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IMPAIRED NON-MOTOR LEARNING AND ERROR DETECTION ASSOCIATED WITH CEREBELLAR DAMAGE

A SINGLE CASE STUDY

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SUMMARY

A previously conducted positron emission tomography (PET) study of normal humans suggested that the cerebellum makes important non-motor contributions to language processing. Beginning with the task which produced right cerebellar PET activation, we studied a 49-yr-old male (RC1) with right cerebellar damage on a variety of tasks involving complex non-motor processing. Whereas RC1's performance on standard tests of memory, intelligence, 'frontal function' and language skills was excellent, he had profound deficits in two areas: (1) practice-related learning; (2) detection of errors. Considered in relation to cerebellar contributions to motor tasks, the results suggest some functions performed by the cerebellum may be generalized beyond a purely motor domain.

INTRODUCTION

The hallmarks of cerebellar damage or degeneration are motor impairments. These have been reported for over 100 years (Dickinson, 1865; Jackson, 1932). Typical symptoms include gait ataxia, dysmetria, dysarthria and vertigo (Holmes, 1939; Gilman *et al.*, 1981). Not surprisingly, both human and animal investigations of the cerebellum have concentrated on understanding the cerebellar functions which underlie these motor disturbances (e.g. Thach, 1970; Mano, 1974). Only fairly recently has it been suggested that the cerebellum may have important non-motor functions. Several investigators have identified cerebellar hypoplasia in individuals with autism (Bauman and Kemper, 1985; Gaffney *et al.*, 1987; Murakami *et al.*, 1989). Reviews of the cerebellum by both Watson (1978) and Bernstein and Torello (1982) conclude that the cerebellum is involved in some emotional processes, such as motivation and reinforcement. Leiner *et al.* (1989), in one of a series of articles on the topic, concluded, 'recent behavioral evidence indicates that the human cerebellum is involved in a wider range of functions: in learning, in planning, in judging time, in some emotional and cognitive disorders such as autism, and in some normal mental activities such as the cognitive processing of words'.

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SUBJECTS

Patient case report

A 49-yr-old right-handed male lawyer with a history of systemic hypertension suffered a sudden onset of nausea, vomiting, intense vertigo, and loss of motor control. Subsequent to his hospital admission, he complained of bifrontal headache, residual vertigo and a mild and difficult to describe visual problem with reading. MRI and CT examination revealed an extensive right-lateralized cerebellar infarct in the distribution of the right posterior inferior cerebellar artery, with no other visible brain abnormalities (see Fig. 1).

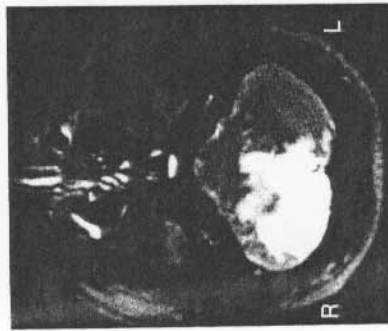


Fig. 1. Horizontal MRI section from patient RC1 showing extensive right cerebellar infarction.

Neurological examinations revealed a smaller right pupillary size as compared with the left. Muscle tone was felt to be slightly decreased in the right arm as compared with the left. Finger-nose-finger testing on the right side revealed a mild degree of ataxia. The remainder of the segmental neurological examination was normal. The patient was discharged 2 wks after his stroke without significant deficits noted by neurologists, and he soon resumed his private law practice on a full-time basis. Twelve months after his stroke, the patient died suddenly and unexpectedly from natural causes. No autopsy was performed. The patient will be referred to as RC1, an abbreviation for the location of his lesion.

Six months after his stroke, RC1 self-reported few remaining problems. He noted occasional episodes of vertigo, which most often followed a rapid head rotation; a decrease in the legibility of his handwriting, most noticeable when writing quickly; a diminished ability to make precise shots in pool; an increased incidence of 'slips of the tongue' (which, based upon his self-explanation, appeared to be semantic paraphasias); a decline in his 'instant recall abilities', e.g. the ability to instantly associate the clients' names with details of their cases; and a shortened attention span, which he attributed to his cessation of smoking. When questioned, RC1's wife also mentioned his 'slips of the tongue', but did not report any other problems or changes in his personality.

RC1 was tested acutely one and a half weeks after his stroke, and subsequently 2, 6, 9 and 10 mths later. Since RC1 did not show marked changes in his performance, the results will be discussed without reference to the date of testing. Informed consent was obtained prior to all testing sessions.

Control subjects

Three right-handed male subjects were used as controls for RC1. In addition to sex and handedness, they were matched for age, education and intelligence (see Table 1). Control subjects participated in two

Claims that the cerebellum contributes to cognitive functions are largely based on anatomical connections and phylogenetic development. The more recently evolved neocerebellum, which consists primarily of the lateral hemispheres and dentate nucleus, may be ideally suited to deal with high-order tasks involving cortical processing (reviewed by Leiner *et al.*, 1986). Phylogenetically, neocerebellar growth has paralleled that of the frontal cortex (Dow, 1942). Input into the neocerebellum is predominantly cortical, via cortical terminations in the pontine and olivary nuclear regions which project to neocerebellar structures (Dow, 1942). Neocerebellar efferent cortical projections are relayed through the thalamus primarily to motor areas, though there is evidence that in higher primates output may extend further frontally (Sasaki *et al.*, 1979; Asanuma *et al.*, 1983; Miyata and Sasaki, 1983).

Only a limited amount of behavioural evidence in humans, and none in other primates, is available to support claims that the cerebellum has important non-motor functions. Ivry and Keele (1989) studied patients with Parkinson's disease, cerebellar damage, cortical damage and peripheral nerve injury on two different tests of timing functions: the first measured the ability of subjects to produce and maintain a simple rhythm, and the second measured the ability of subjects to discriminate differences between interval durations. The cerebellar group showed deficits in both timing production and perception. Bracke-Tolkmitt *et al.* (1989) studied five patients with either cerebellar lesions or atrophy using a battery of standard neuropsychological tests. Compared with age- and education-matched controls, the patients were impaired on verbal, spatial and general ability intelligence measures. Patients also performed significantly poorer than controls on a verbal paired associates test, and a conditional associative learning task in which the subjects had to learn, by trial and error, arbitrary associations between six words and six colours. The patients were not significantly impaired, relative to controls, on most tests of memory (e.g. digit span, delayed recall of stories, etc.), or on the Wisconsin Card Sorting Test. Studies of cerebral blood flow and metabolism in normals have recently shown increased cerebellar activity during tasks in which subjects are instructed to imagine motor movements (Decety *et al.*, 1990), and during the learning as compared with recognition phase of a task requiring tactile discrimination of complicated geometrical objects (Roland *et al.*, 1989).

Our interest in the cerebellum was stimulated by a PET study of language processing previously conducted in our laboratory. As part of this study, subjects were asked to think of and say aloud appropriate verbs for presented nouns. During the control scan, subjects were asked merely to read aloud presented nouns. Unexpectedly, activation of a right lateral cerebellar region was found when subjects generated verbs, but not when they repeated nouns. This activation was clearly distinct from more medial and bilaterally-activated cerebellar regions found during both verb generation and noun repetition. The activation was found regardless of whether the nouns were presented auditorily or visually. In addition to the cerebellar activation, a set of left-lateralized cortical regions was activated during the verb generation but not noun repetition task. This correspondence (the cerebellar hemispheres receive contralateral cortical input, as well as the lack of lateral cerebellar activation during simpler verbal output tasks, made it difficult to account for the cerebellar activation on a purely motor basis (Peterson *et al.*, 1989).

3.5 h testing sessions, with 1–7 d between sessions. Informed consent was obtained from each control prior to both testing sessions. The order of tests was the same for all of the controls.

EXPERIMENTAL INVESTIGATIONS: METHODS AND RESULTS

Equipment, stimulus display and materials

All reaction time tests were administered using a Macintosh Ix computer system for controlling stimulus display and data acquisition. Unless otherwise noted, an electronic circuit (a voice-key) gated by the amplitude of a microphone input was used to measure voice onset times for verbally produced responses. Responses were also recorded onto a cassette tape. Non-verbal responses were made by pressing one of two designated keys on a standard ASCII keyboard. Stimuli were displayed in upper-case letters beneath a 3 × 3 mm cross-hair centred on either an Apple high resolution RGB or monochrome monitor. All words were open-class words with a frequency greater than five occurrences per one million words (Kucera and Francis, 1967). Pattern stimuli were adapted from Raven's Standard Progressive Matrices (Raven, 1956).

General abilities

On the basis of routine social interactions, RC1 appeared perfectly normal and unimpaired. As a means of more formally testing RC1's general level of performance, standard tests of language, memory, intelligence and 'frontal function' were administered. The results are listed in Table 1. RC1's scores on Wechsler

TABLE 1. INCLUSION CRITERIA AND PERFORMANCE ON STANDARD TESTS OF MEMORY, LANGUAGE AND FRONTAL FUNCTION

Inclusion criteria/performance	RC1		Controls	
	R	SD	R	SD
Handedness	49/50	48 ± 5	48 ± 5	SD
Age	17	16 ± 0	16 ± 0	SD
Years of education	131*	133* ± 4	133* ± 4	SD
Intelligence quotient (WAIS-R)	124*	131* ± 1	131* ± 1	SD
Memory	6	6 ± 0	6 ± 0	SD
Digit span	8	7 ± 1	7 ± 1	SD
Tapping span	60/60*			
Delayed match to non-sample				
Language	Spelling error			
Boston Diagnostic Aphasia Exam	60/60*			
Boston Confrontation Naming	No errors			
Token Task	5 errors*			
Frontal	(6 categories)			
Wisconsin Card Sorting Test	20/20*			
Picture Arrangement	42 words			
Word fluency ('CFL' test)				

* = above-average performance according to population normals.

Adult Intelligence Scale, Revised (WAIS-R) (Wechsler, 1981), Wechsler Memory Scale, Revised (WMS-R) (Wechsler, 1987) and Wisconsin Card Sorting Test (Heaton, 1981) were above average to superior. His score on the Picture Arrangement subtest of the WAIS was perfect, and his performance was rapid; he solved 8 out of 10 of the picture arrangement problems in less than half of the allowable time. On the Boston Diagnostic Aphasia Exam (Goodglass and Kaplan, 1983), RC1 appeared to have greater than average difficulty on an oral manipulation subtest, though his performance was in the acceptable range. Apart from

this observation, no evidence for any impairments was found across several diagnostic tests for language disorders (Kaplan *et al.*, 1983; Lezak, 1983).

Rule-based generation tasks

Since our interest in the cerebellum was motivated by our observation of cerebellar activity during a verb generation task, we began our investigations of RC1's deficits by asking him to perform a version of this task while he was still in the hospital. Following this initial testing, RC1 was subsequently tested on a variety of other rule-based generation tasks, in order to determine whether deficits noted initially were stable and limited solely to verb generation.

Verb generation

Methods. Two practice blocks were used to determine an appropriate rate of presentation, and then RC1 was presented with a new list of 40 high-frequency concrete nouns, at a rate of one every 2.2 s. He was asked to produce an appropriate verb for each noun. RC1 was told his answer should be an action word which described what the presented noun might do, or what it might be used for. The same list of nouns, in a different random order, was then presented for five more blocks, to give a total of six blocks with the same list. The instructions were repeated and the importance of speed stressed several times between blocks. For the seventh block, RC1 was asked to read aloud 80 nouns.

To measure both reaction time and response durations, RC1's responses were recorded onto one track of a cassette tape, and a brief tone inaudible to RC1 and synchronized to the onset of stimulus presentation was recorded directly on the second track of the cassette tape. Using a Macintosh Ix computer and MacRecorder software, the tape was digitized and amplitude envelopes were obtained for each response. Reaction times and response durations were calculated by measuring the latencies between tone and response onsets and response offsets.

Control subjects were given the same instructions and block sequence, and words were presented using identical display and rate parameters, as well as order of presentation. Reaction times were determined using a voice-key to measure voice-onset times.

Results. RC1's simple naming speed was slower than that of controls: his median reaction time for reading aloud the nouns presented in block 7 was 642 ms, over 2.5 standard deviations above the mean of 513 ms for controls. However, RC1's median reaction time for verb generation in block 1 was 1045 ms, within the range of control values (mean for controls was 1161 ms ± 348 SD). Most importantly, while all three controls showed a significant 3.9 to 7.5% reaction time decrease per block ($P < 0.015$ for all controls, simple linear regression), RC1 did not show a significant correlation between reaction time and block (slope = 1% decrease per block, $P = 0.38$, simple linear regression). Results are shown graphically in Fig. 2.

In addition to his learning deficit, RC1 also produced an abnormally high number of non-verb associates for the presented nouns. For instance, whereas normal subjects usually respond to the noun 'razor' with the verb 'shave', RC1 said 'sharp'. Further examples are given in Table 2, which lists responses given by RC1 for the first 25 nouns presented in block 1. For comparison, the responses of the first control subject tested and the most common response to each noun are also listed. The typicality of responses made by RC1 and control subjects were evaluated by comparison with a corpus of responses generated by other subjects. A response was defined as atypical if none of 35 previous subjects had generated the same answer. Results are shown in Fig. 3. Controls averaged 13% atypical responses across all blocks of the task. RC1, on the other hand, performed more than eight standard deviations above the control mean, averaging 55% atypical responses; furthermore, he showed no tendency to correct his 'errors' across blocks (0% decrease in errors per block, $P = 0.93$, simple linear regression).

Other rule-based generation tasks

Method. The method used for the verb generation task was modified so that the rate of stimulus presentation was paced by each subject. Each word remained on the screen until either a response was made or 9 s had elapsed since the initial presentation of the word, at which point the word was erased. Following a 1.5 s intertrial interval, during which only a central cross-hair remained on the screen, the next word was presented.

For each of the generation tasks, subjects were given a particular rule by which they were to generate a response to each presented word. In order to ensure subjects understood each task, they were given three practice trials with feedback about the correctness of their responses. Following the three practice

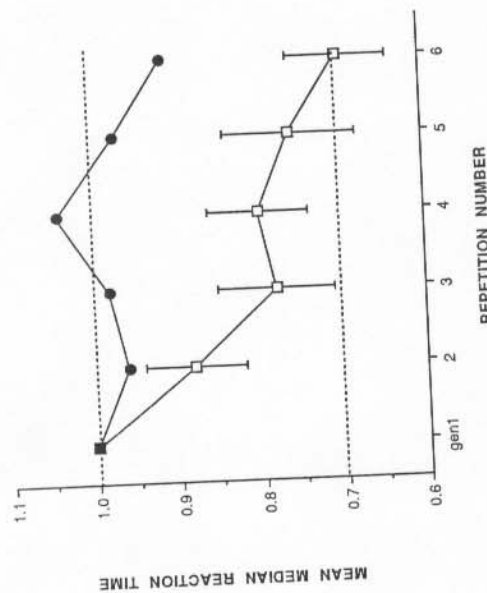


FIG. 2. Reaction times across six repetitions of the verb generation task for RC1 (closed circles) and three controls (open squares). Values are normalized to the mean median reaction time for the first block of the task (gen1). Upper dashed line indicates initial performance, lower dashed line indicates mean performance of the controls on the final repetition. Error bars indicate standard error of the mean for controls.

trials, subjects were presented with 20 words, and asked to verbally produce their responses as quickly as possible. The same 20 words were then presented, in a different order, twice more, and subjects were told they were to work at giving their answers as quickly as possible. No words were used across more than one generation task.

Responses on all tasks but the verb generation were assessed by asking five naive raters to evaluate the correctness of all responses. For each task, a scoring sheet was created which consisted of 20 stimulus words; after each stimulus word all unique responses, in alphabetical order, generated by RC1 and the control subjects across the three blocks of the given task were listed. The instruction for the given generation task was provided at the top of the sheet, and based upon this instruction raters were asked to circle all responses which they felt were incorrect. Total rater error for each block of each generation task was then computed by summing, across raters, all circled responses made by a subject in that block; thus, the maximum total rater error for a given block is 100 (20 responses, each circled as incorrect by the five raters).

The specific generation tasks were as follows. (1) Category generation: 'Each word will be an example of a member of a category; you should try to think of a label for the category represented by the word. For example, if given "colonel" you might say "officer", or for "Columbus" you might say "explorer".' (2) Attribute generation: 'You should think of a characteristic of the word; something the word usually has or possesses. It might be a physical part of the word, or something more abstract. It should be something that "belongs" to the word. For example, if given "rifle" you might say "trigger", or for "continent" you might say "rivers".' (3) Synonym generation: 'You should think of a synonym for each word; a word which means roughly the same thing as the word you see. For example, for "pig" you might say "hog", and for "shove" you might say "push".' (4) Phoneme generation: 'For each word, take the first sound in the word, and give another word that begins with the same first sound. Your answer does not have

TABLE 2. VERBS GENERATED IN RESPONSE TO PRESENTED NOUNS (FIRST 25 RESPONSES PRODUCED IN BLOCK 6)

Presented noun	Generated response	
	RC1	Control (A.F.)
Tree	Treehouse*	Climb
Money	Market*	Spend
Blanket	Warm	Wrap
Razor	Sharp*	Shave
Ice	Cool	Freeze*
Job	Work	Work
Toy	Play	Play
Gun	Hurt*	Shoot
Broom	Clean	Sweep
Scale	Weigh	Weigh
Hose	Fire	Water
Letter	Read	Write
Foot	Ten*	Scratch*
Oven	Heat	Heat
Bed	Sleep	Sleep
Bee	Sing	Make
Lens	See	Spell*
Soap	Clean	See
Dog	Cat*	Wash
Plane	Boat*	Play
Fist	Ten*	Fly
Brick	Red*	Hit
Pill	Small*	Throw
Pool	Swim	Take
Phone	Listen	Swim
		Call

* = response not generated by any of 35 previous subjects; ** = percentage of responding subjects who generated given answer.

to look like the presented word, have the same meaning, or even start with the same letters (for example, "c" and "k" sometimes sound alike). Sometimes the initial sound will not be made from a single letter, for example, the "cl" sound in "club". For example, given the word "ideal" you might say "island", and for "club" you might say "cluck". (5) Verb generation: 'For each word, you should think of an associated verb; something you might do to the word or something it might do. For example, for "picture" you might say "frame", or for "hand" you might say "grasp".' A subset of the nouns used in the previous study of verb generation were used as stimuli. Control subjects were not tested on this task, since they were asked to perform the original version of the verb generation task in the same session.

Results. Results are presented in Table 3. RC1's reaction time decreases on the synonym, attribute and category generation tasks were more than three standard deviations above the decreases shown by controls. Once again, RC1's initial performance was within the range of control values for all but one of the generation tasks; for the category generation task, RC1 was initially faster than all three of the controls, though his median reaction time was still within two standard deviations of the mean for controls. When retested on the verb generation task, RC1 showed a median reaction time decrease of 18%, which, though better than his prior improvement on the generate task, was still below the performance of the controls on the synonym, attribute and category generation tasks (decreases for controls ranged from 26% to 49%). The one generation task for which RC1 did show a normal reaction time decrease with learning was the phoneme generation task; RC1's median RT decreased 64%, compared with 77% for the normals (a difference of less than one standard deviation).

RC1 also produced a large number of incorrect answers. For example, when asked to generate a synonym to 'garbage' he responded with 'old', when asked to generate a category label for 'cookie' he responded

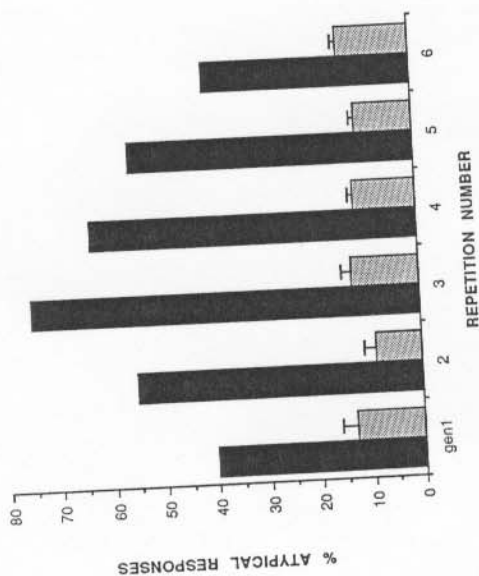


FIG. 3. Percentage of atypical responses across repetitions of the verb generation task for RC1 (filled columns) and three controls (stippled columns). Responses are defined as atypical if none of 35 previous subjects generated the same answer for a given noun. Error bars indicate standard error of the mean for controls.

TABLE 3. INITIAL PERFORMANCE AND LEARNING ACROSS GENERATION TASKS

Task:	Reaction time (ms)				Learning (block 1/block 3 reaction time)			
	Synonym	Category	Attribute	Phoneme	Synonym	Category	Attribute	Phoneme
A.F.	876	1118	1202	1512	0.72	0.63	0.59	0.59
W.A.	1518	1302	2338	3657	0.74	0.72	0.51	0.84
K.A.	1186	1728	1454	1494	0.76	0.53	0.56	0.87
Mean	1193	1383	1664	2221	0.74	0.63	0.55	0.77
SD	321	313	596	1244	0.02	0.10	0.04	0.15
RC1	1236	843	1545	3291	0.91	0.96	0.81	0.64

with 'eat', and when asked to generate an attribute for 'butterfly' he responded with 'insect'. Results from the error analysis are given in Table 4. On none of the blocks for any of the generation tasks was RC1's rater error less than any of the controls. For eight out of 12 blocks, RC1's rater error was more than 2.5 standard deviations above the mean control performance. With the exception of the attribute generation task, RC1 showed no tendency to reduce his errors across blocks; his rater error summed across all of the first blocks of the generate tasks was 87, versus a total of 85 across the third blocks. RC1's responses on the verb generation task were evaluated using the method described for the initial longer version of the task. 0%, 0% and 10% of his responses were atypical on blocks 1, 2 and 3 of the task, respectively.

Discussion. Taken as a whole, RC1's performance on the various generation tasks suggests he had a general deficit in producing typical and correct responses, as well as an abnormal lack of improvement with practice. RC1's improvement on his second exposure to the generate task, and his normal performance on the phoneme generation task, stand as exceptions to his performance on the other generation tasks.

TABLE 4. RATER ERROR ACROSS BLOCKS OF GENERATION TASKS

Task:	Synonym			Category			Attribute			Phoneme		
	1	2	3	1	2	3	1	2	3	1	2	3
A.F.	12	9	9	13	14	14	3	3	3	1	1	3
W.A.	10	8	9	6	6	12	14	12	8	5	8	5
K.A.	10	8	7	15	7	9	4	5	3	8	1	5
Mean	11	8	8	11	9	10	6	7	6	6	2	5
SD	1.2	0.6	1.2	7.4	4.4	4.0	4.9	5.6	5.2	4.0	2.3	2.5
RC1	26	24	25	30	30	27	20	18	12	11	5	16

It seems most likely that RC1's low error rate on the short version of verb generation task reflected his extensive exposure to the verb generation task, as well as the nouns used as stimuli, during his initial testing; this exposure included not only performance of the original generate task, but also more informal use of the noun list and task. However, it is possible that his improvement was due to either some recovery from his lesion, or learning of the task which occurred following the initial testing (due to consolidation, etc.).

It is unclear why RC1 showed normal learning of the phoneme task. Two possibilities seem most likely: (1) a fundamental difference exists between the phoneme and other generation tasks (for example, unlike the other tasks, responses for the phoneme task might be generated without reference to a semantic associate); or (2) based upon block 1 reaction time values, the phoneme is the most difficult of the generation tasks; it is possible that for both RC1 and controls, the learning reflects a general, rather than item-specific, improvement on the task, and had more trials been conducted RC1 would have plateaued at a value much higher than the controls. The available data do not allow us to distinguish between these and other possibilities. Investigations in other patients should clarify this issue and yield valuable information about the mechanisms underlying the learning deficits.

Converging studies

RC1's performance on rule-based generation tasks suggested two specific areas in which RC1 was impaired: (1) practice-related learning; (2) error detection. For each of these areas, a set of converging tasks was designed to evaluate more fully the nature and extent of RC1's difficulties.

Learning task: concurrent discrimination learning

Unlike the generation tasks, subjects were not under time pressure, nor did they have to select an answer using semantic and/or syntactic rules. Both word and pattern versions of the task were administered. For the word version, 20 pairs of words were used, and one word in each pair was arbitrarily preassigned to be the positive member. Subjects were told that they were to learn, through trial-and-error, the positive word in each pair; after indicating a selection by pointing, subjects were told whether they were correct or incorrect. The same set of word pairs was then repeated until a subject made no errors on four consecutive blocks, up to a maximum of 20 blocks. In order to prevent subjects from learning a pattern of pointing, pair order and item position were varied across blocks. Members of each pair were matched for frequency, letter and syllable length, and part-of-speech. Subjects proceeded through the cards at their own pace. For the pattern version of this task the same paradigm was used, except the stimuli consisted of 18 black-and-white pattern pairs repeated across a total of 12 blocks. Both word and pattern pairs were displayed on 4 × 6 index cards.

Results. Results from the word discrimination learning are shown in Fig. 4. For word discrimination learning, all controls showed a significant negative correlation between percent incorrect responses and block number ($P < 0.01$ for all controls, simple linear regression); for each subject, data from all blocks prior to the third consecutive block with no errors was used for the analysis. The controls also showed a similar correlation for the pattern discrimination learning ($P < 0.01$ for all controls, simple linear regression; all blocks were used for each control). RC1, however, failed to show significant improvement across blocks for either the word or pattern discrimination learning ($P = 0.97$ and 0.28 , simple linear regression). Based upon the regression slopes and intercepts, the mean number of trials required to achieve perfect performance for controls extrapolates to 14 ± 4 for the word discrimination and 17.5 ± 7 for the pattern discrimination, versus 1880 and 46 for RC1.

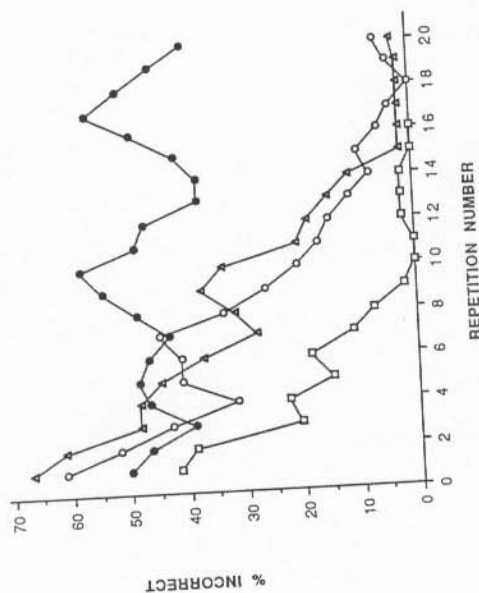


FIG. 4. Percentage of incorrect responses across repetitions of the word concurrent discrimination learning task for RC1 (closed circles) and three controls: A.F. (open circles), W.A. (open squares) and K.A. (open triangles). Values are smoothed across three repetitions by calculating the mean for each repetition and the preceding (if any) and succeeding (if any) repetitions.

Learning task: Tower of Toronto

The Tower of Toronto puzzle, a simplified version of the Tower of Hanoi, was administered according to the procedures outlined by Saint-Cyr *et al.* (1988), with the exception of allowing an unlimited number of moves to complete the puzzle instead of placing a 50-move maximum. Solutions to this puzzle are similar in concept to those for solving the more complicated Tower of Hanoi: a set of discs, each a different colour, must be moved from a starting to a finishing position by shifting individual discs among three pegs. The only rules are that only one disc can be moved at a time, and a darker coloured disc can never be placed on top of a lighter disc. The testing begins with three practice blocks, in which only three discs are used. Immediately after the practice blocks, subjects are requested to complete the puzzle five times in succession, using four discs. After a 1 h to 1.5 h delay, subjects are again asked to complete the puzzle five more times in succession, again using four discs. With three discs, the puzzle can be completed in a minimum of seven moves, whereas with four discs a minimum of 15 moves is required.

Results. An index score was computed according to a formula outlined in the original methodological description of the puzzle (Saint-Cyr *et al.*, 1988). For the 10 blocks using four discs the following is summed:

index score = (no. of blocks with 17 or less moves + 10) - (no. of blocks with 30 or more moves).

A score of less than 9 is considered impaired. RC1's score was 1, four standard deviations below the mean score of 11 for controls. For purposes of comparison, RC1's score is similar to reported values for advanced stage Huntington's disease patients, who show signs of global dementia (Saint-Cyr *et al.*, 1988). RC1 does show improvement on the task. He averaged, for the first five blocks, 52 moves required to complete the puzzle, versus an average of 34 moves required across the last five blocks, a significant decrease ($P < 0.01$, unpaired two-tailed t test). RC1's improvement occurred largely across blocks 1-6;

he plateaued at 33 moves required to complete the puzzle, a value higher than the smoothed mean required by controls on any of the 10 blocks and still above the 30-move ceiling for not deducting points from the index score (see Fig. 5).

RC1's improvement can be analysed by examining the sequences of moves he made to solve the puzzle across the various blocks. If all of the possible legal moves of the Tower of Toronto puzzle are examined, four 'critical choices' can be isolated. These correspond to nodes along various solution sequences in which a non-optimal choice produces the greatest penalty in terms of the number of moves required to recover from the error. Learning puzzles such as the Tower of Toronto involves not only reducing the number of moves required to complete the puzzle, but also applying the solution principles which allow the 'critical choices' to be made correctly. Learning the solution principles appears to be a skill acquired independently of an ability to verbalize a solution strategy or to consciously recollect previous experience with the puzzle (Cohen *et al.*, 1985). While RC1 reduced the number of moves he required to recover from a non-optimal 'critical choice' across blocks 6-10 (primarily because he 'back-tracked' through the puzzle less frequently), he did not appear to learn the solution principles of the puzzle. On block 9, 3 out of 4 of RC1's 'critical choices' were not-optimal; and on block 10, 4 out of 4 of his 'critical choices' were not-optimal; for both blocks RC1's performance was more than a standard deviation above the control means of 1.3 and 1.0 non-optimal choices on blocks 9 and 10, respectively.

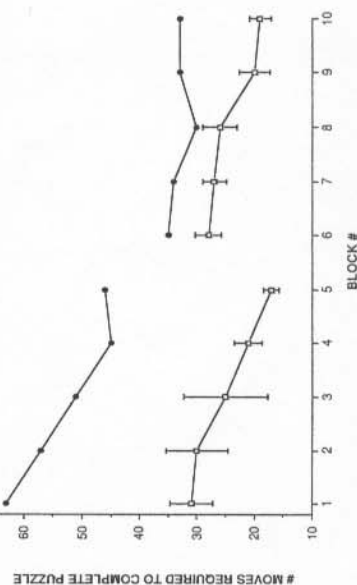


FIG. 5. Number of moves required to complete the Tower of Toronto puzzle across 10 blocks for RC1 (closed circles) and three controls (open squares). For all 10 blocks four discs were used, allowing the puzzle to be completed in a minimum of 15 moves. Following the fifth block there was a 1 h to 1.5 h delay. Values are smoothed across three blocks by calculating the mean for each block and the preceding (if any) and succeeding (if any) blocks; blocks 1-5 were smoothed independently of blocks 6-10. Error bars indicate standard error of the mean for controls.

Error detection: recognition of errors

For the most part RC1 did not seem to realize that his responses were abnormal. When initially tested on the verb generation task, for instance, RC1 only once indicated that he had made a mistake: when he remarked, 'saying more than one word'. At several times during his initial testing, RC1 was auditorily given nouns he had previously seen and asked to generate verbs for them. In some cases, when he produced an incorrect response, he was reminded that a verb should be an action word telling what the noun might do or what it might be used for, and was provided with an example of an appropriate response to the

noun. Under these conditions RC1 still made errors, and only once indicated he had given a non-verb answer ('wire' in response to 'phone'). During subsequent rule-based generation tests he indicated that he thought some of his answers were wrong, but did not explicitly identify any incorrect answers; furthermore, as already discussed, overall he failed to reduce his errors with repeated exposure to the same stimuli.

Error detection: contextual influence

When given stronger constraints for the selection of responses, RC1 made fewer errors. On the day following his initial testing on the verb generation task, RC1 was auditorily presented with 38 of the nouns for which he had generated verbs the previous day. For the first 20 nouns, RC1 was asked once again to produce a verb answer. Immediately following this task, RC1 was asked to respond to the next 18 nouns by replying, 'You (answer) with it', or 'It (answer)'. The typicality of RC1's responses were classified as previously described, and compared with responses produced on his sixth exposure to the nouns the previous day. For the first 20 nouns, 11 out of 20 of his responses were atypical (accepting atypical verb derivations, such as 'swimming' in response to 'pool' as typical responses), versus 8 out of 20 the previous day. For the next 18 nouns, 1 out of 17 of his responses was atypical ('travel' in response to 'boat'), versus 8 out of 17 in the previous day.

Error detection: timed forced-choice adjective/verb discrimination

For a forced-choice test of verb/adjective discrimination, subjects were presented with individual words that they identified as either adjectives or verbs by pressing one of two response keys. Subjects were told that the adjectives would be description words, whereas the verbs would be action words. Each word remained on the screen until either a key was pressed or 9 s had elapsed since the initial presentation of the word. Following a keypress, the word was erased, and after an intertrial interval of 1.5 s the next word was presented.

Results. When asked to decide whether a presented word was an adjective or a verb as quickly as possible, RC1's median reaction time was 2054 ms, more than four standard deviations above the mean of 919 ms for controls. RC1's accuracy (94% correct) was within a standard deviation of the mean for controls (90% correct).

Error detection: untimed forced-choice category and synonym discrimination

RC1 was given a worksheet containing 40 words, some of which had previously been presented as stimuli during the synonym generation task. Beside each word there were two possible answers, some of which were responses he had made previously to the words during the generation task. Only one answer was listed as a synonym in an on-line computer thesaurus (Word Finder, Microlytics, Inc., Pittsford, NY, USA). All possible answers were associated to the stimulus word; for example, for the word 'wed' the possible choices were 'ring' and 'marry', and for the word 'beautiful' the choices were 'glamorous' and 'gorgeous'. He was asked to circle the 'best' synonym for each word. He was told that some of the answers would be close in meaning, and that he should think carefully before making his decision. He was told to take as much time as he wanted to complete the worksheet. Due to an oversight, controls were given a slightly different worksheet, in which the choices for the word 'tall' were 'lanky' and 'high', rather than 'lanky' and 'skyscraper', and one of the stimulus words and associated possible answers was different. A similar worksheet was created also containing 40 words, some of which had previously been presented as stimuli during the category generation task. Once again, possible answers were both associated for a given stimulus word, and some choices were those he had made previously to words during the category generation task. Subjects were told to circle the best category label for each word (e.g. circle 'colour' rather than 'golden' in response to the word 'yellow'). Both RC1 and controls were given the same category worksheet.

Results. In calculating errors, only those stimulus words and associated possible answers which were common to both versions of the synonym worksheet were considered. RC1 made five errors, over three standard deviations above the control mean of 0.7 errors. RC1's errors were all made when asked to select from two closely associated words, e.g. 'unclear' and 'explore' as alternative answers for 'discover'. On the forced-choice category worksheet RC1 made no errors, less than a standard deviation below the mean of 0.7 errors for controls.

Specific dissociations

Delayed non-matching to sample

RC1 may have been unable to distinguish between or remember stimuli used for the word and pattern discrimination learning tasks. As a test of this possibility he was given both word and pattern versions of a delayed non-match to sample task.

Method. A trial consisted of a single word or pattern stimulus displayed in the centre of a sample card for approximately 3 s. The card was then removed from sight. After a 5 s, 15 s or 60 s delay period, a test card was shown containing a novel stimulus and the previously presented sample stimulus. RC1 was asked to point to the novel stimulus. The delay lengths were pseudo-randomly mixed, as was the position of the novel stimulus on the display card.

For the word version of this task, words were printed in bold-faced lower-case letters and taped to a 4×6 inch index card. The sample and novel stimuli words used in each trial were matched for frequency, letter and syllable length, and part-of-speech. Five trials with a delay of 5 s, eleven trials with a 15-s delay, and nine trials with a 60-s delay were given.

For the pattern version of this task, black-and-white patterns were taped to a 4×6 inch index card. Eight trials with a delay of 5 s, 15 trials with a delay of 15 s and 15 trials with a delay of 60 s were given.

Results. RC1 made no errors on either the word (25 out of 25 correct) or pattern (35 out of 35 correct) versions of this test. Control subjects were not tested on either version of the task.

Stroop colour/word interference

It is possible that RC1 knew that his answers were incorrect, but was unable to prevent himself normally from responding with stronger associates to the presented rule than those which match the rule for response generation. In order to determine whether RC1 had a global inability to inhibit pre-potent responses, he was asked to perform a Stroop colour/word interference task, a task in which subjects are provided with strong conflicting information which must be ignored in order to produce a correct response (Stroop, 1935).

Method. For the first block (the incongruent colour block), each stimulus was one of three colour names ('red', 'blue' or 'green') displayed in an incongruent colour (red, blue or green). Subjects were asked to name the display colour as quickly as possible. For the second block (the congruent colour block), a string of Xs was displayed in either red, blue or green, and subjects were again asked to name the display colour as quickly as possible. For the third block (the congruent word block), one of three colour names ('red', 'blue' or 'green') was displayed in black, and subjects were asked to read the colour name as quickly as possible. Only two control subjects were given this task, because the third control subject was colour-blind.

Results. Across all blocks, RC1's median naming time was greater than that of the two tested controls: 760 ms (RC1) versus 702 ms and 702 ms (controls) for the incongruent colour block; 584 ms (RC1) versus 543 ms and 560 ms (controls) for the congruent ink block; and 560 ms (RC1) versus 509 ms and 451 ms (controls) for the congruent colour block. For all three subjects, an incongruity ratio was calculated by dividing the reaction time for the incongruent colour block by the average reaction time value for the two congruent blocks:

$$\text{incongruity ratio} = \text{incongruent colours} / ((\text{congruent words} + \text{congruent colours})/2).$$

RC1's incongruity ratio was 1.33 versus 1.33 and 1.39 for the two controls, indicating the degree of interference caused by conflicting information was the same for both RC1 and controls, despite RC1's slower naming times.

Lexical decision

As mentioned in the analysis of RC1's generation task errors and reaction times, his median response time across all generation tasks was not significantly different from controls, despite the fact that his simple naming time was slower for nouns and stimuli used for the Stroop task. This raises the possibility that RC1 had a global speed/accuracy trade-off abnormality. A lexical decision task was administered as a test of this hypothesis.

Methods. Subjects were presented with letter strings that they identified as either real words or pronounceable non-words by pressing one of two response keys. Each letter string remained on the screen

until either a key was pressed or 9 s had elapsed since the initial presentation of the letter string. Following this, and other generation tasks, was characterized by the production of associated but incorrect answers according to the rule given for response generation. Even when placed in two-alternative forced-choice situations, RC1 still performed below controls. RC1 also failed, unlike controls, to decrease his reaction time with practice on a given set of words. This learning deficit, initially noted as a failure to improve with practice on the generate task, extended to a variety of other tasks, such as word and pattern concurrent discrimination learning.

In contrast to his deficits, RC1's scores of all administered standard neuropsychological tests, including those of intelligence, language, 'frontal function' and memory, were at or above normal. He also performed similarly to controls on specific tasks designed to measure delayed recall and control of response production (both the ability to inhibit a pre-potent response and maintain a normal speed/accuracy trade-off criterion).

Summary

RC1 failed to successfully complete and normally learn the verb generation task. His performance on this, and other generation tasks, was characterized by the production of associated but incorrect answers according to the rule given for response generation. Even when placed in two-alternative forced-choice situations, RC1 still performed below controls. RC1 also failed, unlike controls, to decrease his reaction time with practice on a given set of words. This learning deficit, initially noted as a failure to improve with practice on the generate task, extended to a variety of other tasks, such as word and pattern concurrent discrimination learning.

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DISCUSSION

Attributing causality to the cerebellar damage

A concern with any single-case study must be the extent to which the results may be due to an individual peculiarity, pre-existing impairment or undetected neurological damage. RC1's above-average to superior performance on standard intelligence, memory and language tests makes it difficult to account for his disorders on the basis of a global dysfunction; these tests are sensitive measures of even early stages of senile dementia (Storandt *et al.*, 1984; Adams *et al.*, 1986; O'Donnell *et al.*, 1988). Furthermore, it is unlikely that RC1's deficits can be explained on the basis of task difficulty: even Huntington's disease patients with clear signs of dementia achieve higher scores on the simple Tower of Hanoi task than RC1 (Saint-Cyr *et al.*, 1988). Finally, in three independent readings, radiologists failed to note any evidence in RC1's MRI and CT scans for cortical damage, including excessive cerebral atrophy, infarcts, haemorrhages or other non-specific damage.

It is possible that RC1's cerebral metabolism was affected by his cerebellar damage. Secondly reduced cerebellar metabolism ('crossed cerebellar diaschisis') has been correlated with frontal cortical damage in approximately half of patients examined (Pantano *et al.*, 1986; Baron, 1989); though not as well characterized, similar changes in the contralateral frontal cortex ('reverse cerebellar diaschisis') have been correlated with cerebellar damage in some patients (Broich *et al.*, 1987; Anderson *et al.*, 1988). Functional deficits have been associated with secondary hypometabolism: in general, the hypometabolism and associated deficits have been interpreted as a loss of functional input to the secondary region, rather than a dysfunction of the region (Deuel and Collins, 1984; Powers and Raichle, 1985; Perani *et al.*, 1987; Metter *et al.*, 1989); however, the relationship between secondary metabolic changes and functional deficits is an active area of research, and much remains to be answered. It is reasonable to question whether RC1's deficits might be accounted for by a purely secondary regional dysfunction.

Some aspects of RC1's performance might suggest some frontal impairment resulting

from his cerebellar damage. However, despite RC1's impairments on some language tasks, and his production of errors, he showed no evidence of a 'frontal lobe syndrome'. He was not impaired on standard tests of language difficult for frontal aphasics to perform (Goodglass and Kaplan, 1983), and his word fluency was normal, a language deficit commonly found even in non-aphasic frontal patients (Benton, 1968; Perret, 1974; Miller, 1984). Frontal patients tend to produce responses which are contextually inappropriate, reverting to the production of 'habitual' responses (Luria, 1966, 1980; Stuss and Benson, 1986). Though not systematically investigated, case reports suggest that some frontal patients make errors despite their knowledge that their response is incorrect (Luria, 1980; Konow and Pribram, 1970; Picton *et al.*, 1986); RC1, on the other hand, did not appear to recognize his errors. Furthermore, he was able to inhibit strong habitual responses on the Stroop task, and made only six errors on the Wisconsin Card Sorting Test; both of these tasks are difficult for frontal patients to perform, because of difficulty in maintaining a cognitive 'set' and a tendency for response perseveration (Milner, 1963; Drewe, 1974; Perret, 1974; Robinson *et al.*, 1980). On the Picture Arrangement subtest of the WAIS, a task which appears to be sensitive to difficulties in temporal sequencing and planning associated with frontal damage (Medina *et al.*, 1954; Logue *et al.*, 1968; Hamlin, 1970), RC1's score was perfect. Finally, no changes in RC1's personality were reported by his wife, contrary to common reports that frontal patients tend to lack drive, self-motivation and inhibition of socially-inappropriate behaviour (Penfield and Evans, 1935; Grafman *et al.*, 1986; Stuss and Benson, 1986).

The relationship between the cerebrum and cerebellum

Based upon present theories regarding secondary hypometabolism, and the pattern of deficits seen in RC1, it is most reasonable to conclude that his deficits were more closely associated with his primary cerebellar damage than with a secondary frontal or other cortical dysfunction. This is not to argue, however, that deficits common to patients with cerebral damage and patients with cerebellar damage cannot be identified. In fact, evidence already exists which suggests prism adaptation might be impaired following either frontal or cerebellar damage (Weiner *et al.*, 1983; Canavan *et al.*, 1990), and performance on a task similar to the Tower of Hanoi appears impaired following frontal damage (Shallice, 1982). These results do not mean that the processing required for successful performance on these tasks is solely dependent upon the frontal cortex. Rather, it suggests that for particular tasks there is a strong functional relationship between the cerebellum and the frontal cortex; presumably, each region performs a particular type of processing which may be important for successful task performance, and loss of either one may produce impairments. In other words, mental operations appear to be localized, but performance of a complex task requires an integrated ensemble of brain regions (see Damasio and Damasio, 1990, and Posner *et al.*, 1988 for a discussion of this theory). For instance, in addition to the right cerebellum, a number of frontal cortical regions are activated when normal subjects produce verb associates to visually presented nouns, and these regions are activated by different components of the task (Peterson *et al.*, 1989).

How the cerebellum and the cerebral cortex might interact for successful task performance is a complex question beyond the scope of the present report (see Leiner *et al.*, 1991 for a discussion of this topic). The purpose of the present study was to

examine what particular processing deficits might be associated with damage to the cerebellum. The remainder of the discussion will focus on how RC1's learning and error detection deficits can be understood in light of known motor functions of the cerebellum, and the implications the results may have for mechanisms of memory and learning. Substantiation of the hypotheses developed regarding RC1's deficits, and a more complete ability to place them in the context of deficits associated with damage to other brain regions, will clearly require further investigation, involving cerebellar as well as other patient populations (such as those with frontal or medial temporal cortical damage).

The cerebellum and error detection

RC1 produced a large number of inappropriate responses across a variety of rule-based generation tasks. These errors were particularly striking because they contrasted so markedly with his extremely fluent and grammatically correct conversational skills, as well as his normal performance on standard measures of language function. It is possible that RC1's errors were caused by an inability to control his output. However, RC1's normal performance on tasks which require inhibition of a pre-potent response and establishment of a normal speed/accuracy trade-off criterion argue against this explanation. Furthermore, if RC1's errors resulted from a problem with response control, it seems most likely that he would have been aware of his errors. When RC1 responded once with a multi-word answer, he did comment that he had made a mistake; this suggests RC1 was capable of evaluating at least some type of errors after they had been made. On the other hand, during formal testing RC1 never explicitly identified any of his semantic/syntactic errors. Taken as a whole, the evidence suggests RC1's errors resulted from a diminished ability, on a trial-by-trial basis, to successfully evaluate the correctness of his responses, both before and after their production.

RC1 not only produced errors, but he also had difficulty perceiving errors: when asked in a two-alternative forced-choice test to select synonyms from non-synonyms, his performance was impaired. This suggests RC1's errors reflected a general impairment in both perception and production processes which require the detection of errors in at least some high-order analyses, including tasks requiring particular semantic/syntactic processing of linguistic information. Investigations of timing functions of the cerebellum have similarly led to a proposed role of the cerebellum in both timing production and timing perception (Ivry and Keele, 1989).

RC1's deficits in error detection are consistent with evidence that the cerebellum carries information regarding a variety of motor errors, and that this information can be used to make corrective adjustments to ongoing motor behaviour. This is well demonstrated by the vestibular-ocular reflex (VOR) and smooth-pursuit systems. The VOR helps stabilize visual images on the retina by producing compensatory eye movements in response to vestibular input caused by head movement. When an imperfect compensatory eye-movement occurs, the result is a displacement of an image on the retina (retinal slip) (Miles and Lisberger, 1981; Ito, 1982). In monkeys, some of the same neural machinery is used for accurate tracking of moving visual objects (Miles and Lisberger, 1981). Based upon Purkinje cell discharges in the cerebellar flocculus, it appears that climbing fibres carry information about retinal slip; furthermore, this climbing fibre discharge may be specifically related to retinal slip which needs to be corrected, and

not to other occurrences of retinal slip (such as occur when monkeys are required to fixate and avoid tracking a moving target). Analysis of the known VOR and smooth-pursuit circuitry suggests climbing fibre discharges alter Purkinje cell output, which helps compensate for VOR and smooth-pursuit errors (Stone and Lisberger, 1990).

Though the details are less complete, in other systems climbing fibres also seem to carry information about errors which result in corrective cerebellar output. Studies of cat and ferret locomotion have shown elevated climbing fibre discharges when the step cycle is unexpectedly perturbed (Lou and Bloedel, 1986; Andersson and Armstrong, 1987). In tasks requiring reaching to a spatial target, or movement of a manipulandum to a target zone, perturbations can be caused by changing the manipulandum load to the target. For these tasks also, climbing fibre discharge has been correlated with the perturbation (Gilbert and Thach, 1977; Wang *et al.*, 1987).

In summary, RC1's deficits and physiological recordings made during the performance of various motor tasks suggest that information about ongoing performance which signals a performance error is conveyed to the cerebellum, typically via climbing fibres. As a result, cerebellar output is modified, which in turn produces corrective motor output. In this sense, the cerebellum may act as a central interface between a sensory representation which in some environmental contexts may signal an error, and the motor response to a performance error.

The cerebellum and learning

Marr (1969), in an elegant theoretical demonstration based upon the architecture of the cerebellum, proposed that the cerebellum was a modifiable pattern recognition system which could be used to develop motor skills. Marr's cerebellar learning model was followed shortly by a similar model detailed by Albus (1971). Lesion and physiological studies have since provided compelling evidence to support the involvement of the cerebellum in learning and suggest that climbing fibres serve an important instructive function in the learning process. The role of the cerebellum in motor plasticity has been most extensively investigated in studies of the VOR. Though normally the reflex is extremely precise, performance can be disrupted by requiring subjects (monkeys, cats or humans) to wear magnifying or reducing prisms. Over time, the system adapts to the vestibular-visual gain changes produced by the prisms, and performance returns to initial levels (Jones, 1977; Miles and Eighmy, 1980). Plasticity of the system is lost, or severely reduced, following lesions of the cerebellar flocculus in rabbits and monkeys (Ito *et al.*, 1974; Lisberger *et al.*, 1984). Other types of motor plasticity are also affected following cerebellar damage. For example, performance in a manipulandum task which requires a precise motor output against a known load is disrupted by substitution of a novel load. Adaptation to such load changes is disrupted by cerebellar lesions in humans and monkeys (Gilbert and Thach, 1977; Keating and Thach, 1990). In both of these cases, climbing fibre discharge has been correlated with the learning process: in the early stages of learning, climbing fibre discharge is high, and after appropriate adaptation has been achieved, climbing fibre discharge declines to initiate levels (Gilbert and Thach, 1977; Watanabe, 1984).

Associative learning is also affected by cerebellar lesions. Eye-blinks in rabbits can be classically conditioned by pairing a conditioned stimulus (e.g. a tone or light flash) with an unconditioned stimulus (e.g. an air puff). Following training, the motor response

to an unconditioned stimulus (an unconditioned response) is also produced in response to the conditioned stimulus (a conditioned response) (Gormezano *et al.*, 1962). Lesions of the interpositus nucleus appear to abolish both reacquisition and retention of a conditioned response, while the unconditioned response appears largely intact (Yeo *et al.*, 1985; Lavond *et al.*, 1990; but see Welsh and Harvey, 1989). Cerebellar cortical lesions disrupt, but do not abolish, reacquisition of the conditioned response (Lavond and Steinmetz, 1989; Harvey *et al.*, 1990). Based upon evidence from both lesion and electrical stimulation studies, it appears that climbing fibres carry information about the unconditioned stimulus, while mossy fibres carry information about the conditioned stimulus (Yeo *et al.*, 1986; Lewis *et al.*, 1987; Steinmetz *et al.*, 1989). Initially, climbing fibre discharge is correlated with the presence of the unconditioned stimulus, but as the conditioned response is learned the discharge declines (Thompson, 1986).

Finally, the cerebellum appears to be involved in a variety of other types of conditioning, as well as some types of habituation. For example, the cerebellar vermis appears to be essential for both classically-conditioned bradycardia in rats (Supple and Leaton, 1990), and long-term habituation of the acoustic startle response (Leaton and Supple, 1986). Cerebellar lesions also disrupt conditioned leg flexion in dogs and fish (reviewed by Karamian *et al.*, 1969).

Despite above-average memory abilities, RC1 failed to learn normally a variety of tasks. Those tasks in which RC1 was impaired share similarities to motor tasks also affected by cerebellar lesions. The verb generation task can be thought of in some sense as requiring plasticity in a motor response. It may be that an important aspect of this task is the modification of the most typical but incorrect response to the presented word (either the name of the word or its strongest associate) so that the strongest associate becomes an appropriate verb. The concurrent discrimination task requires the subject to associate, through trial and error, one of two stimuli with a verbal reward. The task is similar to those types of motor conditioning shown to be affected by cerebellar lesions. For all of those tasks which appear to involve the cerebellum, practice results in the development of consistent responses to repeated stimuli. Mishkin and Petri (1984) have theorized that the learning which results automatically from experience with a stimulus-response relationship is distinct from a memory, and might be more accurately termed a 'habit'.

One critical question is the extent to which RC1's errors and failure to exhibit normal learning on the various generation tasks reflect dysfunction of a single underlying process. One possibility is that the process of detecting an error cannot be separated from that of correction and learning. Such an interpretation is consistent with PET evidence that cerebellar activation during performance of the verb generation task occurs in naive subjects who only performed the task once (Petersen *et al.*, 1989), and that reaction times decreased for control subjects upon second exposure to the list of nouns, even though they were unaware that the task would be repeated. Further supporting a possible link between error correction and learning is evidence that, for the VOR and visual/motor arm tasks, error information is used to correct for perturbations in an ongoing motor behaviour, and is correlated with adaptation to a consistent change caused by prisms or load changes. However, in none of these systems has a causal relationship between error information and learning been demonstrated.

Not only are RC1's learning and error-detection impairments consistent with postulated motor functions of the cerebellum, but they are also consistent with a growing body of data which suggests the existence of at least two different long-term memory systems. Studies of humans with severe amnesia caused by medial temporal and midline diencephalic damage have shown amnesics are severely impaired on memory tasks which appear to rely heavily upon conscious recall of previous experience (e.g. see Corkin, 1984; Squire, 1986). On the other hand, it has been shown that amnesics normally benefit from previous experience on some tasks. For instance, amnesics show normal improvement on a variety of skill learning tasks, such as mirror tracing (e.g. Cohen *et al.*, 1985; Squire, 1986; Knopman and Nissen, 1987). Amnesics also tend to show normal priming effects, i.e. the biasing of future responses or alteration of response times due to previous exposure to a particular stimulus (reviewed by Schacter, 1987). In general, the pattern of deficits found in humans has been replicated in monkey models of amnesia (e.g. see Aggleton and Mishkin, 1983; Zola-Morgan and Squire, 1984, 1985).

RC1, in many respects, appears to possess a pattern of deficits opposite to those found in human amnesics. Whereas typical scores for amnesics on the Wechsler Memory Scale are 79.3 (Aggleton *et al.*, 1988), 77.4 (Squire *et al.*, 1988), and 67 (Corkin, 1984), RC1's score of 124 is above average and comparable with his score on the WAIS-R evaluation of intelligence. RC1's delayed recall subscore was 121. Similarly, on both pattern and word versions of a delayed non-match to sample task, RC1 made no errors, while similar studies in monkey and human amnesics have reported greater than 25% errors following only a 30 s delay (Zola-Morgan and Squire, 1985; Squire *et al.*, 1988; Overman *et al.*, 1990).

Conversely, RC1 was dramatically impaired on the Tower of Hanoi task. Even populations with severe memory deficits, as measured by the WMS-R, appear to learn this task normally (Saint-Cyr *et al.*, 1988). Furthermore, there is some evidence that the more complicated Tower of Hanoi can also be learned by amnesics (Cohen *et al.*, 1985). Though amnesics have not been asked to perform the verb generation task, the absence of a significant hippocampal activation during performance of the task suggests it does not make important contributions to the learning of the task (Petersen *et al.*, 1989). Finally, studies with monkeys indicate that the hippocampus and amygdala may not be necessary for normal concurrent discrimination learning (Phillips *et al.*, 1988; Overman *et al.*, 1990). Given RC1's deficit on this task, normal learning may depend upon activation of a cerebellar learning circuit. However, a number of investigators have failed to replicate normal concurrent discrimination learning in human amnesics (Oscar-Berman and Zola-Morgan, 1980; Aggleton *et al.*, 1988; Squire *et al.*, 1988). Several interpretations exist for this discrepancy, including: (1) in humans, both the cerebellum and the hippocampus may be important for normal performance, which would suggest that use of the two structures is not necessarily mutually exclusive; (2) the human amnesics may have confounding cerebellar damage. The memory impairment studies have typically resulted from Wernicke-Korsakoff's syndrome, senile dementia of the Alzheimer type, or medial temporal resections used to treat intractable epilepsy. For all three etiologies, cerebellar as well as hippocampal and/or midline diencephalic damage may occur. Typical motor signs of cerebellar dysfunction occur in the Wernicke's phase of the Korsakoff syndrome, and in many cases it is likely that permanent cerebellar

damage results (reviewed by Butters, 1984). Chronic alcohol abuse by itself also appears to result in cerebellar atrophy (Meigaard and Ahlgren, 1986; Harper and Krill, 1990). Recently, several investigators have reported that amyloid plaques in the cerebellum may not be as rare as initially thought (Cole *et al.*, 1989; Wisniewski *et al.*, 1989). Finally, cerebellar atrophy is not uncommon in severe epileptics; it is unclear whether this typically results from seizure activity or the long-term effects of anti-epileptic medication (Salzman *et al.*, 1978; Botez *et al.*, 1988).

Summary

The pattern of deficits observed in RC1 provide a foundation for further investigations into non-motor functions of the cerebellum and the functional relationship between the cerebral cortex and the cerebellum. RC1 failed to learn and perform normally a variety of tasks which involve complex non-motor ('cognitive') cortical processing. It seems most probable that RC1's deficits were caused by his loss of important cerebellar contributions to the performance on certain types of both motor and cognitive tasks, particularly those involving the development and modification of consistent responses to repeated stimuli. Based upon the differential pattern of deficits between RC1 and amnesics, the contributions made by the cerebellum to learning and memory appear, for at least some tasks, to be dissociable from the contributions made by medial temporal and midline diencephalic structures. This suggests the cerebellum may be a critical part of one of at least two anatomically distinct long-term human memory/learning systems.

We feel our investigations of RC1's deficits demonstrate the utility of using information from PET studies of normal human performance to guide lesion-behaviour studies. Combining information across these two techniques can be particularly valuable when, as occurred in the case of the cerebellar activation, the PET finding cannot be readily accounted for on the basis of existing data. In such instances, beginning a neuro-psychological investigation with a task known to produce activation of a lesioned area may provide novel information about the processing performed by the lesioned area during the chosen task.

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POSTURAL DISTURBANCES DUE TO HOMONYMOUS HEMIANOPIC VISUAL ATAXIA

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SUMMARY

Patients with visual defects often complain of disturbances of equilibrium. In order to measure the influence of visual stimulation on posture, a study was made comparing the posture of hemianopic patients with that of healthy volunteers before and after occlusion of half of the monocular visual field. Hemianopia increases lateral oscillations in patients in the standing position and the projection of the body's centre of gravity shifts towards the hemianopia: in the volunteers, the same shift is noted after masking half the visual field. A tonic effect of visual information is discussed.

INTRODUCTION

Postural control is achieved through a multisensory process to which proprioceptive information from the mechanoreceptors of the joints and the muscles of the legs, and information of vestibular and visual origin contribute. Recently, the importance of visual patterns for postural control and for the equilibrium of the body in space has been demonstrated (Dichgans *et al.*, 1976; Paulus *et al.*, 1984). In fact, Kleint (1936) suspected the pre-eminent role of vision in postural control and Gibson (1958) concluded that the flow pattern of an optic array provides feedback stimulation for the control and guidance of locomotor behaviour which he referred to as 'visual kinesthesia'.

Lee and Aronson (1974), studying the stimulatory effects on children of a moving room, came to the same conclusion, i.e. that visual proprioception is a pre-eminent factor in determining stance. Closing the eyes increases the oscillations of the body in a vertical position. Edwards (1946), Witkin and Wapner (1950) and Hashiba *et al.* (1981) have measured these oscillations with the aid of a platform and shown that 'the visual information from the peripheral field is more effective in body stabilization than from the central visual field'. In confirmation of these results obtained from man, Mirka and Brookhart (1981) have shown in canine postural control that only the peripheral field produced visual feedback that affected postural control.

Clinical observations suggest that very often patients with homonymous hemianopia complain of disturbances of equilibrium. Since experimental results have shown the importance of vision and in particular of peripheral vision in postural control, we have made a study of the posture of patients with visual field defects.

PATIENTS

Thirty-three patients and 56 healthy volunteers having given their informed consent were carefully examined by a neurologist. All patients had a computerized tomographic examination and an examination

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