Poster Papers

1. Use of Memory and Concentration Evaluation in Distinguishing Progressive Supranuclear Palsy from Parkinson’s Disease


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Progressive supranuclear palsy (PSP) and Parkinson’s disease (PD) can be difficult to distinguish in the early stages. This study assessed the utility of neuropsychological assessment in this differential diagnosis among 22 male patients, 15 of whom had PD and seven of whom had PSP. All patients had been diagnosed by clinical neurologic exam and SPECT scan. A battery of tests was administered to each patient. The PSP patients performed worse than the PD patients on Digit Span and the Selective Reminding Test (SRT). Sensitivity, specificity, and predictive value (positive and negative) tests showed SRT, Trail Making A, and Digit Span to be the most robust differentiators between the two groups. Digit Span forward and Trail Making A showed the strongest negative predictive values, suggesting that an attentional deficit may underlie the cognitive differences between the two groups.

Rationale. Progressive supranuclear palsy (PSP) is one of the Parkinson plus syndromes, characterized by both the classic Parkinsonian symptoms of tremor, bradykinesia, rigidity, and postural instability (Stacy & Jankovic, 1992), and additional neurological abnormalities, including supranuclear ophthalmoplegia with down gaze abnormalities, and pseudobulbar palsy. Both PSP and Parkinson’s Disease (PD) are progressive, degenerative diseases of the basal ganglia that can be differentiated upon autopsy by their characteristic patterns of degeneration and inclusion bodies. However, PSP and PD are often difficult to distinguish clinically, as the ocular and pseudobulbar signs characteristic of PSP often do not develop until late in the course of the disorder. Both PSP and PD patients have been found to have cognitive impairments that are classified as “subcortical” in nature (Cummings & Benson, 1988; Pillon et al., 1991). The purpose of this study was to assess the utility of neuropsychological testing in differentiating these disorders early in the process.
Subjects. Twenty-two male patients from the Movement Disorders Clinic of a large VA Medical Center were included in the study. Mean age was 69 years, and their mean level of education was 12 years. Of this group, seven satisfied the criteria for possible or probable PSP, and 15 were diagnosed with PD, based on scores on the Modified Columbia Rating Scale, and the Hoehn and Yahr PD staging system. There was no significant age or education difference between the two groups. Patients with scores greater than 15 on the Hamilton Rating Scales for Depression were excluded from the study, as were patients who scored 7 or higher on the Hachinski Ischemic Rating Scale for vascular dementia and those who scored below 15/30 on the MMSE.

Methodology. A battery of tests tapping skills known to be affected by PD and PSP was assembled and assessed five different areas: Attention and Concentration, Speech and Language, New Learning and Memory, Visual–Spatial Functioning, and Mental Efficiency. This report focuses on the attention and concentration and memory findings.

Attention and Concentration were assessed with three instruments: Digit Span from the WAIS-R, Visual Memory Span from the WMS-R, and the Trail Making Test-Part A.

New Learning and Memory were assessed with four tests: Logical Memory I and II from the WMS-R, the DATATOP Selective Reminding Test, Memory for Design, and the DATATOP New Dot Test.

All subjects were initially screened and diagnosed by a board-certified neurologist according to the criteria outlined above. Within 1 month of the initial screening, each subject underwent a SPECT scan and completed the neuropsychological battery.

Results. Analysis of the data proceeded in several stages. First, mean differences in test performance between the two groups were examined. This was followed by calculations of sensitivity and specificity for each measure, along with estimates of positive and negative predictive values for each test.

Mean differences between the performance of PSP and PD patients were first examined with t-tests of the individual neuropsychological tests. Significant differences \((p < .05)\) were found on four of the measures: the sum of the SRT acquisition trials, Selective Reminding delayed recall, and Digit Span forward and backward. As expected, PSP patients performed worse than PD patients on all of these tests.

Nine instruments were selected for further analyses based on moderately high correlations \((r > .3)\) with the diagnostic categories. For most of these measures, criterion scores were assigned at two standard deviations below the mean. For others, criterion scores were assigned according to established local norms. The data showed that both groups were clearly impaired, with the PSP patients being more severely compromised. The percentage of PD patients scoring below the criteria ranged from 7% (Digit Span backward) to 71% (SRT delayed recall), and the percentages below-criterion scores for
the PSP patients varied from 14% for Digit Span backward to 100% for SRT delayed recall. Failure rates (inability to complete the test) of 1/22 (.045) were noted for SRT delayed recall and Trail Making Part A. Failures were not unique to either diagnostic category.

Sensitivity refers to the probability that a PSP patient tests positively (below the criterion) on a given test. Specificity indicates the probability that a non-PSP patient (PD patient) tests negatively on each measure. Predictive values positive (PVP) show the probability that a positive test score indicates PSP, and predictive values negative (PVN) display the probability that a negative test score contraindicates PSP. A number of tests were found to be highly sensitive to cognitive dysfunction including SRT delayed recall, Trail Making A, and Digit Span forward. The tests most specific to PSP encompassed Digit Span forward and backward, Trail Making A, and Visual Memory Span backward.

When considering the probability that a positive test indicates the presence of PSP (PVP), Trail Making A and Digit Span forward emerge as the most powerful predictors. Predictive value negative (PVN), or the probability that a negative score contraindicates PSP, was above .7 for all tests. The values ranged from a high of 100% probability for SRT delayed recall to a low of .7 for Digit Span backward. These findings suggest that an attentional deficit may underlie the cognitive differences between PD and PSP and may help distinguish these patients early in their progression.

References


2. Impaired Recognition in Parkinson’s Disease

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Parkinson disease (PD) patients’ performance in recognition was assessed with different paradigms aimed at detecting specific impairments that would not appear in traditional testing. Twenty-one non-demented patients and 15 matched control subjects were given several tasks assessing executive functions, recall of verbal
material, and two recognition tasks: a “synonym” task, in which subjects were required to recognize previously learned words among synonyms and neutral distractors, and a source recognition task. PD patients were significantly impaired in few measures of executive functions and memory. In the recognition tasks the discrimination indices were similar in both groups, but qualitative analyses indicated that PD patients recognized as targets a significantly higher proportion of synonyms distractors than the controls, and made significantly more source recognition errors. Some significant correlations were found between executive functions measures and recognition scores in PD patients.

Rationale. Parkinson’s disease (PD) is associated with cognitive deficits and more specifically with episodic memory impairments. This type of memory deficit has been observed on several tasks involving free recall of word lists and short structured stories. In contrast, patients’ performance on tests of recognition memory appears to be normal. It was hypothesized that a more systematic analysis of performance in recognition would show qualitative differences that do not appear in traditional recognition testing, and that these deficits would be correlated to their deficits in tasks of executive functions.

Subjects. Twenty-one patients with Parkinson’s disease and 15 normal controls matched for age (respectively 60.6 and 60.7 years) and education were participated in the study. The patients were neither demented (Mattis DRS: 142) nor depressed. All subjects were given several tasks assessing (1) executive functions: WCST, California Card Sorting Test (CCST), Self-Ordered-Pointing Test (SOPT), and Verbal Fluency; (2) recall of verbal material: logical passages (WMS-R), and CVLT; (3) and two recognition tasks: a “synonym distractor” task in which subjects were required to recognize previously learned words among synonyms and neutral distractors; and a second recognition task in which subjects, after studying words and pictures, were asked to recognize the targets and indicate whether they were originally presented as words or pictures (source memory).

Results. PD patients were significantly impaired on three measures of executive functions and memory [number of errors in the Self-Ordered Pointing Task \( F(1, 33) = 5.8, p = .02 \); CCST total sorts \( F(1, 31) = 4.6, p = .03 \); CVLT list B \( F(1, 32) = 7.2, p = .01 \)]. However in the recognition tasks standard analyses of discrimination indices failed to show any difference between the two groups. In comparison, further analyses indicated that PD patients recognized as targets a significantly higher proportion of synonyms distractors than control subjects \( F(1, 32) = 6.5, p < .02 \) and made significantly more recognition errors concerning the presentation format of targets (words versus pictures) in the second task \( F(1, 32) = 6.7, p < .02 \). Some significant correlations were found between executive functions measures and recognition scores in PD patients.

Conclusions. In conclusion, this study shows that PD patients even with very mild cognitive impairments display deficits indicating that their recognition memory is based on a feeling of familiarity rather than on the recollec-
tion of events, that source recognition is impaired, and that these deficits may be related to frontal dysfunction.

3. Specific Contribution of the Striatum and the Cerebellum in Visuomotor Skill Learning

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The aim of the present study was to examine the specific contribution of the striatum and the cerebellum in visuomotor skill learning. The performance of two groups of patients with Parkinson’s disease, and one group of patients with cerebellar lesions, were compared to that of a group of matched normal control subjects on adapted versions of the Repeated Sequence Test (the Random Visuomotor Task), and of the Mirror-Tracing Test (the Triad Task). For the first time in research on the neural substrates involved in the incremental acquisition of a visuomotor skill, the results yielded a double-dissociation in function between these structures, and suggest that the striatum was preferentially involved in perceptivomotor learning, whereas the cerebellum played a preponderant role in the sequencing of learned movements.

Rationale

Numerous investigators have demonstrated that both the striatum and the cerebellum, in relation with other areas, are involved in the incremental acquisition of visuomotor skills. Considering that these structures are part of two distinct cortico-subcortical circuits, however, it is possible that they may play a different role in the learning of a visuomotor skill. The aim of the present study was to examine the specific contribution of these structures in visuomotor skill learning. In accord with the theoretical models available (Marsden & Obeso, 1994; Inhoff & Rafal, 1990), it was predicted that the striatum would be preferentially involved in perceptivomotor learning based on S-R types associations (Experiment I), whereas the cerebellum would play a preponderant role in the sequencing of learned movements (Experiment II). Finally, Experiment III was conducted to explore the hypothesis that, contrary to patients with damage to the cerebellum, patients with Parkinson’s disease would show a deficit in the ability to adapt to a contextual change in the learned movements.

Subjects

Five groups of subjects participated in this study. All of the patients were recruited via the Department of Neurological Sciences and Neuroradiology at
the Hopital de l’Enfant-Jesus, Quebec, Canada. In contrast, aged and young normal controls were either acquaintances of the experimenters or volunteers from the community. None of the controls had any positive history of a psychiatric or a neurological disorder. Subjects gave informed, written consent for their participation in this experiment. Finally, this study was approved by the hospital’s ethics committee.

Parkinson’s disease groups (PD). These groups were each composed of 15 patients who had received a diagnosis of idiopathic Parkinson’s disease. The first group included 15 patients (5 female, 10 male) in Stage 1 of the disease using Hoehn and Yahr’s scale. On average, they were 58.7 (SD 9.5) years old, and had 12.8 (SD 4.5) years of education. The second group was composed of 15 patients (7 female, 8 male) in Stages 2 and 3 of the disease. On average, they were 59.3 (SD 6.3) years old, and had 13.5 (SD 4.2) years of education. All patients were taking optimal levels of levodopa medication at the time of testing. Patients with drug-induced parkinsonism, multiple system atrophy, cerebro-vascular disease, epilepsy, history of alcoholism, head injury or tumor, cerebellar disturbances, or disproportionate oculomotor and autonomic dysfunction were excluded from the experiment.

Cerebellar group (CE). A heterogeneous group of 15 patients with a radiologically-documented lesion in the cerebellum was also tested. Twelve of them had pure cerebellar atrophy, whilst the last three had lesions extending into the brain stem or spinal cord. They were on average, 40.7 (SD 11.8) years old and had 11.9 (SD 3.0) years of education. All of these patients had dysarthria, ataxia, and dysmetria, although the severity of these cerebellar symptoms differed between patients.

Normal control groups. Two separate groups of normal control subjects were included to match the clinical groups with respect to sex distribution, mean age and mean level of education. Thus, one group of 15 aged normal controls (ANC) and one group of 15 young normal controls (YNC) were respectively used as controls for the Parkinson’s disease and cerebellar groups.

Method

Basic neuropsychological assessment. A short battery of neuropsychological tests including the Mini-Mental State Examination, a General Health Status Questionnaire, the Vocabulary, Digit Span, Picture Arrangement, and Block Design subtests of the WAIS-R, and a French version of the revised Beck Depression Inventory was administered to the patients in the three clinical groups in order to eliminate those showing signs of dementia and/or depression.

Experiment 1

Random visuomotor test: Perceptivomotor skill learning. This experimental task consisted of an adapted version of the Repeated Sequence Test devel-
oped by Nissen & Bullemer (1987). Contrary to the original task in which each block of trials are composed of an embedded sequence, this version used a completely random presentation of the stimuli. The subjects were instructed to use the middle and index fingers of each hand, and to keep one finger on each of the four keys. They were asked to press the button corresponding to the right of the light that was illuminated as quickly as possible, while making as few errors as possible. The stimulus remained displayed until the subject made a response. After the response, the light went off, and this was immediately followed 500 ms later by the display of another stimulus. The subjects completed 6 sessions of 4 blocks, each with 100 random trials (total 2400 trials). In most cases, this protocol was completed in two days, that is three sessions were administered on Day 1 and the last three on Day 2. Each session was separated by three pauses of 90 seconds each.

**Experiment II**

*Mirror-tracing test sequencing of learned movements.* The mirror-drawing task was used to assess the ability to learn another type of visuomotor skill. In this task, the subjects had to learn to outline the shape of a figure by tracing a line between two parallel borders, while viewing their hand and the figure through the reflection of a mirror. Unlike the original paradigm where a single star was used the subjects in this experiment completed two different types of drawings including simple segments of shapes, and triads of these segments. The segments consisted of simple curved or angled figures whereas the triads of segments were composed of the consecutive juxtaposition of three of these segments. Each subject completed four phases of testing: 1) the subjects were first asked to trace 12 simple segments in order to familiarize themselves with the mirror-tracing task; 2) they were then required to draw 12 different triads to get familiar with this type of figure; 3) the actual learning took place in the third phase where each subject completed 10 sessions of training in which 18 new segments were repeatedly presented at random within each session; 4) finally, in the fourth phase, the subjects were then given three other sessions of testing, each consisting of 12 triads which were composed of 6 ‘‘Learned Triads’’ and 6 ‘‘Novel Triads’’. The ‘‘Learned Triads’’ were composed of three segments that were previously practiced individually in the third phase of testing, while the ‘‘Novel Triads’’ were made up of the juxtaposition of three segments that the subjects had never traced before. A pilot study conducted earlier showed no significant difference in the total tracing time or the mean number or errors required to complete both types of triads. Finally, two dependent measures were recorded: Total time (in seconds) taken to complete the figure, and the number of errors committed (i.e. the number of times a subject crossed the borders of a figure).
Experiment III

Mirror-tracing test: Contextual adaptation. This experiment was exploratory in nature, and consisted of an extension of Experiment II. In fact, after the subjects had completed the three sessions of 12 triads required in the latter experiment, they were asked to trace six ‘‘Mixed Triads’’, which were created by juxtaposing at random in the sequence, two ‘‘Learned Segments’’ and one ‘‘Novel Segment’’ together.

Results

The findings of the present study constitute the first demonstration of a double-dissociation in function between the striatum and the cerebellum in visuomotor skill learning. As predicted, in Experiment I, no significant difference were observed between the CE and matched NC group on the Random Visuomotor Task, whereas the results showed that a unilateral striatal dysfunction was sufficient to produce an impairment on this task, when compared to their respective matched NC group. The latter findings suggest that the striatum, but not the cerebellum, play a critical role in perceptivomotor or S-R type learning mechanisms. By contrast, of the three clinical groups who completed the Triad Task (Experiment II), only patients in the CE group showed a significant impairment in the sequencing of learned movements when compared to their matched NC group, suggesting that this structure is preferentially involved in the ability to integrate separate learned movements into a fluid sequence. Finally, the results of the third experiment showed that only PD patients with a bilateral dysfunction were impaired in their ability to adapt to a contextual change in the sequence of learned movements. Overall, these findings provide new functional evidence of a specific contribution of the striatum and the cerebellum in visuomotor skill learning.

References


4. Neural Mechanisms Underlying Encoding and Reproduction of Timed Motor Sequences

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Recent data indicate that the cerebellum may play an important role in both the encoding of temporal information from sensory stimuli and in motor timing. This
PET activation study examined subjects’ ability to retain auditory and visual temporal sequences and to reproduce them by tapping. There were three conditions: simple (ISO), learned (REP), and novel (NOV). The ISO condition revealed modality-specific changes in the cerebellar hemispheres and other cortical regions. In contrast, the well-learned sequences in the REP condition revealed few additional changes. However, the NOV condition showed a consistent pattern of additional activation in the cerebellar vermis and lateral cerebellar hemispheres. These results support a role for the cerebellum in the encoding of temporal information, particularly when it is novel.

Rationale. A wide variety of human activities, from talking to playing the violin, rely on the perception and production of temporal sequences, or rhythms. However, the accurate timing of perceptual input and motor output is an as yet little understood function of the human brain. While timing mechanisms at the level of single muscles are currently being explored, it is not yet clear how the temporal aspect of complex, multi-effector motor programs is encoded and implemented in the human brain. Based on a series of studies in patients and controls, Ivry et al. (1988, 1989) have argued for central control of both perceptual and motor timing functions, mediated by the cerebellum. However, other investigators have found evidence for involvement of the basal ganglia (O’Boyle et al., 1996) and the SMA (Halsband, 1993). In the present experiment, we were interested in examining the role of the cerebellum in control of motor timing and in the hypothesized central control of temporal processing. To do this we designed a PET experiment using a relatively naturalistic rhythm reproduction task in which subjects perceived and reproduced temporal sequences presented in the auditory and visual modalities.

Subjects. Subjects were 12 (6 M/6 F) right-handed normal volunteers (mean age = 22.4 years) selected to have a minimum of musical training or experience (mean = 2.6 years; range = 0–4 years).

Method. There were four task conditions, performed in both the auditory and visual modalities: (1) perception of isochronous sequences [BASE], (2) perception and reproduction of isochronous sequences [ISO], (3) perception and reproduction of a repeated sequence [REP], and (4) perception and reproduction of a series of novel sequences [NOV]. In all conditions, sequences were six elements long and were composed of short (250 msec) and long (750 msec) elements separated by a constant (250 msec) ISI. In the auditory conditions, these elements were 3000 hz tones, in the visual conditions, they were 1” white squares which appeared sequentially at the same location in the center of a computer monitor. In BASE and ISO, the sequences were composed of either all short or all long elements; in REP and NOV, sequences were composed of short and long elements and were constructed to be of equal difficulty.

In all conditions, each sequence was followed by a 6.5-sec pause. In the active conditions, subjects were asked to reproduce the sequences during the
pause by tapping on a single key of the computer keyboard. Subjects were instructed to hold the key down for the number of stimuli in the sequence and for the duration of each stimulus ‘as if you were tapping on a piano key.’ Both key-press and key-release durations were recorded by the computer, and these data were used to score performance in the REP and NOV conditions. Ten to 12 sequences were presented and reproduced in each condition, with 5–6 of the sequences reproduced during a 60-sec period of the scan. Therefore, the number of stimuli and the number of finger movements were the same across all active conditions.

PET scans were obtained with a Scanditronix PC-2048B 15-slice tomograph. CBF was measured during a 60-sec scan using the O¹⁵-labeled waterbolus method. MRI scans were obtained with a Philips Gyroscan ACS (1.5T) which produced 160 continuous, 1-mm sagittal slices. CBF images were reconstructed with a 12-mm Hanning filter and normalized to correct for individual differences in global CBF. MRI and PET scans were transformed into the standardized stereotaxic space of Talairach and Tournoux (1988) (Collins et al., 1994). For each subtraction, a t statistic map was generated (Worsley et al., 1992). The resulting images were coregistered with the average MRI of all subjects in order to examine the anatomical location of observed changes and to compare these locations with the Talairach atlas. Positive and negative changes were considered statistically significant at \( t > 3.5 \), a level at which approximately one false positive peak might be expected to appear for each subtraction examined.

**Results.** Subjects’ key-press responses in the ISO condition were averaged across trials to generate an average short and long response for each subject. Paired t tests for the average and SDs of all responses across modalities showed that only the average long responses differed, with the auditory longer than the visual \( t(1,11) = 4.3, p < .001 \). For the REP and NOV conditions, each subject’s performance was scored by using their average short and long responses within 2 SD of the upper and lower limits for correct response for short and long elements respectively. Performance in the REP and NOV conditions was scored as percent correct at each of the six positions in the sequence. In the REP condition, analysis of variance (ANOVA) revealed a significant interaction of position and modality \( F(5, 55) = 4.95, p < .001 \), largely as a result of two subjects who tended to lengthen their short responses in both modalities. These responses were clearly distinguishable as short in comparison with their long responses, but fell outside of the 2 SD cutoff. In the NOV condition, ANOVA revealed an effect of Position, \( F(5, 50) = 14.68, p < .0001 \), but no difference in the pattern of performance between modalities \( F(5, 50) = 1.35, p < .26 \). In both conditions, the average percentage correct collapsed across position did not differ between the two modalities (REP \( t = .12, p < .50 \); NOV \( t = 1.6, p < .13 \)). Because no consistent differences in performance were observed between the two modalities, any modality-specific differences in CBF can be related
to the modality of sensory input, rather than to a global difference in task difficulty.

References


5. Cerebellar Contribution to Executive-Frontal Function: A Case Study

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A comprehensive neuropsychological evaluation was performed on a patient with an idiopathic cerebellar degenerative disorder. Significant deficits were found in auditory vigilance, semantic concept generation, strategic learning and recall of lists, accessing lexical information, susceptibility to interference, impulsivity, and reduced judgment and planning. These deficits were not readily explained by motor control or coordination difficulties. Due to relatively little cerebral cortical atrophy noted in this patient’s MRI scan, findings support the proposition that the cerebellum is important for some normal cognitive functions and further indicates its possible role in executive functioning. Neuroanatomical considerations are discussed.

Rationale

Neuropsychological studies of patients with cerebellar disorders are demonstrating that the cerebellum contributes to higher cognitive processing (Fiez, 1996; Schmahmann, 1991). Evidence supporting this hypothesis is garnered from neuroanatomical studies (Middleton & Strick, 1994; Schmahmann, 1991), cerebellar activation during effortful and self-determined cognitive tasks (Fiez, 1996), and the development of cognitive deficits following
cerebellar insult (Bracke-Tolkmitt, Linden, Canavan, Rockstroh, 1989). Since cerebellar disorders often result in damage of cortical and brainstem structures in addition to the cerebellum, Akshoomoff et al. (1992) have suggested that it is important to study patients with damage that is principally localized to the cerebellum. Akshoomoff et al. (1992) presented a case of patient C.Z. who had cerebellar degeneration which affected intrinsic structures of the cerebellum but not the brainstem and cerebrum. Cognitive testing revealed deficits in verbal and visual paired associate learning, verbal fluency, visuospatial abilities, and free recall (improved with cueing), and decrements in intellectual abilities. C.Z.’s cognitive profile was viewed as commensurate to that of deficits seen in subcortical dementia and the investigators concluded that the cerebellum is important for some normal cognitive–subcortical functions.

The following case study of patient R.B. depicts the cognitive performance of a woman with marked ideopathic cerebellar degeneration. Similar to C.Z., R.B. has extensive damage of cerebellar structures, but little cortical atrophy, and sparing of brainstem structures. Neuropsychological and functional evaluations were performed to identify any cognitive deficits and daily living difficulties associated with her diffuse cerebellar damage.

Subject

B.R., a 42-year-old, right-handed, high school educated, single, white female developed initial symptoms suggestive of cerebellar dysfunction in 1993, including slurred speech, light-headedness, and balance difficulties. Results of a neurologic exam at that time indicated dysarthria and soft cerebellar signs, including asymmetric lateral gaze nystagmus and mild dysmetria. Repeated MRIs (1993–1996) demonstrated marked, diffuse atrophy of the cerebellum, sparing of the pons and medulla, mild cerebral atrophy, and no focal lesions. Visual, somatosensory, and brainstem evoked potentials are normal. Past medical history is negative with no family history of gait disorder or neurodegenerative disease. Otoneurology evaluation results concluded unquestionable degenerative disorder, with mild dysarthria, left horizontal and down beating nystagmus, ataxia, vertigo, and vestibular dysfunction. Given occasional acute decrements in her clinical course, the form of the degeneration was viewed as rare type.

Method

Neuropsychological testing was administered. Functional evaluations conducted in the home and community were also undertaken.

Results

General cognition. Age scaled intellectual abilities are low average overall (WAIS-R FSIQ = 83). Verbal abilities are low average (WAIS-R VIQ 88); visual-spatial abilities are average (PC, BD) to low average (PA, OA), with
the exception of Digit Symbol performance (age equivalent 5th percentile), which requires quick information processing and motor speed.

Attention and speed of information processing. Attentional capacity ranged from low average to average (WMS-R Attention/Concentration index, low average). Forward digit span is 5–6 digits (22nd percentile) and digits backwards is 3–4 (53rd percentile). Auditory vigilance is impaired for both simple targets (odd numbers) and complex targets (two consecutive odd numbers). Mild distractibility is also noted. Visual scanning and attention (Letter Cancellation) are slow but accurate given extra time. Mental control is good (counting from 1 to 20: 16 sec, 0 errors; reciting alphabet: 9 sec, 0 errors) but performance on complex tasks requiring greater divided attention and concentration shows mild difficulties: adding serial 3′ resulted in multiple errors due to loss of set.

Executive functioning. No loss of set or sequencing difficulties are noted on Trails B (2′38″) although performance was very slow. While concept formation abilities were average on the WCST (6/6 sorts, % perseverations), performance was impaired on an experimental semantic concept generation task (BEEF: 3/6 categories); provision of conceptual cues, however, resulted in average ability (6/6 cued generation). Significant interference effects were noted on the Color–Word Interference condition of the Stroop (7 errors). Cognitive estimation performance was average.

Reasoning judgment. Verbal problem solving and reasoning are variable. Good abilities are noted in identification of logical relationships (Similarities) but with a tendency to interpret information in an overly literal way and to respond with trivial or incorrect associations on more abstract items. Verbal interpretation of proverbs (California Proverb Test) is impaired (2/10); responses on cued proverb test shows pull toward identifying very concrete, literal responses. Similarly, responses to social problem solving questions (If someone pushes you, what should you do?) exhibits tendency toward impulsivity and reduced judgment. Visual–spatial, nonverbal reasoning and problem solving skills are typically low average (e.g., Block Design). Visuomotor performance is hampered by slow and mildly uncoordinated motor responses, however (Object Assembly).

Language and language-related processing. Communication skills are adequately developed. Conversations are engaged with ease and reciprocity, speech is fluent, and linguistic units (syntax, phonology) are normal. Vocabulary knowledge is low average for age, mainly reduced due to poor formulation and organization of responses. Visual confrontation naming is mildly impaired (BNT: 50/60). Ability to generate words for phonemes (Verbal Fluency, FAS) is low average, with significant slowing toward the end of the production periods, suggesting difficulty in sustaining an organized lexical search and accessing lexical information given time demands.

Verbal learning and memory. Learning of verbal and visual paired associates (WMS-R) is at ceiling by three learning trials. Initial acquisition of 16-
item CVLT list (=4) is poor; subsequent learning across trials (8, 9, 10, 11) remained impoverished (−2 SD). There was little evidence of clustering semantically related items. Short and long delayed free and cued recall is impaired (−2 SD); recognition performance is completely average (15/16) with no false positives. In contrast, recall of paragraph-length stories is average for age immediately and after a delay.

Non-verbal processing. There are no anomalies in appreciation of visual field, face-object recognition or location, nor in appreciation of personal space, exploration in space, or navigation in topographic space. Difficulties with visual acuity (jumping” around) are reported during reading but functional performance in reading, writing, and seeing for activities is within normal limits. Visuomotor production output is intact for two-dimensional copies of common objects (Parietal Lobe Battery, clock drawing), but significant planning inefficiencies and strategy miscalculations are observed on three-dimensional copies.

Daily living observations. B.R. was observed to be disinhibited and ineffectual in her daily living skills overall. Reduced ability to generate and follow through with complex behaviors, such as coordinating meals and shopping is noted.

Conclusions. Despite the absence of MRI or SPECT scanning documentation of frontal lobe damage, this cerebellar degeneration patient presents with a number of cognitive deficits that are suggestive of executive dysfunction. Specifically, deficits in auditory vigilance, semantic concept generation, strategic learning and recall of lists, accessing lexical information, and susceptibility to interference, impulsivity and reduced judgment and planning are noted. These deficit areas cannot readily be attributed to motor control, coordination, and speed factors, findings support the positive relationship between some higher order cognitive abilities and cerebellar degeneration. However, unlike the findings by Akshoomoff et al. (1992), who found symptoms likened to subcortical dysfunction in their cerebellar patient, our patient’s deficits conform to deficits commonly associated with a dysexecutive syndrome. Neuroanatomical considerations will be discussed and illustrated with MRI findings.

References
6. The Correspondence between the Rivermead Behavioral Memory Test and Ecological Prospective Memory

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Patients with diffuse and focal brain damage often present with prospective memory deficits in post-acute rehabilitation settings. That is, these patients tend to have difficulties “remembering to remember” to complete plans and intentions in the future. One measure, the Rivermead Behavioral Memory Test (RBMT) purports to measure prospective memory abilities, in addition to providing an ecological estimate of patients’ memory deficits in everyday living environments. In the present study, six patients’ ability to complete daily, assigned responsibilities was correlated with their performance on the RBMT prospective memory items. Results revealed low correlations between prospective memory responses and actual functional performance in the rehabilitation clinic. Conversely, patient’s completion of daily tasks was found to be significantly correlated with the level of anterograde memory severity on the RBMT, indicating that patients with better memory tended to complete more tasks.

Rationale

Patients with neurological impairments due to traumatic brain injuries and other catastrophic neurologic illnesses commonly present with deficits in the ability to plan and carry out everyday tasks within a given time frame. Recent work indicates that such deficits can be thought to reflect impairments in either retrospective memory or prospective memory, or both. Using this categorization, retrospective memory encompasses the ability to recall information in working and short term memory, and recalling events/knowledge from memory when required. Prospective memory, on the other hand, is typically viewed as the ability to “remember to remember.” This construct has been operationally defined as being akin to planning actions over short term retention intervals as well as the ability to remember to complete tasks and/or plan for future actions as warranted. Thus, retrospective memory most closely resembles the construct of “memory” as it is popularly known (i.e., remembering something learned), whereas prospective memory is more closely associated with frontal-executive abilities that correspond to applying appropriate strategies, planning, organizing, and following through with behavioral plans.

One of most challenging aspects of post-acute rehabilitation has been in predicting which neurological patients will experience retrospective and prospective memory failures in everyday life that will subsequently result in deficits in their functional daily living. The most common strategy employed
by neuropsychologists and rehabilitation specialists to predict patients’ retrospective memory has been to examine how well patients’ performance on clinical memory batteries relate to their day-to-day memory functioning. At issue, is that while most of the widely used clinical memory tests and batteries have been found to reliably and validly detect the presence of memory deficits, such tests have not necessarily been useful for predicting the nature and frequency of memory problems that occur in a patient’s everyday life (Mateer, Sohlberg, & Crinean, 1987). Further, of the most popular clinical memory tests used today only the Rivermead Behavioral Memory Test (RBMT) was developed to measure both prospective and retrospective memory. This test is one of the few clinical memory tests available that has been shown to correlate significantly with the capacity of individuals to cope and live independently and remain employed (Wilson, 1991). One issue that remains unclear, however, is in determining how well the prospective memory questions on the RBMT actually correspond to the ability to “remember to remember.”

In the present study, we examined the ecological validity of the prospective items of the RBMT by correlating neurologically impaired rehabilitation patients’ performance on these questions to a measure of their actual, everyday performance.

Subjects

Six neurologically impaired adults (two male, four female) were included in this study. Age ranged from 25 to 68, with a mean age of 42. Upon neuropsychological and functional evaluations in the home. All patients had mild to severe anterograde memory deficits, as well as significant functional impairments in their ability to plan, organize, and carry out tasks and plans in the future. All patients had been employed prior to their injuries, but none of them had been able to return to gainful employment since their injuries. Length of stay in the post acute rehabilitation program ranged from 22 to 101 days, with a mean of 66.2 days.

Method

Treatment program. All patients were attending an outpatient, post-acute community rehabilitation program. This program consists of daily intensive functional, cognitive, vocational, and social skill training that aims at returning patients to their maximum level of vocational and avocational functioning. Training includes group treatment as well as specific remedial training for organization and planning functional activities. The latter type of training typically utilizes maximal rehearsal and routinization of practice in an effort to “proceduralize” how to organize and plan. Cognitive and functional progress is evaluated throughout the program.
Assessment procedure. On 5 predetermined days of the post-acute rehabilitation program, patients’ ability to independently perform several daily assigned tasks was measured. The tasks were mutually agreed upon responsibilities that were to be completed each morning. During the length of the program verbal and visual cues were offered as needed in order to prompt/remind patients to complete these tasks. Prior to each assessment day, verbal reminders were given the day before to all of the clients that neither verbal nor written cues would be given, but they were still encouraged to complete their tasks independently. Patients were allowed to attempt this material in any way they chose. On the morning of each assessment session, rehabilitation staff oriented themselves throughout the clinic so that they could observe the patients’ behavior and yet appear as if they were busy. Inquiries by patients were deferred for 20 min, with no further prompting. Qualitative observations of patients were made as well. A single verbal cue was instituted following the lunch break in the form of reminders by staff to patients that daily responsibilities needed to be completed before the resumption of afternoon activities. Staff again observed whether patients who had not completed their morning tasks used the cue to complete remaining responsibilities.

Results

Pearson product–moment correlations were first computed between the mean number of responsibilities completed without cues by patients and their performance on the prospective memory items of the RBMT (possibility of 0–4 points with “4” corresponding to the most accurate prospective memory). Results of this analysis indicated a very low correlation \( r = -0.13, p = 0.83 \), suggestive of no significant relationship between these two variables. A second correlation was computed between the mean number of responsibilities completed following one verbal cue and the prospective memory score on the RBMT. Results of this correlation resulted in a somewhat larger correlation \( r = -0.32, p = 0.56 \), but it failed to reach significance. A final correlation was calculated between the mean number of responsibilities completed (without cues) and the level of overall anterograde memory severity on the RBMT (out of 24 points possible) to see if there was a relationship between these factors. This significant correlation \( r = 0.83, p < 0.05 \) reflects the relationship between the number of responsibilities completed and retrospective memory impairment.

Discussion

Finding from this study failed to identify a significant relationship between performance on the prospective memory questions of the RBMT and actual performance of daily responsibilities in a heterogeneous group of patients with neurological damage. While there was a relative increase in the correla-
tion between prospective memory performance on the RBMT and the number of daily tasks completed following a verbal cue, this relationship was not significant. Interestingly, there was a highly significant correspondence between the RBMT summative score reflecting overall memory severity and the number of tasks completed; that is, patients with less severe memory impairments performed more of their daily tasks independently. This suggests that either the RBMT prospective memory items are not closely related to prospective memory performance in real-world environments (and thus do not measure this construct) or indicates that the distinction between prospective and retrospective memory systems may be interactive, and that both systems are required in order to “remember to remember” to complete a task.

References


7. Detection of Invalid Profiles on the Interference Learning Test

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The ability of the Interference Learning Test (ILT), a new word-list learning test, to detect poor effort was evaluated in a clinical sample. Invalid cases identified with the Trueblood and Schmidt (1993) criteria (n = 6) were compared to the ILT normative sample (n = 393), post-concussive patients (PCS: n = 84) and closed head-injured (CHI) patients who experienced at least brief unconsciousness (n = 9). Optimal cutoffs were identified on seven measures that discriminated the Invalid group well. At least four of these measures were in the invalid range for all Invalid cases versus 0 Normals, 0 CHI, and 3 PCS (4%). A small cross-validation sample yielded similar results. This invalidity index appears potentially useful in assessment of PCS patients.

Rationale. With the increasing forensic role of neuropsychological evaluation, recent years have seen a large number of studies on malingering and suboptimal effort in test taking. Specific procedures, such as Rey’s 15-Item Test and the Portland Digit Recognition Test, have been refined. The disadvantage of these is that they can lengthen the neuropsychological assessment. Another approach is to examine the effects of suboptimal effort on clinical tests that would be a normal part of the test battery (e.g., Trueblood &
Schmidt, 1993). For example, data about suboptimal performance have been obtained for the Category Test, Wisconsin Card Sort, and WAIS-R. Memory tests may be particularly relevant because memory symptoms are common and data have been obtained for the Rey Auditory Verbal Learning Test, Revised Wechsler Memory Scale, and California Verbal Learning Test. A second important issue in this literature is that many studies have used normal subjects that were instructed to malinger. Some of the findings from these simulation studies have not survived cross-validation in clinical samples (e.g., Trueblood & Schmidt, 1993). Within clinical populations, post-concussion syndrome (PCS) has been an especially relevant group for study because there is controversy regarding long-lasting impairment in this type of injury, diagnosis is often difficult and equivocal, and these cases are often litigated. The present study provides suboptimal performance data for a new word-list learning test, the Interference Learning Test (ILT). Invalid profiles were obtained from an outpatient neuropsychological practice and compared to clinical samples of PCS and closed head injury (CHI), as well as the ILT normative sample.

**Subjects.** The ILT normative sample (n = 393) and three clinical groups referred for outpatient neuropsychological evaluation were used. The PCS group (n = 84) was referred for evaluation of cognitive symptoms following minimal head injuries in which there was no or momentary loss of consciousness. These subjects just met the threshold for the National Congress of Rehabilitation Medicine definition of Mild Traumatic Brain Injury. A CHI group (n = 9) consisted of cases which had clear evidence of at least several minutes of unconsciousness and many had positive neuroimaging findings. The Invalid group (n = 6) consisted of five PCS subjects and one patient referred for evaluation after possible toxic exposure. All produced invalid neuropsychological protocols according to the Trueblood and Schmidt (1993) criteria and several had below-chance performances on Symptom Validity Testing (Hiscock & Hiscock, 1989). A small cross-validation sample was composed from cases that were referred after the main sample using similar criteria. There was 1 Invalid, 2 CHI, and 19 MTBI cases.

**Method.** All subjects were administered the ILT and detailed neuropsychological evaluations. The ILT is a multitrial word-list learning test in which 20 Target words (to be learned) are embedded in a list of Distractor words. The Targets and Distractors are printed on different colored cards, with 1 card presented every 3 sec. Subjects are instructed to read each card aloud and to learn only the words on the white cards (Targets). After four learning trials, a second word list is given for two trials. Free recall for the Targets follows this and is followed by a 30-min delayed free recall, category-cued recall, recognition memory for Targets, and recognition memory for Distractors.

**Results.** One-way ANOVAs were done on 66 ILT variables and post hoc tests indicated that the Invalid group differed significantly from the normative sample on 33 of these. Where variables were computationally related
Table 1
ILT Measures Entering into the Invalidity Index

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Invalid</th>
<th>Normal</th>
<th>CHI</th>
<th>MTBI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>(1)</td>
<td>(0)</td>
<td>(2)</td>
<td>(19)</td>
</tr>
<tr>
<td>Sample characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>37.4 (45)</td>
<td>35.2</td>
<td>46.1</td>
<td>35.3</td>
<td>35.5</td>
</tr>
<tr>
<td>SD</td>
<td>8.4</td>
<td>17.8</td>
<td>14.5</td>
<td>11.4</td>
<td>10.1</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>12.4 (14)</td>
<td>14.1</td>
<td>13.7</td>
<td>13.5</td>
<td>13.4</td>
</tr>
<tr>
<td>SD</td>
<td>0.9</td>
<td>1.9</td>
<td>2.8</td>
<td>2.3</td>
<td>2.4</td>
</tr>
<tr>
<td>Estimated IQ</td>
<td>Mean</td>
<td>84.8 (100)</td>
<td>107.7</td>
<td>99.8 (92.5)</td>
<td>102.0 (103.7)</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>4.8</td>
<td>9.2</td>
<td>13.6</td>
<td>12.3</td>
</tr>
<tr>
<td>Study data</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>List 1 total</td>
<td>&lt;23</td>
<td>5 (1)</td>
<td>4</td>
<td>0 (1)</td>
<td>4 (1)</td>
</tr>
<tr>
<td>Best recall</td>
<td>&lt;9</td>
<td>6 (1)</td>
<td>4</td>
<td>1 (1)</td>
<td>4 (0)</td>
</tr>
<tr>
<td>Added words</td>
<td>&lt;6</td>
<td>3 (1)</td>
<td>5</td>
<td>0 (1)</td>
<td>5 (1)</td>
</tr>
<tr>
<td>Source errors</td>
<td>&gt;9</td>
<td>4 (0)</td>
<td>30</td>
<td>1 (0)</td>
<td>9 (5)</td>
</tr>
<tr>
<td>Cued memory</td>
<td>&lt;5</td>
<td>4 (0)</td>
<td>1</td>
<td>0 (1)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Recog. hits</td>
<td>&lt;14</td>
<td>5 (1)</td>
<td>10</td>
<td>1 (0)</td>
<td>5 (0)</td>
</tr>
<tr>
<td>Indirect hits</td>
<td>&lt;10</td>
<td>6 (1)</td>
<td>0</td>
<td>0 (0)</td>
<td>3 (1)</td>
</tr>
<tr>
<td>Invalidity index</td>
<td>&gt;3</td>
<td>6 (1)</td>
<td>0</td>
<td>0 (1)</td>
<td>3 (0)</td>
</tr>
<tr>
<td>Total pct. correctly</td>
<td>100</td>
<td>100</td>
<td>g1</td>
<td>97</td>
<td></td>
</tr>
<tr>
<td>classified</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note. Cross-validation sample data are in parentheses. The invalid IQs are likely decreased by suboptimal effort.

(e.g., individual trial scores and total learning across all trials), the variable with the greatest difference was selected. A total of 9 variables were selected for further analysis. Using the four subject groups, frequency tables were visually inspected to determine cutoff scores that would identify the greatest number of Invalid cases with the fewest false-positives. Two variables (Recognition False Positives, Indirect Memory False Positives) were excluded since useful cutoff scores could not be established due to large distribution overlaps. Using the 7 remaining variables, an Invalidity Index was developed by tabulating the number of criterion variables that were in the invalid range (Table 1).

An Invalidity Index > 3 identified all 6 Invalid cases, O Normals, O CHI, and 3 (4%) PCS cases. On cross-validation sample, the Invalid case was also identified, along with 1 CHI and O PCS. These data indicate the ILT is sensitive to suboptimal effort and that this can be detected with good accuracy in a relevant clinical sample. This adds to the studies that have examined the effects of suboptimal effort in clinical samples and that have demonstrated the utility of normal clinical tests, particularly memory measures,
for detecting suboptimal effort. The Invalidity Index appears promising, but further cross-validation is needed.

References


8. Memory Distortions in Detoxified Alcoholics

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Both detoxified alcoholics and matched controls demonstrated false recall and recognition in a task previously shown to elicit memory distortions. The important results concerning memory distortions in detoxified alcoholics come from three specific findings in the recall data. Controls clearly recalled a greater proportion of targets than critical lures, while this difference was only marginally significant for alcoholics. Alcoholics also produced the critical lures earlier in their recall than controls. Finally, alcoholics produced more extralist intrusions than critical lures while the opposite was observed for the controls. These results suggest that the nature of the memory distortions differs for these two groups of subjects. The memory distortions exhibited by the alcoholics are consistent with a deficit in monitoring the source of information in memory.

Rationale. While memory distortions have been studied extensively in those with intact memory, they have recently been used as a tool to study those with memory disorders. These studies of false recognition and recall are important because they may provide clues concerning the nature of encoding and retrieval processes in individuals with memory disorders. In the present study, memory distortions were examined in recently detoxified alcoholics and matched controls.

Several neurobiologically based hypotheses concerning the underlying nature of the cognitive deficits observed in detoxified alcoholics point to problems with the frontal and prefrontal areas. Behaviors associated with these areas include the ability to inhibit responses, the planning and allocation of resources, cognitive flexibility, and the monitoring and evaluation of ongoing and completed cognitive activity.

Consistent with these types of deficits, some alcoholics have been shown to have specific impairments in their ability to monitor the source of informa-
tion and to suppress intrusions when remembering (Weingartner, Andreason, Hommer, Sirrocco, Rio, Ruttiman, Rawlings, & Eckardt, 1996). The purpose of the present research was to explore further the nature of cognitive performance in detoxified alcoholics using a task that has been shown to produce memory intrusions reliably in other groups (Roediger & McDermott, 1995; Schacter, Verfaellie, & Pradere, 1996).

Subjects

Thirteen detoxified alcoholics (mean: age, 39.85 years; education, 15.15 years) on an inpatient unit at the Clinical Center of National Institutes of Health and 13 age- and education-matched controls (mean age, 37.78 years; education, 15.84 years) participated in the study. All patients met DSM III-R criteria for alcohol dependence with no other psychiatric diagnosis, were medically healthy, and had been detoxified for a minimum of 3 weeks. All controls had no psychiatric or medical diagnoses.

Method

A modified version of the procedure used by Roediger and McDermott (1995) and Schacter, Verfaellie, and Pradere (1996) was used. Subjects heard 8 lists of 15 words read at a 3-sec rate. Each list was composed of associates (e.g., sour, candy, sugar . . .) of a nonpresented word (sweet). After listening to each list, subjects were required to recall the words by writing them down. A recognition test followed the presentation and recall of all of the lists. The 64-item test was composed of 3 items and the critical nonpresented lure for each of the 8 lists plus 32 distractors made up from the equivalent items for the alternative word set. Subjects made old/new judgments for the words and for those deemed old, made a further judgment as to whether they ‘remembered’ or ‘knew’ the word had been previously studied. Instructions for the judgments followed those used in previous research.

Results

Overall, alcoholics recalled significantly fewer list words (.59) than the controls (.68) \( F(1, 24) = 5.55, p < .03 \), while alcoholics (.46) and controls (.48) did not differ in the number of critical lures recalled. Whereas the controls clearly produced more studied targets during recall than critical lures \( t(12) = 3.99, p < .001 \), this difference was only marginally significant for the alcoholics \( t(12) = 2.07, p = .06 \). An analysis of when the critical lures were produced in recall (controlling for total number of items recalled) revealed that alcoholics produced the critical words significantly earlier in their recall output \( F(1, 24) = 5.52, p < .03 \). That is, controls tended to produce the critical lures at or near the end of their recall output while alcoholics
produced them earlier and often followed them with additional target words. A comparison of the two types of intrusions, critical lures and extralist intrusions (nonstudied words that were not critical lures), revealed a significant intrusion-type by group interaction. While controls and alcoholics produced a comparable mean number of critical lures per list (.48 vs .46), controls produced significantly fewer extralist intrusions [.19, t(12) = 4.18, p < .001] and the alcoholics produced as many extralist intrusions (.57) as critical lures [t(12) = 1.03, p = ns]. For both groups, the majority of extralist intrusions tended to be associated to the other list items. Due to differences in the number and pattern of intrusion for the two groups, the proportion of critical lures intruded as a function of the total number of intrusions was calculated for each subject. Alcoholics intruded a significantly smaller proportion of critical lures (.46) than did control subjects (.77) [ t(24) = 4.19, p < .003].

Both alcoholics and controls claimed to remember critical lures as often as studied words [for alcoholics: studied = .81, lures = .75; for controls: studied = .85, lures = .84; F(1, 24) < 1.88, p = ns]. For both groups, critical lures were more likely to be falsely recognized at recognition if they had been produced on the earlier recall test [recognition given prior recall: for alcoholics = .95, for controls = .97; recognition without prior recall: for alcoholics = .62, for controls .80; t(12) > 2.90, p < .01]. The remember/know analyses did not reveal any significant between group differences. However, alcoholics said that they “remembered” more of the critical lures (.75) at recognition than did controls (.66), although this difference was not reliable. Overall, there was a great deal of variability in the remember/know judgments reflecting a lack of understanding of the task, perhaps, or an inability to use the rule consistently. False alarm rates did not differ for the alcoholics (.04) and controls (.07) on the recognition test [t(24) < 1.00]. It is possible that the way in which the recognition task was constructed (tested for only 3 items from study list plus critical lure but not any of the related extralist intrusions), may not have allowed full assessment of the memory effects of the additional intrusions produced by alcoholics. New tasks are being designed to assess this possibility.

References


9. Acute/Chronic Effects of Smoking on Memory Scanning: Behavioral Performance and Event-Related Potentials in Young and Elderly Adults

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Cigarette smoking has been shown to be a variable risk factor for a number of neurological disorders in that it potentiates the risk for stroke and vascular dementia but reduces the risk for dementia of the Alzheimer type. This investigation utilized scalp-recorded midline (Fz, Cz, Pz) event-related (P300) potential (ERP) and behavioral performance indices within a memory scanning paradigm (under single and dual task conditions) to profile: (a) young and elderly adults with smoking and nonsmoking histories and (b) acute smoking (one cigarette) effects in young and elderly adult smokers. Neither performance nor P300 indices were affected by smoking history but acute smoking shortened reaction times and increased P300 amplitudes elicited by higher memory-set item probes during dual task conditions.

Rationale. Cigarette smoking has been shown to be a variable risk factor for a number of neurological disorders in that it appears to potentiate the risk for stroke and vascular dementia but reduces the risk for dementia of the Alzheimer type. Neurobiological research into the smoking-nicotine habit has focused almost exclusively on young-middle-aged adults and it is yet unknown as to whether a long-term smoking history alters the cognitive status of the aging brain and/or whether cognitive processes associated with aging demonstrate an altered sensitivity to acute smoking-nicotine. As scalp-recorded event-related potentials, and in particular the late positive P300 potential, are sensitive indices of cognition, this investigation examined behavioral performance and P300 indices in a memory scanning paradigm in order to profile: (a) young and elderly adults with smoking and non-smoking histories and (b) acute smoking (one cigarette) effects in young and elderly adults.

Subjects. Forty healthy adult volunteers, 20 young (10 male) aged 18–39 years and 20 elderly (10 male) aged 64–81 years, participated in this study. Half of the young and elderly were nonsmokers with no previous smoking history and the remaining half of the young and elderly were current smokers with average smoking histories of 8.3 and 52.5 years, respectively.

Method. Smokers attended the laboratory (after 12 hr of overnight tobacco abstinence) for two randomized test sessions during which testing was conducted pre- and post-sham (inhaling on a non-lighted cigarette) and cigarette smoking. Smoking in both conditions involved puffing (on their own brand of cigarette) at 1-min intervals for a 10-min duration. The average nicotine and tar levels of the cigarettes were 1.1 and 12.2 mg, respectively.

The memory scanning task involved single presentations of one, three,
and five item (digits) memory sets followed by an in-set (p = .50) or out-
set (p = .50) probe stimulus to which the subjects responded with separate
yes or no response keys, depending on their recognition. Memory sets were
presented in separate blocks (but counterbalanced within and between
groups) and within each block subjects responded under two task conditions.
Half of the memory sets were presented in a neutral (white) color and re-
quired no additional response (i.e., single-task condition). The remaining half
were presented in one of four different colors and immediately prior to the
target digit probe presentation subjects responded (yes or no key response)
to the presentation of a single word describing the colour (e.g., blue) of the
memory set items (i.e., dual-task condition). Performance measures included
reaction times, number of correct detections and commission errors.
ERPs were collected from mid-line (Fz, Cz, Pz) sites (referenced to linked
earlobes) with amplifier bandpass settings and sampling frequency set to
0.1–30.0 Hz and 256 Hz respectively. Ocular-corrected probe-elicited aver-
ages were manually scored for P300 peak latency and amplitude, defined as
the maximum positive deflection within 250–600 milliseconds after stimulus
onset.
Results. Preliminary analysis has indicated that increasing memory set size
is generally associated with significantly reduced accuracy, slower reaction
times, slower P300 latencies, and smaller P300 amplitudes to probe stimuli.
Increasing task difficulty resulted in reduced accuracy in the elderly, slower
reaction times and P300 latencies, and increases in P300 amplitudes to target
probes. Comparison of young and elderly adults showed aging overall to be
correlated with slower reaction times, longer P300 latencies and smaller
P300 amplitudes. The presence of a smoking history in young and elderly
adults did not affect performance or P300 indices. The smoking of a single
cigarette resulted in faster reaction times overall and increased amplitudes
of P300s elicited by three- and five-item memory set target probes in dual-
task conditions. The results will be discussed in relation to cognition in nor-
mal and pathological aging.

10. Lifetime Estrogen Exposure and Cognitive Performance
in Elderly Women

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C. A. Mc Cleary, and V. M. Henderson

University of Southern California

Research has found an association between estrogen levels and cognitive perfor-
mance in pre- and postmenopausal women. This study examined the relationship
between factors associated with estrogen exposure and cognitive performance in 84
Rationale. Fluctuating hormone concentrations have been associated with cognitive performance in both premenopausal (Hampson & Kimura, 1988; Sherwin & Tulandi, 1996) and postmenopausal women (Sherwin, 1988). Studies isolating specific hormone concentrations have noted that increased estrogen concentrations are associated with increased performance on tasks associated with verbal skills (Sherwin & Tulandi). Recent research has suggested that factors associated with estrogen exposure across a woman’s lifetime may be related to the development of hormone-dependent conditions (Nguyen et al., 1995; Rautalahti et al., 1993). Given these associations, it was hypothesized that women who demonstrate traits associated with increased exposure to estrogen over their lifetime will demonstrate better cognitive performance on verbal tasks compared to women who exhibit traits associated with decreased estrogen exposure.

Subjects. This study included 84 neurologically intact women who were enrolled as comparison subjects at the Alzheimer’s Disease Research Center (ADRC) at the University of Southern California (USC). All subjects had undergone neurological and neuropsychological examinations and showed no indication of cognitive or neurological impairment. They had a mean age of 81.00 ± 7.55 years and a mean education of 13.98 ± 2.75 years. The mean age at menarche was 12.95 ± 1.57 years and a mean age at menopause was 47.98 ± 6.64. The subjects had an average of 1.75 ± 1.46 children and breast fed an average of .86 ± 1.12 children. They had an average of .35 ± .65 miscarriages. Years since menopause averaged 31.94 ± 9.84, and 55% of the women indicated that they had been on estrogen replacement therapy (ERT) at some point following menopause. The mean duration of ERT use for all subjects was 4.83 ± 8.74 years. The mean weight since menopause was 135.10 ± 19.64.

Method. Reproductive and menstrual histories were gathered via telephone interviews directly from the participants. Standardized questions were used to gather all information. This information was compared to the subject’s performance on a neuropsychological battery which assessed a variety of cognitive domains. The MMSE and the test of Orientation, Memory, and Concentration (OMC) were included as measures of global functioning. Measures selected to assess verbal skills, such as verbal memory, fluency, and naming, included the total words recalled on three trials from the Consortium to Establish a Registry of Alzheimer’s Disease Word Memory List (TOTAL) and the Delayed Recall (RECALL), the Boston Naming Test...
(BNT); Animal fluency; FAS; Token Test (TT); Aural (AC) and Reading Comprehension (RC), and the Vocabulary (VOC) subtest from the WAIS-R. Measures selected to assess visuospatial skills, such as visual memory and orientation, included the CERAD Drawing (DRAW), the Judgment of Line Orientation (JLO), the Block Design (BD) subtest from the WAIS-R, and the Parietal Lobe Battery (PLB). Short-term memory and attention was assessed with two verbal tests, the Digit Span Forward (DSF) and Digit Span Backward (DSB) subtests from the WAIS-R, and with two non-verbal procedures, the Visual Span Forward (VSF) and Visual Span Backward (VSB) subtests from the WMS-R.

Results. Factors associated with either increased estrogen exposure (age at menarche, parity, miscarriage, time on ERT, and postmenopausal weight) and with decreased estrogen exposure (number of children breast fed and duration since menopause) were standardized for the current sample. The Index of Estrogen Exposure (EE) was calculated by taking the standardized age at menopause and adding the standardized score for parity, postmenopausal weight, the number of miscarriages, and time on ERT. Since lactation and an older age at menarche are associated with decreased estrogen exposure, the respective standardized scores were subtracted from the IEE, as was the number of years since menopause. Controlling for age and education, a hierarchical multiple regression indicated that the IEE was significantly correlated with increased performance on DRAW ($r = .23, p = .05$); TT ($r = .23, p = .04$); BNT ($r = .23, p = .04$); AC ($r = .25, p = .04$) and RC ($r = .26, p = .03$). Although not reaching significance, trends ($p = .10$) were noted for BD and VOC.

Discussion. As hypothesized, a higher exposure index was found to significantly predict cognitive performance in the elderly subjects. In this study, a standardized index of several factors associated with both increased and decreased estrogen exposure across a woman’s lifetime was predominately associated with the performance on verbally loaded measures, such that a higher index of exposure was associated with better naming and verbal comprehension skills.

Research has demonstrated that estrogen levels are associated with improved cognitive performance in estrogen-deficient women, and that this improvement is domain specific (Sherwin & Tulandi, 1996). Adopting the precedence established by Nguyen et al. (1995) and Rautalahti et al. (1993) who examined how estrogen exposure across a woman’s lifetime relates to specific hormone-dependent conditions, this study found that a standardized index of estrogen exposure which combined the duration of menstruation, parity, the duration of ERT use, and the number of children breast fed was associated with better naming and verbal comprehension skills in the elderly subjects.

These results support Sherwin and Tulandi’s (1996) contention that the effects of estrogen exposure are domain specific. Additionally, these results
suggest that it is not only current hormone levels which influence cognitive performance, but that pre- and postmenopausal factors associated with hormone exposure relate to cognitive performance later in life.

**References**


### 11. Longitudinal Effects of HIV on Memory and Attention

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In this prospective longitudinal study, 67 asymptomatic human immunodeficiency virus (HIV) seropositive adults between the ages of 21 and 51 years ($M = 34.9$ years, $SD = 6.7$) were individually administered a comprehensive battery of neuropsychological tests. Fifty-nine were available at Time 2 ($M = 7.1$ months later, $SD = 9$), 39 at Time 3 ($M = 11.7$ months later, $SD = 5.2$), 23 at Time 4 ($M = 19.1$ months later, $SD = 5.2$), and 9 at Time 5 ($M = 22.8$ months, $SD = 7.9$). The total interval time between the first and last session was 58.1 ($SD = 9.0$) months. This study looked at the relationship between CD4 count (a measure of immune functioning) and performance on standard tests of memory and attention. Although CD4 count decreased significantly over time (by 57%), it was not a good predictor of performance in the asymptomatic HIV seropositive adults. However, when groups were created based on a median split of CD4 count, the groups differed on measures of speed and a measure of visual memory, with the lower CD4 groups faring worse.

**Rationale**

Neurobehavioral complications commonly occur in persons with human immunodeficiency virus (HIV). Cell-mediated immunity is important in the protection against many viruses and is orchestrated by the T cell, specifically
the T4 (or CD4) T cell, which is critical in initiating and coordinating the activity of several other immune cells. Acquired immunodeficiency syndrome (AIDS) is a clinical syndrome which results from the collapse of cell-mediated immunity.

HIV-associated dementia has been described among patients in the later stages of AIDS (Navia & Price, 1987). The dementia is characterized initially by disturbances in learning new information, attention, and speeded information processing, followed by amnesia, profound psychomotor retardation, occasional agitation, disorientation, naming difficulties, and changes in mood and behavior. There has been some controversy as to the time of onset of these symptoms. Decreased higher mental functioning, for example, has also been reported in earlier stages of AIDS. This study takes a prospective look at the relationship between CD4 count and performance on standard tests of memory and attention over time.

Subjects. Sixty-seven asymptomatic HIV seropositive adults between the ages of 21 and 51 years (M = 34.9 years, SD = 6.7) and having between 6 and 22 years of education (M = 14.8 years, SD = 3.0) were individually administered a comprehensive battery of neuropsychological tests. Of these, 59 were available at Time 2 (M = 7.1 months, SD = .9), 39 at Time 3 (M = 11.7 months, SD = 5.2), 23 at Time 4 (M = 19.1 months, SD = 5.2), and 9 at Time 5 (M = 22.8 months, SD = 7.9). In addition, 12 non-HIV adults were included as controls. The battery of tests consisted of the Wechsler Memory Scale—Revised (WMS-R), California Verbal Learning Test (CVLT), Rey Visual Design Learning Test (RVDLT), Consonant Tri-grams, Trail Making Test (TMT), Word Fluency (FAS), Shipley Institute of Living Scale, Wisconsin Card Sorting Test (WCST), Stroop Test, and measures of mood and anxiety.

Results. Because of the small sample size at Time 5, the repeated-measures analysis of variance procedures and regression analyses were conducted across the first four testing periods. CD4 counts in individuals with HIV decreased over these four testing periods \( F(3,66) = 5.5, p < .01 \) from an average count of 485.0 at Time 1 to 313.1 at Time 4. Performance on the tests of memory and attention was correlated with CD4 counts. Surprisingly, not one of the memory or attention measures included in this study was significantly related to CD4 count. Discussion focuses on differences between HIV infected adults and the normal controls, sample attrition, HIV-immune status at the time of final testing, and whether CD4 count is related to memory and attention functioning. In addition, issues of statistical versus clinical significance of CD4 change are addressed.

Reference

12. The Relationship between Neuropsychological Memory Performance and Functional Memory Ratings of Acute Rehabilitation CVA Patients

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The Functional Independence Measure (FIM), widely used throughout North America to describe functional levels in patients including those with cerebrovascular accidents (CVA), has been found to predict length of hospital stay and life satisfaction posthospital discharge. The relationship between various psychometrically sound neuropsychological measures of memory and FIM memory scores was compared in 41 CVA acute rehabilitation patients serially referred to the neuropsychology service. This exploratory correlational study demonstrated that the FIM memory score is most closely related with formal measures of visual, rather than verbal, memory when CVA laterality is not used as a grouping factor. As would have been predicted, there were double dissociations observed in verbal versus nonverbal memory performance when laterality of CVA was used as a grouping factor. These effects tend to be masked when using only FIM memory ratings. Face and convergent validity considerations related to the FIM, rehabilitation treatment approaches, as well as psychometric limitations of the current study will be discussed.

**Rationale.** As the health care system is facing cutbacks in funding and in staff, it is important to use all outcome assessment tools in the most efficient manner possible in tailoring learning style and providing the most cost-effective rehabilitation approaches. By increasing our understanding of the type of specific information each of the scores reflects, it may help us to plan and to implement rehabilitation services for patients in a more efficient manner.

Functional improvements of acutely hospitalized patients for a cerebrovascular accident (CVA) are often judged using the Functional Independence Measure (FIM) designed to rate functional disability. Recent research (Linacre, Heinemann, Wright, Granger, & Hamilton, 1994) demonstrated that the FIM is generally quite reliable in terms of internal consistency and test–retest interrater reliability, especially when rated by trained personnel. With respect to the scales’ validity, Granger, Cotter, Hamilton, and Fiedler (1993) found that the FIM is useful in the prediction of patients’ length of stay in hospital. Additionally, the FIM cognitive subscale items contributed significantly to patients’ ratings of their satisfaction with life after discharge from rehabilitation. Disler, Roy and Smith (1993) also found that the FIM was useful in predicting the amount of care a patient required after discharge. Other studies have noted that variables such as age, education, and functional ability at admission contributed to patients’ length of stay in rehabilitation, and significantly to motor functioning at discharge in patients with a variety of conditions including CVA (Heinemann, Liancre, Wright, Hamilton, & Granger, 1994).
Neuropsychological (NP) tests are another form of assessment commonly used to assess cognitive skills in patient populations. NP testing typically includes tests that measure skills rated by the FIM (e.g., memory). There is scant research which considers the relationship between cognitive FIM items and standardized NP measures of memory ability. It is expected that patients who demonstrate better memory skills on the FIM memory items, would also show better performance on various NP tests of memory. Information about the convergent validity of FIM memory items and these relationships could be particularly useful for health care workers in an applied hospital setting in order to help understand the implications of various outcome scores used.

Subjects and Method. This exploratory study examined the relationship between FIM memory items and NP standardized measures of memory in a group of 41 hospitalized patients admitted to acute rehabilitation for treatment following a CT head scan confirmed CVA. Average patient age was 60 years and included 29 males and 12 females. All patients were assessed with the FIM within 3 days after admission to the unit but serially referred for comprehensive NP assessment, most times for differential diagnostics and treatment recommendations, at some point during their stay on rehab. Assessments were tailored to the diagnostic question; therefore, collected measures were not in all cases identical for each subject, resulting in some missing values for several measures. NP measures considered for this study comprised digits backward (DB), visual reproduction (VR), logical memory (LM) and verbal paired associates (PA), all delayed recall scores from WMS-R, Rey Auditory Verbal Learning Test (RAVLT) delayed recall, Benton Visual Retention Test-MC (BVRT), and Rey–Osterreith Complex Figure delayed recall (R-O).

Results. Pearson Product–Moment correlation coefficients ($p < .05$) showed several NP measures were significantly correlated with the FIM memory items. Significant correlation coefficients were highest for VR ($r = .58, p < .01$) and R-O ($r = .55, p < .001$) with the FIM memory item. In contrast, DB ($r = .40, p < .01$), VR ($r = .55, p < .02$), and RAVLT ($r = .35, p < .05$) correlated strongest with the problem-solving FIM item compared to the FIM memory item.

In general, these findings suggest that the FIM memory item is more related to standardized measures of visual memory than of verbal memory. Recall for simple line drawings was significantly related to the FIM memory score, but memory for verbal information, including numbers, words, and stories, was not.

Although the sample sizes were quite small once participants were divided by laterality of CVA, an examination of the relationship between NP memory test and FIM memory items may help to shed some light on how FIM items may have different meaning for different patient populations. Patients with
left-sided CVA demonstrated significant correlations between the FIM memory item and easy PA ($r = .62$, $p < .03$), and LM ($r = .77$, $p < .01$). Significant correlations were found for patients with right-sided CVA between FIM memory items and VR ($r = .72$, $p < .008$) and R-O ($r = .65$, $p < .01$).

**Discussion.** These probabilities need to be interpreted with caution given the exploratory nature of the study and relatively small sample size which can affect correlation coefficients. Bonferroni adjustments to psychometrically control for multiple correlations often attenuated coefficients to none significance.

Overall, with respect to memory items on the FIM, although many of the test items which would have been expected to correlate strongly with functional memory did not, this analysis did provide some insight into just what the FIM memory item seems to assess. It would appear that for the entire group, the FIM memory items are most closely associated with formal measures of visual rather than verbal memory. In this case, VR of simple or complex line drawings which were presented to the subject one half hour earlier, seemed to be most predictive of their functional memory. However, when patients are divided according to laterality of CVA, the pattern appears to change, with verbal memory items showing stronger correlations for left-sided CVA, and the visual items being more important for those with right-sided CVA. The items which were found to be most related to patients’ FIM items were those which involved procedural memory, without an emphasis on complex components.

Future investigations would need to consider each of the cognitive items of the FIM in a similar manner in order to assess more closely what aspects of cognitive functioning each item reflects. The pattern of deficits with respect to memory might differ depending on the laterality of the CVA. Once laterality is factored in, double dissociations were observed. This pattern, which would have been expected based on previous neurocognitive research, cannot be predicted using FIM scores exclusively.

**References**


13. Executive and Memory Impairments in Patients with Anterior Communicating Artery Aneurysm

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Ruptured and repaired anterior communicating artery (ACoA) aneurysm can result in profound impairments in memory and executive function. What is unclear is whether impaired recall is attributable to problems in encoding, accelerated rates of forgetting, retrieval or some combination. Ten ACoA patients were evaluated using the REY-Organizational and Extended Memory (R-OEM) procedure which uses recall and non-recall measures and an organizational procedure for enhancing immediate recall. Our findings were: (1) organization improved immediate recall; (2) Amnesics and Non-amnesics showed similar rates of forgetting; (3) two amnesic subgroups emerged with impairments in acquisition and retrieval; (4) memory on non-recall measures was intact; (5) On CT scan only amnesics had involvement of areas beyond the frontal lobes. Overall, ACoA amnesia does not appear to be global in nature.

Rationale. Neurobehavioral deficits commonly observed following anterior communicating artery (ACoA) aneurysm include impaired memory (Alexander & Freedman, 1984), confabulation (DeLuca & Cicerone, 1991), personality change (Steinman & Bigler, 1986), and impaired executive function (DeLuca & Diamond, 1995). Importantly, traditional cerebral areas implicated in amnesia are not damaged, yet amnesia can still be manifested. While ACoA patients show normal visual-constructional skills (i.e., copy scores) on the Rey-Osterrieth Complex Figure Test (ROCFT), recall is often impaired. What is unclear is whether impaired recall is attributable to problems in encoding, accelerated rates of forgetting, retrieval or some combination.

Therefore, a major goal of the present study was to employ a procedure which allowed us to address whether impaired visual memory in ACoA subjects on the ROCFT is due to inadequate encoding, accelerated rates of forgetting or retrieval failure. Because of methodological limitations, the traditional administration of the ROCFT does not allow for the determination of the specific mechanism(s) responsible for impaired memory. That is, the use of recall measures alone may not adequately reflect the total amount of information that has been encoded (Hanley et al., 1994; Meyers & Lange, 1994).

Subjects. Ten patients, consisting of amnesic and non-amnesics with ruptured aneurysms of the ACoA, comprised the study group. Amnesic and non-amnesic subjects did not differ with respect to age, intelligence, or education.
Method. Subjects were examined using the REY-Organizational and Extended Memory (R-OEM) protocol. The R-OEM uses an organizational procedure for enhancing immediate recall and provides added sensitivity by combining recall with non-recall measures (e.g., recognition and spatial discrimination).

Results. The major findings were: (1) immediate recall in amnesics was improved by providing an organizational strategy; (2) following the organization trials, Amnesics and Non-amnesics retained information to a comparable extent over a 30-min delay; (3) two subgroups of amnesics emerged: those subjects impaired in acquisition (i.e., Facilitation group) and a second group with impaired retrieval (Non-facilitation group); (4) all subjects showed preserved memory on non-recall measures; (5) all of the ACoA subjects showed evidence of frontal lobe involvement on CT scan. However, only amnestic subjects had involvement of areas beyond the frontal lobes. Three of six amnestic ACoA subjects had infarcts in the basal ganglia, while two others had involvement in the Suprasellar region. None of the four Non-amnestic ACoA subjects displayed lesions in regions other than the frontal lobes. Furthermore, two of the three Facilitators displayed left frontal lesions, while two of the three Non-facilitators displayed right frontal lesions.

Conclusions. These findings may have important implications with respect to our understanding of the relationships between lesion site and patterns of impairment in executive and memory functions. Importantly, these results also suggest that amnesia may not represent a global impairment in function. The findings also have implications with respect to the use of organizational strategies in cognitive remediation and the utility of measures of memory that tap multiple domains (i.e., recall, recognition, and spatial discrimination) using both explicit and implicit assessment procedures.

References

14. Memory in Young Adult Survivors of Childhood Brain Tumor

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We studied memory and IQ in 30 adult survivors of childhood posterior fossa tumors an average of 17 years after diagnosis. Twenty subjects were treated with surgery and radiation for medulloblastoma (MB) and 10 were treated with surgery only for astrocytoma (ASTRO). Results were compared with 19 siblings or cousins. Controls performed better than the combined tumor group on all WMS-R Scales and the ASTROs performed better than the MBs for Visual Memory and Attention/Concentration. Controls and ASTROs performed better than MBs on the Attention/Concentration Scale even after the scores were adjusted for IQ. Verbal paired associate learning was impaired in the MB group: 25% had not met the learning criterion at the sixth learning trial, while all of the controls had done so. Memory and IQ are linked in the course of development for adult survivors of childhood posterior fossa tumors. The nature of this link appears to concern difficulty in learning new material.

Rationale. The developmental perspective on the effects of early brain damage requires consideration of the relations among cognitive domains. For example, a deficit apparent in one domain soon after brain injury may influence the acquisition of skills or knowledge in related domains, but those deficits may only become apparent later in development. Brain damage in childhood may be broadly debilitating of cognitive development, first because the ability to learn and remember new information is impaired and, second because that ability is the basis for accrual of an explicit knowledge base. Under this view, early brain damage may affect both memory and knowledge of the kind reflected in IQ scores. Because childhood is a time of active acquisition of new knowledge strategies, the range of cognitive deficits cannot be clearly appreciated during childhood itself. An appropriate group in which to explore the question of memory and IQ would be the one studied here, adult survivors of childhood brain tumors.

We studied memory and IQ in a group of adult long-term survivors of childhood posterior fossa tumors. Our aims were to discern which demographic and treatment-related factors predict later functioning and to document the relation between adult memory and IQ under conditions of early brain damage.

Subjects. Thirty adult survivors (mean age = 26.2; range = 17.2–40.3) of posterior fossa brain tumors were seen for IQ (WAIS-R) and memory assessment (WMS-R: Wechsler Memory Scale—Revised) an average of 17 years after diagnosis (range: 5.7 to 31.4 years). Twenty subjects were treated with surgery and craniospinal radiation (mean of 3500 cGy craniospinal plus a mean of 1600 cGy boost to the posterior fossa) for medulloblastoma (MB),
a malignant primitive neuroectodermal tumor arising in the posterior fossa and typically affecting the cerebellar vermis. Ten subjects were treated with surgery only for astrocytoma (ASTRO), a benign tumor of the cerebellum that is more typically located laterally in one of the cerebellar hemispheres. Results were compared with 19 control subjects who were selected from among the siblings or cousins of the tumor survivors (to provide a control for sociodemographic and family factors).

Results. There were no differences among the three groups with respect to sex or age at test. The two tumor groups did not differ in age at diagnosis or time since diagnosis. As is often true for pediatric patient groups, age at diagnosis and time since diagnosis were correlated.

Group membership affected all of WMS-R Index Scores (Verbal Memory Index, Visual Memory Index, Attention/Concentration, and Delayed Memory Index). This effect was due to better performance by the controls than the combined tumor groups on all scales. Furthermore, the survivors of ASTRO performed significantly better than the survivors of MB on the Visual Memory and Attention/Concentration Scales. Entering FSIQ as a covariate into the profile analysis eliminated the effect on the package of scale scores, although an effect persisted for the Attention-Concentration Scale. Controls and survivors of ASTRO achieved average scores on this scale, whereas survivors of MB had a mean score nearly two standard deviations lower.

The verbal paired associate subtest of the WMS-R represents a measure of new learning in which eight word pairs are presented for learning over three trials or until perfect recall is attained, to a maximum of six trials. Four of the word pairs are highly associated semantically (e.g., rose–flower), and four pairs are unrelated (e.g., school–grocery). All the groups showed learning across trials, and all groups learned the easy pairs faster than the hard pairs. However, the survivors of MB had far more difficulty learning the unrelated word pairs than the controls: despite showing learning across trials, the MB group began at a lower level than the other two groups and remained at a lower level after the three mandatory trials. While 84% of the controls had reached perfect performance after the first three learning trials, less than half of the MB group had reached criterion. By the sixth learning trial, 25% of the MB group had not met the learning criterion, while all of the controls had done so.

Discussion. These results support the view that memory and IQ are linked in the course of development for adult survivors of childhood posterior fossa tumors. The nature of this link appears to concern difficulty in learning new or novel material. Analysis of how cognitive domains are inter-related may prove important in understanding the very long-term effects of early brain damage. Finally, the results highlight the fact that memory and IQ deficits in survivors of childhood posterior fossa brain tumor are extremely long-lasting, being demonstrable in cases surviving more than a quarter of a century.
15. Failure of the NMDA Receptor Antagonist Ketamine to Impair Memory When Administered after Stimulus Presentation

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Glutamatergic dysfunction has been hypothesized to underlie memory deficits in patients suffering from Alzheimer’s and schizophrenia. NMDA receptor antagonists (e.g., PCP, ketamine) impair memory by blocking long-term potentiation in the hippocampus. Limited research in humans has taken place and studies typically administer the antagonists before the learning experience, perhaps resulting in inattention induced by the psychotomimetic effects of these drugs and/or alterations in sensory processing. Bolus injections of ketamine (.01, .03, and 0.5 mg/kg) or placebo were given to 11 normal controls. Immediately prior to injection a verbal memory test and a digit supraspan procedure were administered. Unlike previous studies in which the drug is administered before stimulus presentation, postinjection (30–45 min) scores revealed no differences between the drug and placebo conditions for either task.

Rationale. Substantial evidence points to the important role of NMDA receptors (one type of glutamatergic receptor) in long-term potentiation (LTP), generally considered to be the neurophysiologic basis for memory. Glutamatergic dysfunction has been hypothesized to play an important role in disorders in which memory deficits are common, such as schizophrenia and Alzheimer’s. NMDA-receptor antagonists (e.g., ketamine, PCP) block LTP and antagonizes learning and memory. Conversely, NMDA agonists have been shown to enhance memory retention. Well studied in animal models, few studies have examined the effects of NMDA antagonists on human memory, although existing results with human participants are similar to those found with animals. However, studies typically administer the NMDA antagonist prior to the learning procedure a practice problematic for two reasons. First, these drugs have potent psychotomimetic effects which may cause memory impairment via indirect (secondary) reductions in attention at the time of stimulus presentation. Secondly, metabolic imaging studies in rats reveal a reduction in local cerebral glucose utilization in the somatosensory and auditory areas following administration of ketamine which could reduce the amount of information available for processing, or provide degraded information, either of which might affect the amount or accuracy of later recall.

Given the absence of well-controlled studies comparing the effects of ketamine on the consolidation of memory, we challenged normal control subjects with subanesthetic (0.1, 0.3, and 0.5 mg/kg) doses of ketamine or placebo in a double-blind procedure. Unlike most previous studies we administered the drug immediately following stimulus presentation. It was predicted that
once LTP had occurred, ketamine would have no effect on consolidation of memory.

Subjects. Subjects (n = 12; 9 males, 3 females) were recruited via newspaper advertisement and screened over the phone for potential confounding factors (e.g., drug use, family history of psychiatric disturbance). In-depth structured interviews revealed that none of the subjects met current or past diagnostic criteria for a mental disorder. Average age of subjects was 28 years, most subjects were white (83%), single (50%), and had some college (M = 14.6, SD = 4.4 years of education). Written consent was obtained from all subjects who were informed about the nature of the study and side effects of ketamine including the potential of psychotic-like symptoms.

Method. Thirty minutes prior to infusion an intravenous line was initiated using normal saline. Subjects were monitored via a continuous cardiac monitor, blood pressure cuff, and pulse oxymeter (blood oxygen saturation). In order to rule out generalized impairment, subjects were administered the Serial Digit Learning Test which requires the subject to acquire a supraspan digit sequence (9 digits) within 12 trials, tapping the ability to sustain attention. It is sensitive to generalized changes in cerebral functioning as well as lesions to the hippocampus. Immediately prior to injection subjects were read one of the word lists from the Hopkins Verbal Learning Test. Each list is comprised of 12 nouns from 3 different stimulus categories (e.g., foods). This test has 8 equivalent forms so that different versions could be used on different occasions without a learning effect occurring. Subjects recalled as many words as they could and were immediately administered either ketamine hydrochloride (0.1, 0.3, or 0.5 mg/kg), or placebo infused over 60 sec. Order of drug administration was partially randomized across subjects, with none of the subjects receiving the highest (0.5 mg/kg) dose on the initial session. Approximately 30–45 min postinfusion delayed recall of the word list was obtained and the digit supraspan procedure again administered.

Results. A repeated-measures MANOVA with two within-subjects factors, time (pre- and postdrug) and drug (0.1, 0.3, and 0.5 mg/kg ketamine and placebo), revealed no significant difference between ketamine and placebo on verbal recall \( F(1,24) = .99, p = .35 \), nor were there any time or drug \times time interactions. One-way repeated-measures NOVA comparisons of retention rates (delayed recall/immediate recall \times 100) with one within-subjects factor (drug dose) revealed no difference between the drug and placebo conditions \( F(3,44) = .45, p = .73 \). Finally, scores on the digit supraspan procedure were not affected by administration of ketamine as no significant pre–post differences emerged. These results suggest that although NMDA antagonists are capable of blocking LTP when administered before stimulus presentation, they do not appear to affect the post-LTP cascade of events (e.g., effects of retrograde messengers, protein phosphorylation, entry of calcium into the postsynaptic terminal, etc.) purported to underlie memory con-
solidation. Thus, their effects appear to be related to learning and memory formation but not to consolidation or retrieval of previously learned information.

16. A Functional Imaging Study of Memory Impairment in Schizophrenia

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We examined brain activity in two groups of schizophrenic subjects, one with memory impairment and the other without. All subjects underwent 12 positron emission tomography (PET) scans while engaged in the encoding and recall of word lists. Memory load was manipulated by parametrically varying the length of the lists across scans. Comparisons with a group of age-matched, healthy controls showed a relative failure of left prefrontal activation and of bilateral temporal deactivations in both groups of schizophrenic subjects. Restriction of analyses to those scans in which performance was comparable across groups showed quantitatively normal prefrontal activity in the subjects with schizophrenia. Our results indicate both an abnormality of fronto-temporal interactions in schizophrenia and an abnormality in prefrontal function, the latter relating to memory performance.

Rationale

Schizophrenia is a chronic, deteriorating disorder characterized by, among other things, delusions, hallucinations, social withdrawal, and a number of cognitive deficits. Recent studies have shown that memory impairment can be a major feature, disproportionately exceeding other cognitive abnormalities. The memory impairment tends to be specific to episodic long-term memory and it has been shown that it is not explicable purely in terms of accompanying symptoms such as hallucinations.

Our previous work has suggested that the functional neuroanatomical abnormalities in schizophrenia may be conceptualized as a reversal of the normal interactions between the prefrontal and temporal cortex. Other studies have suggested that the core pathology in schizophrenia lies in a functional abnormality of the prefrontal cortex. Since PET studies of healthy volunteers performing long-term memory tasks have produced data which emphasizes the role of prefrontal cortex in memory, it seems likely that memory provides a useful arena in which to study the functional neuroanatomy of schizophrenia. We therefore used positron emission tomography (PET) to examine changes in brain activity related to the encoding and paced retrieval of word lists in groups of healthy control subjects and in patients with schizophrenia. Memory load was systematically manipulated by parametrically varying word-list length.
Subjects

Twelve subjects with schizophrenia (DSM III-R diagnosis), all on medication, and 6 healthy, age-matched control subjects were scanned. The subjects with schizophrenia were subdivided into two equal groups: Those showing memory impairment and those with preserved memory function.

Method

All subjects underwent 12 PET measurement of regional cerebral blood flow (rCBF) over a 2-hr period. During each PET scan they were engaged in the encoding and paced recall of word lists. Material was presented verbally at a rate of one word per 2 sec. On the completion of the list, subjects were required to retrieve as many items as possible, recall being paced by the experimenter. On completion of the retrieval stage, the list was read and recalled once more; this was repeated throughout scanning. Word list length varied across the 12 scans from 2 to 13 items inclusive.

Statistical parametric mapping (SPM) was used to analyze PET scan data. Scans were realigned and spatially normalized before a correction for changes in global blood flow and pairwise comparisons on a voxel by voxel basis. Data were analyzed for the main effects of memory load (i.e., which brain regions showed increases and decreases in activity in association with varying memory load). In addition, we examined the group-by-task interaction for regions where the subjects with schizophrenia showed significant failures in activation and deactivation in association with the memory task and for regions where brain activation was associated with the presence of memory impairment. A further stage of the analysis assessed activations in light of the degree to which subjects were successful in retrieving material.

Results

Memory-related activations and deactivations in control subjects. The control group showed activations in left lateral prefrontal cortex (PFC) and parietal cortex bilaterally. Deactivations were seen in superior temporal cortex bilaterally and in medial PFC. Analysis of data from subjects with schizophrenia showed a qualitatively similar pattern of activations and deactivations.

Group-task interactions. While showing a qualitatively similar pattern to control subjects, both groups of schizophrenic subjects showed significantly less left PFC activation and temporal deactivation. In addition, the group with impaired memory function showed a significant failure of parietal activation bilaterally. Direct comparison of the two groups of schizophrenic subjects showed a relative failure of parietal activation and of temporal deactivation in the memory-impaired group.
Relation to performance. Across those scans where performance in the schizophrenic subjects was comparable to controls, a normal degree of left PFC activation was observed while failure of temporal deactivation remained significant. In the group with impaired memory, bilateral parietal cortex continued to show an impaired activation.

Discussion

In brief, our study has shown patterns of abnormality in memory-related activity in schizophrenia. First, left PFC activations were significantly less than in control subjects and this can, perhaps, be interpreted as a failure to apply appropriate encoding strategies. The finding that left PFC activation in schizophrenic subjects was statistically indistinguishable from control subjects when effects of impaired performance were removed is an interesting one indicating, as it does, that it is not an inability to activate PFC per se which lies at the core of the abnormality. Rather, it seems that, when the demands of the task become excessive, there is a falling off of normal activity and this is associated with a failure to optimally encode information. The second abnormality, that of a failure of temporal cortex deactivation has been conceptualized as an abnormality of the normal pattern of fronto-temporal integration. This abnormality was not affected by performance and might conceivably indicate a core pathology in schizophrenia.

17. Auditory Short-Term Memory in Schizophrenia: An Event-Related Brain Potentials Study

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This study evaluated the early stages of sensory processing in patients with schizophrenia using the mismatch negativity (MMN), an event-related brain potential associated with auditory memory. Twelve patients with schizophrenia and 12 age-matched controls were presented with: (1) sequences of identical tones that included occasional deviant tones differing in pitch and (2) sequences of tones alternating in pitch with rare deviant repetitions in the alternating pattern. Deviant stimuli elicited an MMN at 120- to 180-msec latencies. The MMNs elicited by the pitch deviations were reduced in amplitude in schizophrenics. No group differences, however, were found in the MMN amplitude to pattern-deviant stimuli. The results suggest reduced specificity in the neuronal response to physically deviant stimuli.

Rationale. Schizophrenia is one of the most devastating psychiatric diseases, characterized by thought disorders and auditory hallucinations. Electrophysiological studies suggest that in schizophrenics, the initial encoding
of auditory stimuli is disrupted because of defective inhibitory mechanisms (e.g., Freedman et al., 1991) similar to those seen in patients with prefrontal damage (Knight, 1994). Conceptually, such defects could allow stimuli to flood in and perturb the integration of auditory inputs, especially in conditions requiring irrelevant stimuli to be dismissed or suppressed.

The mismatch negativity (MMN) of human event-related brain potentials (ERPs) provides a neurophysiological index of early sensory and pattern analyses. The MMN is obtained by presenting subjects, who are engaged in a distracting activity (e.g., reading), with sequences of homogeneous stimuli interleaved with rare deviant stimuli. The deviant sounds may differ from the standard stimuli in pitch, duration, intensity, or spatial location (Näätänen, 1992). The MMN is also generated by deviations in unattended sequences of tones that alternate (Alain et al., 1994) or decrease regularly in pitch (Tervaniemi et al., 1993). The MMN peaks at a latency of 140–240 msec post-stimulus and is maximal over midline frontal areas (Näätänen, 1992). It reflects a neural mismatch between an incoming stimulus and representations of previously presented stimuli (Näätänen, 1992).

Patients with schizophrenia show decreased MMN amplitude to pitch (Javitt et al., 1993) and duration deviant stimuli (Catts et al., 1995). The MMN decrement is present in both medicated and unmedicated patients and is not observed in patients with bipolar disorders (Catts et al., 1995). Since generation of the MMN depends on the ability of the primary auditory cortex to maintain a memory of the types of stimuli presented (Näätänen, 1992), the MMN decrement in schizophrenics raises the possibility that there might be a deficit in auditory short-term memory. The aim of the current study was to evaluate the auditory short-term memory deficit hypothesis using the MMN elicited by pattern-deviant stimuli as well as pitch-deviant stimuli. Deviations of tone patterns place greater demands on auditory short-term memory since auditory pattern memory must include abstract features (e.g., interstimulus relationship) of several stimuli over a multi-second interval. Therefore, deficits in auditory short-term memory should produce even greater abnormalities in the MMN to pattern-deviant stimuli than in the MMN to pitch-deviant stimuli.

Method. Twelve medicated chronic schizophrenic patients and 12 age-matched control subjects attended to visual stimuli and were asked to press a button as fast as possible for thick vertical bars (probability 20%) which were mixed randomly with thin vertical bars (probability 80%). The visual stimuli were displayed for 50 msec at the center of a video monitor at variable stimulus onset asynchrony (SOA, 500–1500 msec). While performing the visual discrimination task, subjects were presented with sequences of identical tones (1000 Hz) that included rare deviant tones differing in pitch (1122 or 1414 Hz) and sequences of two tones alternating regularly in pitch (500 and 2000 Hz tones) with occasional deviant repetitions. Stimuli (100 msec
in duration, 10 ms rise/fall times, 85 dB SPL) were delivered monaurally at fixed SOA (250 msec) with broadband noise (65 dB SPL) presented in the opposite ear.

The EEG (bandpass 0.1–100 Hz) was continuously digitized and recorded from 28 electrodes over the scalp. Vertical and horizontal eye movements were recorded from electrodes lateral and below the left eye. All electrodes were referenced to four interconnected electrodes at the base of the neck, balanced through a potentiometer to cancel electrocardiogram artifacts. For each deviant type, the MMN was measured relative to the mean amplitude of the 200-msec prestimulus activity. The MMNs were compared at Fz for five successive mean voltages obtained for 20-msec windows beginning at 100 msec poststimulus. The results were statistically evaluated using analysis of variance (ANOVA) for repeated measures.

Results and discussion. ERPs of frequently presented auditory stimuli were characterized by a negative (N1) and positive (P2) deflections peaking around 100 and 180 msec from stimulus onset. Deviant tones elicited an N1 wave and an additional negative deflection, the MMN wave. In both groups, this MMN began around 60 msec poststimulus and peaked at about 160 msec over fronto-central sites. The MMN elicited by small and large pitch-deviant stimuli was significantly reduced in patients with schizophrenia compared to age-matched controls between 130 and 190 msec (range of $F(1,22) = 4.43−7.19, p < .05$). This result is consistent with previous research showing MMN reduction to physically deviant stimuli (e.g., Catts et al., 1995).

However, no difference was found between the two groups for the MMN elicited by changes in the alternating patterns ($F(2,22) < 2.77, p > .1$ in all cases). This finding was unexpected. Presumably, if the MMN decrement found for physically deviant stimuli reflects sensory memory deficits in patients with schizophrenia, then the MMN to changes in alternating patterns should have been reduced as well.

An alternative hypothesis to the sensory memory account would be that the MMN decrement observed in schizophrenics reflects primarily a deficit in sensory regulation. Physically deviant stimuli not only disrupt the perceptual context but also trigger new neuronal elements. Therefore, the MMN to physically deviant stimuli may receive contributions from at least two distinct neuronal sources: (1) neurons triggered by changes in the perceptual context and (2) neurons triggered by changes in the physical attributes of the incoming stimulus. Schizophrenia may selectively affect threshold activation of the cortical responses to physically deviant stimuli as shown by the smaller ERP amplitude to the pitch-deviant stimuli. This would account not only for the smaller MMN to physically deviant stimuli but also for the altered startle reflex in patients with schizophrenia (Braff et al., 1978). In summary, patients with schizophrenia appear to have abnormally reduced neuronal sensitivity to new stimuli without impairment in auditory pattern memory. Further research should determine the role of abnormal thresholds for novel stimuli
in addition to factors such as the severity of the symptoms and the effects of medication on the ability to integrate information over time.

References


18. Verbal Memory Disorders in Schizophrenic and Brain-Lesioned Patients

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We compare memory disorders of schizophrenic patients with patients suffering from focal brain lesions. The schizophrenics were classified into three subgroups: paranoid–hallucinatory, disorganized, and negative symptoms. All patients studied a list containing 16 words five times. Dependent measures were learning rate, retention, and indices for the strategic control of learning. The amount of general cognitive impairment and medication was controlled. The left mediotemporal group had general memory deficits, an inflated recency effect, and deficient semantic clustering. Left prefrontal lesions resulted in slowed learning and an increased recall presenting semantic cues. The paranoid–hallucinatory group showed little evidence of memory disorder. Both the disorganized and negative-symptom groups were in absolute terms as impaired as the organic brain-damaged groups. A discriminant analysis revealed that patients with negative symptoms suffered from an impairment pattern similar to that of the brain-damaged patients, particularly to that of the left prefrontal group. The disorganized patients showed a pattern of impairment which differed from all other groups. Recent neuroimaging studies have focused on right ventromedial frontal hypoactivity in these patients. Future research should explore
similarities between disorganized patients and people with right-hemisphere focal lesions.

**Rationale.** Ernst Kraepelin was the first to discuss declarative memory disorders of *dementia praecox* (i.e., schizophrenic) patients, and while waxing and waning, the debate has never subsided entirely (Brand, Hildebrandt, & Scheerer, 1996). Most studies have tended to presuppose a single nosological unit called *schizophrenia*, though more recently this has been subjected to severe criticism. According to current diagnostic criteria, patients who do not share one single symptom all can be labeled *schizophrenic*. However, by means of multivariate statistical methods (e.g., factor analysis), the diversity of schizophrenic disorders can now be mapped unto the three classic syndromes paranoid-hallucinatory, disorganized, and negative symptoms. These classic syndromes are expected to match, in turn, the main types of diverging cognitive deficits.

We have approached this problem by studying the memory performance of schizophrenic patients belonging to different diagnostic subgroups and comparing it to the data from patients suffering from focal cerebrovascular insults in left mediotemporal, left prefrontal, and right postcentral regions.

**Subjects.** Twenty-nine schizophrenic patients and 34 patients with focal brain lesions were studied. The schizophrenic patients were classified by means of the Positive and Negative Syndrome Scale (PANS, Kay et al., 1987) into psychopathological subgroups. This classification relied on the leading symptoms P1 (delusional ideas), P2 (formal thought disorder), and N6 (lack of spontaneity and speech fluency). The brain-damaged patients were classified using CT and NMR. Patient classification, as well as analysis of memory performance, was done in double-blind fashion for all participants. Given the exclusively verbal nature of the learning task, the right postcentral group served as a control group. Overall, the schizophrenic patients were younger than the brain-damaged patients, an unavoidable consequence of the incidence rates of their impairments.

**Method.** The task, a German-language derivate of the California Verbal Learning Test, consisted of five presentations of a 16-item word-list. On the sixth trial, the effects of proactive inhibition were studied by means of a different, *interference* list, comprising in part a switch to different taxonomic categories. On the final trial, cued recall (using the taxonomic categories as retrieval cues) was measured in addition to free recall. Recognition was assessed by presenting a list of 44 items containing the 16 target words, words of the interference list and new words. All learning lists were presented acoustically at a rate of two words per second.

Overall measures were the amount of learning (i.e., number of correctly recalled items), rate of learning (difference between the first and fifth trials), and final performance (after the interference list) under free and cued recall. Effects of interference were measured by the decrement for the interference list. In addition, the serial position curve (recency and primacy effects) was
analyzed, a semantic clustering measure was computed, the consistency of retention (defined by the percentage of items that were correctly recalled on two successive trials) was determined, and recall and recognition were compared.

Results. Schizophrenic patients demonstrated significantly lower levels in learning and retention, reduced retention consistency, and impaired semantic clustering relative to the right postcentral group. For the paranoid–hallucinatory patients, recognition was not impaired.

There were clear differences among the schizophrenic groups. In virtually all learning, retention and recall parameters that were assessed, disorganized and negative-symptoms patients were significantly more impaired than paranoid–hallucinatory patients and often were not significantly different from the patients with left mediotemporal lesion.

Recognition was severely impaired, and accompanied by a shift of the serial position curve in the direction of a greater recency effect. The memory impairment of the disorganized and negative-symptoms patients was almost indistinguishable from that shown by patients with a classic amnesic syndrome, the leading symptom of left mediotemporal brain damage. On all memory measures the negative-symptoms group were not different from the left prefrontal group. The two impaired schizophrenic groups did differ from the left mediotemporal group. The disorganized group had less forgetting and a lower recognition/recall ratio, and the negative symptoms group a reduced recency effect.

Discussion and conclusions. The present investigation documents that memory impairments belong to the core deficits of persons diagnosed as schizophrenic. The pattern of memory impairment revealed by the word-list task suggest that disorganized and negative symptom, but not paranoid-hallucinatory patients, suffer from a disorder that has neuropsychological dimensions and cannot be reduced to a merely functional disorder.

The bulk of the evidence from the negative-symptoms patients is consistent with a prefrontal (though not frontal per se) impairment pattern, consistent with some neuroimaging evidence (Liddle et al., 1992) and an exhaustive literature survey completed by our group (Brand et al., 1996). The disorganized patients were different from all three groups with focal lesions. Their memory was clearly impaired, but the pattern of impairment did not match that found in any of our brain-lesioned groups. Recent neuroimaging studies have focused on right ventromedial frontal hypoactivity in disorganized patients (Liddle et al., 1992). Thus, future research should explore potential similarities between disorganized patients and individuals with right-hemisphere focal lesions.

References

19. Measurement of Medial Temporal Lobe Thickness for the Differential Diagnosis of Dementia

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We measured medial temporal lobe thickness (MTLT) on MRI in Alzheimer’s (AD) patients, vascular dementia (VaD) patients, primary progressive aphasics (PPA), and normal controls (NC). Mean AD MTLT was different from that of NCs, but there was considerable overlap. Likelihood ratios revealed that a MTLT of <7.0 mm yielded an 8-fold increase in the likelihood of AD. Using prevalence statistics for AD, a MTLT <7.0 mm increased the risk of AD 10-fold for ages 65–74, 6-fold for ages 75–84, and 3-fold for ages >85. MTLT also differed between NCs and VaD, but did not differentiate AD from VaD or PPA, unless the left side is considered alone in PPA. Measurement of MTLT could be useful in evaluation of patients at risk for AD, but a combination of MTLT with other imaging parameters will be needed for more accurate differential diagnosis.

Rationale. The medial temporal lobe of the brain is important for normal memory function and this area of the brain has been found to show pathological change in Alzheimer’s disease (AD). Medial temporal lobe thickness (MTLT) measured on CT has been found to be significantly smaller in autopsy-confirmed AD versus normal controls (NC) with little overlap (Jobst, Smith, & Szatmari, 1992). Thus it has been recommended as a diagnostic tool.

Method. To determine the value of measuring MTLT for diagnosis of AD, we measured MTLT in 29 AD subjects meeting NINCDS-ADRDA criteria and in 23 age-matched NCs using magnetic resonance imaging (MRI). Scans were acquired using a 1.5T-MR system (Signa version 4.7, General Electric) and a sagittal T1-weighted 3D volume technique producing 124- to 1.3-mm slices. Slices were obtained with a TR/TE of 35/5 msec, flip angle of 35 degrees, and a FOV of 22 cm in an imaging time of 10.5 min. Images were assessed on a SUN workstation using the ANALYZE software system. All images were reformatted within ANALYZE to be sliced parallel to the long axis of the hippocampal formation in the sagittal view. The minimum width of each MTLT (hippocampus and parahippocampal gyrus) was measured.
using a ruler on printed images adjusted to reflect true brain size. Both left
and right MTLT measures were made on axial scan sections which best rep-
resented the MTLT between its inferior and posterior limits. Widths were
measured in millimeters at the narrowest point of the medial temporal lobe
level with the midbrain (between its anterior and posterior limits). This
procedure is comparable to that of Jobst et al. (1992) who measured the MTLT
on CT scans performed approximately 20 degrees caudad to Reid’s baseline.

We also studied 14 vascular dementia (VaD) patients meeting NINDS-
AIREN criteria (Roman & Tatemichi, 1993) and 11 patients who had frontal
temporal degeneration with primary progressive aphasia (PPA) (Black,
1996).

Results. The inter- and intraclass correlations were >0.82. Mean MTLT
in AD (5.4 mm ± 2.0) was significantly different from NCs (7.8 ± 2.0) (p < .001), but there was considerable overlap. MTLT did not correlate with
age (range 53–84), hippocampal volume, or dementia rating scales in any
group. The area under the ROC curve was 0.78 (p < .001), and the best
model used a cutoff point of 7 mm thickness (similar to that reported by
Jobst et al.) giving a sensitivity of 72% and a specificity of 91% (positive
predictive value = 0.05; negative predictive value = 0.72). Likelihood ratios
revealed that a MTLT of <7.0 mm yielded an 8-fold increase in the likeli-
hood of AD, whereas a MTLT >7.0 mm yielded less than one-third likeli-
hood of AD. Recent Canadian statistics show that prevalence of AD rises
from 1% at ages 65–74 to 6.9% at ages 75–84 and to 26.0% at ages 85 and
over. Based on these statistics the risk ratio for AD given age and a MTLT
of <7.0 mm was calculated. (Pretest odds for the disorder × the likelihood
ratio for the diagnostic result = the posttest odds for the target disorder). A
MTLT <7.0 mm increased the risk of AD 10-fold for ages 65–74 (i.e. 1–
10%), 6-fold for ages 75–84 (i.e. 7–40%), and 3-fold for ages >85 (i.e. 30–
75%). MTLT also differed between NCs and VaD (6.1 ± 2.0) (p < .02),
but only for the left side in PPA (left mean 6.4 ± 3.6, p < .04; right mean
9.4 ± 2.7, p < .05).

Conclusions. Although smaller in AD patients versus NCs, MTLT has
only moderate sensitivity, and does not differentiate AD from VaD or PPA,
unless in PPA the left–right asymmetry is taken into account. It is notable,
however, that our cutoff point observed using a slightly different methodology and different imaging technique concurred with that reported by Jobst
et al. Although CT is more widely available, the protocol used by Jobst et
al. requires unconventional angulation and special positioning. The use of
MRI for this measurement is advantageous because 3D acquisition of images
(7–10 min) allows for reconstruction of images in any view postacquisition.
MRI also allows for quantification of other brain regions involved in Alzhei-
mer’s disease. Interestingly, however, MTLT did not correlate with hippo-
campal volume alone. In fact current research in our lab shows that hippo-
campal volume is a poor discriminant of AD from elderly controls. This
suggests that parahippocampal atrophy contributes to better differentiation achieved by MTLT. A MTLT of <7.0 mm could be useful in clinical evaluation of patients at risk for AD, but a combination of MTLT with other MRI parameters and/or functional imaging patterns will likely be required for accurate differential diagnosis.

References


20. Visuospatial Recall in Cortical and Subcortical Dementias

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Cortical and subcortical dementias differentially affect cognition with visuospatial sequencing particularly susceptible to damage in subcortical dementias. This study examined visuospatial memory and sequencing in cortical vs subcortical dementias. Recall of temporal presentation of visuospatial material was examined in Parkinson’s disease (PD), Alzheimer’s disease (AD), healthy elderly (HE), and healthy young subjects. Predictable pattern vs random sequences assessed ability to utilize pattern information to decrease the memory load of the task. Young subjects performed consistently better than the other groups on random trials. PD performance was consistent with the healthy older subjects. AD subjects were worse than the other groups on some trials. These results indicate that while AD subjects have a deficit in temporal ordering of visuospatial information relative to HE, PD subjects do not.

Rationale. There is evidence that cortical and subcortical dementias differentially affect visuospatial cognition (Cummings, 1986). Both visuospatial memory and visuospatial sequencing involving production of coherent stories, such as on the Picture Arrangement task on the WAIS-R, are impaired in Parkinson’s disease (PD) (Beatty & Monson, 1990). It is unclear how the sequencing deficit is impacted by the language component of the story in
the Picture Arrangement task. The goal of the present study is to examine how cortical vs subcortical dementias impact visuospatial memory and sequencing on tasks with low language dependency. Recall of temporal presentation of visuospatial material was examined in people with PD and Alzheimer’s disease (AD), healthy elderly, and healthy young subjects. The additional variable of predictable pattern vs random sequences was included to assess the ability to utilize pattern information to decrease the memory load of the task.

Subjects. The Subjects comprised four groups: young adults (Y), healthy elderly adults (HE), individuals with a diagnosis of idiopathic PD, and individuals with a diagnosis of probable AD. Mean ages for each group, respectively, are $M = 19.48, SD = 1.08 \ (n = 25); M = 70.16, SD = 5.66 \ (n = 25); M = 61.53, SD = 10.18 \ (n = 17); M = 74.05, SD = 6.62 \ (n = 19)$. The four groups did not differ significantly in mean years of education $[F(3, 78) = 1.23, p = .31]$. The PD group ($M = 7.0, SD = 4.34$) has a significantly longer duration of illness than the AD group ($M = 4.05, SD = 2.57$) $[F(1, 34) = 6.30, p < .02]$. All PD patients were receiving Sinemet. No subjects received anticholinergic medications.

Method. The Mini Mental Status Exam (MMSE) was administered to the AD and PD groups to assess for degree of dementia. To rule out dementia in the HE group, they were given retrospectively a telephone interview of cognitive status (TICS). Results of the TICS showed that the HE Subjects performed within the nondemented range of functioning. As expected, a $t$ test on MMSE performance revealed that the AD group ($M = 22.42, SD = 2.61$) was significantly more demented than the PD group ($M = 28.9, SD = 1.97$) $[F(1, 34) = 89.09, p < .0001]$. Following the dementia assessment, each participant was oriented facing a computer screen on which the task of temporospatial memory (X-test) modified from Kesner et al. was administered. The screen was divided into a $4 \times 4$ grid of 16 boxes. Subjects were instructed to watch and remember the sequence of eight Xs that appeared one at a time in the grid. They were told that the sequence may be random or form a pattern. Following the appearance of the sequence, subjects were asked four questions pertaining to the order of that sequence. For each question, they were to indicate which of two Xs presently appearing in the grid had appeared before the other in the previous sequence of eight Xs. This procedure was repeated for eight sequences, four of which were random and four formed easily recognizable patterns. For each set of questions, the two target Xs varied in order of appearance in the original sequence such that each set of four questions included questions in which the Xs were (1) directly adjacent in the original sequence, (2) separated by two other Xs, (3) separated by four other Xs, and (4) separated by six Xs.

Results. Because the variance in scores in the AD group was significantly
larger than in the other three groups, analyses were conducted on ranked data. A binomial test revealed that overall all groups performed better than chance on the X-test. An ANOVA on number of errors for the eight sequences combined, showed a significant effect of group \( [F(3, 82) = 31.68, p < .0001] \). Simple effects test revealed that the AD group performed significantly worse than the other three groups and the Y group performed significantly better than the other three groups. This same pattern of results was observed in an ANOVA of number of errors for random sequences only \( [F(3, 82) = 22.03, p < .0001] \). However, an ANOVA of number of errors for pattern sequences yielded a significant group difference with only the AD group performing worse than the other three groups. All groups performed better on the pattern than on the random sequences.

Analyses examining the impact of the temporal relationship between the Xs revealed that questions with four Xs between target Xs was the most difficult across groups. An ANOVA of patterned sequences resulted in a significant effect of group (as observed above). An ANOVA of random sequences revealed significant effects of group, temporal relationship and their interaction. AD performed worse than the other three groups when the Xs were further apart (four and six between) and as well as the PD and HE groups when Xs were close together (adjacent and two between). The Y group performed better than all three at temporal distances 0 and 4, better than PD and AD at distance 2, and equivalent to PD and HE groups at distance 6. The HE and PD groups performed similarly at each distance.

Discussion. This suggests that temporal recall of visuospatial information is significantly affected by ability to utilize the cognitive strategy of pattern recognition. PD subjects demonstrated pattern recognition and temporal recall consistent with the HE and Y groups. In addition, the temporal proximity of information influences the ability to recall information especially in random sequences. Depending on how far apart the information is presented temporally in random sequences, AD patients perform like PD patients or HE. These results are consistent with the idea that cortical and subcortical dementias differentially effect visuospatial cognition. In the current study, the PD group had a longer disease duration than the AD group. Although the AD group had lower total scores on the MMSE, the PD group had lower scores on the constructional component. This experiment does not support the notion that PD patients have a deficit in temporal ordering of visuospatial information relative to HE.

References

21. Learning New Face–Name Associations with Spaced Retrieval Strategy on a Patient with Alzheimer-Type Dementia

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This study describes the use of the Spaced Retrieval Strategy (SRS) for learning new face–name associations in a woman with Alzheimer-type dementia (DAT). N.C. shows severe episodic memory deficits but intact implicit memory. As SRS probably relies on implicit memory, it is hypothesized that favoring implicit retrieval, rather than explicit retrieval, could allow for learning to occur. Results seem to indicate that it is the case, as N.C. only learned face–name associations under implicit memory instructions. However, additional testing revealed important proactive interference with both instructions. This could be explained by N.C.’s incapacity to inhibit irrelevant answers. It is suggested that SRS and errorless learning should be combined to optimize acquisition of new information in DAT patients.

**Rationale.** Most researchers agree that episodic memory, which refers to the retention of personal information encoded in a spatio-temporal context, is the memory system most affected by dementia of Alzheimer type (DAT). Several studies have shown preserved procedural and implicit memory in the DAT population. These observations have generated research aiming at improving the learning abilities of DAT patients by using these preserved memory capacities. For example, the Spaced Retrieval Strategy (SRS), in which retention is tested after increasingly long temporal delays, has allowed DAT patients to learn new face–name associations (Camp & Schaller, 1989) to improve their ability to name objects (i.e., Abrahams & Camp, 1993) and to improve their prospective memory (McKitrick & Camp, 1992). According to these studies, the SRS is effortless and probably relies on preserved memory capacities of the implicit type. The aim of the present study was to compare, in a DAT patient, the efficiency of the SRS when favoring an implicit versus an explicit memory instructions. It is hypothesized that learning performance will be better when implicit memory is favored, as it is believed that the SRS relies on this system.

**Subject.** N.C. is a 69-year-old Belgian woman who was diagnosed as probable Alzheimer patient according to the NINCDS-ADRDA criteria. She was tested extensively with language and neuropsychological batteries. This showed absence of disorders of linguistic and praxic types. She showed, however, mild deficits on the Stroop test, as she had difficulties in inhibiting
the nondesired responses. Long-term episodic memory was severely affected for both verbal and nonverbal material. In contrast, short-term, semantic and implicit memories were preserved.

**Method.** Four black and white photographs of faces were chosen according to the following criteria: they represented white males, with similar facial expressions and no distinctive features (i.e., mustache), photographed in a 3/4 profile in front of the same background. The faces were approximately $11 \times 12$ cm in size. A family name was randomly associated with each face. The names were of Belgian origin and equal in length (seven characters). They could not be used as first name and were neither ambiguous nor easily visualized. They were relatively rare and each began with a different consonant.

The patient was tested for 45 min once a week over 3 months. The face with the associated name were first presented for 5 sec. Following a delay period (0 sec for the first trial), the subject was shown only the face, which she then had to name. If the answer was correct, the delay for the next face presentation was increased. Delays were increased exponentially (0, 2, 4, 8, 16, 32, etc. sec) until the subject erred or to the end of the session. If the answer was incorrect the delay was decreased. During the delays, the subject was distracted with diary exercises. At the beginning of the following session, N.C.’s memory of the name was tested. If she could name the face, the criterion for learning was considered to be attained and she was tested on a new face–name association. If she was unable to name the face, learning was ensured, starting with the longest delay achieved in the previous session.

In the implicit instruction condition, N.C. was asked to speak out the first name which crossed her mind when she saw the face. In the explicit memory condition, N.C. was asked to retrieve the learning episode from memory. The order of the two learning conditions was balanced following an ABA design, starting with the implicit condition. At the beginning of every other session, the patient was asked to fill in a questionnaire about the session progress (her explicit knowledge of what happened in the session, the type of material learned, etc.)

**Results and discussion.** N.C. reached the learning criterion for the two associations learned under the implicit memory instruction after two and three sessions, respectively (40 and 30 presentations). In contrast, she was unable to reach the criterion for the association learned under explicit memory instruction for which testing was interrupted after three sessions (80 presentations). These results suggest that implicit memory instructions are necessary for the SRS procedure to generate learning in DAT patients. However, it is possible that results were biased by proactive interference in the association learned under explicit retrieval instruction, as this condition followed a successful implicit memory learning. Indeed, the error analysis in the explicit condition revealed that 25% of N.C.’s errors consisted in producing the previous learned name. No interference was observed in the third trial learned
under implicit instruction, and this might be due to the fact that no learning occurred in the previous association. For this reason, a fourth trial of implicit retrieval was performed. If proactive interference explains our results, there should be difficulties in learning the association, even with implicit retrieval. Indeed, N.C. failed to reach criterion after three sessions (62 presentations). Moreover, she showed 18.57% of intrusion errors. Finally, it must be noted that N.C. had very poor recall of the sessions content, as measured by the questionnaire.

Despite poor recall of the session content, N.C. was able to learn new face-name associations and the learning was somewhat better when implicit retrieval was favored. However, an important proactive interference was observed under both conditions. Baddeley and Wilson (1994) have suggested that the difficulty of amnesic patients to inhibit answers is related to their severe episodic memory deficit. They found that errorless learning was efficient with amnesic patients, since it prevented this production of self-perpetuating errors. It is suggested that SRS and errorless learning should be combined to optimize their acquisition of new information in DAT patients.

References

22. Visual and Semantic Determinants of Object Recognition Deficits in Early Alzheimer’s Disease

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The visual and semantic factors underlying recognition deficits in Alzheimer’s disease were investigated. To control for object form we used triads of computer-generated blobs. Triads either shared visual features or were visually distinct. Triads were artificially labeled using semantically close or distinct, biological, or non-biological names (e.g., lion, tiger, zebra or violin, guitar, banjo vs robin, donkey, frog or kite, wrench, carriage). On test trials blobs were presented alone and patients attempted to recall their ‘name.’ Visually close triads were misidentified significantly more often than visually distinct triads. Irrespective of whether biological or non-biological labels were used, triads labeled with semantically close names were misidentified significantly more often than semantically distinct triads. Hence, prob-
lematic object categories are those whose exemplars are visually and semantically close.

Rationale. Two group studies have shown that patients with Alzheimer’s disease have significantly more difficulty identifying depictions of animal and food exemplars than man-made artifacts (Silveri, Daniele, Giustolisi & Gainotti, 1991). Silveri et al. explained such category-specific deficits by proposing that the knowledge of biological objects is stored in temporal lobes while knowledge of artifacts is stored in frontoparietal lobes. Montanes, Goldblum, and Boller (1995) replicated the findings of the Silveri group in an experiment using black and white line drawings, but failed to replicate these findings in an experiment using colored photographs. They surmised that deficits adhering to the biological/nonbiological distinction may depend on the visual stimuli that are used.

We have argued that use of either line drawings or photographs to understand the factors underlying category-specific recognition deficits is marred by the fact that the shape primitives of the forms depicted by the pictures are unspecified (shape primitives are a fixed set of perceptual features which can be construed as the building blocks of complex object representation). That is, with line drawings we do not know what shape primitives non-brain-damaged subjects use to distinguish a cat from a dog. Hence, exactly what mechanisms, if any, fail at the level of structural shape processing in patients who display category-specific deficits remains a matter of conjecture. Additionally, the form of the object portrayed by a line drawing or photograph is inextricably yoked to the semantics of the object. Thus, without using words, the only way of visually evoking the semantics of “crow” has been to show the object with a head, body, wings, and tail. Hence, if patients can recognize a triad of line drawings comprised of an axe, a tie, and a pen, but not a robin, a crow, and a cardinal, is it because the birds are semantically closer, or simply look more alike?

Our research group has addressed the problems concerning the unspecified nature of line drawings by using simple computer-generated blobs with well-defined underlying shape dimensions to investigate object recognition problems. Shape dimensions are properties like curvature, elongation, and tapering. The exemplars in the visually distinct set have different values on curvature, elongation, and tapering. The exemplars in the visually close set have identical values on tapering. Additionally, in this close set shapes A and B are equally elongated; shapes B and C are equally curved.

To investigate the role of semantics in object recognition we used the following paradigm. Blobs from sets like those above were paired with verbal labels that were either semantically close (cadillac, corvette, mustang), or semantically disparate (kite, door, stapler). On learning trials blobs were presented one at a time with their label. On test trials blobs were presented
alone and subjects tried to give the name that blobs were paired with on learning trials.

Using this paradigm, we demonstrated that a patient with category-specific recognition deficits made significantly more errors for sets of blobs that shared multiple visual features and shared multiple semantic attributes (like the sports cars) than he made for the exact same blobs mapped to semantically unrelated concepts. This paradigm decouples object form and semantics essentially by holding form constant (letting the exact same shapes stand for both semantically close and distinct concepts). Importantly, this combination of visual and semantic proximity lead to performance decrements irrespective of whether blobs bore biological or non-biological labels (e.g., after an initial learning period he made 66% errors with sports car labels, but performed flawlessly when blobs were labeled with unrelated biological labels like shark, rose, and apple).

Taken together this paradigm indicates that the biological/non-biological distinction may merely be an artifact of visually similar and semantically similar objects being harder to recognize. That is, most man-made objects are visually dissimilar and hence pose few problems, or have unique functions which make them more semantically distinct and therefore easier to recognize. Exceptions are categories like makes of car and musical instruments which are both visually and semantically similar (e.g., have overlapping functions). Tellingly, such exceptions often pose problems for temporal lobe stroke patients who otherwise only seem to have difficulties identifying living things.

Like cars and musical instruments, many categories of biological objects share a large number of visual features (all birds have heads, beaks, wings, etc.) and semantic features (sit in trees, lay eggs, sing, etc.). Thus objects like fruits, vegetables, animals, birds, and insects pose the deadly combination of semantic proximity of concepts and shared visual features that precludes object recognition in at least some forms of category-specific visual agnosia.

The current study attempted to see if this combination of visual and semantic proximity contributed to the documented pattern of object recognition problems among Alzheimer’s patients.

Subjects. Four patients with probable DAT as assessed by NINCDS-ADRA criteria completed the study. Patients were English speaking and had Hachinski Ischemia Scale scores of 4 or less without evidence of other neurological disease on neurological exam.

Method. The visually close and visually distinct triads previously described were used. Labels referred to biological objects that were either semantically close (Lion Tiger, Zebra) or semantically distinct (Donkey, Frog, Robin). Artifacts were semantically either close (Banjo Guitar Violin) or distinct (Wrench, Kite, Carriage). The labels in each set were exactly matched for word frequency.
Six learning trials were sequentially presented along with their acoustically presented labels. These were followed by six test trials in which a blob was presented alone, and subjects attempted to “name” it. This six-learning six-test trial pattern continued until 72 learning and test trials were completed. The relevant data were the number of errors subjects made on test trials for the various blob set-label set pairings. For each patient eight sessions were conducted (four triads of verbal labels × two triads of blobs). Sessions were conducted on separate days, usually at a rate of about one session per week. The order of the blob triad-label triad combinations was random.

Results. A three-way analysis of variance was conducted on the error data revealed significant main effects of visual proximity \(F(1, 3) = 25.11, p = .015\) and semantic proximity \(F(1, 3) = 11.56, p = .042\). There was no effect of whether labels corresponded to biological or non-biological objects \(F(1, 3) = 2.40, \text{n.s.}\).

Discussion. These data represent a first in Alzheimer’s object recognition research in that the influence of semantics on object identification was assessed independently from the influence of object form. By using visually close and distinct blobs, and by having the same shapes stand for semantically close and disparate objects, we could control visual influences on object recognition while simultaneously looking directly at the influence of semantics. The results indicate that objects which pose the greatest identification problems for Alzheimer’s patients are those which share multiple visual features and have overlapping semantic attributes. Importantly, it was irrelevant whether labels came from biological or non-biological categories only their degree of semantic proximity contributed to identification errors. As such, these findings fail to support the notion that the brain has separate subsystems devoted to processing biological and non-biological objects. Rather, they suggest that what gets confused in the memory of Alzheimer’s patients are objects with overlapping visual and semantic attributes. In real life such categories include, animals, fruits and vegetables, insects, and birds, but also man-made objects such as cars and musical instruments.

References
23. Toward a Computer Simulation of Large-Scale Brain Systems Associated with Memory Disorders Using Fuzzy Logic

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Traditional functional neuroanatomy combined with functional neuroimaging provide the kind of information needed to simulate the dynamics of large-scale brain systems. A research literature exists linking brain structure interaction and memory, differentiated into declarative, procedural, and other categories based on the brain systems that mediate them. The simulation approach reported here assumes that brain structures are modular, interact dynamically via their projections, and that a fuzzy logic computational approach developed for simulating complex systems can be used to simulate large-scale brain systems.

Rationale. A large and growing research literature has identified brain structures and projections associated with different memory disorders. Known projections among brain structures and changes in brain structure activity continue to focus on medial temporal lobe, thalamic (Squire & Zola-Morgan, 1991; Zola-Morgan & Squire, 1993) and, perhaps, forebrain areas (Moscovitch & Winocur, 1996). What has not been forthcoming are dynamic computer simulations, at the level of brain structure interaction, that are explicit enough to be evaluated. Implementation software based on Zadeh (fuzzy) logic is beginning to be available for simulating dynamic, nonlinear systems (McNeil & Thro, 1993). Using this software, models of brain structure interaction associated with memory disorders can be treated as hypotheses, and results from these simulations can be validated based on results from functional neuroanatomy and neuroimaging studies (Sarter et al., 1996).

Method. Minimal models of brain structures and projections reported to mediate declarative memory were entered in simulation software (McNeill & Thro, 199). Brain structures in the simulation include entorhinal cortex (EC), hippocampus (HIPP), mammillary nucleus (M), anterior nucleus of the thalamus (AN), dorsomedial nucleus of the thalamus (DM), and prefrontal cortex (PFC). Brain structure activity and their projections were first set to reflect normal function, then brain structures and their projections manipulated and changes in different brain structures observed. Among the simulations run were simulated damage to medial temporal lobe structures and, in a separate simulation, frontal lobe damage.

Results and discussion. Simulated damage to EC produced decreased activity in HIPP, less decreased activity in the AN, and minimal decreased activity in PFC. In a separate simulation, reduced activity in PFC resulted in moderately increased activity in EC and HIPP and minimally increased activity in AN. In addition, the dorsomedial nucleus of the DM showed a
moderate decrease in activity, and the M showed no change. Of course, not all changes in brain structure activity are in the predicted direction. An advantage of computer simulations, however, is the rapidity with which simulations can be changed and new simulations tested.

The choice of fuzzy logic for the simulations was based on its use for simulating complex systems (Kosko, 1993). When brain function is conceptually viewed as large scale (Koch & Davies, 1994) dynamic, interacting systems (Farah, 1992), then computer simulations developed to model complex systems can be used to simulate brain function (Reynolds & Getty, 1996). These simulations are currently based on minimal models and are necessarily incomplete. At the same time, simulation results are generally consistent with empirical reports of brain changes associated with memory disorders. Simulations of large-scale brain systems have potential value as experimental models of brain dysfunction associated with memory disorders.

References


24. Neural Correlates of Prospective Memory: A Positron Emission Tomography Study


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Prospective memory is one of the human memory features which involves the activity of remembering to do something in the future. The aim of this study is to
examine neural basis of prospective memory in young normal subjects by measuring regional cerebral blood flow using the positron emission tomography technique. Both functional brain images obtained by subtraction method and analysis of variance showed highly localized activations in the left and the right lateral prefrontal areas and in the anterior medial frontal areas during an event-based prospective memory task compared with a control task. We conclude that the human prefrontal cortices play a critical role for realization of delayed intention of action in appropriate external context.

**Rationale.** It is presumed that memory process we need most in everyday life may be that of not forgetting to do something at a certain time in the future. This aspect of memory in our everyday life has been termed prospective memory (i.e., memory for future events or remembering what we must do), contrasted with retrospective memory (i.e., memory for past events or remembering what we have done) (Meacham & Leiman, 1982). Einstein and McDaniel (1990) classified the prospective memory into two conditions. Time-based prospective memory which involved in the execution of an intended action at the appropriate time, and event-based prospective memory which is involved in the response to an appropriate event. Although reported prospective memory disturbance in normal aging, dementia, and brain damaged patients, have indicated a probable relation between prospective memory disturbance and frontal lobe dysfunction, the neural basis of prospective memory remains speculative. The aim of this study is to clarify the neural correlates of prospective memory by employing recent extensive neuroimaging technology of positron emission tomography (PET).

**Subjects.** Six right-handed male volunteers (19–24 years old, mean 21.5) participated. Each subject’s MRI of the brain was normal and a written informed consent was obtained from each subject prior to the experiment.

**Method.** Subjects performed two a control task and an experimental tasks arranged to be preceded by a prescan study period and to be followed by a post scan recall period. The subjects repeated both tasks in random order. In a study period, subjects were presented auditory lists of 10 Japanese nouns three times and were required to retain these words as cue stimuli throughout the PET scan. In a recall period immediately after the PET scan, subjects were asked to report the 10 stimuli. In a scan period, the subjects heard a set of 5 stimuli of Japanese nouns from a tape recorder through a pair of earphones at the rate of 1 word per second and were required to repeat orally the set of stimuli within a blank duration of 7 seconds. The subjects repeated this sequence 10 times during the scan. In the experimental task list of stimuli was set to include the cue stimuli with very low frequency (2 or 3 occurrences per list) and the subjects were instructed to report if one of the target word appeared by tapping their left hand while repeating the word orally.

Regional cerebral blood flow (rCBF) was measured by using PET (SET2400W Shimadzu, FWHM 4.0 mm) and $^{15}$O labeled water (approximately 35 mCi for each injection). Subjects had a catheter placed into the
right brachial vein for tracer administration, closed their eyes, and wore an individual stereotaxic fixation helmet. Both scan tasks were started concurrent with bolus injection. Each PET data acquisition time was 120 sec. All rCBF images were transformed into the standard anatomical format using Human Brain Atlas system (Roland et al., 1994) and each subject’s MRI. Then all standardized rCBF images were smoothed with a three dimensional Gaussian filter 10 mm wide and normalized for global cerebral blood flow of 50 ml/100 g/min (Herscovitch et al., 1983; Raichle et al., 1983). The comparison between the control task and the experimental task were performed by descriptive $t$ test and two-way analysis of variance (ANOVA). In the $t$ test, subtractions of averaged image of control tasks from averaged image of experimental tasks were calculated for each subject on a voxel by voxel basis, and then the mean and variance image, as well as the descriptive $t$ image, were calculated. In two-way ANOVA (two tasks and six subjects as factors), the image of $F$ values for differences between tasks was calculated on a voxel by voxel basis. Voxels with $t$ values $> 4.03 (p < .005)$ and those with $F$ values $> 12.83 (p < .005)$ were considered to represent regions of significantly increased rCBF. Each activation was then superimposed onto the average reformatted MRI of the six subjects, and anatomical localization of areas of activation in each comparison was estimated in relation to this MRI. Finally, effective activation foci were determined as those seen in both the $t$ image and the $F$ image.

**Results.** The regions activated commonly in subtracted and ANOVA image during the experimental task compared with the control task were as follows: the right inferior frontal gyrus (Brodman Area, B.A. 47), the left superior frontal gyrus (B.A. 10), the anterior cingulate gyrus (B.A. 24), and the medial frontal lobe (B.A. 8). These activations should be associated with realization of delayed intention of tapping the left hand in appearance of cue stimuli. As far as we know, this is the first study which provides an overt evidence that the human lateral and medial prefrontal areas play a critical role in prospective memory performance. Further, we hypothesize that the lateral prefrontal activations (areas of right 47 and left 10) in the present study are related to retrospective component of prospective memory (Einstein & McDaniel, 1990) such as holding of intention and recognition of encoded context, while that the medial frontal activations (areas 24, 8) are the reflection of the prospective component such as decision and execution of future action.

**References**


25. Age-Related Changes in Neural Interactions during Memory Encoding and Retrieval: A Network Analysis of PET Data

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Healthy young and old adults were PET-scanned while they were either encoding or recalling word-pairs. The right prefrontal cortex was more active during recall than during encoding in both groups, whereas a left prefrontal region showed a task × age interaction: it was more active during encoding than during recall in the young, but more active during recall than during encoding in the old. rCBF correlations between this region and the rest of the brain were different in the two groups. The most prominent difference occurred during recall in which a right frontopolar area was negatively correlated with the left prefrontal region in the young but positively correlated in the old. In general, the results suggest a reorganization of memory networks in the aging brain.

Rationale. Cognitive deficits in older adults, such as poor performance in episodic memory tasks, seem to be related to neurobiological changes in the aging brain, such as neuronal atrophy and synaptic loss. What is lacking in the causal chain is evidence of age-related changes in neural function during the performance of cognitive tasks. This missing link can be provided by studies using functional neuroimaging techniques, such as positron emission tomography (PET), which can compare neural activity in young and old adults while they are performing cognitive tasks. Consistent with evidence of neural decline in old age, some PET studies have found age-related decreases in neural activity during cognitive performance, for example, in the left frontal cortex. At the same time, a few of these studies have also found brain regions where old adults show more neural activity than young adults. This type of result has been interpreted as evidence of functional reorganization in the aging brain, which is an idea with important theoretical and practical implications, for example in the domain of cognitive rehabilitation.

The idea of functional reorganization suggest a change not only in the level of activity of the brain regions involved but also in the connections...
between them. If the role of a certain brain region within the network of neural structures subserving a task is different in young and old adults, then the connections of this region with other regions in the network should be also different in the two groups. Changes in functional connections between brain regions, however, cannot be investigated using standard methods of analyzing PET data, because these methods investigate each region independently of the others. In the present study, we employed correlational analyses in order to investigate the effects of aging on the interactions between brain regions involved in memory encoding and retrieval. In particular, we focused on a left prefrontal region (Brodmann Area 47) that in a previous study was found to play a very different role in the encoding and retrieval networks of young and old subjects. In young subjects, this region was more active during encoding than during retrieval, whereas in old subjects, it was more active during retrieval than during encoding. We investigated how the interaction of this region with the rest of the brain changed across tasks and across groups.

Subjects. The subjects were 12 young adults (6 male, 6 female; age range, 19–31; mean age, 26 years) and 12 old adults (five male, seven female; age range 67–75; mean age 70 years). All subjects were right handed and had no history of neurological or psychiatric illness. None of the subjects was taking medication or had a condition that could affect cerebral blood flow (e.g., high blood pressure), with the exception of 1 old subject who suffered from mild hypothyroidism. The two groups were matched in education, self-rated health, and word fluency, but differed in vocabulary (higher in old subjects) and recall on the California Verbal Learning Test (CVLT, higher in young subjects).

Method. Changes in regional cerebral blood flow (rCBF) were measured by PET under different conditions. Two conditions were investigated in the present study: encoding and recall. In each trial of these two conditions, subjects read two words on the screen and said one word aloud. In each trial of the encoding condition, a word-pair (e.g., parents–piano) was presented, and subjects tried to learn the pair by noting meaning relations between the two words, and read the second word aloud (e.g., piano). In each trial of the recall condition, the first word of a pair studied before the scan was presented paired with the word (e.g., parents–word) and subjects tried to recall the original second word. If they could recall it, they said it aloud; if not, they said pass. Each condition was scanned on a GEMS-Scanditronix PC2048-15B head scanner using a bolus injection of 40 mCi (1.48 GBq) of $^{15}O$-H$_2$O.

The analyses of PET data involved four steps. First, using Statistical Parametric Mapping (SPM95) software, the images from each subject were realigned to the first image, transformed into a standard brain space and smoothed using a 10-mm Gaussian filter. Second, the value for each pixel in the images of each subject was divided by the average global CBF for
the subject in the task, and reduced by the average value for the pixel across all tasks. The latter adjustment reduces intergroup errors of registration and other global group differences. Third, a multivariate partial least squares analysis (PLS; McIntosh et al., 1996) was performed on the adjusted rCBF data of the four conditions: Encoding-Young (EY), Recall-Young (RY), Encoding Old (EO), and Recall-Old (RO). (The two scans of each condition were averaged together). Fourth, correlation coefficients were calculated between rCBF in the voxel of interest in left area 47 (xyz = −3628 O) and rCBF in all the other voxels in the brain. The correlation coefficients were calculated separately for the four conditions, and the results were displayed as brain maps in Talairach and Tournoux stereotactic space.

**Results.** The PLS analysis identified two patterns of rCBF changes across conditions. The first pattern corresponded to regions showing similar encoding-recall differences in young and old adults. Regions more active during encoding than during recall included the left prefrontal, and bilateral Sylvian and fusiform regions, and regions more active during recall than during encoding included right prefrontal, cingulate, parietal, midbrain, thalamic, and cerebellar regions. The second pattern corresponded to regions showing age × task interactions, including the region of interest, left area 47, which was more active during encoding than during recall in the young, but more active during recall than during encoding in the old.

As shown by the correlational analyses, the pattern of interaction of left area 47 with the rest of the brain was very different in young and old adults. In EY, this area was positively correlated with the left prefrontal and temporal regions and negatively correlated with occipital and right temporal regions. In EO, positive correlations with the left prefrontal were weaker, and negative correlations occurred mainly with left medial temporal and occipital regions. The largest differences occurred during recall. In RY, there were positive correlations with the left prefrontal and cerebellar regions, and negative correlations with right medial frontopolar, posterior cingulate, and right temporal regions. In RO, there were positive correlations with the left prefrontal and right medial frontopolar regions, and negative correlations with cerebellar and right temporal regions. The most prominent difference occurred during recall in a right medial frontopolar region (area 10) which was negatively correlated with the left area 47 in young adults ($r = −0.9$) but positively correlated in old adults ($r = 0.7$). As indicated by a PLS task × age interaction, this region was more active during recall than during encoding in young adults but not in old adults.

**Discussion.** Frontal activity during recall was right-lateralized in young adults, but bilateral in old adults. The pattern shown by the young subjects has been repeatedly observed and has been described in terms of a Hemispheric Encoding/Retrieval Asymmetry (HERA) model (Tulving et al., 1994; Nyberg et al., 1996). The pattern shown by the old adults suggest a reorganization of the standard lateralized pattern. During recall, old subjects
activated a left frontal region (area 47) which was not activated by young subjects. The difference may be related to the interactions of this region with the right prefrontal cortex. rCBF in the left and right prefrontal cortex was negatively correlated in young adults, but positively correlated in old adults. One possible interpretation is that in young adults, but not in old adults, the right prefrontal had an inhibitory effect on the left prefrontal cortex. The difference in the left prefrontal cortex is also likely to be related to differences in other parts of the retrieval network, an idea we are currently investigating by means of structural equation modeling.

References

26. Functional and Structural Neuroimaging Correlates of Selective Retrograde Amnesia: A Case Study with MRI and PET


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The neuroanatomical and neurophysiological systems underlying episodic memory functioning were assessed in a case of retrograde amnesia without anterograde amnesia following traumatic brain injury (TBI). MRI showed evidence of a focal right inferior frontal injury affecting both cortical tissue and frontal-subcortical pathways, including the uncinate fasciculus, a frontal-temporal band of fibers previously hypothesized to be involved in retrieval of personal episodic memories. On an H$_2$O PET activation paradigm that reliably elicits right frontal activation on retrieval and left frontal activation on encoding, the index case did not show increased right frontal activation on retrieval. The normal pattern of right frontal activation was observed in a matched TBI control subject without retrograde amnesia. Both the index case and the matched control showed additional posterior activations which suggested TBI-related disinhibition, compensation, or both. Taken together, the neuroimaging findings converge to suggest a right frontal-temporal system mediating retrieval of episodic memories.

**Rationale.** Retrograde amnesia (RA) refers to the inability to retrieve information (usually personal episodic memories) which had been acquired prior to a traumatic event. Cases of selective RA, or RA without anterograde
amnesia (the inability to learn new information), are rare and historically have been viewed as psychiatric in etiology. A growing literature of case studies, however, suggests that brain injury can cause selective RA. To the extent that selectively spared/impaired memory systems can be associated with functioning of discrete brain regions, these cases increase knowledge of the neural substrates of memory.

In this report, we describe neuroimaging findings from a 35-year-old man, M.L., with selective RA following a severe traumatic brain injury (TBI). We established that M.L. has structural damage in discrete regions of the frontal lobe which are consistent with emerging theories on the neural systems involved in retrieval of personal memories. We also documented differences between M.L.’s regional cerebral blood flow (rCBF) and that of matched controls during the performance of an episodic retrieval task. Taken together, these findings suggest a specific system for retrieval of episodic memories that can be dissociated from semantic encoding and retrieval.

Subjects. The experimental subject, M.L., sustained TBI from being struck by a car while on his bicycle. He complained of dense RA, a complete loss of all personal episodic memories pre-dating his injury. On measures of autobiographical memory, he produced only memories postdating his accident (see Table 2). Any knowledge of events from his pre-accident life had reportedly been learned from others. M.L. was unable to regain his previous employment in sales.

The control subject, N.R., sustained a severe TBI from a motor vehicle accident. He was matched to M.L. on injury severity and background measures (see Table 2). At the time of testing, N.R. was functioning close to
his pre-morbid level as a student. Neither N.R. nor M.L. has any history of psychiatric problems, substance abuse, prior neurological injury, or serious medical illness. With the exception of M.L.’s RA, both were free of major neuropsychological deficits.

Method. T1 and T2 Images were acquired using a 1.5 T-MR system (Signa version 4.7, General Electric). A sagittal T1 weighted 3-D volume technique produced 124 1.3-mm slices. To obtain lesion coordinates, the T2 images were reformatted parallel to the AC-PC line and matched to the templates in the Talairach atlas using the Analyze software system.

The PET activation paradigm, previously validated in young adults, is designed to compare rCBF during encoding and retrieval of verbal material. To increase the stability of the signal for single-subject comparisons, all eight scans were devoted to either encoding or retrieval; baseline activations were not recorded. Eight lists of 24 word pairs (e.g., PENGUIN TUXEDO) were used, four each for encoding and retrieval. During the encoding scans, subjects noted a meaningful relation between the words in each pair (presented one at a time), then said the second word aloud. During the following inter-scan interval, a different list was studied using the same technique. The pairs on this list served as the encoded stimuli for the retrieval scan. During the retrieval scan, the first word of each pair in this list was presented, followed by ‘‘WORD?’’ Subjects were instructed to give the second word of the pair, or say ‘‘PASS’’ if they could not remember the word.

PET scans were obtained in a standard manner using $^{15}$O-labeled water and analyzed with the Statistical Parametric Mapping (SPM) technique. After realignment, transformation to standard space, and smoothing, the effects of the encoding and retrieval tasks on rCBF for each of the two subjects were compared to data from a set of twelve normal controls using procedures described by Friston et al. (human brain mapping).

Results and discussion. On M.L.’s scan, there is evidence of an old hemorrhage appearing as decreased T2 signal in the R inferior frontal region. Although only 3 to 4 mm in diameter, it extends over approximately 2.7 cm on the dorsal-ventral plane. In Talairach space, its ventral origin is at the gray-white matter junction in the caudal aspect of the inferior frontal gyrus (area 47). It courses dorsally to white matter deep to areas 45, 44, and 10. Additional L hemisphere hemorrhages, situated high in the precentral gyrus, will not be discussed in this report. N.R.’s lesion, much larger in volume than M.L.’s, is situated in L frontal areas 9, 10, 45, and 46.

M.L.’s lesion shows a hemosiderin deposit as a residual from a prior hemorrhage. Such apparently small lesions on the axial slices could easily be dismissed as insignificant, but 3-D mapping shows marked disconnection of frontal from posterior and subcortical regions. In particular, the uncinate fasciculus is affected. This frontal-temporal fiber tract has been previously hypothesized to be involved in the retrieval of episodic memories (Markowitz et al., 1993).
### TABLE 3
Areas in Which rCBF Differed from Normal Controls

<table>
<thead>
<tr>
<th>Area</th>
<th>M.L. interactions</th>
<th>Encoding</th>
<th>Retrieval</th>
</tr>
</thead>
<tbody>
<tr>
<td>R cuneus (18)</td>
<td></td>
<td>-</td>
<td>=</td>
</tr>
<tr>
<td>L post lingual (18)</td>
<td></td>
<td>=</td>
<td>+</td>
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<tr>
<td>L hippocampus</td>
<td></td>
<td>=</td>
<td>+</td>
</tr>
<tr>
<td>L cerebellum</td>
<td></td>
<td>-</td>
<td>=</td>
</tr>
<tr>
<td>L STG/MTG (39)</td>
<td></td>
<td>-</td>
<td>=</td>
</tr>
<tr>
<td>L hippocampus</td>
<td></td>
<td>-</td>
<td>+</td>
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<tr>
<td>L cuneus (18/19)</td>
<td></td>
<td>-</td>
<td>=</td>
</tr>
<tr>
<td>L parahippocampal gyrus</td>
<td></td>
<td>+</td>
<td>-</td>
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<tr>
<td>R frontal pole (10)</td>
<td></td>
<td>+</td>
<td>=</td>
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<tr>
<td>R IOG (18/19)</td>
<td></td>
<td>+</td>
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<tr>
<td>R cingulate (32)</td>
<td></td>
<td>=</td>
<td>-</td>
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<tr>
<td>R MFG (8)</td>
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<td>+</td>
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<tr>
<td>L caudate</td>
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<td>+</td>
<td>-</td>
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<tr>
<td>L PCG (6)</td>
<td></td>
<td>+</td>
<td>=</td>
</tr>
<tr>
<td>R fusiform (18)</td>
<td></td>
<td>+</td>
<td>=</td>
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<tr>
<td>R precuneus (18)</td>
<td></td>
<td>-</td>
<td>+</td>
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<tr>
<td>R med. frontal (9)</td>
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<td>+</td>
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<tr>
<td>R ITG/MTG (20/21)</td>
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<tr>
<td>L lingual</td>
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<tr>
<td>R MFG (10)</td>
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<td>L STG (22)</td>
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<tr>
<td>R IPG (47)</td>
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<tr>
<td>L MFG (6/4)</td>
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<tr>
<td>R caudate</td>
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<tr>
<td>L post. cingulate (31)</td>
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<td>+</td>
<td>=</td>
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<tr>
<td>L putamen</td>
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<td>+</td>
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The PET study augmented the MRI finding through the direct measurement of M.L.’s cerebral functioning using a paradigm which reliably elicits a specific pattern of left and right frontal rCBF activations during encoding and retrieval, respectively, in healthy controls. Although this paradigm does not directly address M.L.’s memory loss for events predating his accident, it does require episodic retrieval. Furthermore, it allows for the investigation of compensatory pathways mediating M.L.’s intact anterograde processes. Considering M.L.’s lesion location and his episodic retrieval disorder, we predicted that he would not show the typical R frontal activation on retrieval. This prediction was supported. In spite of an injury similar in severity to M.L., N.R. showed R frontal activation. Both TBI subjects showed L frontal activation during encoding, although M.L.’s activation in this region was relatively posterior. The normal L frontal activation in N.R. is especially notable considering his large L frontal lesion.
Relative to controls, M.L. showed decreased rCBF in R frontal, L parahippocampal, and L caudate regions during retrieval, with increased rCBF in L temporal regions, including the hippocampus, suggesting that his preserved anterograde encoding and retrieval processes may be mediated by intact L hemisphere systems (see Table 3). A possible implication of this finding is that M.L. relies upon an intact semantic system for anterograde learning. Although N.R. had decreased R inferior frontal rCBF during retrieval, his general pattern indicated increased rCBF in other R frontal area relative to controls, as well as increases in L cingulate and R temporal parietal regions. Both TBI subjects showed a number of increases in subcortical and posterior regions relative to controls during encoding and, to lesser extent, retrieval. The PET results suggest that while TBI causes more widespread rCBF activations in encoding and retrieval (possibly due to disinhibition or compensatory processes), the frontal hemispheric encoding/retrieval asymmetry reported in healthy subjects (see Nyberg, Cabeza, & Tulving, 1996) still holds for TBI.

Conclusions. In conclusion, the structural and functional neuroimaging studies converged to support the hypothesis of Markowitsch and colleagues that retrieval of personal episodic memories are mediated by a prefrontal/anterior temporal system which can be distinguished from other neurocognitive systems involved in memory. Pending further testing of TBI controls (which is ongoing), M.L.’s PET results do not appear to be due to general TBI effects.

References

27. Construct Validity of a Yes/No Recognition Memory Test Used to Predict and Prevent Global Amnesia

J. McGlone, S. E. Black, and A. Sita

Queen Elizabeth II Health Sciences Centre, Halifax, Nova Scotia, Canada

This investigation examined the construct validity of a yes/no recognition memory protocol routinely used to predict amnesia during an injection of intracarotid sodium amobarbital prior to a temporal lobectomy. One patient with global amnesia, two with severe but not global amnesia, and one with Wernicke’s aphasia were administered the protocol without any drug injection. The globally amnesic patient scored below chance on the memory protocol and 100% correct on the language
protocol. Two cases of severe selective amnesia passed both the memory and the language protocols. The aphasic passed the memory protocol, but made errors on the language protocol. Combined, these preliminary results indicate that this yes/no memory protocol has both convergent and divergent validity for differentiating global amnesia and aphasia, but it is not able to differentiate severely from global amnesia.

Rationale

For over 40 years, the intracarotid amobarbital protocol (IAP) has been applied to surgical candidates contemplating temporal lobectomy for the relief of medically intractable epilepsy. Despite its invasive nature and risk of morbidity, surprisingly little research has been conducted on its accuracy in identifying high risk cases of possible post-operative global amnesia. To date, no study has examined whether patients whose global amnesia resulting from permanent brain damage actually fail an IAP memory test. If the memory section of the IAP does indeed identify patients who are at high risk for developing global amnesia subsequent to a temporal lobectomy, then one would also expect that patients who have global amnesia due to other etiologies would fail the memory protocol without the injection of the drug. The purpose of this investigation was to examine the construct validity of a yes/no recognition memory IAP.

Subjects

Thus far, four cases have been assessed, with the prior consent of themselves and next of kin. Their demographics and medical etiologies are found in Table 4. Only K.C. was found to be globally amnesic according to both an interview of significant others and a test of recognition memory for the examiner after a five minute delay. No evidence for acquiring day to day episodic memories could be found in K.C. Two further cases (J.U. and D.S.) acquired some day-to-day memories (e.g., baseball plays, activities enjoyed,

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<td>Left MCA stroke</td>
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<td></td>
<td>Left subdural seizure</td>
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<td></td>
<td>Left PCA infarct</td>
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<tr>
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visitors, etc.). However, their baseline neuropsychological testing indicated that they showed selective, severe memory deficits for both verbal and design materials (Tables 5, 6, 7). Attention, mental status, language, and spatial skills were relatively intact. J.M. was rendered aphasic (Wernicke’s) due to a left hemisphere stroke three months earlier.

### Table 5
**Baseline Memory**

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### Table 6
**General Cognitive Functioning**

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TABLE 7
Language and Constructional Skills

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<td>57/60</td>
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<td>—</td>
<td>—</td>
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<tr>
<td>Body parts</td>
<td>—</td>
<td>—</td>
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<td>—</td>
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<tr>
<td>Western aphasia</td>
<td>98/100</td>
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<td>battery</td>
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<td>Simple yes/no</td>
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<td>Complex yes/no</td>
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**Method**

Patients were seen for about 2 hr each to obtain some baseline neuropsychological measures and LAP memory and language scores.

*Yes-no recognition memory protocol.* Each of the four sets contains four different target items (i.e., 1 object, 2 pictures, and 1 nursery rhyme). Each target item in Set 1 was placed in view, named by the examiner and named by the patient for about 4 sec and then removed from sight. Thereafter followed a distraction interval from 7 to 10 min filled with the language and manual task (grooved pegboard). After the distraction interval, recall and then recognition memory were tested for Set 1. Recognition memory for the object and the nursery rhyme consisted of two foils and the target. There were five foils and 2 targets in picture recognition. The interval between presentation of Sets was filled with 2 minutes of conversation. Sets 2, 3, and 4 were presented in a similar manner to Set 1. For each Set, a percent correct (25, 50, 75, or 100) was assigned and the mean of all four sets is presented in Fig. 1. Failure on the memory protocol is a score less than chance which was 31% for the total.

*Language tasks.* In each set the patient was administered the same items to measure expression, i.e., say the days of the week forward, name eight common objects presented visually, and repeat three phrases, and one comprehension test, i.e., obey verbal commands such as “Point to the large black square.” The cut-off for :aphasia was set at 90% correct or below based on the total expression score (max = 19). Prior research in patients with epilepsy established that when their nondominant hemisphere was injected, fewer than 1% of the sample made more than 10% errors on total expression.

**Results**

The global amnesic failed each memory set, as well as the mean of all four sets, but no language errors occurred. The selective amnesics obtained
passing scores on the memory protocol and the language protocol, whereas the aphasic failed the language protocol but passed the memory protocol.

**Conclusions**

These findings are the first to demonstrate construct validity for a recognition memory protocol that is normally used to predict global amnesia prior to a temporal lobectomy. However, the results suggest that the memory tasks would not predict a severe, but selective memory disorder, which has often been described as “amnesia” in the neuropsychology literature.

**28. Recognition of Complex Visual Scenes by Patients with Closed Head Injury**

S. Pigott

*London Health Sciences Centre, Victoria Campus, London, Ontario, Canada*

Delayed recognition memory for different aspects of complex visual scenes was examined in 14 patients with moderate to severe closed head injury (CHI). This measure has previously been found to be sensitive to right temporal-lobe function (Pigott & Milner, 1993). Relative to 15 normal control subjects, patients with CHI
were significantly impaired on memory for figurative detail (the visual characteristics of objects in a scene), spatial composition (the arrangement of filled and unfilled space in the scene), and the spatial location of specific objects in the scene. This impaired level of performance suggests that right temporal lobe structures and/or their connections are damaged following closed head injury.

Rationale. Memory impairments are frequently observed following closed head injury (CHI), presumably due to damage to temporal-lobe structures or their connections. It is well established that left temporal-lobe damage produces a deficit in the recall of verbal material whereas right temporal-lobe damage impairs the recall and recognition of visual patterns. Although impairments in memory for verbal material have been well documented following CHI, less is known about the existence of and/or the nature of visual memory deficits following such injuries.

Pigott and Milner (1993) recently provided evidence that right temporal-lobe lesions result in deficient recognition memory for different aspects of complex visual scenes. They found that right anterior temporal lobectomy, irrespective of the extent of hippocampal removal, impaired memory for figurative detail (the visual characteristics of the objects in the scene) and spatial composition (the arrangement of the filled and unfilled space in scene), whereas only patients with right temporal-lobe lesions that included extensive hippocampal removal were impaired at detecting changes in the spatial location of specific objects. The performance of patients with CHI was examined on this visual recognition test in order to better define visual memory function following CHI.

Subjects. Adult subjects with moderate to severe CHI participated in this study. The mean time since injury was 2 years 1 month (range 4 months to 7 years). Patients with IQ ratings less than 75, a previous history of learning disabilities, psychiatric history, drug and alcohol abuse, or visual deficits were excluded from participating in this study. Performance was contrasted with that of age- and education-matched normal control subjects with no history of neurological insult. All individuals who participated in this study had normal or corrected to normal vision.

Method. Ten target and 100 test pictures were presented on 35-mm slides of black-and-white line drawings. Each picture contained from 7 to 10 drawings of non-overlapping objects or animals. The 100 test slides consisted of five duplicates of the 10 original pictures and five transformed versions of each of the originals. Memory for figurative detail was assessed in two ways. In the Inventory transformation, one object in the original scene was replaced by an object of the same size and shape but of a different type. In the Figurative-Detail transformation, an object was replaced by another object of the same size, shape and type but differing in the details of its appearance. Two types of transformations were also used to assess recognition accuracy for Spatial Composition. In the Displacement transformation, an object was moved in the horizontal plane through a distance equal to approximately
10% of the width of the picture. In the Deletion transformation, an entire object was removed from the picture. Finally, in the Object-Location transformation two objects of approximately the same size and shape were interchanged.

A Kodak 850H carousel slide projector was used to project the stimuli onto a white screen. Subjects were tested individually, with each subject being seated approximately 1.2 m from the screen in a dark room. The 10 target pictures were presented in series for 60 s each and the subject was asked to study each picture carefully in order to remember it later. They were then presented with 100 test slides for 13 seconds each with an ISI of 1 second. The subject was asked to state if each picture was the same or different from the original.

Results. A one-way multivariate analysis of variance, with group as the between-subjects factor, was carried out on the six dependent measures of the percentage of the original versions correctly recognized and the percentage of the changes correctly identified on each of the five transformations. The overall multivariate analysis for group was significant, $F(6, 22) = 9.48, p < .001$, allowing inspection of the univariate analyses of variance (ANOVA) for the six dependent variables. The number of unchanged scenes correctly identified by subjects did not differ significantly between the CHI and normal controls, $F(1, 27) = 1.3, p > .26$. However, the CHI group were significantly impaired in the five transformed conditions [Inventory ($F(1, 27) = 10.6, p < .001$), Figurative Detail ($F(1, 27) = 40.3, p < .001$), Deletion ($F(1, 27) = 7.5, p < .001$), Displacement $F(1, 27) = 16.0, p < .001$, and Object Location $F(1, 27) = 32.8, p < .001$].

Conclusion. Patients with CHI exhibited an impairment in delayed recognition memory for figurative detail, spatial composition and spatial location information. Performance of these patients was similar to that seen in patients with right temporal-lobe lesions with extensive hippocampal removals in the Pigott and Milner (1993) investigation. This finding supports the notion that CHI produces an impairment in visual recognition memory which may be related to damage to right temporal-lobe structures or their connections.

Reference


29. Neuropsychological Argument for the Activation Approach to Memory: A Case of Phonological Memory Deficit

S. Belleville, I. Peretz, F. Fontaine, and N. Caza

*Centre Hospitalier Côte-des-Neiges, Montreal, Quebec, Canada*

The present study is concerned with a brain-damaged patient, I.R., who shows the typical “selective short-term memory deficit” pattern of performance. It is pro-
posed that this performance pattern could be accounted for without relying on a dual-store approach. In short-term serial recall, the patient did not show normal phonological similarity effects but was highly influenced by the semantic and lexical properties of the items. A similar pattern was found in long-term recall tasks where I. R. showed excellent recall of lexico-semantic material (words) but impaired recall of phonological information (non-words). These results could be explained by the general disruption of a phonological memory with preserved semantic memory, without regard to the short-term/long-term memory distinction.

Rationale. One classical memory distinction involves the interplay of a temporary memory system (short-term memory or working memory, STM) and of a long-term memory system (LTM). A widespread theoretical position holds that these two systems rely on independent and dissociable stores (Broadbent, 1984; Shallice & Warrington, 1970; Shallice, 1988). In this framework, these two stores are believed to hold different locations in the brain and/or in the cognitive architecture. However, the increasing influence of activation models of memory challenges the structural independence of STM and LTM. For instance, Crowder (1993) proposed that memory is a by-product of information processing that extends over time. A similar view was proposed in Craik and Lockhart’s (1972) levels of processing approach. Other investigators have suggested that working memory could represent the activated portion of long-term traces (Cowan, 1988). According to these views, the distinction between STM and LTM tasks might be explained by their reliance on different features: phonological features would be required for STM tasks while semantic features would be used in LTM tasks. If this view was correct, brain damage leading to STM deficit would spare most but not all of LTM. Moreover, such damage would spare lexicon–semantic effects in STM. The present study reports the case of a patient who shows the typical “selective short-term memory deficit” pattern of performance. It is proposed that the patient’s pattern of memory performance is better accounted for within an activation than within a dual-store approach to memory.

Subject. I.R. is a 37-year-old woman who worked as a restaurant manager before her first accident. In 1985, she was hospitalized and operated on because a giant aneurysm located on the left middle cerebral artery had ruptured. Acute language problems followed but recuperation was complete. One year later, she was operated on again in an attempt to clip a second silent aneurysm, symmetrical to the first on the right middle artery. There were surgical complications and the patient suffered postoperatively from left hemiplegia, psychomotor slowing and dysarthria. A recent neuropsychological examination evidenced dysarthria, severe amusia, and short-term memory deficits. I.R.’s language and executive functions were normal and her I.Q. was 94. She also performed normally on classical tests of long-term episodic memory. She showed a memory quotient of 98 on the Wechsler-Memory Scale and performed within normal limits on the Bushke procedure. In contrast, her STM span was severely reduced for digits (3 and 4 in the
auditory and visual modalities, respectively), consonants (2 and 3 in the auditory and visual modalities, respectively) and words (3 in both modalities). Her visuo-spatial span was nonetheless normal for faces (4) and for spatial locations (4). I.R.’s performance is compared to that of normal controls matched for age, sex, and education.

**Method.** I.R.’s sensitivity to phonological structure was assessed by comparing her immediate serial recall of phonologically dissimilar (non-rhyming) and similar (rhyming) letters. Short-term recall capacities for series of short (monosyllabic) and long (four-syllable) words were also compared in order to assess her sensitivity to articulatory properties. This was done using the auditory and visual modes of presentation. For each mode and stimulus type tell sequences of three items were presented for recall. I.R. was tested with three-item lists as this corresponds to her word span. Recall was oral. The influence of lexico-semantic properties on short-term recall was assessed in the following manner. First, her recall of series of frequent and rare words were compared. Second, the recall of series of concrete and abstract words were compared. Third, the recall of series of semantically dissimilar (belonging to different taxonomic categories) and semantically similar words (belonging to the same taxonomic category) were compared. Finally, the recall of series of abstract words, grammatical words and non-words were compared. Items compared in the different series were equivalent with respect to other parameters known to affect immediate serial recall in normal subjects (phonological similarity, length, etc).

I.R.’s LTM for lexico-semantic material was measured with lists of eight pairs of words (word–word paired-associate task). Each pair was presented visually for 5 sec. The subject was then asked to count backward for 30 sec. Following this delay, the first word of a pair was presented visually and I.R. was asked to recall the second word. I.R.’s phonological LTM was measured in the same manner except that the lists were made of 8 nonwords paired with 8 words (word–non-word paired-associate task). At recall, the word was presented as a cue and I.R.’s task was to recall the non-word associated with the cue. In both conditions, the pairs were presented three times and a recall phase followed each presentation. Other LTM tasks are currently being tested with I.R.

**Results.** The patient failed to show the typical effect of phonological similarity in STM. She recalled more phonologically similar than dissimilar words, as opposed to normal subjects who showed better recall for phonologically dissimilar lists. Furthermore, she recalled as many long words as short words, thus failing to show the typical word length effect. In contrast, I.R.’s immediate serial recall was very much influenced by the semantic and lexical properties of items. Her short-term serial recall was better for concrete than for abstract words; for frequent than for rare words; and for semantically dissimilar than for similar items. Such a large and consistent lexico-semantic effect is never observed in normal subjects.
A comparable pattern of performance was found in long-term recall. I.R. showed good performance in the word word paired-associated task. In contrast, her performance was below that of normal controls in the word non-word paired associated task.

Conclusions. In conclusion, we have presented a patient who shows the pattern of performance suggestive of an isolated short-term memory deficit. However, closer examination of her memory performance suggests impairment of a phonological memory which extends beyond short-term recall. A phonological memory impairment is clearly present in I.R. without regard to her being tested in short-term or long-term memory tasks. In contrast, she shows preserved use of lexicosemantic information in both short- and long-term memory tasks. Moreover, her reliance on lexico-semantic representations appears to be enhanced in short-term recall which has been reported in normal subjects when tested in condition of articulatory suppression. This is the first study reporting this pattern of data. However, our hypothesis is that other patients with a selective short-term memory deficit should exhibit a similar pattern of performance.

References


30. Word Production: Dissociation across Time of Working and Semantic Memory Contributions

O. Almkvist and S-E. Fernaeus

Huddinge Hospital, Huddinge, Sweden

The possible contribution of memory systems for word production was studied. Patients (n = 126) referred to a Memory Clinic for suspected cognitive impairment underwent a neuropsychological examination including the FAS word fluency test. The number of words produced during six consecutive 10-sec periods...
followed a negatively accelerated curve. All the FAS variables (3 letters \( \times 6 \) periods) were entered into an exploratory factor analysis resulting in two factors. One factor, linked to working memory tests, loaded on the initial periods and a second factor, linked to semantic memory tests, loaded on the later periods of the FAS test. The contribution of working and semantic memory seem to be dissociated across time of the FAS test, which may have theoretical as well as practical implications.

**Rationale.** The contribution of different memory systems (e.g., semantic memory, working memory) for word production was examined.

**Subjects.** Subjects were individuals who were referred to the Memory Clinic at Huddinge Hospital for suspected cognitive impairment. A total of 126 individuals (64 men and 62 women), ranging in age from 37 to 88 (\( M = 64.4, SD = 11.7 \)), and who had 6 to 20 years of formal education (\( M = 11.2, SD = 3.6 \)), participated in the study.

Clinical diagnoses were made according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV). The most common diagnosis was mild cognitive disorder that did not fulfill any dementia diagnoses (\( n = 40 \)). This was followed by dementia of the Alzheimer’s type (\( n = 29 \)), vascular dementia (\( n = 4 \)), unspecified dementia (\( n = 1 \)), diabetes mellitus (\( n = 1 \)), alcohol-induced persisting dementia (\( n = 1 \)), and primary progressive aphasia (\( n = 1 \)). Forty-nine subjects did not receive any diagnosis, because they did not fulfill any diagnostic category of DSM-IV, although they had subjective memory or other cognitive symptoms.

**Method.** All subjects underwent a comprehensive diagnostic examination including medical history, laboratory analysis of blood urine and cerebrospinal fluid, brain imaging and neuropsychological assessment. The neuropsychological assessment included the FAS word fluency test, and a number of working memory and semantic memory tests including: Information, Similarities and Digit Span from the Wechsler Adult Intelligence Scale—Revised, Free Recall and Recognition of Words (Backman & Forsell, 1994), and a vocabulary test. In addition, tests of visuospatial ability, attention, learning, and motor performance were administered.

The FAS test was administered according to the standard procedure, i.e., to say as many words as possible. The number of words reported in each 10-sec interval during 1 min was observed and scored by the examining psychologist. Repetitions and other errors were omitted from these scores. The other neuropsychological tests were administered according to standard instructions.

**Results.** The number of words produced across the six 10-sec periods followed a negatively accelerated curve for all three letters. According to a 6 (periods) \( \times 3 \) (letters) repeated-measures ANOVA, there was a significant main effect of period \( [F(5, 605) = 145.5, p < .0001, MS_c = 1.37] \), and letter \( [F(2, 242) = 51.0, p < .0001, MS_c = 1.27] \), but no significant interaction
between the two \( (p > .1) \). Tests of simple effects showed that the significant effect of period was due to the fact that a greater number of words was produced in period one as compared to all other periods \( (p’s < .001) \). The significant effect of letter was due to the fact that letter \( (A) \) demonstrated a lower word production as compared to the other two letters that exhibited similar levels of word fluency.

The number of words produced in each 10-sec period and each letter (18 variables) was subjected to a principle components analysis (PCA) with varimax rotation. Pairwise deletion of correlations were used when missing values occurred. Two factors emerged with eigenvalues above 1 accounting for 27 and 26% of the variance, respectively. The first factor was associated with performance from the initial three periods of the FAS test, and the second factor was related to the performance in the three later periods.

A second PCA on the six memory tests and the factor scores of the two FAS factors was computed with pairwise deletion of missing values. The vocabulary test was completed by 77 subjects, whereas all other tests were based on 100 subjects or more. Two factors emerged with eigenvalues above one and they were interpreted as a Working Memory factor because of high loadings on Digit Span Forward, Digit Span Backward, Free Recall and Recognition of Words, and a Semantic Memory factor because of high loadings on Information, Similarities, and Vocabulary.

The initial periods of the FAS test (factor I scores from the first PCA) and the later periods of the FAS test (factor II scores from the first PCA) demonstrate a separable pattern of loadings. The initial periods of the FAS test loaded on the Working Memory factor. The subsequent periods loaded primarily on the Semantic Memory factor. This result suggests a dissociation of memory systems across time of the FAS test, with the initial periods being linked to working memory processing and the later periods linked to semantic memory processing.

The initial periods of the FAS test (factor I scores from the first PCA) and the later periods of the FAS test (factor II scores from the first PCA) were not attenuated by age or education. Age was unrelated to either factor, while education was significantly related to both factors \( [r = .304, F(1, 89) = 9.08, p < .01; r = .286, F(1, 89), p < .01] \).

Conclusion. The contribution of working and semantic memory during word production of the FAS test appears to be dissociated across time. This result may have theoretical as well as practical implications.

Reference

31. Eye Tracking of a Right Parietal Patient and Normal Subjects during the 7/24 Spatial Recall Test and Object Memory Tests

S. Shimozaki, A. Weinstein, M. Hayhoe, W. Merigan, G. Zelinsky, and D. Ballard

University of Rochester

In previous studies a right parietal patient has demonstrated a visuospatial deficit possibly related to spatial memory. To assess this deficit, the eye movements and fixations of the patient and normal subjects were measured while performing the 7/24 Spatial Recall Test. The subjects also performed analogous tasks testing object memory (images and words), and a task testing spatial and object memory simultaneously. Accuracy results confirmed the patient’s earlier finding of a deficit specific for spatial memory. Analysis of the fixations during the initial 10-sec memorization period of the 7/24 Spatial Recall Test showed the patient tends to fixate individual spatial locations more often than normal subjects, suggesting a relative loss in the visuospatial ability to cluster individual objects into groups.

Rationale. In previous studies a right parietal patient has demonstrated a visuospatial deficit that appears to be related to spatial memory (Shimozaki, Merigan, Zelinsky, Hayhoe, & Ballard, 1996). The goal of this study is to assess this deficit by measuring the eye movements and fixations of both the patient and normal subjects while performing the 7/24 Spatial Recall Test. To assess the specificity of the patient’s deficit subjects also performed tasks testing object image memory, object text memory, and a task testing both spatial and object image memory simultaneously.

Subject. The patient is a 62-year-old right-handed male with a localized right posterior parietal lesion caused by a thrombotic stroke approximately 1.5 years ago. All testing was performed at least 1 year after the stroke. Neuropsychological testing on the patient showed no apparent hemineglect, hemianopia, or loss in verbal and short-term memory. The patient showed a decline in performance in some visuospatial tests compared to estimates of premorbid functioning. These tests are Block Design (part of the Wechsler Adult Intelligence Scale—Revised, WAIS-R), the Hooper Visual Organization test, and the 7/24 Spatial Recall test.

Method. In the 7/24 Spatial Recall Test, subjects are shown seven checkers placed randomly on a 6 × 4 grid. After viewing the grid for 10 sec, the checkers are removed, and the subject is asked to reproduce the random pattern after being given nine checkers. Typically eight trials are given, five trials with the same pattern, followed by a trial with a different pattern, a recall trial of the first pattern, and finishing with a trial in which the checkers are not removed and the subject must copy the pattern. The last copy trial assesses any motor or perceptual difficulty that might confuse the interpreta-
tion of performance in the task. A delayed recall trial of the first pattern may be given after 30 min.

In this study, subjects performed in a computer version of the 7/24 task (condition 7/24 Memory) while their eye positions were measured with a head-mounted eye tracker (Applied Sciences Laboratories infrared bright pupil). Three computer monitors were placed in front of the subject, which were designated as the model monitor, the resource monitor, and the workspace monitor. At the beginning of each trial, a $6 \times 4$ grid pattern with seven checkers randomly placed on the grid appeared on the model monitor for ten seconds. After the model grid pattern disappeared, subjects viewed an empty $6 \times 4$ grid on the workspace monitor and an array of seven checkers on the resource monitor. Subjects attempted to reproduce the model grid pattern by using a computer mouse to select the checkers on the resource monitor and to place them in the empty grid on the workspace monitor. Subjects also performed in a 7/24 copy condition in which the model grid pattern remained visible for the duration of the trial (condition 7/24 Copy).

In addition to the 7/24 Spatial Recall Test, subjects performed in tests of object image memory [condition Object Image] and object text memory [condition Object Text]. With the same arrangement of monitors as above, either the images or the words of seven objects appeared for 10 sec in a $4 \times 2$ grid on the model monitor. After 10 sec, subjects viewed 24 objects on the resource monitor, and an empty $4 \times 2$ grid on the workspace monitor. Using the mouse, subjects attempted to choose the seven objects displayed on the model monitor and place them on the workspace monitor. This placement could be done without regard to the original location of the object in the grid on the model monitor. The 24 objects were fixed across trials, and were chosen from a set of 260 object images developed by Snodgrass and Vanderwart (1980). These 260 objects were ranked by their “ease to be encoded” by using a combined $z$ score from the four scales measured in the original paper (familiarity, image agreement, complexity, and name agreement). From this ranking the 24 most easily encoded objects were chosen.

A final condition tested the ability to retain object image and spatial location information simultaneously [condition LOC+OBJ]. Subjects viewed four images of objects (from the set of 24 described above) placed randomly in a $4 \times 3$ grid on the model monitor for 10 sec. After the model grid pattern disappeared, the subjects viewed 20 objects on the resource monitor and an empty $4 \times 3$ grid on the workspace monitor. With the mouse, subjects attempted to choose the correct 4 objects and place them in the correct location in the $4 \times 3$ grid. The number of grid locations and objects in the resource area were chosen to equate the complexity of the task, as measured by the total number of possible combinations, with the 7/24 and object memory tasks.
Overall, subjects performed in five conditions: 7/24 Memory, 7/24 Copy, Object Image, Object Text, and LOC + OBJ. In each condition, subjects performed in 10 trials, with each trial containing a different model. All subjects viewed the same set of model patterns. Besides the patient subject, 4 normal subjects in participated the study (Normals Eye). In addition, 10 normal subjects participated in the study without eye tracking (Normal No Eye).

**Results.** Table 8 gives the average number of objects selected and/or placed correctly on each trial (out of seven objects, except for LOC + OBJ, which is out of four objects). The patient has nearly equivalent performance to the normal subjects for the Object Images and 7/24 Copy conditions, and is less accurate than normals in the LOC + OBJ, the 7/24 Memory, and the Object Text conditions. Table 9 gives performance in the LOC + OBJ condition considering separately just the correct spatial location or just the correct object identity. Consistent with a spatial memory deficit the patient performs as well as the normal subjects in the LOC + OBJ condition when considering

**TABLE 8**
Accuracy = Number Correct/Trial and Standard Deviations

<table>
<thead>
<tr>
<th></th>
<th>7/24 Memory</th>
<th>7/24 Copy</th>
<th>Object images</th>
<th>Object text</th>
<th>Loc + Obj</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normals no eye</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>5.38</td>
<td>6.90</td>
<td>5.93</td>
<td>5.62</td>
<td>3.63</td>
</tr>
<tr>
<td>SD</td>
<td>1.94</td>
<td>.54</td>
<td>1.02</td>
<td>1.10</td>
<td>0.82</td>
</tr>
<tr>
<td>Normals eye</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>5.76</td>
<td>7.00</td>
<td>6.10</td>
<td>5.60</td>
<td>3.77</td>
</tr>
<tr>
<td>SD</td>
<td>1.76</td>
<td>0</td>
<td>1.33</td>
<td>1.04</td>
<td>.67</td>
</tr>
<tr>
<td>Patient</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>3.60</td>
<td>7.00</td>
<td>5.70</td>
<td>4.80</td>
<td>2.70</td>
</tr>
<tr>
<td>SD</td>
<td>2.17</td>
<td>0</td>
<td>.95</td>
<td>.09</td>
<td>1.16</td>
</tr>
</tbody>
</table>

**TABLE 9**
Accuracy = Number Correct/Trial, LOC + OBJ Condition, Separated by Object Identity and Spatial Location

<table>
<thead>
<tr>
<th></th>
<th>Object identity only</th>
<th>Spatial location only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normals no eye</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>3.89</td>
<td>3.86</td>
</tr>
<tr>
<td>SD</td>
<td>.27</td>
<td>.47</td>
</tr>
<tr>
<td>Normals eye</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>3.92</td>
<td>3.85</td>
</tr>
<tr>
<td>SD</td>
<td>.27</td>
<td>.59</td>
</tr>
<tr>
<td>Patient</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>3.90</td>
<td>3.00</td>
</tr>
<tr>
<td>SD</td>
<td>.32</td>
<td>.94</td>
</tr>
</tbody>
</table>
Table 10 gives the time-of-completion for each condition. Generally the patient is slower in all conditions compared to the normal subjects. This relative slowing, however, does not affect the patient’s performance in the Object Images and 7/24 Copy conditions. Thus, results from accuracy and time-to-completion seem to confirm a specific difficulty in spatial memory for the parietal patient, except for performance in the Object Text condition. Looking at serial effects on performance, however, suggests that the patient’s difficulty with object text differs markedly from his spatial memory deficit. Table 11 gives the proportion of objects selected correctly with respect to the order in which they were selected. For the Object Text condition, initially the patient performs as well as normals (collapsed over Eye and No Eye), then he suffers from a steeper memory decay rate than normals as he selects more items. For the 7/24 Memory condition, the patient’s performance is worse

**TABLE 10**
Time of Completion per Trial in Seconds

<table>
<thead>
<tr>
<th></th>
<th>7/24 Memory</th>
<th>7/24 Copy</th>
<th>Object images</th>
<th>Object text</th>
<th>Loc + Obj</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal no eye</td>
<td>M</td>
<td>26.2</td>
<td>16.1</td>
<td>41.6</td>
<td>47.2</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>11.6</td>
<td>7.56</td>
<td>13.9</td>
<td>18.8</td>
</tr>
<tr>
<td>Normal eye</td>
<td>M</td>
<td>24.2</td>
<td>19.4</td>
<td>34.2</td>
<td>36.2</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>4.55</td>
<td>12.3</td>
<td>9.66</td>
<td>11.4</td>
</tr>
<tr>
<td>Patient</td>
<td>M</td>
<td>39.7</td>
<td>25.9</td>
<td>46.0</td>
<td>45.6</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>9.02</td>
<td>9.44</td>
<td>13.3</td>
<td>10.3</td>
</tr>
</tbody>
</table>

only object identity, but worse than normal subjects when considering only spatial location.

Table 10 gives the time-of-completion for each condition. Generally the patient is slower in all conditions compared to the normal subjects. This relative slowing, however, does not affect the patient’s performance in the Object Images and 7/24 Copy conditions. Thus, results from accuracy and time-to-completion seem to confirm a specific difficulty in spatial memory for the parietal patient, except for performance in the Object Text condition. Looking at serial effects on performance, however, suggests that the patient’s difficulty with object text differs markedly from his spatial memory deficit. Table 11 gives the proportion of objects selected correctly with respect to the order in which they were selected. For the Object Text condition, initially the patient performs as well as normals (collapsed over Eye and No Eye), then he suffers from a steeper memory decay rate than normals as he selects more items. For the 7/24 Memory condition, the patient’s performance is worse

**TABLE 11**
Proportion Correct across All Trials with Respect to Order of Selection

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>7/24 Memory</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal eye and no eye</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>.892</td>
<td>.883</td>
<td>.893</td>
<td>.813</td>
<td>.760</td>
<td>.746</td>
<td>.667</td>
</tr>
<tr>
<td>SD</td>
<td>.112</td>
<td>.114</td>
<td>.160</td>
<td>.145</td>
<td>.249</td>
<td>.215</td>
<td>.282</td>
</tr>
<tr>
<td>Patient</td>
<td>.600</td>
<td>.500</td>
<td>.600</td>
<td>.700</td>
<td>.667</td>
<td>.330</td>
<td>.333</td>
</tr>
<tr>
<td>Object text</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal eye and no eye</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>.979</td>
<td>.943</td>
<td>.914</td>
<td>.886</td>
<td>.779</td>
<td>.650</td>
<td>.530</td>
</tr>
<tr>
<td>SD</td>
<td>.043</td>
<td>.094</td>
<td>.117</td>
<td>.129</td>
<td>.208</td>
<td>.265</td>
<td>.210</td>
</tr>
<tr>
<td>Patient</td>
<td>1.00</td>
<td>1.00</td>
<td>.800</td>
<td>.800</td>
<td>.600</td>
<td>.500</td>
<td>.111</td>
</tr>
</tbody>
</table>
from the first item selected, and decays at about the same rate as normal subjects. This suggests that, unlike the difficulty with text, the patient’s spatial memory deficit is unrelated to decay rate and might be due to the initial storage or retrieval of spatial information.

To assess a possible difference in encoding between the normal subjects and the patient, the eye tracking data in the 7/24 Memory condition during the initial 10-sec period of memorization were analyzed. In general, normal subjects appear to fixate the individual checkers less frequently than the parietal patient. The average number of fixations upon an individual checker per trial is lower for the normal subjects (16.1, SD = 5.15) compared to the parietal patient (22.8, SD = 6.12). Also, the proportion of the checkers in the model grid that were fixated upon individually is slightly lower for the normal subjects (77.5%) than for the parietal patient (88.6%). Finally, fixating upon a checker location during the memorization interval does not correlate with performance at that same location for the normal subjects (r = .077). The same correlation for the parietal patient, however, is r = .355, suggesting that performance is more closely tied to fixation locations during the memorization period for the parietal patient. Thus, the normal subjects perform the 7/24 Spatial Recall Test better than the patient, yet with less regard to individual checkers. One possibility is that the patient may lack the visuospatial ability to cluster, or “chunk,” several checkers into a single group, forcing the patient to remember more objects, and leading to worse performance compared to normals.

**Conclusions.** Results from studies assessing spatial, object text and object image memory confirmed an earlier finding of a deficit specific for spatial memory for a right parietal patient. During the initial memorization period of the 7/24 Spatial Recall Test, the patient tends to fixate individual spatial locations more often than the normal subjects, possibly suggesting a relative loss in the visuospatial ability to cluster individual objects into groups.

**References**


32. **Event-Related Potential Evidence of Right Prefrontal Activity during a Visuospatial Working Memory Task**

D. J. A. Moulden, T. W. Picton, and D. T. Stuss

*Rotman Research Institute at Baycrest Centre, North York, Ontario, Canada*

Event-related potentials were recorded from eight healthy adults as attention randomly switched between one of two visuomotor task-sets. Cues designating the task goal and response hand occurred 1200 msec before a target. The target was a circle
occurring in one of four boxes of a 2 × 2 grid. The spatial location of the target within the grid indicated which of two buttons to press using the precued left or right hand. Irrespective of the responding hand, a sustained right prefrontal positive slow wave was recorded only during the delay interval between perception of the task identifying cue stimulus and its associated response rule activating target. This may represent the on-line monitoring and manipulation of temporally distant events (cue and target sets) within spatial working memory.

**Rationale.** Numerous PET and fMRI studies of the human brain support the role of the dorsolateral prefrontal cortex as a key site of activation during performance of working memory tasks (Cohen et al., 1994). Most studies report a predominant right hemisphere activation for spatial (location processing) tasks, and a left hemisphere predominance for verbal tasks (Awh, Smith, & Jonides, 1995). Some of the imaging research has further pinpointed areas 9 and 46 as functional sites in the normal performance of spatial working memory processes (McCarthy et al., 1994); For example, Petrides et al. (1993) present human PET scan results suggesting a right dorsolateral prefrontal dominance for monitoring of working memory during spatial attention demanding tasks. Posner and Petersen (1990) have described a similar right lateral midfrontal system involved in sustained attention (vigilance) when one needs to suspend activity while waiting for low probability events. In a recent formulation, Petrides (1995) postulates that the mid-dorsolateral frontal cortex (i.e., areas 9, 46) is especially active when several pieces of information in working memory need to be monitored and manipulated on the basis of the task requirements or the subject’s current plans.

The current event-related potential (ERP) study represents an attempt to provide convergent evidence for the PET and fMRI reports of a right lateral prefrontal spatial working memory system. The paradigm that was used required subjects to hold visual cue information in working memory while awaiting for an associated task-relevant target, which had to be processed for its spatial location in order to correctly execute a discriminative button press. It was hypothesized that a right prefrontal lateralized waveform might emerge during the delay interval between the cue and target, thus supporting the recent PET and fMRI evidence for the role of the right prefrontal region in spatial working memory.

**Subjects.** Eight healthy right-handed male subjects (mean age = 34 years) participated in the experiment. All subjects were university graduates with a negative history for neurological impairment.

**Method.** Task stimuli were presented on a computer monitor positioned 75 cm in front of the subject. Each subject completed 1000 task-set trials over 10 separate trial blocks. Each trial consists of a cue, target, and response. Cue arrows designating the task and response hand were located either to the left and right (Left Hand Task) or on the top and bottom (Right Hand Task) of a 2 × 2 grid. The target was a circle occurring in one of the four grid boxes. The Left Hand Task involved deciding whether the circle was in the Left or Right half of the grid and pressing a button with the index or
middle finger of the left hand. The Right Hand Task involved deciding whether the circle was in the Top or Bottom half of the grid and responding with the right hand. Task-hand cues preceded the target by 1200 msec thereby allowing subjects to use the task identifying cues to switch conceptual sets and prepare the correct response hand prior to the target, although the cue information had to be retained in working memory in order to correctly respond to the target.

The sequence of tasks within a block occurred randomly so that on each trial the subject either repeated the task from the previous trial (e.g., left hand task preceded by a left hand task—repeat left hand), or switched to the other task (left hand preceded by a right hand task—switch to the left hand). Subjects were instructed to respond as quickly and accurately as possible and to use the arrow cues to prepare the correct response hand in advance of the target location decision as this would facilitate a faster RT.

The EEG was recorded with a Neuroscan Syn-amp amplifier system using an electrode cap with 32 standard 10-10 scalp locations. All electrodes were referenced to the inion (Iz) and converted to an average reference off-line prior to analyses. Impedance was maintained below 5 kOhm. EEG was recorded with a bandpass of DC (3 subjects) and 0.1 (5 subjects) to 50 Hz at a rate of 250 samples/sec. Epochs were collapsed off-line to 180 points representing one sample every 16.67 msec over a 3-sec sweep including a 200-msec pre-cue baseline. Rejection for movement artifact was set at ±600 µV on any channel. Ocular source components were used to remove ocular artifacts from each subjects averaged ERP data.

Results. ERPs were analyzed for correct response 1200 ms cue-target interval trials. Mean area under the curve was obtained from left and right lateral prefrontal (F7, F8) and left and right central (C3, C4) electrode sites during the delay interval between perception of the cue (450 msec post-cue) and perception of the target stimuli (200 msec post-target). The independent variables were sequence (switch vs repeat), task-hand (left vs right), and hemisphere (left vs right). Two separate repeated-measures ANOVAs were performed for the homologous electrode pairs.

When the brain is preparing to make a motor response a slow negative wave develops at the central scalp location contralateral to the preparing response hand. This readiness potential (RP) or Bereitschaftspotential is generated in the precentral and supplementary motor cortex and is a sign of specific response hand preparation. The analysis at the central electrodes (C3, C4) gave rise to a significant task-hand by hemisphere interaction ($F(1, 7) = 67, p < .001$) and revealed a greater negativity at the electrode site contralateral to the cued response hand. This indicates that subjects used the cue information to prepare the correct response hand in anticipation of the cue-dependent spatial location decision for the target.

Consistent with the initial hypothesis, a significant hemisphere effect ($F(1, 7) = 6.33, p < .05$) was obtained at the frontal electrode pair. A sus-
tained positive slow wave was recorded over the right (mean = +1.6 µV) but not the left (mean = +0.4) prefrontal site during the cue-target delay. This sustained positivity remained right frontal lateralized during both a left and right hand response (task-hand, \( p > .05 \)) and for switch and repeat trials (sequence, \( p > .05 \)) and returned to baseline immediately after the button-press response. No higher-order interaction approached significance (\( p > 0.1 \)). That this waveform remained right frontal lateralized even while subjects were preparing either a right or left hand response suggests that this activity is not an artifact of the preparatory response set (i.e., the lateralized readiness potential). Thus, the obtained results are in accord with recent fMRI and PET studies which have suggested a right frontal dominance for monitoring of spatial (location processing) working memory during attention demanding tasks (Petrides et al., 1993) especially when behavior must be suspended, and integrated, across a short temporal delay.

References


33. Neural Correlates of Episodic Memory: The Effects of Divided Attention

J. A. Mangels, T. W. Picton, and F. I. M. Craik

Rotman Research Institute at Baycrest Centre, North York, Ontario, Canada

Divided attention (DA) in young subjects has been used as a model for the memory deficits associated with aging. Following this model, we assessed the effects of DA at encoding on the electrophysiological activity (ERPs) of young subjects.
Individuals studied visually presented words under focused attention or while performing an auditory-motor task. Early positive (P120) and negative (N180) parieto-occipital deflections were invariant across encoding conditions. These peaks may reflect perceptual processes automatically initiated by words within the focus of visual attention. However, DA markedly attenuated two later positive components, the P280 and P580, maximally recorded over right parietal regions. These components may index conscious evaluation of word meaning (P280) and integration of the word with the encoding context (P580), suggesting that reduced attentional resources disrupt episodic encoding at both a conceptual and contextual level.

**Rationale.** Episodic memory stores events from one’s personal past together with the spatio-temporal context in which the event occurred. Integration of content and context into an episodic memory trace requires the allocation of a sufficient level of attentional resources to the encoding task. If attentional resources are reduced by concurrent performance of a secondary task, as in a divided attention (DA) paradigm, episodic memory will be impaired (Craik & Byrd, 1982). The specific effects of DA on episodic memory are supported by the finding that DA at encoding impairs conscious recollection of a prior encounter with an item, but does not affect retrieval based on feelings of relative familiarity (e.g., Gardiner & Parkin, 1990).

Aging also selectively impairs conscious recollection (Parkin & Walter, 1992). DA in young subjects might therefore be used as a model for the effects of aging on memory (Craik, 1982). Following this model, we assessed the effects of DA on encoding on the electrophysiological activity (ERPs) of young subjects. ERPs were measured as subjects learned visually presented words under either focused attention or while performing an auditory-motor task. By comparing the time course and distribution of neural activity associated with learning under focused and divided attention, we were able to determine how reduced attentional resources modulate activity related to episodic encoding.

**Subjects.** Ten young (range, 24–37 years; mean, 34.6) right-handed subjects were tested.

**Method.** ERPs were recorded as subjects studied and recognized words. At study, subjects learned a series of 45 concrete, medium-frequency nouns presented at a rate of 2 sec each. Between words, subjects fixated on a cross-hair for 1.5 sec. In the full attention condition (FA), subjects performed the encoding task alone. In the DA condition, subjects performed the encoding task concurrently with an auditory continuous performance task (ACPT).

In the ACPT, subjects heard low-, medium-, and high-pitched tones over speakers and responded to these tones by pressing a button on a response box with their right hand. The next tone was presented immediately after the subject pressed a button or 3 sec had elapsed. There were two levels of difficulty to the secondary task. In the difficult DA condition, the tones were presented in a random order. In the easy DA condition, the tones were presented in a sequential order. The easy DA task was less attentionally demanding than the difficult DA task but involved the same perceptual-motor
components. Subjects received two blocks of each encoding condition in a counterbalanced order.

Each block of studied items was followed by a 30-sec distractor task and a free recall test. Subjects then began a recognition test during which ERPs were again recorded. In the recognition test, targets and an equal number of distractors were presented in a random order for 2 sec each. At the end of the 2 sec interval, a response cue appeared beneath the word and subjects made a remember (R), know (K), or new (N) response. Subjects made a R response if recognizing the item brought back to mind specific associations or images experienced at when the word was first presented, a K response if they recognized that the item had been on the study list but did not consciously recollect its presentation, or a N response if they had not seen the word before.

EEG was recorded from 46 electrode sites with an average reference. Signals were amplified, filtered (.05–50 Hz), digitized (250 Hz) and stored for off-line analysis. Following artifact rejection, ERP sweeps were selected from 100 msec before word onset to 3.5 sec after word onset. EOG artifacts were compensated using ocular source components.

Results. Recall and recognition memory performance declined systematically with the increase in secondary task demands. In addition, DA reduced the proportion of R responses but did not affect the proportion of K responses, indicating that DA selectively impaired consciously controlled encoding processes. In addition, for the difficult DA condition, there was a 300 msec cost to RT in the secondary task when it was combined with the memory task compared to when it was performed alone. The cost to both the encoding task and secondary task verified that subjects were attempting to dividing their attention equally across the two tasks in this condition.

Early posterior positive (P120) and negative (N180) deflections were observed in all encoding and retrieval conditions and were invariant across encoding conditions. Significant effects of DA were observed, however, at two mid-latency positive components maximally recorded over right parietal regions. The first component, maximal at 280 msec post-stimulus (P280), was attenuated in the difficult DA condition at encoding, but was consistent across R, K, and N response categories at retrieval. The second component peaked at 580 msec post-stimulus (P580) and was recorded maximally over right centro-parietal regions. At encoding, this component was delayed by an average of 60 ms in the easy DA condition, although its amplitude was not significantly reduced. In the difficult DA condition, however, the amplitude of the P580 was attenuated to baseline levels. The P580 was also observed at retrieval. At retrieval, items associated with conscious recollection (R responses) evoked the largest P580. The P580 for items recognized on the basis of familiarity (K responses) did not differ from new items.

Discussion. The early deflections, P120 and N180, have been associated with perceptual processing of words (Compton et al., 1991). Specifically, the P120, which was lateralized to right temporal-parietal regions, appears
to index pre-lexical analysis of visual features, whereas the N180, recorded maximally over left parietal-occipital regions, may index lexical access or word-form identification. Although the amplitudes of these early peaks can be modulated by spatial selective attention, these peaks were invariant across FA and DA encoding conditions. Thus, the perceptual processes they represent appear to be automatically initiated whenever a word is within the focus of visual attention and are not affected by reduced central processing resources.

The invariance of the P280 across response category at retrieval suggests that it does not index episodic memory processes, but rather may reflect conceptual processes, such as access to word meaning. The interpretation gains support from both electrophysiological and behavioral findings. The latency and distribution of the P280 is similar to a vertex recorded potential that is sensitive to the conscious recognition of meaningful verbal stimuli (Rudell & Hua, 1996). Furthermore, studies of DA effects on priming indicate that DA impairs cross-modality priming more than same-modality priming (Jacoby, Yonelinas, & Jennings, in press). This may occur because cross-modality priming depends more on conceptual processes than same-modality priming, which can utilize both perceptual and conceptual processes.

The similar distribution of the P580 to that of the P300 suggests that this component may index the conscious evaluation of the stimulus in its episodic context (Donchin & Fabiani, 1991). The less demanding DA task (easy) may have simply delayed evaluation of the stimulus within the encoding context, resulting in less opportunity for subsequent elaborative processing. The difficult DA task, however, may have reduced attentional resources to the extent that conscious evaluation was prevented. The relationship between the P580 and conscious processes related to episodic memory is supported further by the finding that this component indexes conscious recollection at retrieval (i.e., R responses).

In summary, divided attention did not affect early positive (P120) and negative waves (N180) associated with perceptual processing, but did attenuate later components associated with conscious evaluation of semantic (P280) and episodic (P580) information. These findings support behavioral studies indicating that reduced attentional resources resulting from either experimental (DA) or neurophysiological means (normal aging) selectively impair conscious processes. Furthermore, these results indicate that attention is not only necessary for binding content and context into an episodic memory trace, but also for processing at a conceptual, semantic level (see also Craik, Moscovitch, & McDowd, 1994).

References


34. Semantic Priming in an Object Decision Task in Normals and Alzheimer’s Disease: An Electrophysiological Study

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Semantic memory deterioration is a major symptom observed in dementia of the Alzheimer’s type (DAT). However, the nature of this deficit remains uncertain, some researchers postulate difficulty in accessing and retrieving semantic information while others point to a degraded storing. In this study, we used the event-related potential, specifically the component N400, to assess semantic functions. Ten DAT patients and 10 controls were visually presented with 120 prime-targets pairs, 50% of them belonging to the same category and the other 50% mismatching the prime. Statistical analysis revealed significant differences just for the incongruent targets while the amplitude of the congruent ones was similar for both groups. The lack of this component in DAT patients appears to indicate that there is a lack of efficient access and deficient associative links within the semantic network and therefore seems to indicate a breakdown in the structure and organization of semantic memory.

Rationale. Semantic memory deterioration is a mayor component of the cognitive decline seen in patients with dementia of the Alzheimer’s type (DAT). However the exact nature of this deficit remains unclear, some re-
search data support a procedural deficit where there is an inability to access or retrieve the contents of semantic memory, while other work is suggestive of a degraded semantic storing, whose contents are disrupted. According to the network theory of semantic memory postulated by Collins and Loftus (1975), concepts are represented by nodes interconnected by a variety of relationships, such as membership in a common category, functional and property relationships. Whenever a concept is presented, the corresponding node in semantic memory is activated, this activation spreads automatically to related nodes, increasing the accessibility of these for processing. Experimental evidence for such a spread of activation comes from studies of semantic priming, where behavioral studies have shown that the processing of related targets is enhanced or facilitated in comparison with the processing of unrelated targets. Additional information about semantic processing in DAT can be obtained by the use of the N400 event-related potential (ERP) component. Priming has a substantial effect on this component, several studies have shown that this negative deflection is enhanced for written endings of sentences with semantically incongruent words, relative to sentences with a congruent ending. This component has also been demonstrated using written words, speech sounds and pictures as stimuli (Barret & Rugg, 1990) with a larger N400 elicited by semantically unrelated pairs than by semantically related ones. Until now, few studies have been published using N400 to assess semantic functions in DAT. Recently, Hamberger et al. (1995) used a verbal lexical decision task, and found that the N400 amplitude was identically responsive to semantic relatedness in young normal and DAT groups. Research using reaction time measures has found that unlike normals DAT patients did not show semantic priming when the prime was a picture of an object, while priming was observed for DAT patients when the prime was a word. There are differences between the processing of words and pictures (Potter & Faulconer, 1975), therefore, the follow-up of these results may provide important information about the limitations of semantic functioning in DAT. The purpose of the present study was to provide an objective analysis of semantic abilities of DAT patients using an active categorization task with pictures as primes.

Subjects. Ten normal elderly subjects (5 male and 5 female, mean age = 67.8, SD = 4.7) and 10 patients with DAT (4 males and 6 females, mean age = 75.4, SD = 5.2) participated. The criteria for inclusion of the normal group were: not demented according to the Diagnostic and Statistical Manual of Mental Disorders criteria (DSMIV), a score equal to or higher than 23 in the Mini-Mental State Examination, and no history of neurological or psychiatric illness. The patient group was clinically demented and met the criteria for dementia of DSM IV for primary degenerative dementia and the criteria of the NINCDS/ADRDA for probable DAT. Patients were mildly to moderately impaired. Other possible sources of dementia were excluded by appropriate laboratory evaluations, such as computed tomography (CT).
and electroencephalography (EEG). Their scores on the Hachinski ischemic rating score were used to aid in excluding multifarct dementia.

**Method.** The stimuli consisted of 120 related pairs of line drawings taken from the Snodgrass and Vanderward (1980) stimuli, adapted and standardized in a Spanish-speaking population. Stimuli were presented sequentially in prime-target pairs with one-half of the targets ‘matching’ the primes via categorization relationships (violin–guitar) and the other half mismatching the prime (cat–guitar). The subjects had to discriminate between semantically related and unrelated pairs. Subjects sat in a comfortable chair in front of a computer monitor and were instructed to minimize body and eye movements. The EEG recording was synchronized with the picture onset. A typical trial proceeded as follows: the letter string XXXX was presented as a warning stimuli, a picture was presented 1 sec followed by a blank screen for 180 msec, a second picture was presented for 1 sec, and the screen was again blanked. The word ‘RESPONDA’ (answer) appeared and the subjects responded verbally (yes or no). The response was delayed until EEG recording was complete in order to reduce artifacts, thus reaction time was not measured. Scalp electrical activity was recorded from 32 monopolar derivations of the 10–20 International System. All electrodes were referenced to linked ear lobes. An additional bipolar derivation recorded EOG activity used to reject sweeps contaminated with eye movements. Electrode impedance was always below 5 Kohms. The signal was filtered between 0.5 and 30 Hz (3 dB down). In each trial 256 points of digitized EEG (12 bit resolution) were recorded at a sampling rate of 250 H7, totaling 1 sec, and stored on a magnetic disk for off-line analysis. A pre-stimulus baseline of 100 msec was obtained in each trial and data acquisition continued 900 msec after stimulus onset. Each sweep was visually inspected and those with eye movements and muscular artifacts were eliminated. Trials with incorrect responses were also eliminated. For each subject, ERP’s evoked for each recording site were obtained for each stimuli condition. The morphology of the waveform consisted of a negative peak N100, followed by a positive P200, then a negative modulation N400 and a slow positivity P600. The average amplitude on the components of the ERP waveforms were measured for each individual in predefined time windows.

**Results.** Analysis of variance for repeated measures (ANOVA) with the factors of Condition (congruent vs incongruent), Site (F7,C7,P7,07), and Group (normal vs DAT) were performed due to limitations in the number of subjects; only five derivations were submitted to statistical analysis, but qualitative analysis was performed with the remaining recording derivations ($n = 32$). No significant effects in the amplitude or latency of the ERPs were found before 300 msec for any factor. In the normal group, after 300 msec the recordings associated with the incongruent pictures became more negative than those associated to the congruent targets. This negativity (N400) appeared around 325 msec and lasted up to 650 msec, with its maximum at
about 504 msec. The mean amplitude of the difference waveform subtraction of ERP of congruent from those of incongruent trials) was calculated over a 325-msec window that was centered for each group on the corresponding N400 peak. The ANOVA on the mean amplitude of the difference waveform (N400 effect) revealed a significant difference ($p < .05$) between the factors of Group and Site ($p < .05$). The normal group showed a posterior distribution of this negativity with larger amplitude at PZ and CZ, whereas DAT patients showed a reduced amplitude with no significant topographic effects. The analysis of the N400 effect was complemented by a separate analysis of congruent and incongruent trials. The ANOVA revealed a significant difference ($p < .05$) between Condition and Group. A further analysis reflected that the amplitude of incongruent recordings was larger for the normal subjects than DAT patients, while the amplitude for congruent recordings was similar for both groups.

Discussion. It has been postulated that the N400 is sensitive to semantic processing and that the N400 amplitude varies inversely with the extent to which a word or picture has been primed by its preceding semantic context. Although the amplitude of the N400 component was reduced in DAT, a separate analysis of congruent and incongruent trials revealed than only the incongruent trials were different for patients with respect to controls. Thus, the results of this study indicate that DAT patients show both normal and abnormal patterns of ERP. On one hand, they showed a normal ERP for congruent trials, but on the other hand they exhibited abnormal ERP for the incongruent targets. Semantic memory has been conceptualized as a network in which semantically related items are closely linked, whereas more distantly related items share fewer connections and are represented more remotely within the network (Collins & Loftus, 1975). The difficulty that DAT patients showed in processing only the incongruent stimuli could be due to damage to the associated cortical areas that affect the access to unrelated stimuli. Neuronal loss may lead to deterioration in the associative network which form the skeletal structure of semantic memory. These findings are consistent with a lack of efficient access and deficient associative links within the network, and therefore seem to indicate that in DAT there is a breakdown in the structure and organization of semantic memory.

References
Improving Age-Related Deficits in Recollection: Application of an Opposition Procedure

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Previous research has revealed striking age-related deficits in conscious recollection (Jennings & Jacoby, in press). To reverse those declines, we attempted training older adults by giving them a continuous recognition task where recollection was easy, then gradually increased the difficulty to shape recollective processing. Specifically, participants were asked to recollect items at very short presentation-test delays, which gradually increased in length. On the first day of training, older adults could only show equivalent performance to young adults when two intervening items occurred between presentation and test. However, after 6 hr of training, they showed comparable recollection to young adults with 26 intervening items. These gains could not be attributed to practice or bias effects, but seemed to arise from the shaping technique. Moreover, improvements lasted over a 3- to 4-month period.

Rationale. Previous research has revealed that aging and traumatic brain injury are associated with striking deficits in conscious recollection (Jennings & Jacoby, in press; Ste-Marie, Jennings, & Finlayson, 1996). Consequently, it is important to explore rehabilitation techniques for reversing those declines. The method examined here was designed to improve memory performance by placing individuals in a situation where recollection is easy, then gradually increasing the difficulty to shape recollective processing. Slowly moving subjects from a situation where they can perform competently may allow them to adapt their recollective process to more demanding situations.

To test this idea, we adopted an “opposition” task designed to examine recollection across different delays (Jennings & Jacoby, in press). In that procedure, young and elderly subjects were asked to read aloud and learn a list of words, followed by a yes/no recognition test, in which they were shown study and new words with each new word repeated once after 0, 3, or 12 intervening items occurred. Subjects were asked to respond “yes” to words they had seen at study, but “no” to new words and repetitions. The repetitions are the critical items. The first presentation of those items should increase their familiarity, and subjects may misattribute this familiarity to the prior study phase, confuse repetitions with old words, and mistakenly respond yes. However, if subjects can recollect the source of a word’s initial
presentation (study versus test), or recollect that they have already responded to a word, then any influence of familiarity is opposed, and subjects will correctly respond no. Older adults responded yes to significantly more repetitions than young adults when only 3 intervening items occurred, indicating poor recollection at a very short delay.

We adapted this task to try to train older adults and had them use recollection when it was easy to do so (i.e., 1 intervening item between repetitions), then gradually increased that interval to see if they could show accurate recollection across longer delays. If performance did improve, three questions have to be addressed: (1) Did these improvements arise from practice or bias effects? (2) Did these effects show generalization to other memory tests? (3) Did improvements last over time? To address these issues, we compared the performance of an experimental group who received 5–6 hr of training with the shaping procedure to that of control subjects who received 5–6 hr of practice without shaping. We also looked for transfer of performance to standard recognition, and maintenance of training over a 4-month interval. If training proved viable with older adults, one could consider applying it to other memory disorders.

Subjects. Eleven elderly adults (mean age = 72.1) made up the experimental group; an additional 8 elderly adults (mean age = 74.2) comprised the control group. All subjects were community dwelling residents in self-reported good health, with an average of 17.2 years of education, and 83.9% on the Mill Hill Vocabulary Test. Control and experimental subjects were matched for age, gender and memory performance.

Method. Subjects were given four training sessions a day for 7 days. For each training session subjects studied 30 words, followed by a training phase where they were shown the 30 study words, 30 new words, and those 30 new words were repeated once at one of two delay intervals. Subjects were asked to respond “yes” to old items, and “no” to new and repeated items, and given positive feedback whenever they responded correctly. The shaping procedure was implemented by gradually increasing the lag intervals. In Session 1, words were repeated after one or two intervening items. If subjects performed to criterion (the level of performance shown by young adults in previous experiments) then in Session 2, the lag conditions increased to one and three items, then two and four, and so on to 20 and 48. Thus, subjects were always working at one easy lag interval that they had already mastered and one that was new and more difficult. If subjects did not achieve criterion at both lags, they continued at those intervals till criterion was met.

Control subjects were given the same training program except for the shaping procedure. Rather than gradual increases in the lag pairs from 1 & 2 to 1 & 3 etc., control subjects were presented a randomly ordered set of lag pairs across the 28 sessions. Each control subject was yoked to an experimental subject, so that the control received the same lag intervals and the same number of sessions for each lag interval as their experimental counterpart.
On the first day, control subjects received intervals 1 & 2, 1 & 3, 2 & 4, 2 & 8, and on the last day, they received the highest lag interval pairs as their experimental partners. We tested control subjects in this manner to evaluate their level of performance on the first and last training days. The order of lag intervals for the remaining 5 days were scrambled.

Training follow-up: Four months later experimental subjects were asked to return for eight more training sessions (2 days) after a 4-month delay. We used the first day to pinpoint the level of performance that subjects had maintained, and the second day to determine how much they could improve with 4 more sessions.

Results. Gains in performance were measured by comparing the length of the interval where subjects reached criterion on the first versus the last training day. If interval length increased significantly between the first and last day of training, it would suggest that we have improved performance. On the first day of training, the experimental group, on average, could only perform to criterion when the lag interval consisted of 1.8 intervening items. However, by the last day of training, the average lag interval at which they reached criterion performance was 26.1 intervening items (Table 12). Overall the training group showed a marked improvement in recollection. The control group also showed moderate gains, performing to criterion with 12.1 intervening items by the last day of training. They demonstrated a practice or training effect that was unrelated to shaping, however, the experimental group exceeded the control group’s gains, suggesting that shaping had an additional influence on performance.

Although recollection seemed to have improved, we may have merely altered subjects bias to respond no. To ensure that bias was not a factor, we calculated a bias measure for the first and last day of training based on performance with study and new items. The estimates of bias by the last day of training were similar for the two groups, and both groups showed a change in bias overall (Table 12). These results indicate that bias shifts cannot completely account for the training advantage of the experimental group.

The next questions to examine were whether these improvements generalized to other memory tasks and whether any effects of training lasted after the procedure had ended. Because subjects were given repeated study lists, and asked to recognize old and new items as part of the task, we could
examine generalization by looking for improvements on that standard recognition component. Unfortunately, comparing hits-fas for the first and last day of training did not reveal any change in recognition performance for either group. The form of recollection benefited here did not transfer to simple recognition, although it may generalize to more comparable ‘‘monitoring’’ situations. As for whether training endured, five subjects returned for retraining after 4 months. Four of those subjects showed some maintenance of performance on the first day of testing: three subjects showed maintenance of 25–33% of their original training effect, and one subject showed 100% preserved benefit. Moreover, a second day of training revealed that subjects did not require much effort to return to post-training performance, returning to 72% of their previous gains.

Conclusions. Our training procedure produces an improvement in recollection that reflects more than a simple effect of practice or bias, and this effect has lasting potential, although further work must be done to examine generalization. Finding that deficits in recollection can be improved with elderly adults though offers hope that this procedure may be beneficial with other memory-disordered populations. For example, traumatic brain-injured patients show a very similar pattern of memory deficits as elderly adults when tested at short study-test intervals (Ste-Marie et al., 1996). Given this correspondence in performance, it is reasonable to hope that we may see comparable training results.

References


36. A Comparison of Two Training Methods for Teaching Name–Face Associations to Elderly Subjects with Self-Reported Memory Loss

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Eight community-dwelling elderly subjects with self-reported memory loss volunteered to participate in a training study to improve memory for name–face associa-
Rationale. The age of retirement is increasing and many elderly individuals value social involvement. The ability to remember peoples’ names is important for many work and social situations and therefore impacts overall quality of life. Research has shown that the elderly have more difficulty than younger individuals remembering faces and their associated names (Yesavage & Rose, 1984). Cohen (1990) suggested that “…it is difficult to put names to faces for the same reason that it is difficult to put non-words to faces. Both are lacking in the semantic associations that allow other kinds of person identity information to be related to stored knowledge” (p. 297). Cognitive intervention, such as providing a strategy for linking the name to stored knowledge and enhancing the visual processing of the face through dynamic views, may be an effective means of helping elderly persons to remember peoples’ names. The present study compared the effectiveness and the efficiency of two methods used in name–face association training with amnestic subjects (Thoene & Glisky, 1994).

Subjects. Eight subjects over the age of 65 volunteered in a memory for name–face associations training study. None of the subjects had a positive neurological history, hearing impairment, or visual impairment. All of the subjects complained of memory problems in everyday situations. All of the subjects were within two standard deviations on a facial recognition test and a test of new learning. None of the subjects had clinical depression or other psychiatric conditions. All of the subjects were dwelling in the community and functioning independently.

Method. A multiple N intervention design was chosen such that every subject was trained with both training methods. In the mnemonic imagery condition, the first and last names were associated by means of a verbal elaboration provided by the experimenter and photographs of student actors. The first and last names were also provided on an index card. The subject
was asked to associate the verbal elaboration of the name with the face in the photograph by using visual imagery provided by the experimenter. Example ‘This is Sandy Peas. Here are some hints to remember her name: Think of her first name, Sandy, like a sandy beach, and her last name, like the vegetable peas. Try to imagine Sandy Peas sitting on a sandy beach eating peas. This might help you to remember her name.’

In the video condition, the name was presented on a card and spoke by the experimenter as well as by the student actor on the videotape. The student actor on the videotape stated his or her name and future occupation. The student then read some information about the University of Cincinnati. For example, the experimenter told the subject, ‘you are going to see Sandy Peas.’ The videotape began with ‘Hello, my name is Sandy Peas. I am studying at the University of Cincinnati and I want to become a teacher. The University of Cincinnati is located in the southwestern corner of the state of Ohio...’ Two sets of target faces, eight first and last names, and the order of the conditions within a session were all counterbalanced. In each condition, subjects attempted to learn the names associated with a set of four faces. The exposure time to the faces was approximately equivalent in both conditions. The subjects participated in 1-hr sessions until they reached the within trial criterion and the between trial criterion. The between trial criterion for the training was that the subject produced all eight names after a 3- to 5-day delay; this test was conducted at the beginning of each session except for the first. A trial consisted of a presentation of the four names with one of the two conditions. The within trial criterion was that the subject produced all four first and last names on two consecutive tests or until four learning and test trials were complete. A session consisted of a total of four to eight trials with both conditions; the exact number depended on when the subject reached the within session criterion.

Five of the subjects returned 1 week later to meet the student actors presented in the pictures and videotapes used in the two conditions. Each subject was seated in a room with an examiner. The subjects were asked to say the name of the student when the student entered the room. This procedure continued until all five subjects had the opportunity to independently name all eight subjects.

Results. The mean number of trials to reach between session criteria was similar in the mnemonic ($M = 10.63$) and video ($M = 11$) conditions. With the mnemonic imagery, 2 subjects reached criterion (between sessions) in the second session, four in the third session, one in the fifth session, and one in the eighth day of training. In the video condition, four subjects reached criterion by the third session, and five subjects reached criterion at the fourth session, and one never reached criterion.

For the real life meeting, three out of the five subjects who participated in this component of the study were able to correctly produce all first and last names. One subject correctly produced six names and one subject correctly
produced three names. Only one of the five subjects was able to identify more names learned in the mnemonic imagery condition than in the videotape condition. The other four subjects recalled the same number of names learned in each condition.

Discussion. Both techniques were effective and there were no systematic differences in the efficiency of these two techniques. All subjects reached the criterion of accurately providing all eight names (four learned with the imagery technique and four learned with the mnemonic technique) after a one-half hour delay and seven of the eight subjects recalled all eight names after a 2- to 5-day delay. In addition, recall of the names and faces was tested for five of the subjects in a simulated real life meeting. Although there was some decrement in performance, the subjects were able to generalize the training to a novel situation. There were no systematic differences in the subjects’ ability to recall the names learned with the imagery technique and names learned with the video technique in the simulated real life meeting. The results suggest that normal elderly subjects benefit from the training methods described in this study and were able to generalize the training to a simulated real life meeting. There were no differences related to training method.

References

37. Semantic Memory and Aging: Is it More Difficult to Organize Information in Time or in Space?

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This study examined whether older adults’ capacity to organize knowledge was dependent on the spatial or temporal nature of the information and-or on the level of difficulty. Two tasks were administered to 16 younger and 16 older adults: (1) generation of 16 familiar scripts with high spatial or high temporal content, difficulty being controlled by asking subjects to generate the scripts in a forward or backward sequence; (2) two tests that provided estimates of the capacity to manipulate knowledge in a space or a time frame. Elderly people demonstrated greater difficulty to order events in a backward sequence. Results also showed that spatial
organization of knowledge in older adults is impaired. Findings are discussed in light of recent neuropsychological models of cognitive aging.

Rationale

Shallice (1988) and Grafman (1989) have proposed that the frontal lobes are involved in organizing the representation of large-scale conceptual units, called scripts. Scripts refer to rehearsed sequences of events that have a typical temporal and semantic structure (e.g., going to a restaurant). Recently, Godbout and Doyon (1995) have tested patients with frontal-, temporal-, or parietal-lobe damage on different scripts in forward and backward conditions. Results showed that the prefrontal lobes, together with the parietal cortex, play a special role in establishing the spatio-temporal position of events within a script (Godbout & Doyon, 1995).

Because of the known frontal-lobe dysfunction associated with age (see West, 1996, for a review), a first set of studies conducted in our lab sought to examine whether the organization of scripts would also be affected in normal elderly people. Large samples of young and older adults were tested on generation of scripts in a forward or a backward sequence. Our findings indicated that the ability to organize script-related actions declines with age, as elderly displayed significantly more sequencing and perseverative errors as well as non pertinent intrusions in the script generation tasks.

More recent studies, also performed in our lab, provided valuable insights regarding the spatio-temporal nature of the scripts in patients with frontal or parietal lobe damage. In these studies, scripts that have a more prominent spatial or temporal content and tests that were developed to estimate the capacity to manipulate semantic information in a spatial or a time frame were administered to patients and matched control participants. Our preliminary results suggest that parietal patients are impaired on tasks that emphasized the spatial organization of information. In contrast, the performance of frontal patients appears to be poorer on tasks requiring manipulation of temporal information. The aim of the present study was to clarify if older adults’ impairment on script production tasks is tributary to the spatial or temporal nature of the information and/or to the level of the difficulty of the task.

Subjects

Sixteen younger (18–35 years old) and older adults (65–78 years old) volunteered for the study. None of the subjects showed any indication that suggests a dementia syndrome, neurological or psychiatrical antecedents or alcohol or drug dependency.

Method

The subjects were initially required to complete three questionnaires. First, they were asked to fill out the Personal Identification Questionnaire which
consists of a short demographic inquiry. Second, a Script Familiarity Questionnaire was administered in order to determine the degree of familiarity with the 16 scripts. These particular scripts were chosen because reliability ratings and norms for a francophone population are available. Finally, they were asked to complete the Events and Objects Familiarity Questionnaire in order to determine the degree of familiarity with the elements that they had to organize mentally in the two tests. They also had to fill out the Edinburgh Handedness and the Information subtest of the Wechsler Adult Intelligence Scale—Revised (WAIS-R). Moreover, older adults were tested on the Folstein’s Mini Mental State Exam.

Subjects were then tested under four conditions of a script-generation task: four scripts with high spatial content in a forward order; four scripts with high spatial content in a backward order; four scripts with high temporal content in a forward order; and four scripts with high temporal content in a backward order. For each of the 16 scripts, subjects were asked to enumerate a list of 10 to 20 actions describing what people generally do over the course of an activity and to place the actions in the correct chronological or reverse order. They were also told to not include idiosyncratic actions based on personal behaviors. An example was given to illustrate what was expected from them. Moreover, they were asked to answer a series of questions that was comprised in two tests that required organization of semantic knowledge (geographical locations, historical events) in a spatial or temporal order. The proportion of correct answers was used as a dependent variable in the statistical analyses.

Scoring of the script generation task. The subjects’ responses were evaluated following the same criteria as those used in our previous work (Godbout & Doyon, 1995). Amongst the various measures, two types of errors were very important for the purpose of this study: sequence errors consist in a displacement in the natural sequence of actions within a script; perseverative errors consist in repeating an action more than once within a script.

Results. Because sequence or perseverative errors have a low probability of occurrence, Fisher exact probability tests were computed to compare the number of older and younger adults who produced sequence and perseverative errors in each experimental condition. In the script-generation task, older adults demonstrated greater difficulty to order events in a backward sequence, regardless of the nature of the information. Also, older adults showed deficits on the spatial organization of semantic memory as revealed by a lower performance on one of the tests.

References
38. Awareness of Memory Deficit in Nursing Home Residents

G. J. McDougall

*Case Western Reserve University*

This study examined cognitive disorders in 106 nursing home residents: cognitively impaired (31), depressed (19), cognitive impaired and depressed (34), and controls (22). Dependent measures were health, recall, and the metamemory components of capacity, change, locus, and strategy. The mixed group’s recall score was lower than that of the depressed group. The cognitively impaired group’s recall score was lower than both the control and depressed group. The capacity and change subscales differentiated between the cognitively impaired and the mixed group, with the mixed group indicating unstable memory capacity (lessening) and memory change (worsening). The control group’s health scores were greater than either the cognitively impaired group or the depressed group; the mixed group’s health scores were significantly higher than the depressed group’s scores.

**Rationale.** According to the 1990 Census Bureau Report, a major public health concern in the United States is the nursing home population, which increased by 24.2% in the period from 1980 to 1990. Nearly 1.8 million people lived in nursing homes in 1990. 1.6 million of these were 65 or older. The incidence of mental disorders, specifically cognitive impairments and the dementias, are the most prevalent and they may include mixed affective disorders, such as depression. In 1985 for every 1000 residents, 674 had at least one cognitive disability. This growing cognitively impaired cohort of nursing homes residents therefore presents a challenge to rehabilitation professionals, whose goals are to restore, preserve, and enhance physical and cognitive function.

Health care providers often believe that individuals with cognitive disturbance are unaware of their deficits. The term unawareness of deficits was initially used to describe a neuropsychological syndrome known as anosognosia for dementia and has since been applied to unawareness of any neurological or neuropsychological deficit. However, two methodological shortcomings are present in the literature. First, clinicians and investigators often rely on their subjective observations of the patient and few investigators have developed quantitative methodologies for objectively evaluating the presence or degree of awareness disturbance. Second, although the relation of intellectual impairment to anosognosia is an important issue, the nature and severity of these deficits are rarely assessed in a systematic fashion. Memory complaints can provide insight into how individuals view their own cognitive functioning. Individuals with depression may underestimate their memory...
ability, while individuals with dementia may overestimate their ability. However, there has been relatively little study of awareness of cognitive function in nursing home residents.

Metamemory is closely related to memory and is defined as: (a) factual knowledge about memory tasks and memory processes, (b) memory monitoring or awareness of how one typically uses memory as well as the current state of one’s memory system, (c) memory beliefs or one’s sense of mastery or ability to use memory effectively in memory-demanding situations, and (d) memory-related emotional states including anxiety, depression, and fatigue. Examination of metamemory has implications for the remediation of memory deficits in the elderly since strategic and adaptive behaviors are often more amenable to change than are cognitive deficits such as dementia. Therefore, the study reported here examined cognitive function, depression, health status, and metamemory in four groups of nursing home residents: the cognitively impaired, depressed, those with both cognitive impairment and depression, and controls.

Subjects. Subjects included 31 elderly with cognitive impairment (1 male and 30 female), 19 who were depressed (2 male and 17 female), 34 with mixed depression and cognitive impairment (8 male and 26 female), and 22 who had neither depression nor cognitive impairment (4 male and 18 female). Subjects were residents of six nursing homes in the greater Cleveland area.

Method. Assessment of cognitive function was made by trained registered nurse interviewers using the Mini Mental State Examination (MMSE). The instrument contains 11 questions and scores may range from 0–30, with a score of 23 or less indicating cognitive impairment. Usually a score between 18 and 22 indicates mild cognitive impairment and a score between 0 and 17 indicates severe cognitive impairment. Individuals scoring <15 on the MMSE were excluded since the ability to report about memory is questionable below that score. The MMSE contains three recall questions scored 0–3 which are not actual measures of memory performance but give some indication of recall ability. The 4-point score was therefore included in the analysis as a reference point.

The Geriatric Depression Scale (GDS) is a 30-item Yes–No questionnaire. The depressive responses are tallied, and the score indicates the level of depression (0–10 = normal; 11–20 = mild depression; 21–30 = moderate or major depression).

The Health Scale, a subscale of the Multilevel Assessment Instrument, measures perceived health. Subjects rate the quality of their health using a 4-point response format. Anchors are ‘‘better’’ to ‘‘not so good’’ and ‘‘excellent’’ to ‘‘poor.’’ Total scores on the 4-item tool range from 4 to 13 with higher scores indicating better health.

The Metamemory in Adulthood Questionnaire (MIA), a measure of the memory components of knowledge, beliefs, and affect, was used to assess
memory awareness and knowledge. The MIA consists of 108 statements, with responses rated on a 5-point Likert scale. Four of the seven subscales, measuring capacity, change, locus, and strategy, were utilized in this study because they were most relevant to the residents. Capacity is the perception of memory capacities as measured by predictive report of performance on given tasks (+ = high capacity). Change is the perception of memory abilities as generally stable or subject to long-term decline (+ = stability). Locus is the individual’s perceived personal control over remembering abilities (+ = internal locus). Strategy is knowledge of one’s remembering abilities such that performance in given instances is potentially improved; it includes reported use of both internal and external strategies (+ = high use).

Results. One-way analysis of variance, two-factor ANOVA, and Pearson correlation coefficients were used to compare the cognitively impaired, depressed, mixed, and control groups on various measures. Assumptions of homogeneity of variance were not violated in any analyses. Comparisons of group and task means was carried out using the Fisher PLSD post hoc test.

The MMSE scores of the cognitively impaired were, as expected, significantly lower than those of either the depressed or control groups [F(3, 102) = 54.22, p < .0001]. There was no significant difference between the cognitively impaired and the mixed groups’ scores, or between the depressed and the control groups’ MMSE scores. Also as expected, the GDS scores for the depressed group indicated that they were significantly more depressed than the cognitively impaired and control groups [F(3, 102) = 69.66, p < .0001], with all subjects above the cutoff score of 11 for clinical depression. There were no significant differences between the mixed group’s depression scores and the depressed group’s scores or between the cognitively impaired group’s depression scores and the control group’s scores. Subjects in the cognitively impaired group were older than all other groups but only significantly older than the control group. The depressed group were taking more medications than other groups and significantly more medications than the cognitively impaired group [F(3, 102) = 1.84, p < .05]. There were no differences between the groups in the number of diseases or years of education.

The perceived health status score for the control group was significantly higher than for either the cognitively impaired group or the depressed group [F(3, 102) = 6.49, p < .001]. The mixed group’s score was significantly higher than the depressed group’s score.

The mixed group’s recall score on the MMSE was lower than that of the depressed group. The cognitively impaired group’s recall score was significantly lower than the score of both the control and depressed group [F(3, 102) = 11.13, p < .0001]. The cognitively impaired group’s score on memory capacity were significantly lower than the mixed group’s scores [F(3, 102) = 2.93, p < .05], but there were no differences in memory capacity between the other groups. The mixed group’s memory change scores were
significantly lower than the cognitively impaired group’s scores \( F(3, 102) = 5.05, p < .005 \). There were no other group differences in memory change scores, and no group differences on the metamemory subscales of locus and strategy.

When the entire sample was divided into depressed and non-depressed groups using a score of 11 or above on the GDS as the cutoff, ANOVA indicated significant differences between the depressed and non-depressed groups on the metamemory subscales of capacity, change, and locus. The depressed group scored significantly lower on memory capacity \( (3.00 \text{ vs. } 3.27) \) \( F(1, 104) = 5.37, p < .05 \) and on memory change \( (2.33 \text{ vs. } 2.76) \) \( F(1, 104) = 13.38, p < .0005 \). The depressed group also scored significantly \( (3.15 \text{ vs. } 3.38) \) lower on memory locus. There were no differences between the groups on the use of strategies.

Of the six nursing homes participating in the study the large percentage (43%) of individuals in the sample with depression \((M = 16.4, SD = 4.5)\) was unexpected. Depression had a substantial influence on perceptions of memory capacity and change. This sample had a mean age of 84.18 \((SD = 10.01)\) years, and they had an average of six comorbid medical conditions and varying levels of recall ability. Although memory performance was not measured, there was sufficient variability in the recall scores of the cognitively impaired, mixed, and control groups to suggest that they had some awareness of their deficits.

39. An Investigation of Glucose Effects on Learning and Memory Impairments Induced by High Fat Diets and Environmental Factors

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We previously demonstrated that feeding rats high fat diets impairs performance on learning and memory tests. This study examined the combined effects of environmental factors and diet on cognition to determine if glucose administration could enhance performance adversely affected by these factors. Subjects were tested on a variable interval delayed alternation task which measures learning and memory functions that differentially involve specific brain regions. The results confirmed the negative effects of high fat diets and showed that environmental enrichment improved acquisition of the basic habit. By comparison, glucose selectively enhanced trial-specific memory performance at longer delays. We conclude that high fat diets generally disrupt cognitive function. The enriched environment reduced learning impairment associated with frontal lobe function whereas glucose mediated its beneficial effects on hippocampus-related memory function.
Rationale. In our previous work, we observed that post-weanling rats fed high fat diets over a 3-month period were severely impaired relative to rats fed standard laboratory chow on several tests of learning and memory. The results revealed that diets high in saturated or polyunsaturated fat produced widespread cognitive impairment that included deficits in spatial and non-spatial episodic memory, alternation and conditional associative rule learning, and complex maze performance. Given the variety of cognitive tasks which were impaired by feeding high fat diets we interpreted the data to suggest that dietary fat produced a global deficit which showed no specificity in terms of either the brain region involved or the specific component of cognitive function which was influenced. While our studies have not elucidated the specific biochemical mechanism mediating the dietary fat impairment, we have provided evidence that both the overall level of dietary fat and specifically the intake of saturated fatty acids are important components of this effect.

The objective of the present study was to further explore the dietary fat impairment in cognitive function by examining its sensitivity to other factors known to influence performance. To address this objective, we relied on two other factors which have been shown to modify cognitive functions. There is considerable evidence that age differences in cognitive function can be reduced by environmental influences and glucose administration. While it is unlikely that these two manipulations improve cognitive performance by common mechanisms, both are able to offset some of the deficits observed with normal aging. The degree to which these factors can recover deficits accompanying a different biologic model of cognitive impairment, i.e. dietary fat induced, was the focus of this study.

Subjects. Subjects were experimentally naive, male Long-Evans rats. When the rats were 1 month of age and weighed 60–80 g, they were randomly assigned to one of three environmental conditions: normal, enriched, or deprived. At the same time, rats were placed on the experimental diets containing either 20% by weight of soybean oil or beef tallow. Rats were provided diet and water ad libitum until they were 4 months of age. At this time, they were gradually reduced, over a 2-week period, to 80% body weight. Throughout the experiment, food intake was adjusted to maintain rats at about 80% normal body weight.

Method. Cognitive function was measured using a variable interval delayed alternation (VIDA) task. We have previously shown this task to be sensitive to impairment associated with aging or dietary fat feeding and to produce differential effects on specific components of performance associated with lesions to different brain regions. Initially food restricted rats were shaped to press a lever for food according to a continuous reinforcement (CRF) schedule. During CRF training, each lever press was rewarded by a single Noyes pellet. After each session, rats were returned to their home cages and provided their respective diets for the remainder of the day. VIDA
testing was initiated the day after criterion was reached on CRF training. Each session consisted of 12 reinforced (go) trials alternating with 12 nonreinforced (no-go) trials. The go and no-go trials were separated by a variable inter-trial interval (ITI), during which the lever was retracted. ITIs were 0, 5, 10, 20, 40, or 80 sec long, with each delay occurring twice after the go trials and twice after the no-go trials, for a total of four times per session. Time to first response at each trial was measured by use of a microcomputer. Data were converted to go/no-go latency ratios at each ITI by dividing mean latency to first response in the go trials by mean latency to first response in the no-go trials. After 21 days of VIDA training, rats were administered 10 additional daily sessions in which testing was preceded on alternate days, by injections of 100 mg/kg glucose or an equal volume of saline. Repeated measures factorial analysis of variance was used to test the main effects of diet, environmental condition and glucose as well as their interactions. For ease of comparison, data were collapsed for ITIs 0, 5, and 10 sec (short intervals) and 20, 40, and 80 sec (long intervals).

**Results.** In agreement with our previous studies, rats fed the high fat diets showed impaired performance on the VIDA task, with increased latency ratios observed at both the short and long intervals suggesting that they had difficulty in both acquiring the basic alternation rule and remembering the event of the preceding trial. Environmental enrichment impacted on performance of these impaired animals. However, the benefit of environment was only observed at short, but not long, latencies, suggesting that its primary effect was on task acquisition. That is, latency ratios were significantly lower in the environmentally enriched group at short intervals ($p < .001$) in comparison to animals raised in either the control or environmentally deprived setting. No difference amongst groups was observed at the longer intervals ($p = .77$).

In contrast to the effect of environment, glucose administration enhanced performance at long latencies but had less impact at the shorter intervals suggesting that its effect was targeted toward the memory components of task performance. That is, significant main effects of both glucose and interval as well as a glucose $\times$ interval interaction were observed (all $p$’s $< .001$). The magnitude of effect of glucose was influenced by the environmental setting of the rats (glucose $\times$ environment interaction, $p = 0.013$). There was evidence that animals in the control and environmentally impoverished conditions responded more to glucose at long delays in comparison to animals in the enriched condition.

**Conclusions.** In conclusion, the data confirmed a widespread deficit in cognitive performance associated with high fat feeding that involves multiple aspects of performance. Both an enriched environment and glucose administration can offset cognitive deficits observed in young adult rats fed high fat diets. However, environment and glucose differentially affect specific components of cognitive performance. The task acquisition component
VIDA testing has been previously shown to be sensitive to lesions of the frontal lobe suggesting that the impact of environment is most apparent in functions associated with this brain region. By contrast, the memory component of the VIDA task demonstrates specific sensitivity to hippocampal lesions suggesting that glucose is predominantly enhancing hippocampal functions. We speculate that dietary fat, in part, exerts negative effects by interfering with glucose utilization. The glucose treatment effect at long delays is in line with this interpretation. However, not all of the dietary effects are mediated this way. The fact that environmental factors, but not glucose treatment, reduced impairment at short delays suggests that high fat diets affect cognitive function through additional mechanisms.

40. Patterns of Cerebral Glucose Metabolism in Behaviorally Disturbed Acquired Brain Injury Patients

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Acquired brain injuries (ABI) lead to a variety of amnesic syndromes associated with cognitive deficits, disturbances of emotional response, and personality changes, particularly in post-traumatic cases. We have studied cerebral glucose metabolism in 15 ABI patients using FDG and positron tomography. The lowest rates of cortical glucose metabolism were found in two cases classified as amnesic confusional. Three cases of more stable amnesia showed more localized areas of hypometabolism, mostly in the temporal lobes. In the one case of Korsakoff syndrome, hypometabolism was observed in the frontal lobes during the confabulatory stage; this case lost its confabulations and showed a concomitant improvement in frontal metabolism. The three post-traumatic mild brain injury and six post-concussive syndromes were clinically heterogeneous. Patterns of metabolic disturbances were identified when clinical variables were considered.

Rationale. Acquired brain injuries (ABI) lead to a variety of amnesic syndromes associated with cognitive deficits, disturbances of emotional response, and personality changes, particularly in post-traumatic cases. A tentative clinical classification developed at the ABI provincial program of the Hamilton Psychiatric Hospital includes amnesic confusional states, usually early post-traumatic or post-encephalitic, stable amnesic syndromes, amnesic syndromes with confabulations or Korsakoff syndromes, and the attentional-amnesic syndromes associated with post-concussional symptoms or mild brain injuries.

Subjects. We studied 15 patients: 9 post-concussive or mild brain injury syndromes, 2 (1 post-traumatic, 1 post-encephalitic) cases of prolonged confusional amnesic states, 3 cases of stable amnesic syndromes with well-
preserved cognitive skills (2 post-traumatic, 1 post-encephalitic), and 1 case of Korsakoff following an attempt at hanging during an alcoholic binge. All patients were clients of the ABI provincial program of the Hamilton Psychiatric Hospital. We also examined, as a control group, 16 subjects who were not suspected of having any psychiatric disorders.

Methods. Each subject was studied 45 min after the intravenous injection of between 4.5 and 5.5 mCi of 18F-fluoro-deoxyglucose (FDG). Ambient light and minimal background noise defined the environment. Subjects were positioned in an ECAT-ART positron tomograph, and a head-holder was used to immobilize the head in a comfortable position that allowed the brain, from the vertex to the cerebellum, to be covered by the axial field of view. Subjects were asked not to move and were not spoken to for the duration of the examination. Each study was corrected for attenuation using the automated software provided by the scanner’s manufacturer. Regions of interest were defined interactively with reference to a standard anatomical atlas. Each regional value was converted to a reference ratio by dividing values for specific regions by the mean value for the whole brain. Group comparisons were examined using a two tailed t test.

Results. The ABI patients showed a 15% decrease in cortical glucose metabolism in the frontal lobes (M = 1.85, SD = 0.13) as compared to controls (M = 2.00, SD = 0.13); this difference was significant (p = .001). Similarly, a 10% decrease in striatal glucose metabolism was found in the ABI group (M = 1.19, SD = 0.13 as compared to M = 1.30, SD = 0.09 in controls; p = .01); this difference appeared to be greatest in the caudate nucleus. We also found a significant increase (p = .025) in glucose metabolism of the temporal lobes in the patient group (M = 1.14, SD = 0.16 as compared to M = 1.01, SD = 0.12 in controls).

Low rates of cortical glucose metabolism were found throughout the brain in the two cases classified as amnesic confusional. The three cases of more stable amnesia showed more localized areas of hypometabolism, specifically in the frontal and parietal lobes; we suggest that the distinction between amnesic confusional and amnesic syndromes may be one of stage of the disorder only. In the one case of Korsakoff, hypometabolism was observed in the frontal lobes during the confabulatory stage; this case lost its confabulations and showed a concomitant improvement in frontal metabolism.

The results of the six post-concussive syndromes were heterogeneous. Three patients appeared to have patterns of glucose metabolism that were near normal in all regions examined; it is interesting to note that the diagnosis of post-concussive syndrome had been questioned by several observers in this group. A further three patients with severe post-concussive syndromes showed marked hypometabolism in the frontal lobes, and a lesser degree of hypometabolism in the striatum, particularly in the caudate nucleus. The one patient with post-traumatic movement disorders showed a global hypometabolism, one patient with post-traumatic dementia showed decreased metabo-
lism in the parietal lobes and striatum, and one patient with post-traumatic hystrionic symptoms showed hypermetabolism in the frontal lobes and hypometabolism in the striatum.

**Conclusions.** Patterns of metabolic activity in different lobes may be related to specific symptom clusters. The most obvious relation was found in the disappearance of confabulation as a Korsakoff symptom with concomitant improvement in the glucose metabolism of the frontal lobes. Other correlations among patterns of metabolic activity and symptoms are more speculative at this time.

41. Cross-Modal Priming in the Densely Amnesic Subject K.C.

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If repetition priming is a perceptual phenomenon, why is it not eliminated when the modality is shifted between study and test? We investigated cross-modal priming in a densely amnesic subject (K.C.) with bilateral hippocampal lesions using a fragment completion task. After making semantic judgments on words in the visual and auditory modality, K.C. was asked to complete visual word fragments with the first word that came to mind. On three separate occasions, K.C. showed robust within-modality priming but no reliable cross-modal priming, suggesting that the latter relies on brain structures damaged in this patient. Our data are compatible with the notion that cross-modal priming in healthy individuals reflects explicit contamination from episodic memory. Conditions that compromise episodic memory, such as amnesia, can abolish the effect.

**Rationale.** Much research on implicit memory suggests that repetition priming is perceptual in nature and is based on presemantic representations. It is sensitive to changes in perceptual characteristics of target information from study to test and can be observed following study tasks that do not require any semantic processing. Yet, many studies have also demonstrated a small but robust priming effect when the presentation modality is shifted between study and test (e.g. Craik et al., 1994). If priming is a perceptual phenomenon, why is it not reduced to ‘0’ when there is no perceptual overlap between items at study and cues at test? It has been suggested that cross-modal priming reflects the contamination of performance on an implicit test by intentional uses of explicit memory (Jacoby et al., 1996). According to this view, cross-modal priming reflects ‘‘leakage’’ from explicit episodic memory rather than true implicit memory processing. Alternatively, cross-modal priming may be a truly implicit form of memory that is not perceptual in nature but based on conceptual or lexical processing. We decided to investigate this issue by testing cross-modal priming in a densely amnesic subject...
who has severe episodic memory impairments but shows no deficits on implicit memory tasks. If the cross-modal priming effect observed in normal subjects reflects "leakage" from episodic memory and is dependent on the integrity of structures damaged in amnesia (e.g., hippocampus), then it should be absent in a densely amnesic patient who has severe damage to these structures and, hence, suffers from a nearly complete loss of episodic memory.

Subject. K.C. is a 45-year-old male who, at the time of this experiment, had been amnesic for 15 years following a closed-head injury in a motorcycle accident. His neuropsychological profile and neuroimaging data have been reported elsewhere (Tulving, Schacter, & McLachlin, 1988). Data from a recent reexamination will be reported at the conference. K.C.'s most recent MRI shows multiple lesions, predominantly in the left hemisphere. His medial temporal lobes show substantial damage bilaterally. We quantified his hippocampal damage using volumetric planimetry. The residual volume of his left hippocampus is only 21% (4 cm³) of that measured for an age-matched normal control. The volume of his right hippocampus is 39% (7 cm³) of that of the control. Additional brain damage included left occipital infarction and white-matter encephalomalacia deep to the left frontal and parietal cortex. His IQ, as determined by the WAIS-R, is in the lower normal range (FIQ 88, VIQ 96, PIQ 79). In contrast, his episodic memory functions are severely impaired for verbal and non-verbal material. He scores at chance level on the Warrington Recognition Memory Tests for faces and words. On CVLT immediate recall, he shows virtually no learning across multiple learning trials. He scores five standard deviations below average on delayed recall and recognition of the CVLT.

Methods. We tested priming within the visual modality and from the auditory to the visual modality on three separate occasions. Each session included a study phase that was immediately followed by a test phase. The study phase involved the presentation of 25 words in the visual and 25 words in the auditory modality for a semantic judgment. K.C. had to decide for each word whether it referred to something living or non-living. The test phase involved the visual presentation of 75 word fragments and required their completion with the first word that came to mind. Twenty-five fragments were parts of words that had been studied visually, 25 corresponded to words heard at study, and 25 were fragments of non-studied words. To examine long-term retention of priming, the test phases for items studied in Sessions 1 and 3 were readministered 8 weeks after the completion of Session 3. New non-studied items were used to establish the baseline completion rate. At this point in time, we also administered a recognition memory test for the same items. K.C. was shown the complete words and was asked for each of them whether it had been presented to him before in the context of the living/non-living task. The recognition memory test was administered after the fragment completion task.
Results and discussion. In each of the three test sessions, K.C. completed a substantially larger proportion of fragments for visually primed items than for non-studied items, indicating preserved within-modality priming (Table 13). For the cross-modal condition, there was virtually no advantage of studied over non-studied items (one item in each session). Considering the total number of items presented and the amount of priming demonstrated within the visual modality, we interpret these data to indicate the absence of cross-modal priming.

To shed more light on K.C.’s priming performance, we also investigated long-term retention effects. Priming on the fragment completion task was examined for the complete sets of items from Session 1 (10 weeks earlier) and Session 3 (8 weeks earlier). Performance on this task was compared with performance on an explicit recognition memory test. There was no sign of cross-modal priming after delays of 8 and 10 weeks, whereas within-modality priming was still present (Table 14). Together with the immediate delay results, these data indicate no evidence for cross-modal priming in K.C. Priming within the visual modality, by contrast, is preserved and long-lasting.

When asked to recognize the previously studied words on the explicit recognition memory test, K.C performed very poorly regardless of whether items had been studied in the visual or the auditory modality (Table 15). The rate of hits minus false alarms was .20 for both conditions, indicating that K.C.’s severe episodic memory impairment extends to the material used in the present study. It is, thus, extremely unlikely that his performance on the fragment completion task could have been influenced by intentional uses of explicit episodic memory.

<table>
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<th>Study condition</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>Mean</th>
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<tbody>
<tr>
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<td>.64</td>
<td>.63</td>
<td>.58</td>
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<tr>
<td>Auditory (across-modality)</td>
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<td>.42</td>
<td>.24</td>
<td>.32</td>
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<tr>
<td>Nonstudied</td>
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<table>
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<tbody>
<tr>
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<td>.37</td>
<td>.41</td>
</tr>
<tr>
<td>Auditory (across-modality)</td>
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<td>.23</td>
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<tr>
<td>Nonstudied</td>
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TABLE 15
Proportion of Old Responses in Delayed Visual Recognition Memory Test as a Function of Study Condition and Delay

<table>
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<th>Study condition</th>
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<th>10</th>
<th>Mean</th>
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<tbody>
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Conclusions. K.C. showed no evidence for reliable cross-modal priming from the auditory to the visual modality on the fragment completion task. This suggests that brain structures damaged in K.C., possibly the hippocampus, mediate cross-modal priming in normals. Our data are compatible with the notion that cross-modal priming in normals reflects explicit contamination, i.e. leakage from episodic memory, and that conditions which compromise episodic memory can eliminate the cross-modal priming effect.

References


42. Impaired Short-Term Memory and Intact Temporal Memory in Amnesic Patients

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*National Institutes of Health*

The continual-distractor paradigm was used to investigate the recency effect in amnesic patients. Amnesics’ recall displayed normal recency effects in lists ranging from 18 to 60 sec long. In contrast, overall recall was impaired compared to normals in all lists and across all positions, including the final position. These findings dissociate the recency effect from overall levels of recall. Performance by the controls suggests that the amnesic patients performed worse overall due to an inability to benefit from rehearsal. Current theorizing about the recency effect suggests that amnesics’ normal recency effect may be evidence of an ability to encode and retrieve temporally-associated information.
**Rationale.** In the immediate-memory paradigm, where subjects are required to recall immediately after list presentation, amnesic patients recall final items normally while having reduced recall at early list positions (Baddeley & Warrington, 1970; Brooks & Baddeley, 1976). Within the framework of the classical dual-store theory, these findings have been interpreted as showing that amnesic patients have an intact short-term memory store and a damaged long-term memory store (cf., Carlesimo, Marfia, Loasses, & Caltagirone, 1996).

However, a number of researchers have demonstrated that the size of the recency effect changes when within-list temporal intervals change (Bjork & Whitten, 1974). This finding, described as the ratio rule, suggests that serial-position effects might be caused by temporal distinctiveness (Crowder, 1976). The ratio rule has been extended beyond the recency effect and seems to be able to account for performance at every serial position except position 1 (because the ratio is undefined at position 1; Neath & Crowder, 1990). Many findings suggest that much of the primacy effect disappears when rehearsal processes are reduced. These results allow temporal distinctiveness and rehearsal to account for the effect of serial position without proposing multiple memory stores. This provides an alternative interpretation for amnesic patients’ normal recency effect. If we interpret amnesic patients’ normal recency effect within the temporal-distinctiveness framework, there are at least two important implications for theories of amnesia. The first implication is that it suggests that amnesics can demonstrate normal temporal-associative processing. Temporal-distinctiveness theory proposes that recency is caused by the encoding and retrieval of the temporal relations between list items. Therefore, if amnesic patients produce a normal recency effect, it follows that they are able to encode and retrieve the temporal relations between list items. This conclusion runs counter to a number of theories of amnesia that assume or predict that amnesic patients are unable to encode and/or retrieve temporally associated information. The second implication of the temporal-distinctiveness explanation of the recency effect is that it suggests that amnesics perform more poorly than controls at primacy simply because of their poor rehearsal strategies (Cermak, Naus, & Reale, 1976) or the correlates thereof.

These implications of temporal-distinctiveness theory make two predictions which we tested in the present study. The first prediction is that amnesic patients should have reduced recall in shorter term memory paradigms. We tested this prediction by using a list that lasted only 15 seconds but was followed by 3 sec of distracting activity (for a total of 18 sec). This method provides a more valid test of recent memory than the standard immediate memory paradigm because it is not contaminated by normal perceptual or attentional processes (it does not include an “immediate-report” condition).

The second prediction of temporal-distinctiveness theory is that amnesic patients will be sensitive to temporal manipulations, even in lists in which
they have reduced recall. That is, they should show normal temporal memory even under conditions where they show abnormal memory performance. In order to test this prediction, we manipulated the interpresentation interval to retention interval (IPI/RI) ratio in lists ranging from 18 to 51 sec long. Temporal distinctiveness theory predicts that the amnesic patients’ recency effect should be as sensitive as the controls’ recency effect to changes in this ratio. This should be true even when they are remembering less than controls, as we expected to be the case in at least the longest lists.

**Subjects.** Twelve amnesic patients, 6 patients with alcoholic Korsakoff’s syndrome and 6 patients with amnesia from varying etiologies, including anoxia \(n = 3\), encephalitis \(n = 2\), and head injury \(n = 1\), were tested. The mixed-etiology group of patients all presumably had amnesia due to damage to the medial-temporal lobes. Control subjects who had substance abuse histories of 10 years or longer, but who had been abstinent for a minimum of 4 to 6 weeks at the time of testing, were matched to the amnesic patients with Korsakoff’s syndrome with respect to age, years of education, and WAIS-R VIQ. Six additional healthy control subjects were matched to the medial-temporal group of amnesics on the same variables.

**Method.** The design was a 2 × 3 × 5 mixed-factorial manipulating group (amnesics and controls) between subjects and IPI/RI ratio (low, constant, or high) and serial position (1–5) within subjects. Nouns were chosen and randomly paired from a pool of 300 words. Word pairs were presented for 3 sec. A screen filled with randomly generated digits was presented for 3 sec for the digit-shadowing distractor task.

A trial consisted of the presentation of five word pairs, each pair separated by digit shadowing, followed by free recall of the word pairs. The number of distractor tasks separating each word pair was determined by the ratio condition. In the low-ratio condition, no distractor tasks were presented between each word pair, in the constant-ratio condition, 1 distractor task was presented between each word pair, and in the high-ratio condition, three distractor tasks were presented between each word pair. The final word pair in each list was followed by one distractor task. Hence, the ratios in the three conditions were as follows: low ratio \((0/3 \text{ sec}) = 0\), constant ratio \((3/3 \text{ sec}) = 1\), high ratio \((9/3 \text{ sec}) = 3\).

**Results.** Because the interpresentation interval for position 1 is undefined, the ratio rule is undefined, and therefore temporal-distinctiveness theory makes no predictions, for position 1. Hence, the data for only positions 2–5 were analyzed. We note, however, that controls’ recall was much greater than was amnesics’ recall at position 1.

Controls remembered more words overall than the amnesics. This was true at every position, but more so at Position 2 and less so at Position 5. Controls remembered more than amnesics in all three conditions; however, they recalled an even greater amount in the high-ratio condition, suggesting that they were able to benefit from rehearsal in spite of the distracting activ-
ity. The ratios affected performance in both groups equally and as predicted by the ratio rule.

After Glenberg, Bradley, Kraus, and Renzaglia (1983), we defined the slope of the recency effect as the slope of the least-squares line relating percentage recalled to serial position over the last three serial positions. As predicted by the ratio rule, the slope increased with increases in the ratio. This effect was most apparent in the recency effects of the amnesic subjects, however, the effect of ratio on the slope of the recency effect was not reliably different between the two groups.

After Glenberg et al. (1983), we examined the level-of-recall effect, which is the fact that performance at the final list position is positively related to the ratio. Considering performance at the final serial position only, both groups showed the predicted level-of-recall effect. Recall was highest in the high-ratio condition, and lowest in the low-ratio condition, with recall in the constant-ratio condition falling in between. This pattern was evident in the recall performance of the amnesic patients even though they were recalling reliably less than the controls at this position.

References


