Repetition Priming With Nonverbal Stimuli in Patients With Dementia of the Alzheimer Type

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Perceptual repetition priming was examined in patients with dementia of the Alzheimer type (DAT) and normal control (NC) participants using a task involving the discrimination of geometric designs that had either a continuous ("closed") or discontinuous ("open") perimeter. With the open stimuli, the groups displayed significant and equivalent levels of priming after immediate repetition of the stimuli, whereas only the NC group primed significantly over a delay of three intervening items. Neither group demonstrated significant priming with the closed stimuli. Results indicate that under some conditions DAT patients can exhibit normal repetition priming with stimuli that do not have preexisting representations but that (due possibly to a deficiency in the level of steady-state cortical activation) this priming dissipates more rapidly in DAT patients than in NC participants.

A number of studies have shown that patients with dementia of the Alzheimer type (DAT) are impaired on word-stem completion (Bondi & Kasznia, 1991; Burke, Knight, & Partridge, 1994; Carlesimo, Fadda, Marfia, & Caltagirone, 1995; Heindel, Salmon, Shults, Walicke, & Butters, 1989; Keane, Gabrieli, Fennema, Growdon, & Corkin, 1991; Randolph, 1991; Salmon, Shimamura, Butters, & Smith, 1988; Shimamura, Salmon, Squire, & Butters, 1987) and word-fragment completion (Heindel, Cahn, & Salmon, 1997), repetition priming tasks that are thought to assess memory implicitly by measuring the degree to which prior exposure to a stimulus facilitates the subsequent identification of that stimulus. The impaired performance of DAT patients is not likely to be a consequence of the medial temporal lobe damage that is thought to underlie their severe explicit memory deficit, because amnesic patients with similar explicit memory impairment and medial temporal lobe damage exhibit normal priming on these tasks (Graf, Squire, & Mandler, 1984; Shimamura, 1986; Shimamura & Squire, 1984; Squire, Shimamura, & Graf, 1987). Rather, this priming deficit seems likely to result from additional neuropathology that is uniquely associated with DAT and that is not present in patients with circumscribed amnesic syndromes (Salmon & Heindel, 1992).

In contrast to their deficits on word-stem and word-fragment completion tasks, DAT patients have been found to exhibit normal repetition priming on perceptual identification tasks that require them to identify very briefly presented words (Abbenhuis, Raaijmakers, Raaijmakers, & van Woerden, 1990; Fleischman et al., 1995; Keane et al., 1991; Koivisto, Portin, & Rinne, 1996; but see Ostergaard, 1994). Keane and colleagues (1991), for example, found that the identification threshold for briefly presented words was lowered to the same extent in DAT patients and in normal control (NC) participants by prior exposure to those words and that this normal facilitation in perceptual identification occurred despite impaired priming in the word-stem completion task in these same patients. To account for the observed dissociation between the DAT patients' priming ability on the word-stem completion and perceptual identification tasks, these investigators proposed the existence of two anatomically and functionally distinct processing systems that mediate performance on tests of repetition priming: (a) a structural–perceptual system in the occipital cortex that supports perceptual priming, and (b) a lexical–semantic system in the temporoparietal cortex that supports conceptual priming. Given that DAT patients have marked pathology in the neocortical association areas of the temporal, parietal, and frontal lobes, but have a relative preservation of primary sensory cortices, these patients should demonstrate impaired performance on those word-stem completion and other conceptually based lexical and semantic priming tasks that are mediated by the lexical–semantic system but should demonstrate intact performance on perceptual identification and other perceptually based priming tasks that are mediated...
by the structural–perceptual system. Consistent with this prediction, DAT patients have also previously been found to display impaired priming performance on such conceptual tasks as word association (Brandt, Spenser, McSorley, & Folstein, 1988; Carlesimo et al., 1995; Salmon et al., 1988) and category exemplar generation (Monti et al., 1996).

Although there is rather strong evidence that DAT patients are generally impaired on conceptually based repetition priming tasks, there is surprisingly little clear-cut support for the notion that they perform normally on perceptually based repetition priming tasks. It is possible, for example, that the normal priming exhibited by DAT patients on the perceptual identification task occurs through some residual capacity for lexical or semantic activation of words despite the patients' damaged temporal and parietal association areas. In this view, DAT patients may display intact performance on the perceptual identification task simply because the task requires less lexical or semantic activation than the word-stem and word-fragment completion tasks and not because these patients possess a general preservation of perceptual priming ability. In addition, a number of studies have shown that DAT patients display substantial impairments on repetition priming tasks that involve the identification of fragmented pictures (Bondi & Kaszmiaak, 1991; Bondi, Kaszmiaak, Rapcsak, & Butters, 1993; Corkin, 1982; Heindel, Salmon, & Butters, 1990; but see Gabrieli et al., 1994), a task thought to depend primarily on perceptual rather than on conceptual processes (Weldon & Roediger, 1987) and, consequently, one that they should perform normally.

A major source of difficulty in interpreting the results of studies that use the fragmented pictures and perceptual identification tasks to assess perceptual priming in DAT patients is that both tasks involve the activation of preexisting lexical or semantic representations. Although the fragmented pictures task utilizes pictorial stimuli, the pictures are line drawings of real animate and inanimate objects, which may allow priming on this task to be supported by activation of their representations within the same semantic memory system that mediates performance on the word-fragment and word-stem completion tasks (Heindel et al., 1990). Similarly, the perceptual identification tasks used with DAT patients have exclusively utilized word or word-like (i.e., pronounceable nonwords; Keane, Gabrieli, Growdon, & Corkin, 1994) stimuli, so that the intact priming exhibited by DAT patients may be mediated by residual lexical or semantic processes. Given this possible ambiguity in the relative contribution of perceptual and conceptual processes to priming in the fragmented pictures and perceptual identification tasks, the status of perceptual priming in DAT patients remains unknown. A strong test of the notion that perceptual priming is normal in DAT patients and is mediated by an intact structural–perceptual system would be to determine whether or not these patients exhibit normal priming with nonverbal stimuli that do not have preexisting lexical or semantic representations.

The purpose of the present study was to directly examine the perceptual repetition priming ability of DAT patients using nonverbal stimuli. The repetition priming task that was used was similar to one developed by Kerstean-Tucker (1991) and involved the discrimination of geometric designs that had either a continuous ("closed") or discontinuous ("open") perimeter. The effect of repetition on the speed with which these perceptual discriminations were made was assessed with either immediate repetition or after a lag of three intervening items.

Method

Participants

Seventeen patients with probable DAT (10 males, 7 females) and 19 older persons who were NCs (9 males, 10 females) participated in this study. All participants were native English speakers. Written informed consent was obtained from each participant (or their conservator).

The diagnosis of probable DAT was made by a senior staff neurologist at the University of California, San Diego, (UCSD) Alzheimer's Disease Research Center (ADRC) on the basis of the criteria developed by National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA; McKhann et al., 1984). As part of their ADRC participation, the DAT patients received neurological and neuropsychological evaluations and a number of laboratory tests that are used to rule out other causes of dementia. Patients with a history of severe head injury, alcoholism and serious and prolonged psychiatric illness were excluded. To reduce the possibility of inadvertently including patients with multi-infarct dementia, those with a score of 5 or greater on the modified Hachinski ischemia scale (Hachinski et al., 1975; Rosen, Terry, Fuld, Katzman, & Peck, 1980) were excluded from the DAT group.

NCs were volunteers recruited from the UCSD ADRC or were paid participants recruited through newspaper advertisements. All NCs included in the study denied a history of alcoholism, drug abuse, learning disabilities, or serious neurologic or psychiatric illness.

The mean ages, years of education, and Dementia Rating Scale (DRS; Mattis, 1976) scores of the two participant groups are shown in Table 1. Because of an inability to accurately perform the basic repetition priming task, data from two DAT patients were excluded from all statistical analyses (see Data Analysis section). Thus, the results of the study are based on a total of 15 patients with DAT. The final groups of DAT patients and NCs did not differ significantly in age or years of education. The DAT patients scored significantly lower than the NCs on the DRS, t(18) = 7.35, p < .01.

Apparatus and Stimuli

A Macintosh IIci computer with a 14-in. color monitor was used for programming experimental events, presenting stimuli, and

Table 1

Means and Standard Deviations of Participant Characteristics of Patients With Dementia of the Alzheimer Type (DAT) and Normal Controls (NCs)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>NCs (n = 19)</th>
<th>DAT (n = 15)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
</tr>
<tr>
<td>Age (years)</td>
<td>73.2</td>
<td>4.7</td>
</tr>
<tr>
<td>Education (years)</td>
<td>15.6</td>
<td>2.7</td>
</tr>
<tr>
<td>DRS score</td>
<td>140.6</td>
<td>2.7</td>
</tr>
</tbody>
</table>

Note. DRS = Dementia Rating Scale.
recording participants' responses. A response box with two keys that could be labeled "open" and "closed" or "yes" and "no" was attached to the computer keyboard.

The stimuli were 128 novel, nonverbal line figures. Sixty-four of the stimuli were closed figures, which had a continuous perimeter consisting of 5 to 11 connected lines. The remaining 64 stimuli were open figures that had a discontinuous perimeter created by removing one line from each closed stimulus. As presented, each figure was approximately 1.0 square inch in size. Examples of the open and closed stimuli are shown in Figure 1.

Four open and four closed stimuli were used in a brief practice session that preceded the priming task. Forty stimuli were used in the repetition priming task; 20 presented as closed figures and 20 as open figures (see Appendix). The remaining 20 stimuli (10 open and 10 closed) were used as distractor items in a recognition test that followed the priming task.

Procedure

Repetition priming task. The participants sat in front of the computer monitor and the response box that contained two response keys labeled "open" and "closed." The participants were told that a series of line figures would be presented in the center of the computer screen and they were to press the key marked "open" if the figure was open (i.e., had a discontinuous perimeter) or the key marked "closed" if the figure was closed (i.e., had a continuous perimeter). They were then shown examples of the open and closed stimuli. The participants were instructed to respond as quickly and accurately as possible.

Each trial began with the presentation of a fixation point (a black dot) for 1,000 ms that directed the participants' attention to the center of the computer screen. Immediately after the fixation point was extinguished, an auditory tone warning of the impending presentation of the stimulus was presented for 33 ms. At the end of the tone, the stimulus was presented and remained visible until the participants responded by pressing one of the two keys. The computer recorded the accuracy of the participants' response and the reaction time (RT). RT was measured to the nearest millisecond from the onset of the stimulus to the participants' response.

![Example of Open and Closed Stimuli](image)

Figure 1. An example of the "open" and "closed" versions of three of the stimuli used in the experiment.

During the repetition priming task, each stimulus was presented twice. Half of the stimuli (10 open and 10 closed figures) were shown immediately following their first presentation (i.e., immediate repetition) and half (10 open and 10 closed figures) were shown after three intervening items (delayed repetition). Therefore, a total of 80 test trials were completed. The open and closed trials were presented in a fixed random order. No single stimulus was shown in both its open and its closed forms in the repetition priming task, and the open and closed versions of the stimuli were counterbalanced across the participants in each group.

A 15-trial practice test preceded the repetition priming task to acclimate the participants to the experimental procedures and to ensure that the test instructions were understood. The practice test used four open and four closed stimuli. Seven of the practice stimuli were repeated immediately after their initial presentation or after one or more intervening items.

Recognition test. Immediately following the repetition priming task, a recognition memory test was administered to examine the participants' ability to recognize items used in the priming task. Twenty of the items that had been presented previously in the priming task (10 open and 10 closed), and 20 new items (10 open and 10 closed), were randomly presented, one at a time, in the center of the computer screen. The participants were told that some of the stimuli may have been presented in the previous task and were asked to press the response key labeled "yes" on the response box if the stimulus had been previously presented or to press the key labeled "no" if the stimulus had not been previously presented. The stimulus remained visible until participants responded.

Data Analysis

We calculated median RTs for each participant separately for the initial (i.e., baseline) and repeat (i.e., target) presentations of the stimuli in the following four conditions of the repetition priming task: open stimulus with immediate repetition, open stimulus with delayed repetition, closed stimulus with immediate repetition, closed stimulus with delayed repetition. Each condition consisted of 10 baseline trials and 10 target trials. In the calculation of the median RT, we included only trials in which the participant's responses were correct for both the baseline and the target presentation of a particular stimulus. For example, if a participant's response was accurate on the baseline presentation of a stimulus but was inaccurate on the repeat (i.e., target) presentation of that stimulus, we did not include either trial in the calculation of the median RT for that condition. If more than half of the 10 baseline-target trials were eliminated in any of the four conditions, we dropped the participant from all analyses. This resulted in the elimination of two DAT patients. We performed the final statistical analyses with data from 15 patients with DAT and 19 NCs.

Results

Repetition Priming Task

Response accuracy. The mean percentage of target–baseline stimulus pairs from each condition that were correctly classified by the NC and DAT participants are shown in Table 2. Although the DAT patients performed significantly worse than the NCs in the closed–delayed, $t(32) = 2.54, p < .05$, open–immediate, $t(32) = 2.35, p < .05$, and open–delayed conditions, $t(32) = 2.40, p < .05$,
both groups achieved at least 90% accuracy in all conditions of the discrimination task.

**Reaction time measures of repetition priming.** Table 3 shows the mean of the median RTs produced by the NCs and DAT patients on the baseline and target trials in each condition of the repetition priming task. A mixed-model repeated measures analysis of variance (ANOVA) with group (DAT vs. NC) as a between-subjects factor and with condition (baseline vs. target), delay (immediate vs. delayed), and stimulus type (open vs. closed) as within-subjects factors revealed significant main effects of group, F(1, 32) = 12.07, p < .001, and condition, F(1, 32) = 12.22, p < .001. The significant group effect indicates that DAT patients were generally slower to respond than NCs. The significant effect of condition indicates that responses were faster on the second presentation of a stimulus (i.e., in the target condition) than on its first presentation (i.e., in the baseline condition). This latter effect demonstrates that repetition priming occurred with these nonverbal stimuli. The main effects of type and delay were not statistically significant.

None of the interaction effects involving group attained statistical significance. Thus, the NCs and DAT patients demonstrated similar magnitudes of priming and appeared to be similarly affected by the type of stimulus presented and the imposition of a delay interval. However, the Type X Delay, F(1, 32) = 4.48, p = .04, Condition X Delay, F(1, 32) = 5.92, p = .02, and Condition X Type X Delay, F(1, 32) = 3.99, p = .05, interaction effects were significant. The significant Type X Delay and Condition X Delay interaction effects indicate that there was a greater decline in RT for both baseline and target stimuli across the delay interval with the open stimuli than with the closed stimuli and that the magnitude of priming was greater with immediate repetition of the stimulus than with delayed repetition, respectively. The significant Condition X Type X Delay interaction effect indicates that the magnitude of priming declined across the delay interval to a greater extent with the open stimuli than with the closed stimuli. This effect is shown for the NCs and patients with DAT in Figure 2, which presents the mean difference between the median RTs for target and baseline stimuli (i.e., the absolute magnitude of priming) as a function of stimulus type (i.e., open and closed) and delay (immediate and delayed).

To further explore this apparent difference in the processing of open and closed stimuli, we performed separate Group (DAT vs. NC) X Condition (baseline vs. target) X Delay (immediate vs. delayed) repeated measures ANOVAs with each stimulus type. The analysis with the closed stimuli revealed a significant main effect of group, F(1, 32) = 10.4, p < .01, but no significant effect of condition or delay and no significant interaction effects. The analysis with the open stimuli, in contrast, revealed significant main effects of group, F(1, 32) = 10.92, p < .01, and condition, F(1, 32) = 18.84, p < .0001, and a significant Delay X Condition interaction effect, F(1, 32) = 8.35, p < .01. No other main or interaction effects were statistically significant. These results indicate that the DAT patients had generally slower response times than the NCs with both closed and open stimuli. Furthermore, both groups exhibited repetition priming with the open stimuli but not with the closed stimuli, and the magnitude of the priming effect was similar in the two groups. Finally, the repetition priming that occurred with the open stimuli decreased for both groups when a delay was interposed between the baseline and target presentations of a stimulus.

**Proportional priming scores.** Previous research suggests that the magnitude of priming observed in a repetition priming task increases as a function of absolute RT in the baseline condition (Ostergaard, 1994; Stanovich & West, 1979). Because the DAT patients were generally slower to respond than the NCs in the present study, we created proportional priming scores to at least partially adjust for absolute differences in baseline RT. We calculated a participant's proportional priming score for each condition (i.e., open—immediate, closed—immediate, open—delayed, closed—immediate, open—delayed, closed—delayed).
PERCEPTUAL PRIMING IN DAT

Figure 2. The mean difference between the target and baseline reaction times (i.e., priming) for the normal control (NC) participants and the patients with dementia of the Alzheimer type (DAT) as a function of delay (immediate vs. delayed) and stimulus type (closed vs. open).

Table 4
Mean Proportion Scores (and Standard Deviations) Derived From the Median Reaction Times (RT) in Each Condition of the Repetition Priming Task

<table>
<thead>
<tr>
<th>Group</th>
<th>Closed-immediate</th>
<th>Closed-delayed</th>
<th>Open-immediate</th>
<th>Open-delayed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
</tr>
<tr>
<td>NC</td>
<td>.023</td>
<td>.11</td>
<td>.018</td>
<td>.07</td>
</tr>
<tr>
<td>DAT</td>
<td>.044</td>
<td>.16</td>
<td>.037</td>
<td>.12</td>
</tr>
</tbody>
</table>

Note. NC = normal control; DAT = dementia of the Alzheimer type. Proportion score = ([Baseline RT - Target RT]/Baseline RT).

*p < .001.
Discussion

The neurologically intact NCs demonstrated significant facilitation (i.e., decreased RT) in their ability to make perceptual decisions regarding novel geometric line drawings as a result of previous exposure to these same stimuli. Although the magnitude of this priming effect decreased over a delay period, significant priming was obtained with immediate repetition of the stimulus and when a lag of three items intervened between repeated presentations. This facilitation in the ability of NCs to make perceptual decisions occurred despite their inability to recognize these same stimuli on a recognition memory test, suggesting that the repetition priming effect was due to an implicit facilitation within the processing structures involved in performing the perceptual decision task rather than by conscious, explicit memory for the particular stimuli. These findings confirm and extend those of previous studies that have demonstrated priming of novel, nonverbal stimuli in normal participants and amnesic patients (Kersten-Tucker, 1991; Musen & Squire, 1992; Schacter, Cooper, Delaney, Peterson, & Tharan, 1991), and they provide further support for the notion that priming can occur with stimuli that have no preexisting representations.

As in previous studies, the repetition priming effect exhibited by the NCs was limited to one of two versions of the nonverbal stimuli. Specifically, the NCs demonstrated significant priming with the open figures that had a discontinuous perimeter but no priming with the closed figures that had a continuous perimeter. This result is similar to the results of Kersten-Tucker (1991) who observed repetition priming effects for symmetrical but not asymmetrical two-dimensional polygons and to those of Schacter et al. (1991) who obtained significant priming for two-dimensional drawings of possible, but not impossible, novel three-dimensional objects. Kersten-Tucker (1991) and Schacter et al. (1991) offered similar explanations to account for the presence of stimulus-specific priming effects in their studies; namely, that a visual stimulus must possess a regular pattern that forms a strong whole (such as symmetrical polygons) or a structural coherence (such as possible objects) to be primed. It is not clear, however, that this type of explanation can account for the present findings, because the closed figures that were not primed appear to be at least as regular and as structurally coherent as the open figures that were primed.

A possible alternative explanation for the stimulus-specific priming exhibited by the NCs in the present study is that the perceptual decisions for open and closed stimuli entail different information-processing demands. Whereas a figure with a discontinuous perimeter can be classified as open as soon as the discontinuity is observed, correct classification of a closed stimulus requires an exhaustive search of the entire figure, because the presence of continuity in one part of the figure's perimeter does not imply continuity throughout the perimeter. It may be the case that prior exposure to a closed stimulus, in contrast, may have minimal impact on the exhaustive search required for a correct closed decision. Regardless of whether this particular explanation is correct or not, the general phenomenon of stimulus-specific nonverbal priming is quite robust, having been repeatedly observed across very different priming paradigms. Additional studies are clearly needed to better characterize the boundary conditions under which nonverbal priming will or will not occur.

A second major finding from the present study is that patients with DAT exhibit normal repetition priming with nonverbal stimuli under some conditions. The DAT patients, like the NCs, displayed significant priming with the open but not the closed figures in the immediate condition, and the magnitude of the priming effect (expressed as proportion of baseline RT) was comparable in the two groups. This demonstration of normal priming with nonverbal stimuli that do not have preexisting representations provides critical evidence in support of the claim that perceptual priming is normal in DAT patients and is mediated by an intact structural–perceptual system (Keane et al., 1991). This result also provides strength to the argument that the normal performance of DAT patients on the perceptual identification task (Abbenhuis et al., 1990; Fleischman et al., 1995; Keane et al., 1991; Koivisto et al., 1996) is mediated through their intact perceptual processes rather than through some residual capacity for lexical or semantic activation and that their impairment on fragmented picture identification tasks (Bondi & Kaszniaik, 1991; Bondi et al., 1993; Heindel et al., 1990) may be due to an impairment in activating the
semantic representations associated with the depicted objects rather than to a perceptual priming deficit.

Although the DAT patients and NCs displayed equivalent levels of priming with the open stimuli in the immediate condition, there are indications that the perceptual repetition priming of the DAT patients was not entirely normal. Specifically, the magnitude of priming declined at a faster rate in the DAT patients than in the NCs as indicated by the failure of the DAT patients, but not the NCs, to prime above baseline after a lag of three intervening items. This finding is not consistent with the notion that perceptual priming is completely preserved in patients with DAT and cannot be easily accounted for in terms of the perceptual–conceptual distinction postulated by Keane and colleagues (1991). When this abnormality in perceptual priming is considered in conjunction with the extensive evidence of impaired conceptual priming in patients with DAT, it suggests that some general factor might be contributing to the priming deficits exhibited by these patients across a variety of tasks.

One general factor that may contribute to the repetition priming deficit of patients with DAT is a deficiency in the level of steady-state cortical activation, or cortical tonus (Sara, 1985), that modulates the efficiency of cortical information processing (Salmon & Heindel, 1992). This steady-state cortical activation is thought to be maintained by the noradrenergic projection system (i.e., the locus coeruleus; Sara, 1985) that is often damaged in patients with DAT (Zweig et al., 1988). It may be the case that damage in the noradrenergic system reduces cortical tonus and the efficiency of cortical information processing in DAT patients to a level that is still sufficient to support immediate activation in the present repetition priming task but is not sufficient to maintain this activation over a delay.

It should be noted that this explanation of DAT patients' priming deficits in terms of deficient activation is not mutually exclusive with the perceptual–conceptual explanation proposed by Keane et al. (1991). These two explanations may invoke orthogonal pathophysiological processes that combine to produce the particular pattern of priming deficits that is observed in these patients. That is, patients with DAT may have a general activation deficit that reduces information-processing efficiency within the entire neocortex, but the effect of this impairment on priming is modulated by the structural integrity of different regions of the neocortex. Because the temporoparietal nocorcellar association areas that are thought to store semantic and lexical representations are more compromised than the primary sensory cortices in patients with DAT, for example, repetition priming deficits arising from deficient activation are more pronounced on conceptually based tasks than on perceptually based tasks.

Isolating the relative contributions of activation and structural integrity to the repetition priming performance of patients with DAT may prove to be extremely difficult to achieve experimentally given the highly interactive relationship that exists between these factors. From a neural network perspective, representations are actually defined by a pattern of activation across a set of distributed nodes. Thus, a disruption in the structure of preexisting representations may manifest itself as a general inability to effectively activate those representations, or a preexisting representation may appear to be degraded because of a general deterioration in cortical activation. In light of this proposed melding of activation and structural representation, further investigations of the nature of DAT patients' repetition priming with novel stimuli that do not have preexisting representations may be particularly pertinent for understanding the processes that contribute to the priming impairment displayed by these patients.

References


### Appendix
Repetition Priming Stimuli

<table>
<thead>
<tr>
<th>OPEN</th>
<th>CLOSED</th>
</tr>
</thead>
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Received February 11, 1997
Revision received May 12, 1997
Accepted May 13, 1997