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Article *in* Neurology · December 2000

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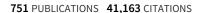
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The FAB

A frontal assessment battery at bedside

B. Dubois, MD; A. Slachevsky, MD; I. Litvan, MD; and B. Pillon, PhD

Article abstract—Objective: To devise a short bedside cognitive and behavioral battery to assess frontal lobe functions. Methods: The designed battery consists of six subtests exploring the following: conceptualization, mental flexibility, motor programming, sensitivity to interference, inhibitory control, and environmental autonomy. It takes approximately 10 minutes to administer. The authors studied 42 normal subjects and 121 patients with various degrees of frontal lobe dysfunction (PD, n = 24; multiple system atrophy, n = 6; corticobasal degeneration, n = 21; progressive supranuclear palsy, n = 47; frontotemporal dementia, n = 23). Results: The Frontal Assessment Battery scores correlated with the Mattis Dementia Rating Scale scores (rho = 0.82, p < 0.01) and with the number of criteria (rho = 0.77, p < 0.01) and perseverative errors (rho = 0.68, p < 0.01) of the Wisconsin Card Sorting Test. These variables accounted for 79% of the variance in a stepwise multiple regression, whereas age or Mini-Mental State Examination scores had no significant influence. There was good interrater reliability ($\kappa = 0.87, p < 0.001$), internal consistency (Cronbach's coefficient alpha = 0.78), and discriminant validity (89.1% of cases correctly identified in a discriminant analysis of patients and controls). Conclusion: The Frontal Assessment Battery is easy to administer at bedside and is sensitive to frontal lobe dysfunction. NEUROLOGY 2000:55:1621–1626

Assessing frontal lobe function and thus being able to identify a dysexecutive syndrome are helpful for the diagnosis and prognosis of brain diseases such as frontotemporal dementias¹ and for evaluation of the severity of brain injuries. It can also help to identify vascular dementias² and parkinsonian disorders, particularly progressive supranuclear palsy (PSP), in which the presence of frontal lobe dysfunction supports the diagnosis.³ It may also be useful for differentiating between degenerative disorders involving subcortical structures and for evaluating the progression of these disorders over time.⁴

The functions of the frontal lobes are difficult to assess clinically. There is no test that reliably identifies a dysexecutive syndrome.⁵ In practice, extensive neuropsychological batteries are needed to assess the frontal lobe processes.^{6,7} Given the modular functional organization of the frontal lobes,^{8,9} searching for a possible dysexecutive syndrome requires time-consuming tests exploring functions associated with different frontal areas. Therefore, there is a need for a brief tool exploring different domains of executive function that are impaired in several neurologic diseases.

We devised a bedside battery to assess the presence and severity of a dysexecutive syndrome affecting both cognition and motor behavior, and to evaluate it for 1) content and concurrent validity, 2) discriminant validity, comparing normal controls

and patients with various degrees of executive dysfunction, and 3) interrater reliability.

Methods. Description of the Frontal Assessment Battery (FAB). According to current theories, the frontal lobes control conceptualization and abstract reasoning, mental flexibility, motor programming and executive control of action, resistance to interference, self-regulation, inhibitory control, and environmental autonomy. 6,10-14 Each of these processes is needed for elaborating appropriate goaldirected behaviors and for adapting the subject's response to new or challenging situations—functions that are mediated by the prefrontal cortex. For that reason, the designed battery consists of six subtests, each exploring one of the aforementioned functions related to the frontal lobes. Moreover, these subtests were chosen because the score of each of them significantly correlated with frontal metabolism, as measured in terms of the regional distribution of 18-fluorodeoxyglucose in a PET study of patients with frontal lobe damage of various etiologies.9 The processes studied and the corresponding subtests of the FAB are presented below. The content, instructions and scoring of each subtest are provided in the Appendix. The total scores are calculated by adding the notes of the six subtests. The overall duration of the battery is approximately 10

 Conceptualization: Abstract reasoning is impaired in frontal lobe lesions.¹¹ This function is currently investi-

See also pages 1601, 1609, and 1613

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Supported by INSERM. Funded by a grant from Mideplan-Chile (A.S.).

Received June 12, 2000. Accepted in final form September 13, 2000.

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Table Study group characteristics

Population	n	Age, y	MMSE	Mattis DRS	FAB
Controls	42	$58.0 \pm 14.4^{\rm a}$	28.9 ± 0.8^{a}	$141 \pm 2.4^{\rm a}$	17.3 ± 0.8^{a}
Patients	121	$64.4\pm9.3^{\rm a}$	$25.5\pm4.8^{\rm a}$	$118.0 \pm 19.1^{\rm a}$	$10.3\pm4.7^{\rm a}$
PD	24	$59.4 \pm 12.9^{ m c,g}$	$28.0\pm1.9^{i,j}$	$134.0\pm15.2^{\rm c,g,i}$	$15.9 \pm 3.8^{c,g,i}$
MSA	6	65.0 ± 10.5	$25.7\pm3.9^{\mathrm{j}}$	$127.0\pm16.2^{\rm e}$	$13.5\pm4.0^{\rm e,f}$
CBD	21	$67.4 \pm 8.1^{ m b,c}$	$26.4\pm3.8^{\rm b}$	$123.7\pm15.0^{\rm b,c}$	$11.0 \pm 3.7^{\rm b,c,d}$
PSP	47	$66.9 \pm 7.0^{ m g,h}$	$26.2\pm3.7^{\rm h}$	$117.7\pm15.2^{\rm g,h}$	$8.5\pm3.4^{\rm d,f,g}$
FTD	23	$60.3 \pm 8.5^{\mathrm{b,h}}$	$20.7\pm6.3^{\rm b,h,i}$	$101.5\pm20.0^{\rm b,e,h,i}$	$7.7\pm4.2^{\rm b,e,i}$

Values are presented as mean \pm SD. Significantly different at p < 0.05 for: "controls and patients; "frontotemporal dementia (FTD) and corticobasal degeneration (CBD) patients; "PD and CBD patients; "progressive supranuclear palsy (PSP) and CBD patients; "FTD and multiple system atrophy (MSA) patients; "PSP and MSA patients; "PD and PSP patients; "FTD and PSP patients; "PD and FTD patients; "PD and MSA patients.

MMSE = Mini-Mental State Examination; DRS = Dementia Rating Scale; FAB = Frontal Assessment Battery.

gated by card-sorting tasks, proverb interpretation, or similarities.¹⁵ The last task is easier for bedside assessment and scoring. Subjects have to conceptualize the links between two objects from the same category (e.g., an apple and a banana). Patients with frontal lobe dysfunction may be unable to establish an abstract link between the items (i.e., fruit), adhering to the concrete aspects of objects (i.e., both are yellow), or may be unable to establish a link of similarity (i.e., one is round but the other is elongated).

- 2. Mental flexibility: Patients with frontal lobe lesions are specifically disturbed in nonroutine situations in which self-organized cognitive strategies have to be built up. 16,17 Literal fluency tasks are unusual, require self-organized retrieval from semantic memory, and are easy to score. Frontal lesions, regardless of side, tend to decrease verbal fluency, with left frontal lesions resulting in lower word production than right frontal lesions. 18 In this task, subjects need to recall as many words as they can beginning with a given letter in a 1-minute trial.
- 3. Motor programming: Patients with frontal lobe lesions are also impaired in tasks requiring temporal organization, maintenance, and execution of successive actions. 12,13,19 In Luria's motor series, such as "fist-palmedge," less severely impaired patients are unable to execute the series in correct order, whereas the most severely affected are unable to learn the series. Simplification of the task (two gestures instead of three) and perseveration (inappropriate repetition of the same gestures) may be observed.

Sensitivity to interference: Deficits in behavioral self-regulation may be observed in tasks in which verbal commands conflict with sensory information. This occurs in the Stroop test, in which the subject must name the colors of words while inhibiting the natural tendency to read the words. This also occurs in the case of conflicting instructions, in which subjects must provide an opposite response to the examiner's alternating signal, e.g., tapping once when the examiner taps twice. Thus, subjects should obey verbal commands and refrain following what they see. Patients with a frontal lobe lesion usually fail to obey the verbal command and

tend to execute echopractic movements, imitating the examiner. 14

Inhibitory control: Withholding a response may be difficult for patients with damage to the ventral part of the frontal lobes.²¹ In tasks anticipated to elicit a false-alarm motor response, these patients are often unable to inhibit inappropriate responses.²² This difficulty in controlling impulsiveness can be assessed with the go—no go paradigm,²³ in which the subjects must inhibit a response that was previously given to the same stimulus, e.g., not tapping when the examiner taps twice.

Environmental autonomy: Patients with frontal lobe lesions are excessively dependent on environmental cues.24 Sensory stimuli can activate patterns of responses that are normally inhibited in normal controls. For example, the patient conceives the sight of a movement as an order to imitate (imitation behavior); the sight of an object implies the order to use it (utilization behavior); and the sight or sensory perception of the examiner's hands compels the patient to take them (prehension behavior). In some cases, the patients can elicit these behaviors even if they have been explicitly told not to do so. These abnormal behaviors (the spontaneous tendency to adhere to the environment) express the lack of inhibition normally exerted by the prefrontal cortex on the activation of patterns of behavior triggered by sensory stimulations.

Subjects. Subjects gave informed written consent to participate. Forty-two normal control subjects (mean \pm SD; age, 58 \pm 14.4 years), without any neurologic or psychiatric history, were included (table). All control subjects had a Mattis Dementia Rating Scale (DRS)²⁵ score >136 or a Mini-Mental State Examination (MMSE)²⁶ score >27.

To evaluate the discriminative power of the FAB, 121 patients with mild (PD, n = 24; multiple system atrophy [MSA], n = 6), moderate (corticobasal degeneration [CBD], n = 21), or severe (frontotemporal dementia [FTD], n = 23; progressive supranuclear palsy [PSP], n = 47) frontal lobe dysfunction^{27,28} were included (see table). All patients underwent an extensive clinical evaluation to confirm their diagnosis and all met currently accepted diagnostic criteria. The diagnostic criteria for PD were based on the pres-

ence of a parkinsonian syndrome with unilateral onset characterized by a resting tremor or an akinetorigid syndrome, a good response to levodopa that persisted at the time of evaluation, and the absence of exclusion criteria (e.g., supranuclear gaze palsy).^{29,30} The diagnostic criteria for MSA included the presence of an extrapyramidal syndrome poorly responsive to levodopa, associated with an autonomic or urinary dysfunction in the absence of exclusion criteria.31 The diagnostic criteria for CBD included a slowly progressive asymmetric akinetorigid syndrome and one or more of the following signs of cortical involvement: ideomotor apraxia, myoclonus, cortical sensory deficit, or alien limb syndrome.32 The criteria for PSP included the presence of a gradually progressive disorder with an age at onset of 40 years or later; a supranuclear limitation of vertical gaze; a prominent postural instability, with falls occurring in the first year of symptom onset; and no evidence of another disease that could explain the symptoms; in the absence of exclusion criteria.33 The diagnosis of FTD was based on a progressive onset of behavioral changes fulfilling the Lund and Manchester criteria, a severe dysexecutive syndrome on neuropsychological evaluation, and the absence of any other neurologic disorder sufficient to explain the frontotemporal cortical deficit. The neuropsychological evaluation of patients consisted of the MMSE²⁶ and Mattis DRS for all patients,25 and the Wisconsin Card Sorting Test (CST)³⁴ for 86 patients. The MMSE ranges were 30 to 24 for patients with PD, 30 to 21 for patients with MSA, 30 to 13 for patients with CBD, 30 to 17 for patients with PSP, and 30 to 6 for patients with FTD.

Technical properties of the battery. Validation. Concurrent validity. The validity of the FAB, i.e. how well the battery evaluates the existence of a frontal lobe syndrome, so was analyzed by correlating the FAB total score with the patient's performance on 1) the Wisconsin CST, a test considered to be sensitive to executive dysfunction the Mattis DRS, a global scale reported to be correlated with the degree of executive dysfunction in neurodegenerative diseases. For the Wisconsin CST, the number of criteria achieved and the number of perseverative errors were considered because both have been shown to be sensitive to frontal lobe dysfunction. We performed a correlational validity study because there is no "gold standard" that determines the existence and severity of a frontal lobe syndrome.

<u>Discriminant validity.</u> We determined the ability of the FAB to discriminate between normal control subjects and patients with cognitive impairment according to the Mattis DRS scale. Patients without cognitive impairment were excluded for this analysis. Only 95 patients with a Mattis DRS score below 136 were included.

The ability of the FAB to differentiate the frontal dysfunction of patients with cortical and subcortical lesions was studied by using a stepwise discriminant analysis in two groups of patients with frontal lobe dysfunction of different origins—subcortical (47 patients with PSP) and cortical (23 patients with FTD).

Reliability. Interrater reliability was determined by comparing the scores of two independent raters who were present during the administration of the FAB by one of them. Each rater was blind to the ratings made by the other. Interrater reliability was conducted in 17 patients and determined by calculating the kappa value.

We studied the internal consistency of the battery, i.e.,

the extent to which the six items of the FAB reflect the same underlying construct, by calculating the Cronbach's coefficient of alpha.³⁷

Results. Technical properties of the battery. Validation. Concurrent validity. A correlation was found between the FAB scores and the Mattis DRS performance in 121 patients ($r=0.82,\ p<0.001$). Similarly, the FAB scores correlated with the number of criteria ($r=0.77,\ p<0.001$) and perseverative errors (rho = 0.68, p<0.001) achieved in the Wisconsin CST. A stepwise multiple regression was used to evaluate the influence on the FAB performance of the following independent variables: age of patient, MMSE and Mattis DRS scores, and the number of criteria and perseverative errors in the Wisconsin CST. The Mattis DRS score and number of criteria achieved in the Wisconsin CST accounted for 79% of variance in the FAB (F [2,82] = 152.9; p<0.001; $r^2=0.79$). Interestingly, age and MMSE scores had no significant influence.

Discriminant validity. The FAB discriminated between controls and patients after adjusting for age as a covariate (analysis of covariance: F[1,131] = 17. 24; p < 0.001). The performance on the FAB correctly identified 89.1% of the cases (Wilke's lambda = 0.43, F[1,135] = 176.2; p < 0.001). A stepwise discriminant analysis in patients with FTD and PSP using the six FAB subscores as independent variables showed that similarities and prehension behavior correctly classified 69.7% of the patients (Wilke's lambda = 0.865; χ^2 [ddl = 2] = 10.6; p = 0.005).

Reliability. Two raters independently evaluating a subset of 17 patients with the FAB achieved an optimal interrater reliability ($\kappa=0.87, p<0.001$). The Cronbach's coefficient alpha between the items of the FAB of 121 patients was 0.78, suggesting good internal consistency.

Discussion. In order to provide a simple tool for assessing frontal lobe function that could be applied by any practitioner, we designed a short assessment battery, the FAB, based on our experience with focal frontal lobe lesions²⁴ and movement disorders associated with striatofrontal dysfunction.4 Other tools have already been designed to evaluate frontal lobe function at the bedside.38-41 A brief assessment of frontal and subcortical functions was proposed for patients with suspected subcortical pathology, but patients with AD scored significantly lower on this scale than those with Huntington's disease or PD.38 The EXIT 25, an executive interview, correlates not only with tests sensitive to frontal lobe dysfunction but also with the MMSE (r = -0.85). This suggests that the EXIT 25 is also sensitive to functions that are not executive.³⁹ Another brief tool sensitive to executive control, the CLOX (a clock drawing test),⁴⁰ has been proposed, but only investigates one domain of cognitive function: drawing. Lastly, Ettlin and Kischka⁴¹ proposed the "frontal lobe score," which is, however, not convenient for bedside assessment because it includes tasks such as the Trail-Making Test and takes up to 40 minutes to complete. The FAB is an easy test to administer, requires less than 10 minutes to complete, and is well accepted by patients. The six FAB subtests explore both cognitive and behavioral domains under the control of the frontal lobes, each of them having been shown to be significantly correlated with frontal lobe metabolic activity measured by 18-fluorodeoxyglucose using PET scan. Moreover, each subtest is associated with specific areas of the frontal lobes on the basis of neuropsychological, electrophysiologic, and functional arguments: conceptualization with dorsolateral areas, 42,43 word generation with medial areas, 44,45 and inhibitory control with orbital or medial frontal areas. Therefore, performance on the six subtests of the FAB can give a composite global score, which evaluates the severity of the dysexecutive syndrome and may suggest a descriptive pattern of executive dysfunction in a given patient.

The FAB presents good metric properties. The study demonstrated good internal consistency (Cronbach's alpha was 0.78),37 optimal interrater reliability ($\kappa = 0.87$), and concurrent validity. Indeed, the FAB score was strongly associated with the performance of patients on the Mattis DRS (rho = 0.82) and Wisconsin CST (rho = 0.77 for the number of criteria), both of which evaluate different cognitive functions under frontal lobe control. These functions include initiation, conceptualization, and attention for the Mattis DRS scale²⁵ and conceptualization and cognitive flexibility for the Wisconsin CST. Several recent studies have demonstrated that performance in the Wisconsin CST is related to functional activity in the prefrontal cortex. 42,48-50 In contrast, the FAB score is correlated neither with the MMSE score, a measure of more general cognitive function, nor with age (see the results of the stepwise multiple regression). The battery also presents good discriminant validity, allowing differentiation to be made between control subjects and patients with frontal or subcorticofrontal cognitive impairment. However, the FAB global score does not allow discrimination between patients with predominantly subcortical (PSP) or cortical (FTD) dysfunction. Only two subtests discriminated between these patients to some extent prehension behavior (more severely impaired in patients with PSP) and similarities (more severely impaired in patients with FTD). This result is not unexpected because patients with frontal and subcorticofrontal lesions usually present similar cognitive deficits and share only subtle neuropsychological differences.51-53

Some points should be stressed, however. Testretest reliability was not assessed. The anatomic correlation of the different subtests of the battery was derived from data obtained with similar tests, but not from the subtests themselves. Finally, although highly significant correlations were shown between the FAB and tests sensitive to frontal lobe functions, but not between the FAB and MMSE, it would be necessary to demonstrate that patients with nonfrontal lobe injuries perform at a higher level than that observed for patients with frontal lobe injuries, to definitively consider the FAB as a measure of frontal lobe dysfunction.

Appendix

Content, instructions, and scoring of the FAB

1. Similarities (conceptualization)

"In what way are they alike?"

A banana and an orange (In the event of total failure: "they are not alike" or partial failure: "both have peel," help the patient by saying: "both a banana and an orange are..."; but credit 0 for the item; do not help the patient for the two following items)

A table and a chair

A tulip, a rose and a daisy

Score (only category responses [fruits, furniture, flowers] are considered correct)

Three correct: 3 Two correct: 2 One correct: 1 None correct: 0

2. Lexical fluency (mental flexibility)

"Say as many words as you can beginning with the letter 'S,' any words except surnames or proper nouns."

If the patient gives no response during the first 5 seconds, say: "for instance, snake." If the patient pauses 10 seconds, stimulate him by saying: "any word beginning with the letter 'S.' The time allowed is 60 seconds.

Score (word repetitions or variations [shoe, shoemaker], surnames, or proper nouns are not counted as correct responses)

More than nine words: 3

Six to nine words: 2

Three to five words: 1

Less than three words: 0

3. Motor series (programming)

"Look carefully at what I'm doing."

The examiner, seated in front of the patient, performs alone three times with his left hand the series of Luria "fist-edge-palm." "Now, with your right hand do the same series, first with me, then alone." The examiner performs the series three times with the patient, then says to him/her: "Now, do it on your own."

Score

Patient performs six correct consecutive series alone: 3

Patient performs at least three correct consecutive series alone: 2
Patient fails alone, but performs three correct consecutive series with the examiner: 1

Patient cannot perform three correct consecutive series even with the examiner: $\mathbf{0}$

4. Conflicting instructions (sensitivity to interference)

"Tap twice when I tap once."

To be sure that the patient has understood the instruction, a series of three trials is run: 1-1-1. "Tap once when I tap twice." To be sure that the patient has understood the instruction, a series of three trials is run: 2-2-2. The examiner performs the following series: 1-1-2-1-2-2-2-1-1-2.

Score

No error: 3

One or two errors: 2

More than two errors: 1

Patient taps like the examiner at least four consecutive times: 0

5. Go-No Go (inhibitory control)

"Tap once when I tap once."

To be sure that the patient has understood the instruction, a series of three trials is run: 1-1-1. "Do not tap when I tap twice." To be sure that the patient has understood the instruction, a series of three trials is run: 2-2-2. The examiner performs the following series: 1-1-2-1-2-2-1-1-2.

Score

No error: 3

One or two errors: 2

More than two errors: 1

Patient taps like the examiner at least four consecutive times: 0

6. Prehension behavior (environmental autonomy)

"Do not take my hands."

The examiner is seated in front of the patient. Place the patient's hands palm up on his/her knees. Without saying anything or looking at the patient, the examiner brings his/her hands close to the patient's hands and touches the palms of both the patient's hands, to see if he/she will spontaneously take them. If the patient takes the hands, the examiner will try again after asking him/her: "Now, do not take my hands."

Score

Patient does not take the examiner's hands: 3

Patient hesitates and asks what he/she has to do: 2

Patient takes the hands without hesitation: 1

Patient takes the examiner's hand even after he/she has been told not to do so: 0

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Hippocampal and cortical atrophy predict dementia in subcortical ischemic vascular disease

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Article abstract—Background: The cause of dementia in subcortical ischemic vascular disease (SIVD) is controversial. Objectives: To determine whether cognitive impairment in SIVD 1) correlates with measures of ischemic brain injury or brain atrophy, and/or 2) is due to concomitant AD. Methods: Volumetric MRI of the brain was performed in 1) elderly subjects with lacunes (L) and a spectrum of cognitive impairment—normal cognition (NC+L, n = 32), mild cognitive impairment (CI+L, n = 26), and dementia (D+L, n = 29); 2) a comparison group with probable AD (n = 28); and 3) a control group with normal cognition and no lacunes (NC). The authors examined the relationship between the severity of cognitive impairment and 1) volume, number, and location of lacunes; 2) volume of white matter signal hyperintensities (WMSH); and 3) measures of brain atrophy (i.e., hippocampal, cortical gray matter, and CSF volumes). Results: Among the three lacune groups, severity of cognitive impairment correlated with atrophy of the hippocampus and cortical gray matter, but not with any lacune measure. Although hippocampal atrophy was the best predictor of severity of cognitive impairment, there was evidence for a second, partially independent, atrophic process associated with ventricular dilation, cortical gray matter atrophy, and increase in WMSH. Eight autopsied SIVD cases showed variable severity of ischemic and neurofibrillary degeneration in the hippocampus, but no significant AD pathology in neocortex. The probable AD group gave evidence of only one atrophic process, reflected in the severity of hippocampal atrophy. Comparison of regional neocortical gray matter volumes showed sparing of the primary motor and visual cortices in the probable AD group, but relatively uniform atrophy in the D+L group. Conclusions: Dementia in SIVD, as in AD, correlates best with hippocampal and cortical atrophy, rather than any measure of lacunes. In SIVD, unlike AD, there is evidence for partial independence between these two atrophic processes. Hippocampal atrophy may result from a mixture of ischemic and degenerative pathologies. The cause of diffuse cortical atrophy is not known, but may be partially indexed by the severity of WMSH.

NEUROLOGY 2000;55:1626-1635

Subcortical ischemic vascular disease (SIVD) is characterized by lacunar infarcts and deep white matter changes. The proportion of vascular dementia (VaD) attributed to SIVD ranges from 36 to 50%, with higher rates noted among African Americans¹ and Asian Americans² than whites.^{3,4} A few studies re-

port risk of dementia to be higher among subjects with lacunar infarcts versus other subtypes of stroke,⁴ and among patients with AD with concomitant lacunar versus large-artery infarcts.⁵ Thus, SIVD is an important subtype of VaD either alone or in combination with AD.

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Supported by the National Institutes of Health (P01-AG12435, P50-AG10129, R01-AG10897), the State of California Department of Health Services Alzheimer Program, a National Research Service Award (DA-05683-02), and a Career Scientist Award (G.F.) from the Department of Veterans Affairs. Received August 5, 1999. Accepted in final form October 2, 2000.

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