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Impaired skill learning in patients with severe closed-head injury as demonstrated by the serial reaction time (SRT) task☆

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Abstract

A group of 20 patients who sustained closed-head injury (CHI) and a matched control group of 20 individuals were tested on the serial reaction time (SRT) task. Three different sequence-learning measures were generated from the task: two implicit and one explicit. The two implicit sequence-learning measures include: (1) the learning rate on the first five blocks of the repeated sequence, assumed to reflect primarily general reaction time learning, and (2) the difference between the fifth block of the repeated sequence and the sixth block, a random sequence that reflects implicit sequence-specific learning. In addition, an explicit measure of sequence learning was generated. The results indicate that the CHI group was impaired on the explicit measure of sequence learning. The groups did not differ on general reaction time learning, one of the implicit measures of sequence learning. However, the control group was superior to the CHI group in learning the specific sequence repeated in the SRT task. This pattern of results is unique to the CHI group, corresponding with neither that of amnesic patients nor with that of patients with dysfunction of the basal ganglia (i.e., Parkinson's diseases).

Keywords: Closed-head injury; Serial reaction time; Skill learning

1. Introduction

Preserved skill learning in amnesic patients led to the distinction between two forms of memory, *declarative* and *procedural* or *skill learning* (Cohen & Squire, 1980; Cohen, Eichenbaum, Deacedo, & Corkin, 1985). Skill learning was found to be preserved in amnesics when tested by a wide variety of tasks such as Tower of Hanoi puzzle (TOHP) (Cohen et al., 1985) and serial reaction time (SRT) (Nissen & Bullemer, 1987). Declarative memory has been studied quite extensively with patients who sustained closed-head injury (CHI) (for review, see Levin, 1989), but only

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a limited number of studies have tested skill learning with these patients. Some of the skill learning tasks involve sequence learning (e.g., TOHP and SRT). CHI patients were shown to have impaired memory for temporal order when measured directly (Vakil & Tweedy, 1994) but showed preserved temporal order when measured indirectly (Vakil, Blachstein, & Hoffien, 1991, 1998).

Based on the findings with memory for temporal order, it could be predicted that CHI patients will present normal performance on skill learning tasks that involve sequence learning (e.g., TOHP and SRT), because sequence in these tasks is measured indirectly. Although sequence learning is a crucial component in the TOHP and SRT skill learning tasks, they differ in several ways from the temporal order tasks reported above (Vakil et al., 1991, 1998). Despite the fact that temporal order was tested indirectly, it was done in the context of direct memory testing of words. The latter differs from skill learning tasks in which sequence learning is embedded in a task that is not perceived as a memory test. Thus, generalization from the performance of CHI patients on temporal order to performance on skill learning tasks, even when it involves sequence learning, is not inconsequential.

In a recent study, CHI patients were shown to be impaired in learning the TOHP, even though it measures sequence learning indirectly (Vakil, Gordon, Birnstok, Aberbuch, & Groswasser, 2001). However, the researchers pointed out the possibility that the CHI group failed on this task because it is a problem solving task that requires planning and a strategic approach, and the latter are among the cognitive processes known to be impaired in CHI patients (Levin, Benton, & Grossman, 1982; Lezak, 1983).

One of the advantages of the SRT task, which is the focus of the present study, is that several sequence-learning measures could be extracted from it. First is *learning rate*, which is reflected in reduction in reaction time (RT) across training blocks (blocks 1–5) when the same sequence is presented repeatedly. In addition to the sequence-specific learning, this measure reflects a more generalized skill learning (e.g., mapping the specific response to the specific stimulus position) (Ferraro, Balota, & Connor, 1993; Knopman & Nissen, 1987). Second is *indirect sequence learning* measured as the increase in RT when a block with a random sequence is presented (block 6), compared to the previous repeated sequence (block 5). Third is *direct sequence learning* measured by the "generate" task in which the participant is asked to predict the next position of the stimuli.

Mutter, Howard, and Howard (1994) and McDowall and Martin (1996) tested CHI patients with the SRT task and reached contradictory results. In addition, as we are going to point out, there are certain difficulties with these studies that prevent making conclusive statements about sequence learning ability of CHI patients, when measured directly and indirectly. Mutter et al. tested mild and severe CHI patients on the SRT task. The mild CHI patients showed intact performance on the direct (i.e., generate) as well as on the indirect measures of the sequence. The severe CHI patients were impaired on the indirect measure of sequence learned but demonstrated normal performance in the direct measure of the sequence learned. Commenting on these findings, the authors observe that "In combination, these findings present a rather odd picture of indirect and direct pattern memory after moderate to severe head injury" (Mutter et al., p. 283). Mutter et al. applied the generate task following *three* additional repeated sequence blocks after the random block. The problem with this procedure is that the explicit knowledge about the sequence measured at this stage (i.e., block 8) does not necessarily reflect the explicit knowledge available when indirect sequence learning was measured (i.e., block 4). This procedure may have lead to the relatively high rate of accuracy (about 70–80% correct, see Fig. 3 in Mutter et al.). Other studies that tested the generate task following only one block after the random block report a 40–50% accuracy rate (Jackson, Jackson, Harrison, Henderson, & Kennard, 1995; Knopman & Nissen, 1987; Vakil, Kahan, Huberman, & Osimani, 2000). Moreover, under these conditions, the lack of group effect may be due to ceiling performance of the control participants. Thus, the administration of the generate task in this study raises difficulties in relating these results to results obtained in previous studies with the SRT task.

By contrast with Mutter et al.'s (1994) results, McDowall and Martin (1996) reported normal performance of the severe CHI patients in the indirect sequence learning measure of the SRT task. Since these researchers did not apply the generate test, they do not have a direct sequence learning measure. Furthermore, the indirect measure of sequence learning was calculated by subtracting block 4 RT (i.e., repeated sequence) from that of block 5 (i.e., random sequence). This score was significantly different from zero for both groups. The authors did not report whether the mean difference between the blocks, which was 110 and 60 ms for the control and CHI group, respectively, reached significance. The nonsignificant Group by Blocks interaction (when all six blocks with repeated and random sequence are analyzed) cannot be taken as evidence of lack of interaction if only blocks 4 and 5 were analyzed. It is possible that the differences were masked by the similarities among the groups in the other blocks.

The goal of the present study was to rectify some of the difficulties pointed out in the previous two studies (McDowall & Martin, 1996; Mutter et al., 1994) that tested severe CHI patients with the SRT task. Hence, participants were first presented with five blocks with repeated sequence and then the block with random sequence. The generate task was administered following just one additional block with the repeated sequence. This procedure allowed a more adequate comparison of the groups on direct and indirect measures of sequence learning.

2. Method

2.1. Participants

Two groups participated in the present study: a control group (nonbrain damaged) and a CHI group. The control group consisted of 20 volunteers (14 males and 6 females) ranging in age from 22 to 53 years ($M = 30.85$, $SD = 10.97$). Their education ranged from 12 to 18 ($M = 14.65$, $SD = 1.66$) years of schooling. The CHI patients were recruited for the study from a population of patients admitted to the Loewenstein Rehabilitation Hospital (Israel) for rehabilitation following a head injury. This group was composed of 20 patients (15 male and 5 female) ranging in age from 18 to 55 years ($M = 32.85$, $SD = 12.13$). Their education ranged from 8 to 20 ($M = 13.30$, $SD = 2.87$) years of schooling. The groups did not differ significantly either on age, $t(38) = .55$, $p > .05$, or educational level, $t(38) = 1.82$, $p > .05$. Table 1 provides a more detailed description of the patient group including the length of coma, the Glasgow Coma Scale, and time after onset. An interdisciplinary team in the department had evaluated patients referred to the study at least one month earlier, as being out of Post-Traumatic Amnesia. Thus, patients' intellectual and linguistic functioning was at a level enabling adequate responsiveness to the task requirements based on the tests conducted. Participants in both groups were proficient in Hebrew, and had no history of mental illness, alcoholism or drug use.

2.2. Tests and procedure

2.2.1. Serial reaction time

In this task, a red light appears in one of four squares (3.3×3.3 cm) arranged horizontally on the computer screen. Participants were given the following

Table 1
Demographics of the CHI patient group

Patient	Age	Sex	Educ	TAO	Coma	GCS
1	44	M	12	14	14	06
2	43	M	15	13	02	08
3	18	M	12	05	04	13
4	21	M	12	23	14	04
5	28	F	18	21	17	06
6	24	M	12	06	14	10
7	52	M	08	17	21	06
8	55	M	10	41	60	11
9	21	M	12	15	07	08
10	49	F	16	18	14	03
11	31	F	20	27	45	05
12	46	F	17	23	30	03
13	43	M	16	47	21	03
14	20	M	12	08	01	07
15	33	M	12	26	05	05
16	24	F	12	29	14	06
17	21	M	12	17	14	06
18	21	M	12	13	06	06
19	27	M	14	32	07	04
20	36	M	12	30	14	06

Educ, education (years); TAO, time after onset (months); COMA, length of coma (days); GCS, Glasgow Coma Scale.

instructions: "A red light will appear in one of the four positions on the screen. Using the index finger of your dominant hand, your task is to press as fast as possible one of the first four horizontal numerical buttons on the keyboard that corresponds to the position of the red light. In other words, for the red light appearing from the left most to the right most position, you have to respond with the keys 1–4, respectively." The red light position appeared in a 10-trial sequence of repetitions, i.e., 2131431241. Ten repetitions of this sequence (i.e., 100 trials) constituted one block. Participants were presented with five blocks, with a one-minute rest between blocks. The starting position of the sequence (i.e., "2") was always the same across blocks. As soon as a response was made, or if the participant did not respond within 5 s, the next target spatial location appeared on the screen, whether or not the response made was correct. RT was defined as the time from onset of the stimulus to pressing of the response key. RT was recorded automatically by the computer for correct responses only. Incorrect responses or failing to respond within the 5 s were recorded as errors. Following the five blocks with repeated sequence, the sixth block was presented with a random sequence, followed by the seventh block that consisted of the original repeated sequence. (Accuracy of measured RT was more reliable in one-hundredth of a second than one-thousandth of a second.)

2.2.2. Generate

This task was designed to test the explicit memory of the repeated sequence. Following the seventh block, participants were informed that they had been presented with a repeated sequence in the first five blocks and in the seventh block. They were presented with a series of stimuli, in the repeated order, and were asked to push the response button in the location where they thought the next stimulus would appear. Following the response, whether it was right or wrong, the target moved to the next correct position. Participants were also told that in this task they are not timed and should focus on being accurate, rather than fast. The number of correct positions selected out of the 10-position sequence was recorded.

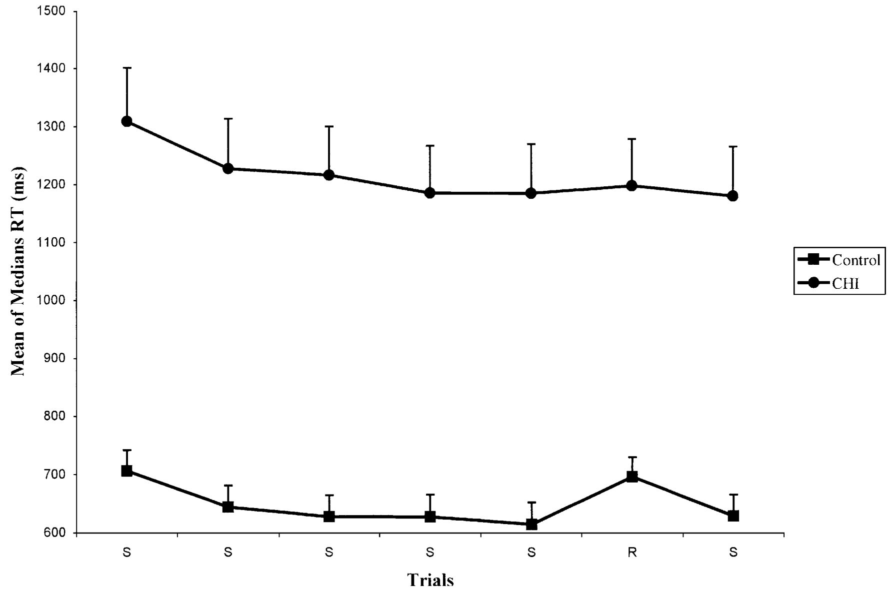


Fig. 1. The mean of the median RT (and SE), of the CHI and control groups in the seven blocks of trials in the SRT task. S, sequenced stimuli; R, random stimuli.

2.2.3. Statistical analyses

As in previous studies, the mean of the median (of 10-item sequence) RT per block (i.e., 100 trials) was analyzed (Ferraro et al., 1993; Nissen & Bullemer, 1987). In addition the number of errors (i.e., incorrect responses) was analyzed as well. All participants responded within the 5-s time limit. As mentioned above, RT was recorded automatically by the computer for correct responses only. Figs. 1 and 2 present the mean of the median RT and the number of errors, respectively, as a function of blocks of the SRT task for both groups. The groups (CHI and control) were compared on different learning measures of the SRT task. In this task implicit

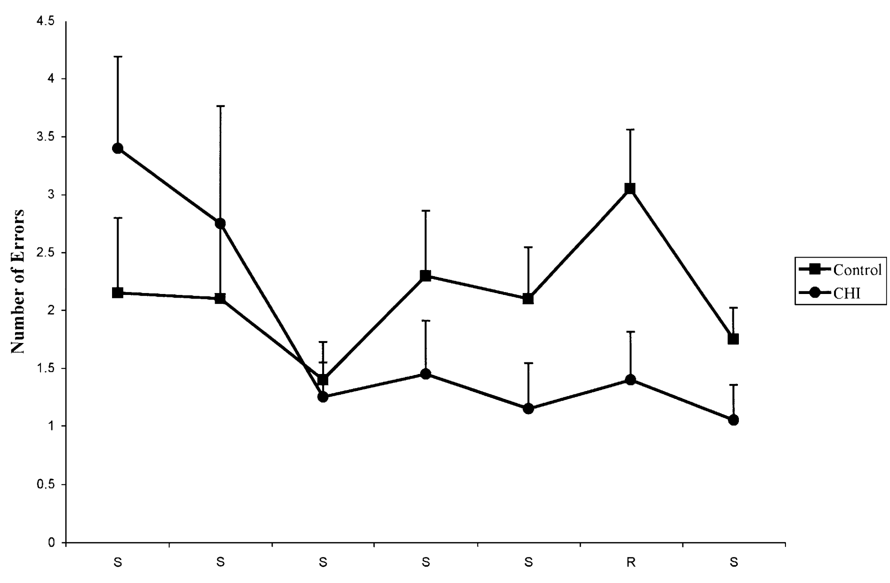


Fig. 2. The mean number of errors (and SE), of the CHI and control groups in the seven blocks of trials in the SRT task. S, sequenced stimuli; R, random stimuli.

sequence learning is expressed in two ways: first as the rate of reduced RT over the first five blocks of the repeated sequence, and second as the comparison of the repeated sequence (i.e., fifth block) and the RT to a random sequence-interference (i.e., sixth block). The recovery from interference was also assessed by comparing the groups' RT to a random sequence (i.e., sixth block) compared to the repeated sequence (i.e., seventh block). In addition, the groups were compared on the generate task which reflects explicit knowledge of the repeated sequence. The results were submitted to a mixed-design ANOVA with group and blocks as factors; the first is a between subjects factor, and the second is a within subjects factor.

3. Results

3.1. Learning-blocks 1–5

3.1.1. Reaction time

In the analysis of the mean of median RT of the two groups in the first five blocks of the SRT task, the RT of the control group was faster than that of the CHI group, $F(1,38) = 41.58$, $p < .001$. There is also a significant reduction in RT over blocks 1–5, $F(4,152) = 9.60$, $p < .001$. The Group by Learning block interaction did not reach significance, $F(4,152) = .37$, $p > .05$.

3.1.2. Number of errors

In the analysis of number of errors it was found that the overall number of errors made by the groups were not significantly different, $F(1,38) = .01$, $p > .05$. The number of errors significantly decreased over the five learning trials, $F(4,38) = 3.13$, $p < .05$. The Group by Learning block interaction did not reach significance, $F(4,152) = 2.04$, $p > .05$.

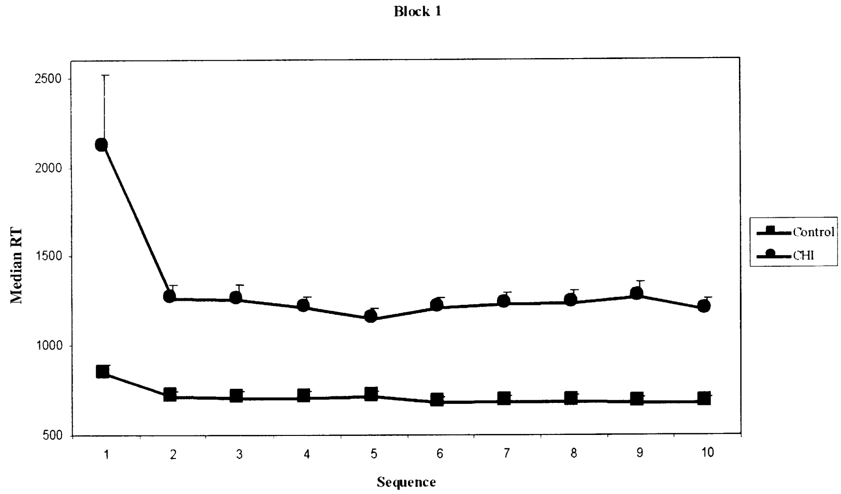
As can be seen in Fig. 1, for both groups the most significant learning rate took place in the first two blocks. There is a possibility that analysis of the learning blocks was not sufficiently sensitive to detect differences in the learning rates of the groups because each block is composed of 10 repeated sequences. Hence, to address this possibility the median RT of each of the 10 sequences of the first two blocks were analyzed. Figs. 3A and B present for both groups the median RT of each sequence, in blocks 1 and 2, respectively.

Analysis of the median RT of the first block found that overall the control group's RT was faster than that of the CHI group, $F(1,38) = 36.94$, $p < .001$. There is also a significant reduction in RT over the 10 learning sequences, $F(9,342) = 7.72$, $p < .001$. The Group by Learning sequences interaction was also significant, $F(9,342) = 4.02$, $p < .001$. As can be seen in Fig. 3A the significant interaction is due to the steeper change, from first to second sequence, of the CHI group over the control group. In the analysis of the 10 sequences of the second block, group was the only effect that reached significance, $F(1,38) = 39.47$, $p < .001$. The learning sequence within this block did not reach significance, $F(9,342) = 1.37$, $p > .05$, and the Group by Learning sequences interaction was also nonsignificant, $F(9,342) = 1.51$, $p > .05$.

3.2. Sequence learning (Interference)—block 5 vs block 6

3.2.1. Reaction time

As can be see in Fig. 1, the overall RT of the control group was faster than that of the CHI group, $F(1,38) = 35.95$, $p < .001$. There is an overall increase in the RT to the random sequence (block 6) as compared to the repeated sequence (block 5), $F(1,38) = 35.20$, $p < .001$. The Group by Blocks interaction reached significance,



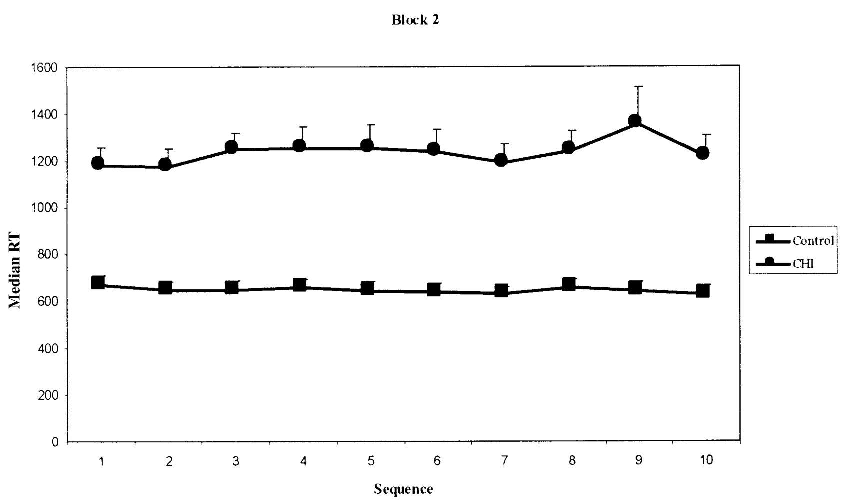


Fig. 3. (A) and (B) The median RT (and SE) of the CHI and control groups of each sequence in blocks 1(a) and 2(b).

$F(1,38) = 18.74$, $p < .005$. This interaction indicates that the difference between repeated as compared to random sequence (i.e., interference) is greater for the control group than for the CHI group. Fig. 4 presents, for the two groups, a scatterplot of the individual interference scores (mean RT of 10 medians of block 6 minus mean RT of 10 medians of block 5); the higher the score, the stronger is the interference. As can be seen in this figure all the control participants showed interference, while only about half of the CHI group showed such interference. The demographic measures (i.e., age and education) and the severity of injury measures (i.e., GCS, length of coma, and time after onset) were not significantly correlated with the interference score. In addition, to detect possible variables that distinguish between these groups the CHI group was divided into two subgroups, those that showed interference ($n = 12$) and those that did not show interference ($n = 8$). Using t test for independent sample to compare the groups, we found that these CHI subgroups did not differ either on age or on education. The subgroups were not reliably different on the severity of injury measures although, the measure closest to reaching significance was the length of coma, $t(18) = 1.62$, $p > .05$. The CHI subgroup, that like controls showed interference, had fewer days of coma ($M = 12.08$, $SD = 8.03$) compared to the group that did not show interference ($M = 22.38$, $SD = 19.94$).

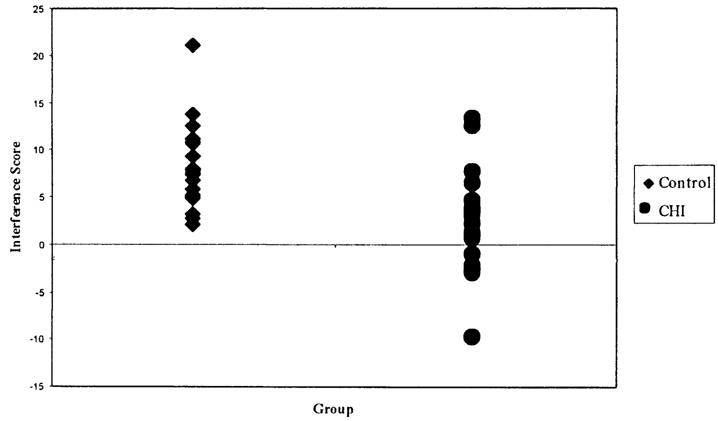


Fig. 4. A scatterplot of the individual interference scores for the CHI and control groups.

3.2.2. Number of errors

Analysis of the number of errors revealed that only group effect reached significance, $F(1,38) = 6.04$, $p < .05$. As can be seen in Fig. 2, due to the interference, the control group made more errors than the CHI group. The increase in the number of errors from block 5 to block 6 did not reach significance, $F(1,38) = 3.21$, $p > .05$, nor the Group by Blocks interaction, $F(1,38) = 1.09$, $p > .05$.

3.3. Recovery from interference—block 5 vs block 7

3.3.1. Reaction time

The significant group effect, $F(1,38) = 34.66$, $p < .001$, indicates the faster RT of the control group as compared with the CHI group. As can be seen in Fig. 1, the significant Group by Blocks interaction, $F(1,38) = 6.09$, $p < .05$, is due to the fact that while the controls' RT was faster in block 7 compared to block 6, the patients RT did not change. Thus it follows that the significant block effect, $F(1,38) = 17.70$, $p < .001$, is due only to the controls' change in RT from block 6 to block 7.

3.3.2. Number of errors

In this analysis the two main effects, but not the interaction between them, reached significance. Overall, the control group made more errors than the patient group, $F(1,38) = 8.32$, $p < .01$. There is a significant decrease in errors from the block with the random sequence (block 6) back to the repeated sequence (block 7), $F(1,38) = 5.15$, $p < .05$; this decrease in the number of errors was similar in the two groups, $F(1,38) = 1.71$, $p > .05$.

3.4. Generate

In this task the sequence learning is measured directly. The control group ($M = 6.25$, $SD = 1.94$) and the CHI group ($M = 4.75$, $SD = 2.24$) differed significantly in the number of correct sequence positions generated, $t(38) = 2.26$, $p < .05$.

To assess the relations between the different measures of sequence learning, Pearson product–moment correlations were calculated separately for the control and patient groups. In both groups, the correlation between the generate task and the two indirect learning measures (i.e., block 1 vs block 5 and block 5 vs block 6) did not reach significance. The correlation between the two indirect learning measures reached significance only in the control group, $r(20) = .49$, $p < .05$, but not in the CHI group, $r(20) = .29$, $p > .05$. This positive correlation indicates a consistency

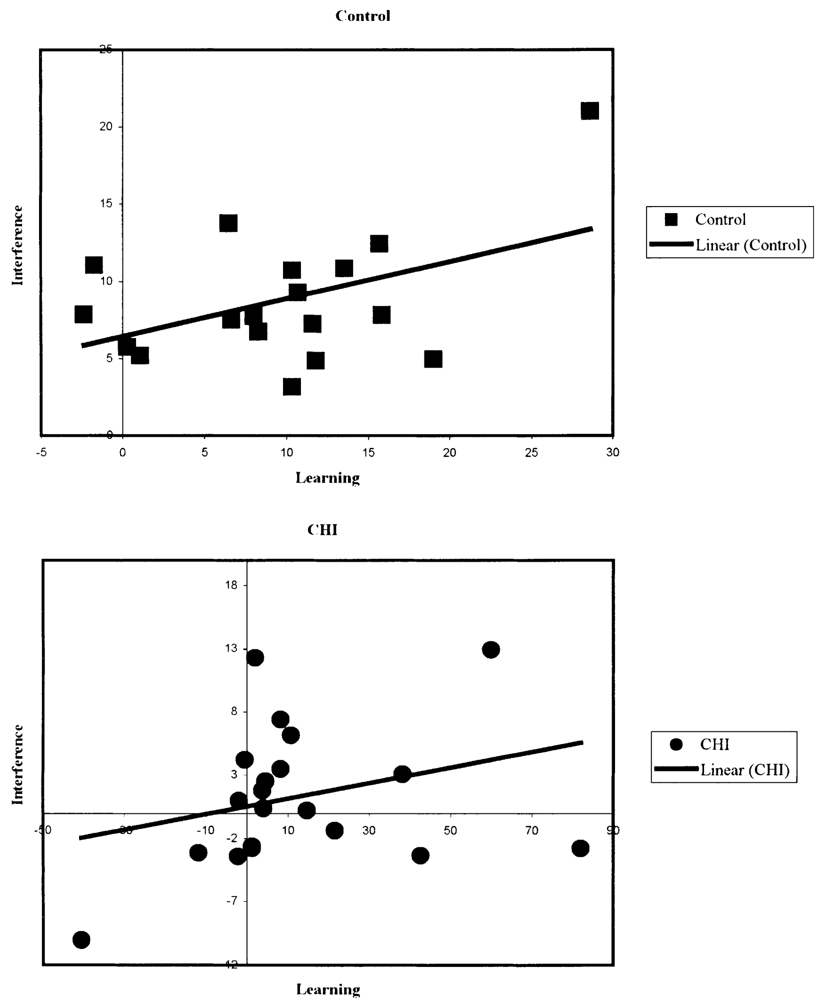


Fig. 5. A scatterplot and regression line as a function of the learning rate and interference score, for the CHI and control groups.

between the two learning measures of the SRT task in the control group but not necessarily in the CHI group. Fig. 5 present a scatterplot and a linear regression line for each group. As can be seen in Fig. 5, in the control group the higher the learning rate (i.e., block 1 vs block 5), the greater is the interference (i.e., block 5 vs block 6), but these variables are much less related to each other in the CHI group.

Finally, Pearson product-moment correlations were calculated to assess the relations between the severity of the patients' head injury to their performance on the different memory measures. The only correlation that reached significance was between the length of coma and the total number of errors in the first five learning trials, $r(20) = .689$, $p < .001$.

4. Discussion

Two earlier studies (McDowall & Martin, 1996; Mutter et al., 1994) that tested CHI patients with the SRT reached conflicting results. Furthermore, as noted above there are some difficulties with these studies, particularly with regard to the generate task. In the study by McDowall and Martin the generate task was not measured at all. Mutter's et al. administered the generate task following three additional blocks after the random block. At this stage (i.e., block 8) the explicit knowledge available does not necessarily reflect the explicit knowledge about the sequence that was available when indirect sequence learning was measured (i.e., block 4).

In the present study the CHI group did differ from the control group on the generate task, which requires direct retrieval of the repeated sequence of the stimuli. This finding indicates that the CHI patients differ from controls in terms of development of explicit awareness of the sequences. Although overall the RT of the control group was faster than that of the CHI group, the groups did not differ on the learning rate of the task as measured by the first five blocks. However, the difference between the fifth block (i.e., repeated sequence) and the sixth block (i.e., random sequence) was significantly greater for the control group as compared to the CHI group, indicating impaired learning of the repeated sequence by the patient group even when measured indirectly.

Other studies have also reported dissociation between "learning" as expressed in the first learning blocks versus the difference between the repeated and random sequence (i.e., interference). That is, the second but not the first was found to be impaired (e.g., Ferraro et al., 1993, *re* Parkinson's disease patients; Knopman and Nissen, 1987, *re* Huntington's disease patients; Vakil et al., 2000; *re* basal ganglia patients). Ferraro et al. (1993) and Knopman and Nissen (1987) suggest that these two indirect learning measures derived from the SRT task reflect two types of learning: First is "reaction-time-task learning" as defined by Knopman and Nissen, and "generalized skill" as termed by Ferraro et al. that is related to proficiency in execution of the RT task (e.g., mapping the specific response to the specific stimulus position). Second is the "sequence-specific learning" in Knopman and Nissen's terms, or "implicit learning" as defined by Ferraro et al. that reflects implicit learning of the specific sequence in which stimuli were presented. These two learning aspects are reflected in the learning rate from the first to the fifth block, because in these initial blocks participants are familiarized with general aspects of the task and learn the sequence (i.e., implicitly) at the same time. The difference between the fifth block of the repeated sequence and the sixth block (the random sequence) reflects only the implicit sequence-specific learning. For this reason all studies using the SRT task viewed the comparison between the repeated and the random blocks as reflecting procedural learning, or more specifically, sequence learning (e.g., Ferraro et al., 1993; Jackson et al., 1995; Knopman & Nissen, 1987).

Two findings with the CHI group further confirm the dissociation between the two aspects of the implicit learning occurring in the SRT task (i.e., "generalized skill" and "sequence-specific learning"). First is the finding that the CHI group did not differ from the control group on the former aspect, but did differ on the latter. The second finding is the nonsignificant correlation between these two measures in the CHI group. This pattern of results helps to characterize which aspect of learning is preserved and which aspect of learning is impaired following closed head-injury. What is primarily learned in the CHI group is probably "reaction-time-task learning" or "generalized skill." However, the CHI patients have difficulties in sequence-specific learning.

The pattern of results of the CHI group is quite unique compared to findings with other patient samples. On the one hand, CHI patients, just like amnesic patients (Nissen & Bullemer, 1987) have difficulties in explicit retrieval of the learned sequence as measured by the generate task. On the other hand, they differ from amnesics in that they are impaired on implicit sequence learning as measured by the interference of the random block. A comparison of CHI patients to patients with damage to the basal ganglia (Ferraro et al., 1993; Knopman & Nissen, 1987; Vakil et al., 2000) shows that only CHI patients are impaired on explicit sequence learning, but on the other hand also shows impaired implicit learning of the sequence, just as in basal ganglia patients.

Previous studies have reported that CHI patients have memory impairment for temporal order when measured directly (Vakil & Tweedy, 1994) but are preserved when measured indirectly (Vakil et al., 1991, 1998). Based on these studies it was predicted that CHI patients when tested with the SRT task would be impaired on the direct measure of the sequence learning (i.e., generate), but not the indirect measure of the sequence learning. Thus, impaired performance in the direct measure of the sequence learning was predicted, but the impairment in the indirect measure of the sequence learning is contrary to our prediction.

In a previous study (Vakil et al., 2001) we tested the performance of CHI on a skill learning task, the TOHP (implicit sequence learning), and on an explicit nonverbal sequence learning task. Consistent with the present findings, the CHI group was impaired on the implicit and explicit sequence learning. These findings that the CHI patients show impaired implicit sequence learning are also inconsistent with previous reports that showed preserved temporal order of words when measured indirectly (Vakil et al., 1991, 1998). A possible explanation offered in the study by Vakil et al. (2001) is that the TOHP is a problem-solving task whose solution requires planning and a strategic approach, which are among the cognitive processes known to be impaired in CHI patients (Levin et al., 1982; Lezak, 1983). This explanation would not be valid for the findings of the present study, where the CHI group was impaired in the implicit sequence learning measured by the SRT task. A conceivable explanation could be that in the SRT task, although the sequence is learned indirectly, since it is a fundamental element of what is learned in this task, the CHI patients found it difficult to acquire. By contrast, the temporal order of a list of words is secondary information to the learning of the words. In this case the CHI patients could demonstrate indirect learning to the same degree as controls (Vakil et al., 1991, 1998). In conclusion, this study demonstrates that direct or indirect learning is not the exclusive criterion that predicts whether CHI patients will be impaired in sequence learning. Further studies are required to define the factors that determine when sequence learning, even when learned indirectly, is impaired or preserved in CHI patients.

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