickut, B. A., Dierckx, R. A., & De Deyn, P. P. (1996). Cerebellar induced aphasia: Case report of cerebellar induced prefrontal aphasic language phenomena supported by SPECT findings. *Journal of Neurological Sciences*, *144*, 34–43.
- Marr, D. (1969). A theory of cerebellar cortex. *Journal of Physiology, London*, *202*, 437–470.
- Middleton, F. A., & Strick, P. L. (1994). Anatomical evidence for cerebellar and basal ganglia involvement in higher cognitive function. *Science*, *266*, 458–461.
- Middleton, F. A., & Strick, P. L. (1997). Cerebellar output channels. In J. D. Schmahmann (Ed.), *The cerebellum and cognition* (pp. 61–82). San Diego: Academic Press.
- Minshew, N. J., Luna, B., & Sweeney, J. A. (1999). Oculomotor evidence for neocortical systems but not cerebellar dysfunction in autism. *Neurology*, *52*, 917–922.
- Mostofsky, S. H., Reiss, A. L., Lockhart, P., & Denckla, M. B. (1998). Evaluation of cerebellar size in attention-deficit hyperactivity disorder. *Journal of Child Neurology*, *13*, 434–439.
- Muir, H., Nagata, K., Hirata, Y., Satoh, Y., Watahiki, Y., & Hatazawa, J. (1994). Evolution of crossed cerebellar diaschisis in middle cerebral artery infarction. *Journal of Neuroimaging*, *4*, 91–96.
- Murakami, J. W., Courchesne, E., Press, G. A., Yueng-Courchesne, R., & Hesselink, J. R. (1989). Reduced cerebellar hemisphere size and its relationship to vermal hypoplasia in autism. *Archives of Neurology*, *46*, 689–694.
- Orgogozo, J. M., & Larsen, B. (1979). Activation of the supplementary motor area during voluntary movements in man suggests it works as a supramotor area. *Science*, *206*, 847–850.
- Owen, A. M., James, M., Leigh, P., Summers, B., Marsden, C., Quinn, N., Lange, K., & Robbins, T. (1992). Frontostriatal cognitive deficits at different stages of Parkinson's disease. *Brain*, *115*, 1727–1751.
- Owen, A. M., Roberts, A. C., Hodges, J. R., Summers, B. A., Polkey, C. E., & Robbins, T. W. (1993). Contrasting mechanisms of impaired attentional set shifting in patients with frontal lobe damage or Parkinson's disease. *Brain*, *116*, 1159–1175.
- Page, J., & Boucher, J. (1998). Motor impairments in children with autistic disorder. *Child Language Teaching and Therapy*, *14*, 233–259.
- Pantelis, C., Barnes, T. R., Nelson, H. E., Tanner, S., Weatherly, L., Owen, A. M., & Robbins, T. W. (1997). Frontostriatal cognitive deficits in patients with chronic schizophrenia. *Brain*, *120*, 1823–1843.
- Passingham, R. E. (1985). Premotor cortex: Sensory cues and movement. *Behavioural Brain Research*, *18*, 175–185.
- Passingham, R. E. (1988). Premotor cortex and preparation for movement. *Experimental Brain Research*, *70*, 590–596.
- Paulesu, E., Connelly, A., Frith, C. D., Friston, K. J., Myers, R., Gadian, D. G., & Frackowiak, R. S. (1995). Functional MR imaging correlations with positron emission tomography. Initial experience using a cognitive activation paradigm on verbal working memory. *Neuroimaging Clin North America*, *5*, 207–225.
- Paulesu, E., Frith, C. D., & Frackowiak, R. S. (1993). The neural correlates of the verbal component of working memory. *Nature*, *362*, 342–345.
- Piek, J. P., Pitcher, T. M., & Hay, D. A. (1999). Motor coordination and kinaesthesia in boys with attention deficit-hyperactivity disorder. *Developmental Medicine and Child Neurology*, *41*, 159–165.
- Raichle, M. E., Fiez, J. A., Videen, T. O., MacLeod, A. M., Pardo, J. V., Fox, P. T., & Petersen, S. E. (1994). Practice-related changes in human brain functional anatomy during nonmotor learning. *Cerebral Cortex*, *4*, 8–26.
- Robbins, T. W., James, M., Owen, A. M., Lange, K. W., Lees, A. J., Leigh, A. J., Marsden, C. D., Quinn, N. P., & Summers, B. A. (1994). Cognitive deficits in progressive supranuclear palsy, Parkinson's disease, and multiple system atrophy in tests sensitive to frontal lobe dysfunction. *Journal of Neurology, Neurosurgery, and Psychiatry*, *57*, 79–88.
- Roland, P. E., Larsen, B., Larsen, N. A., & Skinhoj, E. (1980). Supplementary motor area and other cortical areas in organization of voluntary movements in man. *Journal of Neurophysiology*, *43*, 118–136.
- Romo, R., & Schultz, W. (1992). Role of primate basal ganglia and frontal cortex in the internal generation of movements, III. Neuronal activity in the supplementary motor area. *Experimental Brain Research*, *91*, 396–407.
- Rovee-Collier, C. (1990). The "memory system" of prelinguistic infants. In A. Diamond (Ed.), *The development and neural bases of higher cognitive functions* (Vol. 608, pp. 517–542). New York: Annals of the New York Academy of Sciences.
- Rovee-Collier, C. (1997). Dissociations in infant memory:

- Rethinking the development of implicit and explicit memory. *Psychological Review*, 104, 467–498.
- Rypma, B., Prabhakaran, V., Desmond, J. E., Glover, G. H., & Gabrieli, J. D. (1999). Load-dependent roles of frontal brain regions in the maintenance of working memory. *Neuroimage*, 9, 216–226.
- Sasaki, K., Jinnai, K., Gamba, H., Hashimoto, S., & Mizuno, N. (1979). Projection of the cerebellar dentate nucleus onto the frontal association cortex in monkeys. *Experimental Brain Research*, 37, 193–198.
- Schlosser, R., Hutchinson, M., Joseffer, S., Rusinek, H., Saarimaki, A., Stevenson, J., Dewey, S. L., & Brodie, J. D. (1998). Functional magnetic resonance imaging of human brain activity in a verbal fluency task. *Journal of Neurology, Neurosurgery, and Psychiatry*, 64, 492–498.
- Schmahmann, J. D. (1996). From movement to thought: Anatomic substrates of the cerebellar contribution to cognitive processing. *Human Brain Mapping*, 4, 174–198.
- Schmahmann, J. D., & Pandya, D. N. (1995). Prefrontal cortex projections to the basilar pons in rhesus monkey: Implications for the cerebellar contribution to higher function. *Neuroscience Letters*, 199, 175–178.
- Schmahmann, J. D., & Sherman, J. C. (1998). The cerebellar cognitive affective syndrome. *Brain*, 121, 561–579.
- Selemon, L. D., & Goldman-Rakic, P. S. (1985). Longitudinal topography and interdigitation of corticostriatal projections in the rhesus monkey. *Journal of Neuroscience*, 5, 776–794.
- Selemon, L. D., & Goldman-Rakic, P. S. (1988). Common cortical and subcortical target areas of the dorsolateral prefrontal and posterior parietal cortices in the rhesus monkey: Evidence for a distributed neural network subserving spatially guided behavior. *Journal of Neuroscience*, 8, 4049–4068.
- Slavoff, G. R., & Bonvillian, J. D. (1997). *Motor functioning of children with autistic disorder*. Paper presented at the biennial meeting of the Society for Research in Child Development, Washington, DC.
- Solomon, P. R., Stowe, G. T., & Pendlebury, W. W. (1989). Disrupted eyelid conditioning in a patient with damage to cerebellar afferents. *Behavioral Neuroscience*, 103, 898–902.
- Stelmach, G. E., & Worringham, C. J. (1988). The preparation and production of isometric force in Parkinson's disease. *Neuropsychologia*, 26, 93–103.
- Stewart, M. A., Pitts, F. N., Craig, A. G., & Dieruf, W. (1966). The hyperactive child syndrome. *American Journal of Orthopsychiatry*, 36, 861–867.
- Szatmari, P., Offord, D. R., & Boyle, M. H. (1989). Correlates, associated impairments, and patterns of service utilization of children with attention deficit disorders: Findings from the Ontario Child Health Study. *Journal of Child Psychology and Psychiatry*, 30, 205–517.
- Tanaka, M., Kondo, S., Hirai, S., Ishiguro, K., Ishihara, T., & Morimatsu, M. (1992). Crossed cerebellar diaschisis accompanied by hemiataxia: A PET study. *Journal of Neurology, Neurosurgery, and Psychiatry*, 55, 121–125.
- Tanji, J. (1994). The supplementary motor area in the cerebral cortex. *Neuroscience Research*, 19, 251–268.
- Taylor, A. E., Saint-Cyr, J. A., & Lang, A. E. (1987). Parkinson's disease. Cognitive changes in relation to treatment response. *Brain*, 110, 35–51.
- Taylor, A. E., Saint-Cyr, J. A., & Lang, A. E. (1990). Memory and learning in early Parkinson's disease: Evidence for a "frontal lobe syndrome." *Brain and Cognition*, 13, 211–232.
- Taylor, A. E., Saint-Cyr, J. A., Lang, A. E., & Kenny, F. T. (1986). Parkinson's disease and depression. *Brain*, 109, 279–292.
- Teicher, M. H., Ito, Y., Glod, C. A., & Barber, N. I. (1996). Objective measurement of hyperactivity and attentional problems in ADHD. *Journal of the American Academy of Child and Adolescent Psychiatry*, 35, 334–342.
- Thach, W. (1998). A role for the cerebellum in learning movement coordination. *Neurobiology of Learning and Memory*, 70, 177–188.
- Thompson, R. F. (1990). Neural mechanisms of classical conditioning in mammals. *Philosophical Transactions of the Royal Society (Section B)*, 329, 161–170.
- Thompson, R. F., Bao, S., Chen, L., Cipriano, B. D., Grethe, J. S., Kim, J. J., Thompson, J. K., Tracy, J. A., Weninger, M. S., & Krupa, D. J. (1997). Associative learning. In J. D. Schmahmann (Ed.), R. J. Bradley, R. A. Harris, & P. Jenner (Series Eds.), *International review of neurobiology: Vol. 41. The cerebellum and cognition* (pp. 152–189). San Diego: Academic Press.
- Topka, H., Valls-Sole, J., Massaquoi, S. G., & Hallett, M. (1993). Deficit in classical conditioning in patients with cerebellar degeneration. *Brain*, 116, 961–969.
- Vaidya, C. J., Austin, G., Kirkorian, G., Ridlehuber, H. W., Desmond, J. E., Glover, G. H., & Gabrieli, J. D. (1998). Selective effects of methylphenidate in attention deficit hyperactivity disorder: A functional magnetic resonance study. *Proceedings of the National Academy of Sciences*, 95(24), 14494–14499.
- van Mier, H., Petersen, S. E., Tempel, L. W., Perlmutter, J. S., Snyder, A. Z., & Raichle, M. E. (1994). Practice related changes in a continuous motor task measured by PET. *Society for Neuroscience Abstracts*, 20, 361.
- Weiner, M. J., Hallett, M., & Funkenstein, H. H. (1983). Adaptation to lateral displacement of vision in patients with lesions of the central nervous system. *Neurology*, 33, 766–772.
- Wiesendanger, M. (1981). Organization of the secondary motor areas of the cerebral cortex. In V. B. Brooks (Ed.), *Handbook of physiology: The nervous system: Vol. 2. Motor control* (pp. 1121–1147). Bethesda, MD: American Physiological Society.
- Williams, G. V., & Goldman-Rakic, P. S. (1995). Modulation of memory fields by dopamine D1 receptors in prefrontal cortex. *Nature*, 376, 572–575.
- Wise, S. P. (1985). The primate premotor cortex: Past, present, and preparatory. *Annual Review of Neuroscience*, 8, 1–19.
- Wolff, P. H., Michel, G. F., Ovrut, M., & Drake, C. (1990). Rate and timing precision of motor coordination in developmental dyslexia. *Developmental Psychology*, 26, 349–359.
- Woodruff-Pak, D. S., Logan, C. G., & Thompson, R. F. (1990). Neurobiological substrates of classical condition-

- ing across the life span. In A. Diamond (Ed.), *The development and neural bases of higher cognitive functions* (Vol. 608, pp. 150–178). New York: Annals of the New York Academy of Sciences.
- Yamamoto, T., Yoshida, K., Yoshikawa, H., Kishimoto, Y., & Oka, H. (1992). The medial dorsal nucleus is one of the thalamic relays of the cerebellocerebral responses to the frontal association cortex in the monkey: Horseradish peroxidase and fluorescent dye double staining study. *Brain Research*, 579, 315–320.
- Yeo, C. H., & Hardiman, M. J. (1992). Cerebellar cortex and eyeblink conditioning: A reexamination. *Experimental Brain Research*, 88, 623–638.
- Zametkin, A. J., Nordahl, T. E., Gross, M., King, A. C., Semple, W. E., Rumsey, J., Hamburger, S., & Cohen, R. M. (1990). Cerebral glucose metabolism in adults with hyperactivity of childhood onset. *The New England Journal of Medicine*, 323(20), 1361–1366.
- Zilbovicius, M., Garreau, B., Samson, Y., Remy, P., Barthelemy, C., Syrota, A., & Lelord, G. (1995). Delayed maturation of the frontal cortex in childhood autism. *American Journal of Psychiatry*, 152, 248–252.