The Role of the Cerebellum in Cognition and Behavior: A Selective Review

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The cerebellum has traditionally been seen primarily to coordinate voluntary movement, but evidence is accumulating that it may play a role in cognition and behavior as well. This is a selective review of studies assessing potential cognitive deficits and personality changes associated with cerebellar disease. Preliminary studies of the role of the cerebellum in schizophrenia, dementia, and other psychiatric disorders are also discussed. Efforts to understand the neurological substrates of behavior should consider the role of the cerebellum.

(The Journal of Neuropsychiatry and Clinical Neurosciences 2000; 12:193–198)

The role of the cerebellum has traditionally been seen as limited to the coordination of voluntary movement, gait, posture, speech, and motor functions.[1] The cerebellum has not conventionally been seen as relevant to the field of psychiatry or to the study of brain–behavior relationships. There is evidence, however, that the cerebellum may have a role to play in cognition, behavior, and psychiatric illness. This paper critically reviews selected published literature targeting this hypothesis, with the goal of raising awareness of recent developments and stimulating increased research interest in the role of the cerebellum in cognition and behavior. The literature search began with a MEDLINE search from 1992 to the present combining the keyword "cerebellum" with the following keywords: psychiatry, psychosis, delusions, hallucinations, depression, dementia, Alzheimer's disease, and cognition. Next we searched relevant references cited in these studies, often from articles prior to 1992, and incorporated these where appropriate in addressing the hypothesis. The search was limited to human studies in the English language, and studies were individually selected if they were of interest in addressing our hypothesis and goal.

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ANATOMICAL CONSIDERATIONS

Motor Functioning

Lesions of the midline area of the cerebellum, the vermis, are associated with disorders of the trunk, whereas lesions of the lateral areas, the hemispheres, produce limb asynergia.[1] Cerebellar diseases can be generally localized by their clinical features: Lesions in the flocculonodular lobe are seen to cause disequilibrium with ataxic gait, a wide-based stance, and nystagmus; lesions of the anterior lobes are associated with an even more impaired gait and abnormal coordinated movements of the lower limbs; lesions of the lateral posterior lobes are associated with hypotonia, dysmetria, dysarthric speech, and dysdiadochokinesia.[1]

Nonmotor Functioning

From an anatomical standpoint, it should not be surprising that the cerebellum may play a role in nonmotor brain functioning. Although the cerebellum constitutes only 10% of the total brain weight, it contains more than half of all the neurons in the brain.[1] The cerebellum is connected to the cerebrum via three cerebellar peduncles. There are connections, largely via the thalamus, to many brain areas relevant to cognition and behavior, including the dorsolateral prefrontal cortex, the medial frontal cortex, the parietal and superior temporal areas, the anterior cingulate, and the posterior hypothalamus.[2,3] There are also noradrenergic, serotonergic, and dopaminergic inputs to the cerebellum from brainstem nuclei.[2] Given these connections, a role for the cerebellum in nonmotor functioning would seem likely. Gao et al.[4] recently suggested that the lateral cerebellum is involved in the acquisition and discrimination of sensory information. Behavioral aspects of the cerebellum have not been directly examined until recently.

REVIEW OF THE LITERATURE

Cases of intellectual impairment and aberrant behavior in patients with cerebellar disease were described as early as 1831.[5] Through the latter part of our century, there have been selected reviews of the potential role of the cerebellum in cognition and behavior.[6–8] However, the role of the cerebellum has remained largely ignored by psychiatry until relatively recently. By analogy, the basal ganglia initially were felt to subserve primarily motor functions, and it was not until the early 1970s, when interest developed in "subcortical dementia,"[9] that the role of the basal ganglia in cognition and behavior became appreciated. Since that time, supported by a growing anatomical and theoretical literature in nonhuman primates,[10,11] psychiatrists have become very interested in the role of the basal ganglia in the psychiatric features associated with Parkinson's disease,[12] Tourette's syndrome,[13] and obsessive-compulsive disorder,[14] among others. It may be useful to investigate the role of the cerebellum in understanding the complex neural circuitry underlying cognition, affect, and behavior in a similar manner. Ultimately, a thorough understanding of this circuitry may lead to improved outcomes for individuals suffering from psychiatric disorders related to these circuits.

The Cerebellum and Cognition

Schmahman and Sherman,[15] using bedside cognitive testing as well as neuropsychological testing in a group of 20 patients with isolated cerebellar disease, described a syndrome that included impaired spatial cognition, dysprosody, and anomia, as well as executive dysfunction with difficulties in planning, set-shifting, abstraction, working memory, and verbal fluency. Abnormalities of the posterior cerebellum, especially if bilateral, were particularly associated with these cognitive difficulties. Although this study detailed both bedside cognitive abnormalities and neuropsychological testing in subjects with isolated cerebellar lesions, the patient group was heterogeneous, including patients with various diseases of the cerebellum. Additionally, neuropsychological testing was analyzed by using z-scores, with no control group for comparison. Moderate to severe executive dysfunction was similarly found by Storey et al.[16] in an Australian pedigree of spinocerebellar ataxia. Although this study assessed executive functioning by use of various measures, there were only 5 subjects who completed all of the neuropsychological testing, and a control group was again lacking. Subjects with cerebellar disease have been often found to have "frontal-like" cognitive impairment, with much more variable findings in the areas of visuospatial dysfunction, language, and memory (see more detailed review by Daum and Ackermann[17]).

The cerebellum may also be relevant in the cognition of normal subjects without overt cerebellar disease. Cerebellar size has been found to be weakly correlated with memory retention and to show a trend for correlation with general IQ, even when covaried for cerebral volume in normal subjects.[18] The relatively weak associations suggest that the role of the cerebellum in the cognition of normal subjects may well be mediated through the cortical areas with which it is intimately linked. In functional neuroimaging studies of normal subjects, the cerebellum has been seen to activate in tasks involving learning and word generation.[19] These cerebellar effects do not occur in isolation and are rarely the areas of the most robust change, suggesting that the role of the cerebellum in cognitive changes in normal subjects is mediated by cortical areas.

The Cerebellum and Mood/Behavior

Apart from its potential role in "coordinating" movement and cognition, the cerebellum may also be implicated in emotional and behavioral control. Schmahman and Sherman[15] found that in their group of patients with isolated cerebellar disease, particularly those with midline and vermal pathology, personality changes of either flattening of affect or disinhibited and inappropriate behavior were common. The lack of standardized measures of these behavioral changes in subjects and the lack of a control group make this conclusion rather tentative. On the other hand, in a controlled study by Kish et al.,[20] patients with olivopontocerebellar atrophy had significantly higher depression scores than control subjects, and depression correlated weakly with cognitive testing. Mayberg et al.[21] found that induction of transient sadness in healthy volunteers and patients with depression was associated with increased cerebral blood flow in the cerebellar vermis. However, this was but one of the brain areas found to have changes in cerebral blood flow with induction of sadness, and it is difficult to ascertain the role that the cerebellum plays independently of cortical and limbic changes.

An earlier study by Heath et al.[22] showed that anterior cerebellar electrode stimulation improved some refractory cases of depression, psychosis, and behavioral problems in patients with diagnoses of schizophrenia, depression, epilepsy, and organic brain syndrome. With the availability of pharmacological treatments, now the mainstay of treatment for depression and schizophrenia, these observations may be seen as historically interesting but of limited practical value. However, the emerging use of transcranial magnetic stimulation,[23] other methods such as vagal stimulation, and stereotactic surgery for refractory cases in psychiatry may refocus attention on this previous observation.

The Cerebellum in Schizophrenia

There has been a growing interest in the role of the cerebellum in schizophrenia. An uncontrolled study showed that young male patients with schizophrenia who were on medications but not using alcohol had a preponderance of mild lower-extremity cerebellar signs[24] suggesting cerebellar involvement. Additionally, abnormal smooth-pursuit eye tracking has been found to be more common in schizophrenic patients (off neuroleptics) than in control subjects.[25] The abnormal eye movements may well be related to cerebellar pathology, although it is likely that alternative cortical systems including frontal eye fields were also involved.[26] These studies did not control for cortical involvement.

Some structural imaging studies have found cerebellar atrophy in schizophrenia,[27–29] but others have failed to replicate this.[30–32] One study in fact showed hyperplasia of the vermis.[33] Differences in both inclusion criteria and imaging methods may have accounted for these differences in the results. More precise MRI volumetric measures will be instrumental in resolving this debate.

Postmortem pathological studies in schizophrenia have shown smaller vermal area compared with subjects with no psychiatric illness or with other psychiatric illnesses;[34] smaller Purkinje cell size;[35] and decreased linear density and increased surface density of Purkinje cells compared with age-matched controls.[36] The influence of chronic treatment was not considered in these limited sample studies, nor have they been replicated. Additionally, although the control subjects when living had had no known psychiatric illnesses, they had not been thoroughly screened for the absence of psychiatric problems. Firm conclusions on structural changes of the cerebellum in schizophrenia therefore cannot yet be made.

A functional neuroimaging study by Volkow et al.[37] suggested that individuals with schizophrenia have lower cerebellar metabolism compared with control subjects. In this study, the subjects with schizophrenia were receiving neuroleptics and the control subjects were not; therefore it is unclear whether the cerebellar hypometabolism in the schizophrenic subjects was related to the illness or the medication. Additionally, the role of concomitant cortical changes was not explored. An intriguing new study by Crespo-Facorro et al.[38] of Andreasen's group[39] has suggested that subjects with schizophrenia have less blood flow in the cerebellum than control subjects during the performance of a novel memory task. This group has suggested the presence of a "cognitive dysmetria" in schizophrenia patients that relates to their cerebellar activity, analogous to the motor dysmetrias demonstrated in cerebellar patients. Their findings also suggest involvement of cortical-thalamic-cerebellar loops, since the cerebellum was but one area of altered blood flow, in addition to the frontal cortex, thalamus, and other areas. The role of metabolism or blood flow of the cerebellum in isolation in schizophrenia remains unclear. Validation of the paradigm in subjects with known cerebellar disease will be important for testing the specificity of these findings.

The Cerebellum in Other Psychiatric Disorders

With respect to bipolar disorder, there has been some suggestion of cerebellar atrophy in patients with bipolar disorder or mania,[28,40] and another study showed a trend to this effect in patients over the age of 50.[32] The role of alcohol abuse, however, may be a confounder. In one of the studies,[28] only the subjects with concomitant bipolar disorder and alcohol abuse had smaller cerebellar dimensions or vermis than control subjects. The other studies[32,40] did not control for alcohol abuse. Anticonvulsant medication use may be an additional confound.

Autism has been associated with hypoplasia of lobules VI and VII of the cerebellar vermis in a study by Courchesne et al.,[41] although this finding has not been consistently replicated. (A recent review by Courchesne and others[42] has demonstrated that in several MRI studies, patients with autism may have two types of cerebellar pathology—hypoplasia and hyperplasia—of the posterior vermis.) Kates et al.[43] studied a pair of monozygous twins, one of whom met criteria for strictly defined autism and the other of whom showed constrictions in social interaction and play but did not meet these criteria. Smaller cerebellar vermis lobules VI and VII were found in the affected twin compared with the nonaffected twin, further suggesting a role for the cerebellum in autistic disorder; however, there were differences in other brain regions as well, making this conclusion tentative. A recent study has shown smaller volumes of the posterior inferior lobe of the cerebellum in children with attention-deficit/hyperactivity disorder than in age-matched control subjects, even adjusting for brain volume and IQ.[44] Adults with Down's syndrome have also been found to have smaller cerebellar volumes than age-matched control subjects, also controlling for total intracranial volume and total brain volume. This difference did not appear to change over time in a small subset of patients followed serially.[45] These studies had the benefit of both a control group and covariate analysis controlling for brain volume. Specificity for symptoms in these disorders is not addressed in these studies, and dissimilarities in clinical presentations across syndromes likewise have not been addressed.

The Cerebellum in Aging and Dementia

The cerebellum also appears have relevance to mechanisms in aging and dementia. With aging, a 10% to 40% decrease in Purkinje cell layer[46] and a reduction in the area of the dorsal vermis[47] have been reported, suggesting the possibility that any functions (motor and nonmotor) that are subserved by the cerebellum may be affected to some degree by the aging process. The role of the cell loss in mental or postural stability has not yet been studied. Alcoholic dementia is one of the classic dementias associated with cerebellar atrophy.[48] Although alcoholic dementia is commonly complicated by medical comorbidity, patients with this illness may have more ataxia and stereotypic behavior changes but less overt cortical dysfunction (e.g., less anomia, less deterioration in cognitive status) than do those with Alzheimer's disease (AD).[48] In contrast, Kish et al.[20] found that patients with olivopontocerebellar atrophy (OPCA) demonstrate multiple deficits in intellect, memory, attention, language, and visuospatial and executive functions compared with a control group. It is unclear whether these cognitive skills deteriorate over time in this population and to what extent these subjects had subtle cortical involvements implicating other sites of involvement in the absence of MRI correlation. Thus, although both alcoholic dementia and OPCA are associated with cerebellar abnormalities, it is uncertain how static these deficits are, and specificity remains uncertain because cortical and subcortical areas are also involved.

The cerebellum is not considered to be a primary focus of pathology in AD. However, diffuse amyloid plaques and increased microglia (but an absence of neurofibrillary tangles) can be found in the cerebellum, usually later in the AD process.[49] Purkinje cell density is decreased, especially in familial AD.[50] Ishii et al.[51] found decreased cerebellar metabolism in severe AD, and this decrease was correlated with Mini-Mental State Examination (MMSE) scores. It is important to note, however, that this association may be an artifact of the temporal and parietal hypometabolism in these same patients, since this correlation was not corrected for cortical hypometabolism. In one autopsy study by Barclay and Brady,[52] gross cerebellar atrophy had been found on CT scan in 2/8 (25%) of subjects with mixed dementia, but in none of 15 subjects with AD or 14 with multi-infarct dementia (diagnoses confirmed at autopsy); in view of these results, cerebellar atrophy on CT was tentatively suggested as a marker for mixed dementia. If replicated, this could be most helpful clinically.

The cerebellum may be implicated in the behavioral aspects of dementia as well. Gutzmann and Kuhl[53] found that affective lability and emotional incontinence in dementia are associated with cerebellar atrophy, third ventricular width, and interhemispheric fissure width, but not with other measures of cortical atrophy. However, it was unclear how affective lability and emotional incontinence were quantified, despite a clear attempt at attaining a homogeneous sample. Meguro et al.[54] found that wandering in vascular dementia was associated with sparing of the metabolic rate in the cerebellum as well as frontal, left parietal, temporal-parietal-occipital, and left occipital areas of the cortex. This finding only tentatively points to a role of the cerebellum and may be due to reciprocal functional connections between the cerebellar and cortical areas. In contrast to the finding of hypometabolism in the cerebellum in severe AD,[51] Dolan et al.[55] found that patients with cognitive impairment in depression show higher cerebellar blood flow in the vermis and less blood flow in the left medial frontal cortex than depressed patients without cognitive impairment. This effect appears to be related specifically to cognitive dysfunction, since the investigators controlled for depression severity. If this finding is replicated, cerebellar activation may help distinguish between AD and the cognitive impairment of depression.

CONCLUSIONS

Caution must be exercised in interpreting the above data because many of the studies have not as yet been replicated, and in many cases control groups are lacking. Experience warns that it is highly unlikely that a specific area of the brain causes cognitive or emotional changes, since mental functions tend to be widely distributed in various brain circuits.[11] It is also difficult to know whether changes in the cerebellum are responsible for symptoms or syndromes of mental illness or are instead secondary to changes in other areas of the brain. The intimate connections of the cerebellum with much of the rest of the brain make this particularly difficult to sort out.[3,15]

Nonetheless, these many studies provide strong support for a nonmotor role of the cerebellum. It will be clinically prudent to be on the alert for cognitive, affective, and behavioral disturbances in assessing, treating, and rehabilitating patients with cerebellar illness. Further, it may be important to consider the possibility of cerebellar disease in patients presenting with a new onset of changes in these behavioral domains. From a research perspective, the use of the cerebellum as a control or reference region in functional neuroimaging studies may need to be reconsidered, or at least adopted cautiously in subjects with psychiatric disturbances. Clearly much more may yet be learned about the cerebellum's role in both normal and patient populations, and it will be important for imaging studies of disorders of mood, behavior, and cognition to take the cerebellum into account.

Frick[8] viewed the cerebellum as having a crucial integrating and organizing function and proposed that it may form a major neurological component of the ego, particularly subserving the autonomous ego functions. Like the basal ganglia, the cerebellum may have a fundamental coordinating role in cognition and emotions. It is likely that future research into the role of the cerebellum will confirm Dow's prediction[7] that just as the cerebellum maintains balance, integration, and stability in the somatic motor sphere, it may also help with balancing, integrating, and stabilizing other functions of the brain of particular relevance to psychiatry.

References

1. Ghez C, Fahn S: The cerebellum, in Principles of Neural Science, 2nd edition, edited by Kandel ER, Schwartz JH. New York, Elsevier, 1985, pp 502–522
2. Dolan RJ: A cognitive affective role for the cerebellum. Brain 1998; 121:545–546
3. Middleton FA, Strick PL: Cerebellar output channels. Int Rev Neurobiol 1997; 41:61–82
4. Gao JH, Parsons LM, Bower JM, et al: Cerebellum implicated in sensory acquisition and discrimination rather than motor control. Science 1996; 272:545–547
5. Schmahman JD: Rediscovery of an early concept. Int Rev Neurobiol 1997; 41:3–19
6. Snider RS: Recent contributions to the anatomy and physiology of the cerebellum. Arch Neurol Psychiatry 1950; 64:196–219
7. Dow RS: Some novel concepts of cerebellar physiology. Mt Sinai J Med 1974; 41:103–119
8. Frick RB: The ego and the vestibulocerebellar system: some theoretical perspectives. Psychoanal Q 1982; 51:93–112
9. Albert ML, Feldman RG, Willis AL: The subcortical dementia of "progressive supranuclear palsy." J Neurol Neurosurg Psychiatry 1974; 37:121–130
10. Goldman-Rakic PS: Regional and cellular fractionation of working memory. Proc Natl Acad Sci USA 1996; 93:13473–13480
11. Alexander GE, DeLong MR, Strick PL: Parallel organization of functionally segregated circuits linking basal ganglia and cortex. Annu Rev Neurosci 1986; 9:347–381
12. Starkstein SE, Bolduc PL, Mayberg HS, et al: Cognitive impairments and depression in Parkinson's disease: a follow-up study. J Neurol Neurosurg Psychiatry 1990; 53:597–602
13. Comings DE: Tourette's Syndrome and Human Behavior. Duarte, CA, Hope Press, 1990
14. Baxter LR, Schwartz JM, Bergman KS, et al: Caudate glucose metabolic rate changes with both drug and behavior therapy for obsessive-compulsive disorder. Arch Gen Psychiatry 1992; 49:681–689
15. Schmahman JD, Sherman JC: The cerebellar cognitive affective syndrome. Brain 1998; 121:561–579
16. Storey E, Forrest SM, Shaw JH, et al: Spinocerebellar ataxia type 2: clinical features of a pedigree displaying prominent frontal-executive dysfunction. Arch Neurol 1999; 56:43–50
17. Daum I, Ackermann H: Cerebellar contributions to cognition. Behav Brain Res 1995; 67:201–210
18. Paradiso S, Andreasen NC, O'Leary DS, et al: Cerebellar size and cognition: correlations with IQ, verbal memory and motor dexterity. Neuropsychiatry Neuropsychol Behav Neurol 1997; 10: 1–8
19. Raichle ME, Fiez JA, Videen TO, et al: Practice-related changes in human brain functional anatomy during non-motor learning. Cereb Cortex 1994; 4:3–26
20. Kish SJ, El-Awar M, Schut L, et al: Cognitive deficits in olivopontocerebellar atrophy: implications for the cholinergic hypothesis of Alzheimer's dementia. Ann Neurol 1988; 24:200–206

21. Mayberg HS, Liotti M, Brannan SK, et al: Disease and state specific effects of mood challenge on rCBF (abstract). Neuroimage 1998; 7:S901
22. Heath RG, Llewellyn RC, Rouchell AM: The cerebellar pacemaker for intractable behavioral disorders and epilepsy: follow-up report. Biol Psychiatry 1980; 15:243–256
23. George MS, Wasserman EM, Kimbrell TA, et al: Mood improvement following daily left prefrontal repetitive transcranial magnetic stimulation in patients with depression: a placebo-controlled crossover trial. Am J Psychiatry 1997; 154:1752–1756
24. Martin P, Albers M: Cerebellum and schizophrenia: a selective review. Schizophr Bull 1995; 21:241–250
25. Cooper PM, Pivik RT: Abnormal visual-vestibular interaction and smooth pursuit tracking in psychosis: implications for cerebellar involvement. Journal of Psychiatry and Neurosciences 1991; 16:30–40
26. Sweeney JA, Luna B, Srinivasagam NM, et al: Eye tracking abnormalities in schizophrenia: evidence for dysfunction in the frontal eye fields. Biol Psychiatry 1998; 44:698–708
27. Heath RG, Franklin DE, Walker CF, et al: Cerebellar vermal atrophy in psychiatric patients. Biol Psychiatry 1982; 17:569–583
28. Lippmann S, Manshadi M, Baldwin H, et al: Cerebellar vermis dimensions on computerized tomographic scans of schizophrenic and bipolar patients. Am J Psychiatry 1982; 139:667–668
29. Nasrallah HA, Jacoby CS, Chapman S, et al: Third ventricular enlargement on CT scans in schizophrenia: associations with cerebellar atrophy. Biol Psychiatry 1985; 20:443–450
30. Coffman JA, Mefferd J, Golden CJ, et al: Cerebellar atrophy in chronic schizophrenia (letter). Lancet 1981; i:666
31. Mathew RJ, Partain CL: Midsagittal sections of the cerebellar vermis and fourth ventricle obtained with magnetic resonance imaging of schizophrenic patients. Am J Psychiatry 1985; 142:970–971
32. Yates WR, Jacoby CG, Andreasen NC: Cerebellar atrophy in schizophrenia and affective disorder. Am J Psychiatry 1987; 144:465–467
33. Nasrallah HA, Schwarzkopf SB, Olson SC, et al: Perinatal brain injury and cerebellar vermal lobules I–X in schizophrenia. Biol Psychiatry 1991; 29:567–574
34. Weinberger DR, Kleinman JE, Luchins DJ, et al: Cerebellar pathology in schizophrenia: a controlled postmortem study. Am J Psychiatry 1980; 137:359–361
35. Tran KD, Smutzer GS, Doty RL, et al: Reduced Purkinje cell size in the cerebellar vermis of elderly patients with schizophrenia. Am J Psychiatry 1998; 155:1288–1290
36. Reyes MG, Gordon A: Cerebellar vermis in schizophrenia. Lancet 1981; ii:700–701
37. Volkow ND, Levy A, Brodie JD, et al: Low cerebellar metabolism in medicated patients with chronic schizophrenia. Am J Psychiatry 1992; 149:686–688
38. Crespo-Facorro B, Paradiso S, Andreasen NC, et al: Recalling word lists reveals “cognitive dysmetria” in schizophrenia: a positron emission tomography study. Am J Psychiatry 1999: 156:386–392
39. Wiser AK, Andreasen NC, O’Leary DS, et al: Dysfunctional cortico-cerebellar circuits cause “cognitive dysmetria” in schizophrenia. Neuroreport 1998; 9:1895–1899
40. Nasrallah HA, Jacoby CG, McCalley-Whitters M: Cerebellar atrophy in schizophrenia and mania (letter). Lancet 1981; i:1102
41. Courchesne E, Yeung-Courchesne R, Press GA, et al: Hypoplasia of cerebellar vermal lobules VI and VII in autism. N Engl J Med 1988; 318:1349–1354
42. Courchesne E, Townsend J, Saitoh O: The brain in infantile autism: posterior fossa structures are abnormal. Neurology 1994; 44:214–223
43. Kates WR, Mostofksy SH, Zimmerman AW, et al: Neuroanatomical and neurocognitive differences in a pair of monozygous twins discordant for strictly defined autism. Ann Neurol 1998; 43:782–791
44. Berquin PC, Giedd JN, Jacobsen LK, et al: Cerebellum in attention deficit hyperactivity disorder: a morphometric MRI study. Neurology 1998; 50:1087–1093
45. Aylward EH, Habbak R, Warren AC, et al: Cerebellar volume in adults with Down syndrome. Arch Neurol 1997; 54:209–212
46. Hall TC, Miller AKH, Corsellis JAN: Variations in human Purkinje cell population according to age and sex. Neuropathol Appl Neurobiol 1975; 1:267–292
47. Raz N, Torres IJ, Spencer WD, et al: Age-related regional differences in cerebellar vermis observed in vivo. Arch Neurol 1992; 149:412–416
48. Atkinson RM, Ganzini L: Substance abuse, in The American Psychiatric Press Textbook of Geriatric Neuropsychiatry, edited by Coffey CE, Cummings JL. Washington, DC, American Psychiatric Press, 1994, pp 297–321
49. Larner AJ: The cerebellum in Alzheimer’s disease. Dement Geriatr Cogn Disord 1997; 8:203–209
50. Fukutani Y, Cairns NJ, Rossor MN, et al: Purkinje cell loss and astrocytosis in the cerebellum in familial and sporadic Alzheimer’s disease. Neurosci Lett 1996; 214:33–36
51. Ishii K, Masahiro S, Kitagaki H, et al: Reduction of cerebellar glucose metabolism in advanced Alzheimer’s disease. J Nucl Med 1997; 38:925–928
52. Barclay LL, Brady PA: Cerebellar atrophy as a CT marker for mixed dementia. Biol Psychiatry 1992; 31:520–524
53. Gutzmann H, Kuhl KP: Emotion control and cerebellar atrophy in senile dementia. Arch Gerontol Geriatr 1987; 6:61–71
54. Meguro K, Yamaguchi S, Yamazaki H, et al: Cortical glucose metabolism in psychiatric wandering patients with vascular dementia. Psychiatry Res: Neuroimaging 1996; 67:71–80
55. Dolan RJ, Bench CJ, Brown RG, et al: Regional cerebral blood flow abnormalities in depressed patients with cognitive impairment. J Neurol Neurosurg Psychiatry 1992; 55:768–773