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Research report

Impaired procedural learning in obsessive–compulsive disorder and Parkinson's disease, but not in major depressive disorder

Daphna Joel[a,*], Orly Zohar[a], Michal Afek[a], Haggai Hermesh[b], Lidia Lerner[c], Ruth Kuperman[d], Ruth Gross-Isseroff[e], Abraham Weizman[b], Rivka Inzelberg[d,f]

[a] *Department of Psychology, Tel Aviv University, Ramat-Aviv, Tel Aviv 69978, Israel*
[b] *Anxiety Disorders and Behavior Therapy Unit, Geha Mental Health Center, Petach Tikva, Israel and Sackler Faculty of Medicine, Tel Aviv University, Israel*
[c] *Department of Psychiatry, Hillel Yaffe Medical Center, Hadera, Israel*
[d] *Department of Neurology, Hillel Yaffe Medical Center, Hadera, Israel*
[e] *Research Unit and Outpatient Department, Geha Mental Health Center, Petach Tikva, Israel*
[f] *Rappaport Faculty of Medicine, Technion, Haifa, Israel*

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Abstract

The striatum has been consistently implicated in the pathophysiology of obsessive–compulsive disorder (OCD), yet, studies assessing the performance of OCD patients in procedural learning tasks, assumed to rely on the intact functioning of the striatum, have yielded inconsistent results. Recently, Rauch et al. [Rauch SL, Savage CR, Alpert NM, Dougherty D, Kendrick A, Curran T, et al. Probing striatal function in obsessive–compulsive disorder: a PET study of implicit sequence learning. J Neuropsychiatry Clin Neurosci 1997;9:568–73] have obtained evidence suggesting that seemingly intact performance of OCD patients in such tasks may be achieved by recruiting systems which in normal subjects are reserved for explicit or declarative, rather than implicit or procedural, processing. The present study assessed procedural learning in OCD patients using a card betting task in which explicit processing impairs, rather than assists, acquisition. In addition, we tested a group of Parkinson's disease (PD) patients, in order to better establish the dependence of the task on procedural learning, and a group of major depressive disorder (MDD) patients, in order to test the possibility that impaired learning in the card betting task may be a result of concurrent depression. The majority of OCD (15/18) and PD patients (14/16) did not acquire the task, whereas MDD patients acquired the task similarly to normal control subjects. These results demonstrate that OCD patients are impaired on a procedural learning task in which explicit processing impairs acquisition. Two different interpretations are suggested: that the striatal system is dysfunctional in OCD, or that inappropriate explicit processing in OCD interferes with the functioning of the striatal system.

Keywords: Procedural learning; Explicit processing; Card betting; Striatum

1. Introduction

Obsessive–compulsive disorder (OCD) is a common psychiatric disease, affecting 2–3% of the population worldwide [38]. The Diagnostic and Statistical Manual of Mental Disorders [3] classifies OCD as an anxiety disorder characterized by obsessive thinking and compulsive behavior. Evidence from functional neuroimaging studies has most consistently implicated dysfunction of the orbitofrontal cortex and of the striatum in the pathophysiology of OCD (for review see [47,53]). Consistent with the former, several studies have reported that OCD patients are impaired in paradigms assumed to tap orbitofrontal function, including the decision making task of Bechara et al. [5], Object Alternation Test, and tests of response inhibition (e.g. [1,2,4,9,10,12,22,23,40,41,50,60],

* Corresponding author. Tel.: +972 3 6408996; fax: +972 3 6409547.
E-mail address: djoel@post.tau.ac.il (D. Joel).

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but see [31]). In contrast, the performance of OCD patients in tasks assumed to rely on the intact functioning of the striatum, that is, procedural learning tasks (for review see [13,21,28-30,33,34,42,43,46,58]), has been assessed in a few studies, and these have yielded inconsistent results, reporting either impaired performance [9,11] or no deficit [39,48,56]. There is some evidence suggesting that seemingly intact performance of OCD patients in such tasks may be achieved by recruiting systems which in normal subjects are reserved for explicit or declarative, rather than implicit or procedural, processing. Thus, Rauch et al. [39] reported that in OCD patients performing an implicit sequence learning task, increased metabolism (assessed using PET) was seen in the hippocampus, rather than in the striatum, which was activated in normal controls performing the task, although the two groups acquired the task similarly. On the basis of these results, Rauch et al. suggested that OCD patients have a dysfunctional striatal system, and have therefore attempted to solve the task by recruiting the hippocampal system, which is thought to subserve explicit forms of learning and memory (for review see [51]). This hypothesis was supported in a later study, which found that OCD patients were impaired in the implicit sequence learning task when they were required to perform concurrently an additional, explicit task [16].

The aim of the present study was to assess procedural learning in OCD patients using a task which appears to be insolvable using non-procedural strategies—thus, any attempts by OCD patients to utilize explicit learning would still result in worse performance compared to normal controls. In the task, a card betting game developed by Friedland [19], participants have to bet on one of four decks of cards. Each deck has a different probability of winning, which is unknown to the participants. However, they can learn by trial and error which deck will maximize their likelihood of winning. Friedland [19] used this task to study how differences in personal orientation towards event attribution, affect subjects ability to acquire a card betting game. He found that subjects who habitually attribute the outcome of random events to chance (“chance-oriented persons”) gradually learned the task, whereas those who attribute such outcomes to luck (“luck-oriented persons”) did not show any evidence of learning. The gradual acquisition of the task by chance-oriented subjects suggests that these subjects have used a procedural strategy. Since it is highly unlikely that normal subjects have a deficient procedural learning mechanism, the lack of evidence that luck-oriented subjects acquired the task raises the possibility that these subjects have attempted to solve the task using a non-procedural strategy, and that this strategy is unsuitable for solving the task (see ref. [19] for discussion of the possible strategy employed by luck-oriented subjects). Thus, although it is not clear why chance–luck orientation is correlated with the tendency to use procedural versus non-procedural strategies in Friedland’s card betting task, this task seems to have the essential feature for assessing procedural learning in OCD patients, namely, being unsolvable using non-procedural strategies.

In order to better establish the dependence of the card betting task on procedural learning, we tested a group of Parkinson’s disease (PD) patients, as it is well documented that these patients are impaired on tasks assessing procedural learning (e.g. [18,26,27,42,54,55,57]). In addition, because both OCD and PD patients may also suffer from depression, a group of patients with major depressive disorder (MDD) was included, in order to test the possibility that impaired learning in the card betting task may be a result of concurrent depression. In order to rule out the possibility that differences in luck score between patients and control groups underlie differences in performance of the card betting task, all participant filled out the Chance–Luck questionnaire.

2. Materials and methods

2.1. Patients

The study population consisted of 18 (7 men) patients with OCD, 16 (11 men) patients with PD, 18 (6 men) normal healthy young control subjects, 17 (8 men) healthy elderly control subjects, and 14 patients with MDD (mild to severe), out of which 8 (3 men) were young, and 6 (3 men) were elderly (see Table 1). OCD and MDD were diagnosed by two senior psychiatrists according to DSM IV criteria. Severity of OC symptoms was assessed using the Yale-Brown Obsessive–Compulsive Scale (Y-BOCS [20]; this score is missing for one patient). The mean and standard error of the mean score of the OCD patients was 31.2 (9.0). PD was diagnosed according to standard criteria [8]. PD patients were at stages II and III of Hoehn and Yahr [24]. Severity of depression was assessed in all participants using the Beck Depression Inventory (BDI [6,7]; this score was not obtained from 12 elderly controls, 2 young controls, 1 OCD patient, and 5 PD patients). In addition, all participants filled out the obsessive–compulsive personality scale from the Wisconsin Personality Disorders Inventory (WISPI [25]) to assess any possible relation between obsessive–compulsive personality traits and task performance (this score was not obtained from one elderly control, one young control, and four PD patients). Fifteen out of the 16 PD patients were treated with L-Dopa and received in addition different combination of Amantadine, Entacapone and Selegiline. Of the 18 OCD patients, 12 were treated with one of the selective serotonin reuptake inhibitors (SSRI, fluoxetine, fluvoxamine, paroxetine or citalopram), two were treated with a combination of an SSRI and risperidone, and four were not under medication. Of the 14 MDD patients, five were treated with an antidepressant (fluoxetine, fluvoxamine, paroxetine or mianserine), two were treated with a combination of an antidepressant and perhenazine, one was treated with olanzapine, one with carbamazepine and one with a combination of Carbamazepine and Chlorpromazine. Three MDD patients were not under medication. All patients were tested while on their usual medication. The study was approved by the Review Ethics Board of

Table 1
Demographic and clinical data of the different diagnostic groups (mean and standard deviation)

	Men (*n*)	Women (*n*)	Age (years)	Education (years)	BDI	WISPI
Control-young	6	12	30.0[a] (7.1)	15.1 (2.1)	3.6 (3.6)	4.0[a] (1.2)
Control-elderly	8	9	63.35[*] (12.0)	13.7 (2.9)	3.2 (2.6)	5.4[*] (1.6)
OCD	7	11	32.5[a] (10.6)	13.7 (2.6)	21.4[*,a] (17.2)	5.7[*] (1.9)
MDD	6	8	49.3[*,a] (18.0)	12.7[*] (2.1)	24.0[*,a] (11.3)	4.9 (2.1)
Young	3	5	36.0 (9.2)	13.1 (1.9)	27.3 (9.5)	4.8 (2.4)
Elderly	3	3	67.0 (7.8)	12.2 (2.3)	19.7 (13.0)	5.0 (1.8)
PD	11	5	65.4[*] (11.7)	10.9[*,a] (3.7)	10.2 (6.1)	6.4[*] (1.8)
			$F(4,78) = 32.97$, $P < 0.0001$	$F(4,78) = 5.31$, $P < 0.001$	$F(4,58) = 9.89$, $P < 0.0001$	$F(4,72) = 4.18$, $P < 0.005$

[a] Significantly different from the elderly-control group ($P < 0.05$).
[*] Significantly different from the young-control group ($P < 0.05$).

the Hillel-Yaffe Medical Center, Gehha Mental Health Center and Tel Aviv University, and all participants signed an informed consent form after the nature of the study was fully explained to them.

2.2. Procedure

Each subject was tested individually in an isolated and quiet room, and required approximately 25–50 min (depending on the specific questionnaires administered and his/her pace). Subjects were thanked for giving their consent to participate in this experiment, and were told that a computer game had been developed in Tel-Aviv University, and that the aim of the present experiment was to assess the game and to determine the suitable target audience for it. To this end, they were therefore asked to play the game and fill out several questionnaires. After the conclusion of the card betting game, subjects filled out the Chance–Luck, BDI, WISPI, and Y-BOCS (OCD patients only) questionnaires.

2.3. Instruments

2.3.1. Card betting task

The card betting task [19] was conducted on a laptop computer and required the usage of the computer mouse only. Four decks of blue and red cards facing downwards were presented on a computer screen (Fig. 1). Each deck had a constant and pre-defined probability of red cards of either 75%, 60%, 40% or 25%. The order of cards in each deck was pseudo-random—it was randomly chosen by the software but was restricted by the following rules: (1) the assigned probability had to be expressed in the entire deck, as well as within each sequence of 10 cards in the 40%- and 60%-red decks, or in each sequence of 20 cards in the 25%- and 75%-red decks. (2) The maximal length of a same-color card sequence could not exceed three cards in the 40% and 60% probabilities, and four cards in the 25% and 75% probabilities.

At the beginning of the task, the subject was presented with a screen presenting task instructions (see Appendix A). After clicking on a “Start” button, the task begun. On each trial, the subject was given 100 points, and required to choose a betting sum between 10 and 100 points by mouse clicking on 1 of 10 small buttons, each representing one betting sum in increments of 10 (Fig. 1). After choosing a betting sum, the subject had to click on one of the four decks in order to turn over its uppermost card. If this card turned out to be red, the betting sum was doubled and credited to the subject; if it turned out to be blue, the betting sum was lost. Amounts not bet were also credited to the subject (i.e. if a subject bet $10 and did not win, s/he was nevertheless credited with $90). Participants were unaware of the total number of trials (150), the number of cards in each deck (150), or the probability assigned to each deck.

The following measures were recorded on each trial: the deck chosen; the sum wagered; the time between choosing a deck on the previous trial and selecting a betting sum on the current trial (time to bet); the time between sum selection and deck selection on the same trial (time to deck).

2.3.2. Chance–Luck questionnaire

This questionnaire [19] presents short descriptions of four events (see Appendix B). Each portrays an outcome that the subject has to account for by splitting 100 points between two factors—luck and chance. For example:

You were about to take a trip abroad. Upon arrival at the airport you realized that the time of departure indicated on your ticket was incorrect, and that your flight had departed already. You took the next scheduled flight. After landing you found out that your original flight had been hijacked en route.

Please divide 100 points between chance and luck to indicate the weight of the two factors in accounting for the outcome:

$$\underset{\text{Chance}}{\underline{\qquad}} + \underset{\text{Luck}}{\underline{\qquad}} = 100$$

In a pilot study, with 30 healthy subjects, we found that of the four original events, the mean luck score of the third and fourth events had the highest correlation with task acquisition. We have therefore used this mean to characterize participants as luck- or chance-oriented in the present study.

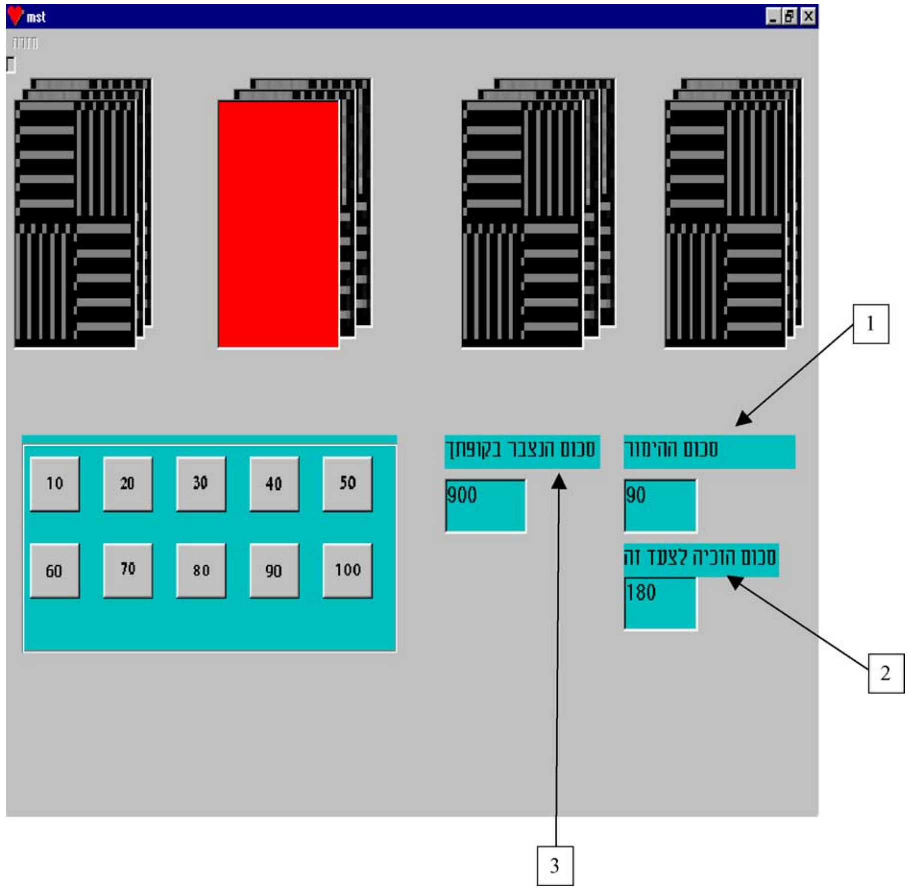

Fig. 1. The computer screen of the card betting task after the subject had clicked on a deck and the uppermost card had turned over. Translation from Hebrew: Box No. 1: "Betting sum" (90 in this example); Box No. 2: "The sum won on the current trial" (180 in this example); Box No. 3: "The sum accumulated up to the current trial" (900 in this example).

2.4. Statistical analysis

One-way ANOVAs were used to examine differences between the groups on the clinical and demographic variables, as well as on the scores on the Chance–Luck questionnaire.

Acquisition of the card betting task was assessed by (1) analyzing the frequency of bets placed on the 75%-red deck in each of the seven 20-trials blocks (of trials 11–150; the first 10 trials served as training trials). In order to achieve a near normal distribution of these data, this statistic was arcsin-transformed ($P' = 0.5[\arcsin\sqrt{X/(n+1)} + \arcsin\sqrt{(X+1)/(n+1)}]$, where X is the number of bets placed on the 75%-red deck in each block and n is the number of trials in each block) [59]. The transformed proportion of bets was analyzed using a 5 (Diagnosis) × 7 (Blocks) mixed ANOVA. (2) Analyzing the frequency of "Learners" and "Non-learners" on the last 20-trial block, using a 5 (Diagnosis) × 2 (Learners/Non-learners) χ^2-test. "Learners" were defined according to the binomial distribution as subjects who chose the 75%-red deck significantly more than expected by chance, that is, more than eight times out of 20 ("Non-learners", subjects who chose the 75%-red deck 8 times or less out of 20). In addition, in order to assess the relation between task acquisition and Chance–Luck orientation, subjects were divided into chance- or luck-oriented according to their luck score, and the transformed proportion of bets was analyzed using a 5 (Diagnosis) × 2 (Chance–Luck orientation) × 7 (Blocks) mixed ANOVA, and the frequency of "Learners" and "Non-learners" on the last 20-trial block was analyzed using a 5 (Diagnosis) × 2 (Chance–Luck orientation) × 2 (Learners/Non-learners) χ^2-test. Finally, in order to detect perseverative responding on the betting task, we checked whether the frequency of bets placed on any of the other three decks (i.e. the 25%-, 40%- and 60%-red decks) on the last block was higher than expected by chance (i.e. higher than 8).

Speed of performance on the card betting task was assessed by analyzing the average time to choose a betting sum and the average time to choose a deck, using 5 (Diagnosis) × 7 (Blocks) mixed ANOVAs (data from participants that experienced difficulties in using the mouse, and for whom the mouse was operated by the experimenter, were excluded from these statistical analyses). Because the two analyses did not yield a significant interaction between Blocks and Diagnosis, data were collapsed over blocks and analyzed using one-way ANOVAs with a main factor of Diagnosis.

Finally, correlations between the transformed proportion of bets on the 75%-red deck on the last training block and the different clinical and demographic variables were calculated.

3. Results

3.1. Demographic and clinical data

There were no significant differences between the elderly and the young MDD patients on years of education, BDI, WISPI, luck score, number of bets on the 75%-red deck, time to bet and time to choose a deck (all Ps > 0.14). We have therefore combined the data of the two MDD groups for further analysis.

There were significant differences between the five diagnostic groups in years of age, years of education, BDI score, and WISPI score (Table 1 presents the demographic and clinical data and the results of the statistical analysis).

3.2. Scores on the Chance–Luck questionnaire

There were no significant differences between the luck scores of the five diagnostic groups (mean (S.E.): control-young: 60.3 (6.2); control-elderly: 43.8 (7.5); MDD: 63.8 (7.4); OCD: 57.5 (7.1); PD: 54.3 (11.6), $F < 1$).

3.3. Acquisition of the card betting task

None of the participants in any of the groups showed perseverative responding—that is, chose the 25%-, 40%- or 60%-red decks more than expected by chance on the last training block.

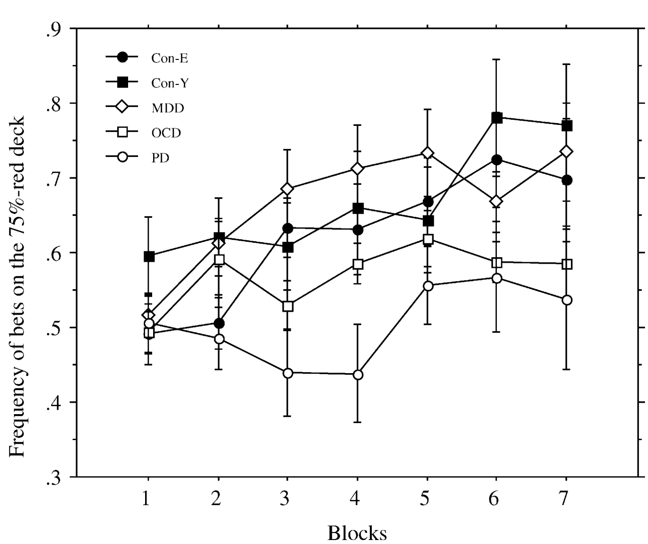

Fig. 2. Mean and standard error of the mean transformed number of bets placed on the 75%-red deck in 20-trial blocks in the five diagnostic groups. Examples for the relation between non-transformed and transformed data: 2 bets, 0.351; 5 bets, 0.537; 8 bets, 0.689; and 11 bets, 0.833.

Fig. 2 presents the mean and standard error of the transformed number of bets placed on the 75%-red deck in 20-trial blocks in the five groups. As can be seen, the frequency of bets placed on the 75%-red deck gradually increased in the control and MDD groups, whereas the performance of the PD and OCD groups remained at chance level throughout training. An ANOVA performed on these data revealed significant effects of Diagnosis, $F(4,78) = 2.813$, $P < 0.05$, and Blocks, $F(6,468) = 8.659$, $P < 0.0001$. Although the Diagnosis × Blocks interaction did not reach statistical significance, a planned contrast comparing the linear trend for the control and MDD groups versus the PD and OCD groups approached significance $F(1,78) = 3.49$, $P = 0.065$.

As groups' means can obscure individual differences in performance, and because Friedland [19] has reported that normal subjects may fail to acquire the task, we have also analyzed the frequency of "Learners" and "Non-learners" in the five diagnostic groups on the last 20-trial block (Table 2). This analysis revealed that whereas the proportion of "Learners" (i.e. of subjects choosing the 75%-red deck more than expected by chance) in the control and MDD groups was above 40%, the proportion of "Learners" in the OCD and PD groups was much lower (16.7% and 14.3%, respectively). A Diagnosis × "Learner"/"Non-learner" χ^2-test revealed mutual dependence between the two variables ($\chi^2(4) = 11.43$, $P < 0.025$). Further contrasts comparing each of the patients groups to the control group (elderly and young combined) confirmed that the frequency of "Learners" was significantly lower in the PD ($\chi^2(1) = 3.552$, $P < 0.05$) and OCD groups ($\chi^2(1) = 3.548$, $P < 0.05$).

3.4. Relations between task acquisition and Chance–Luck orientation

As there were no significant differences between the luck scores of the five diagnostic groups, participants were characterized as luck- or chance-oriented according to their ranking above or below the median luck score of the entire sample (which was 55).[1] Participants with ranking identical to the median were characterized as luck-oriented.

Fig. 3 presents the mean and standard error of the transformed number of bets placed on the 75%-red deck in 20-trial blocks in the 10 groups (Diagnosis × Chance–Luck orientation). As reported by Friedland [19], young chance-oriented control subjects gradually increased their frequency of betting on the 75%-red deck, whereas luck-oriented young control subjects performed at chance level throughout training. A

[1] The median luck score of the entire sample was used as this statistic is assumed to provide a better estimate of the population parameter than the median obtained in each diagnostic group. We would like to note that using the median of the entire sample yielded division into chance- and luck-orientation that was very similar to the division obtained by using each diagnostic group's median (the attribution of chance/luck orientation was changed for only four participants (one from each group, except for the PD group), out of the 81 participants with a luck score (luck score was missing for two PD patients).

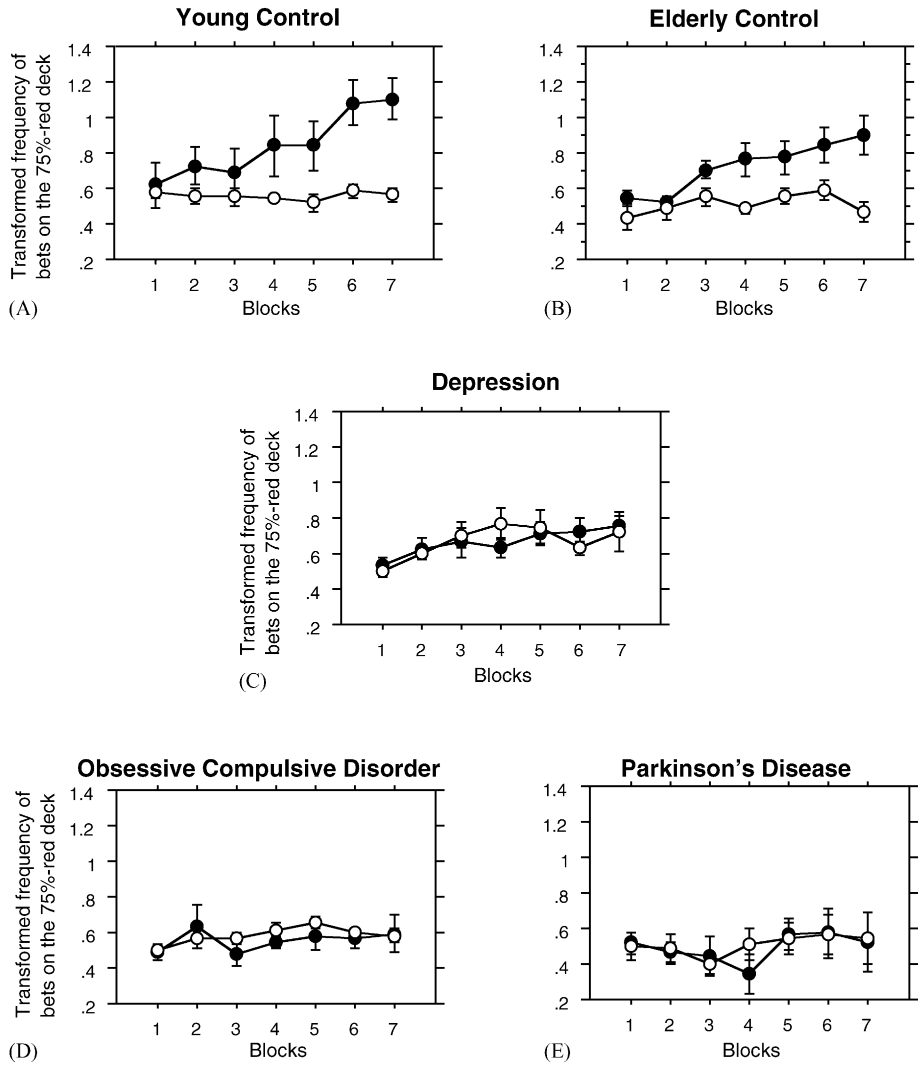

Fig. 3. Mean and standard error of the mean transformed number of bets placed on the 75%-red deck in 20-trial blocks in the (A) young control, (B) elderly control, (C) MDD, (D) OCD, and (E) PD groups (chance-oriented: full circle, luck-oriented: open circle). A 5 × 2 × 7 mixed ANOVA revealed significant effects of Diagnosis, $F(4,71) = 4.20$, $P < 0.005$; Chance–Luck orientation, $F(1,71) = 6.79$, $P < 0.02$; and Blocks, $F(6,426) = 9.85$, $P < 0.0001$, as well as significant Diagnosis × orientation ($F(4,71) = 4.00$, $P < 0.01$), orientation × blocks ($F(6,426) = 23.13$, $P < 0.01$), and Diagnosis × orientation × blocks ($F(24,426) = 1.55$, $P < 0.05$) interactions. Examples for the relation between non-transformed and transformed data: 5 bets, 0.537; 8 bets, 0.689; 11 bets, 0.833; 14 bets, 0.981; and 17 bets, 1.151.

similar pattern of results was obtained with the elderly control group, that is, chance-oriented, but not luck-oriented, elderly control subjects gradually acquired the task. In contrast, there were no differences between the performance of luck- and chance-oriented subjects in the OCD, PD, and MDD groups. In addition, the two subgroups of OCD patients and the two subgroups of PD patients performed at chance level throughout training, whereas the two subgroups of MDD patients gradually increased their frequency of betting on the 75%-red deck, albeit to a lesser extent than chance-oriented control subjects (Diagnosis × Orientation interaction $F(4,71) = 4.00$, $P < 0.01$; Diagnosis × Orientation × Block interaction $F(24,426) = 1.55$, $P < 0.05$).

Table 2
The frequency of “Learners” and “Non-learners” in the five diagnostic groups

	Young control	Elderly control	OCD	PD	MDD
Learners	**8**	**7**	**3**	**2**	**9**
Chance	7	7	1	1	4
Luck	1	0	2	1	5
Non learners	**10**	**10**	**15**	**12**	**5**
Chance	0	2	7	6	2
Luck	10	8	8	6	3

An analysis of the frequency of “Learners” and “Non-learners” in the 10 groups (Diagnosis × Orientation) on the last 20-trial block (Table 2) revealed that whereas in the two control groups most chance-oriented subjects acquired the task (young: 7/7, elderly: 7/9), and most luck-oriented subjects did not acquire the task (young: 10/11, elderly: 8/8), in

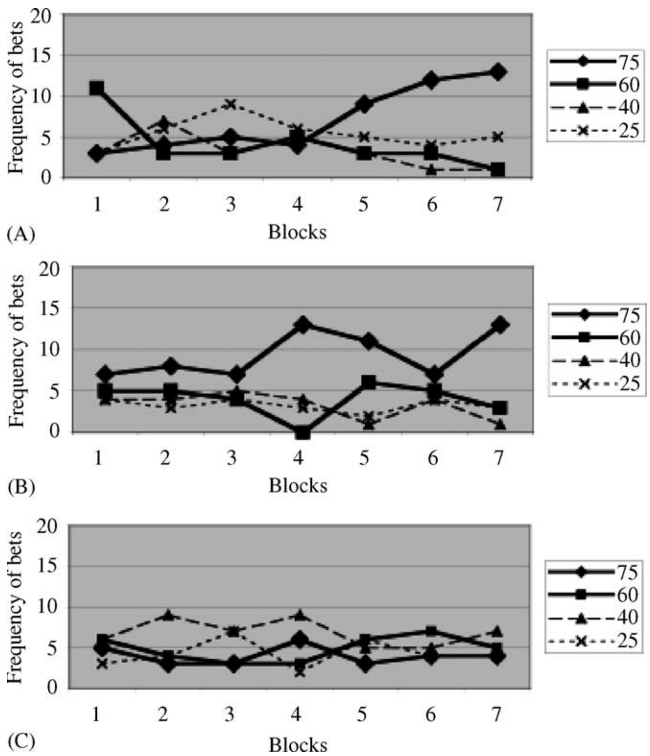

Fig. 4. The frequency of bets placed on the 75%-, 60%-, 40%- and 25%-red decks in 20-trial blocks of typical “Learners” (A and B) and a typical “Non-learner” (C).

the MDD group there was a similar proportion of “Learners” and “Non-learners” in the chance- and luck-oriented subgroups. Chance–Luck orientation also did not differentiate between “Learners” and “Non-learners” in the OCD and PD groups (the two PD patients for whom luck scores were missing performed at chance level). A three-dimensional (Diagnosis × Chance–Luck orientation × “Learner”/“Non-learner”) χ^2-test revealed mutual dependence between the three variables ($\chi^2(13) = 37.98$, $P < 0.001$). Further 2 × 2 × 2 χ^2-tests revealed that the frequency of “Learners” and “Non-learners” in the chance- and luck-oriented subgroups was different in the patients groups compared to the control groups (all Ps < 0.005).

3.5. Individual acquisition curves

The gradual increase of bets on the 75%-red deck seen in the control and MDD groups suggests that the acquisition of the card betting task depends on procedural learning. However, the curves presented in Figs. 2 and 3 were obtained by averaging over the performance of the individuals in each group and do not necessarily represent the form of the individuals’ curves. Most importantly in the present context, such a curve may also be obtained if individual curves are in the form of a step function, as would be expected from “insight” learning. Examination of the acquisition curves of each of the “Learners” reveals, however, that they show either a gradual monotonic increase of bets on the 75%-red deck (Fig. 4A) or a “zigzag”-like curve (Fig. 4B).

3.6. Performance speed

Fig. 5A and B presents the mean average time to select a betting sum and to choose a deck, respectively, in the five groups. Four MDD patients (three elderly and one young), two OCD patients, and four PD patients were not included in these analyses because they needed the experimenter’s help to operate the computer mouse. As can be seen, the young-control group had the shortest times to select the betting sum and to choose a deck, the PD group had the longest times, and the elderly-control, OCD, and MDD groups had an intermediate response speed (time-to-bet: $F(4,68) = 4.57$, $P < 0.005$, time-to-deck: $F(4,68) = 18.88$, $P < 0.0001$, see Fig. 5A and B for least significant difference post hoc comparisons).

3.7. Correlations

Table 3 presents the correlations of performance level on the betting task on the last block with the different clinical and demographic variables, in each of the five diagnostic groups. Performance level was not correlated with age, years of education, WISPI score, and BDI score in none of the groups, nor was it correlated with Y-BOCS scores in the OCD group. Performance level was also not correlated with performance

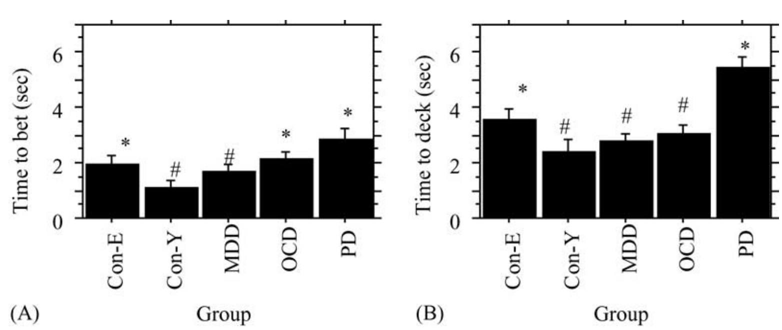

Fig. 5. Mean and standard error of the mean average time to (A) select the betting sum and (B) choose a deck in the five groups (Con-Y, young control; Con-E, elderly control; MDD, major depressive disorder; OCD, obsessive–compulsive disorder; PD, Parkinson’s disease). *Significantly different from the young-control group ($P < 0.05$). #Significantly different from the PD group ($P < 0.05$).

Table 3
Correlations of the transformed number of bets placed on the 75%-red deck in the last 20-trial block with demographic and clinical variables in the five diagnostic groups (significant correlations are depicted in bold)

	Age (years)	Education (years)	Luck score	BDI	WISPI	Y-BOCS	Time to bet	Time to deck
Elderly control	0.003 (P = 0.990, n = 17)	0.151 (P = 0.568, n = 17)	**−0.674** (P = 0.002, n = 17)	−0.489 (P = 0.450, n = 5)	0.080 (P = 0.773, n = 16)		−0.206 (P = 0.435, n = 17)	−0.342 (P = 0.183, n = 17)
Young control	−0.068 (P = 0.793, n = 17)	0.132 (P = 0.606, n = 18)	**−0.668** (P = 0.0018, n = 18)	−0.268 (P = 0.321, n = 16)	0.064 (P = 0.810, n = 17)		−0.179 (P = 0.483, n = 18)	−0.059 (P = 0.819, n = 18)
MDD	0.085 (P = 0.777, n = 14)	−0.142 (P = 0.636, n = 14)	−0.158 (P = 0.598, n = 14)	−0.150 (P = 0.616, n = 14)	0.252 (P = 0.393, n = 14)		0.064 (P = 0.866, n = 10)	0.158 (P = 0.673, n = 10)
OCD	0.176 (P = 0.492, n = 18)	0.284 (P = 0.258, n = 18)	−0.060 (P = 0.816, n = 18)	−0.087 (P = 0.743, n = 17)	0.236 (P = 0.352, n = 18)	0.143 (P = 0.590, n = 17)	−0.014 (P = 0.959, n = 16)	−0.048 (P = 0.863, n = 16)
PD	−0.162 (P = 0.556, n = 16)	−0.223 (P = 0.414, n = 16)	0.008 (P = 0.978, n = 14)	−0.258 (P = 0.456, n = 11)	0.240 (P = 0.464, n = 12)		0.400 (P = 0.203, n = 12)	0.363 (P = 0.254, n = 12)

speed in any of the groups. As can be expected from the results described above, performance level was negatively correlated with luck score in the young and elderly control groups, but not in the MDD, OCD, and PD groups.

4. Discussion

The present study replicates Friedland's [19] findings that young chance-oriented normal subjects gradually increase their frequency of bets on the 75%-red deck, whereas luck-oriented subjects continue to perform at chance level. The same pattern of results was also obtained in a group of elderly normal subjects, which, although slower to respond on each trial, acquired the task similarly to young control subjects. The gradual acquisition of the task by chance-oriented subjects (evidenced also in individual's curves) indicates that task acquisition depends on the slow and accumulating process of procedural learning. The performance pattern of luck-oriented control subjects, however, cannot be taken as a proof that these subjects did not learn the task, because we cannot rule out the possibility that luck-oriented subjects have learned the different probabilities of red cards in the different decks, but have failed to act according to this knowledge for some reason [19]. The latter does not seem to be the case, however, because informal interviews conducted with subjects following task completion have suggested that none of the subjects that performed at chance level had noticed that the different decks had different probabilities of red cards, let alone was able to describe the different probabilities of the different decks. The same was also true for subjects that have learned the task, and testifies for the task's procedural nature.

In line with the latter, and in accordance with reports in the literature (e.g. [18,26,27,42,54,55,57]), the performance level of the PD group remained at chance level throughout training. In fact, of the 16 PD patients, only 2 chose the 75%-red deck significantly more than expected by chance on the last training block. These two patients had no unique characteristics, in terms of stage of disease, medication, age, years of education, luck score, BDI score, WISPI score, and response times.

The lack of task acquisition by PD patients in the present study strengthens the possibility that acquisition of the card betting task depends on an intact procedural system, and suggests that the card betting task cannot be solved using non-procedural strategies, that is, that the PD patients were not able to compensate for their deficient procedural system by using other, non-procedural, systems (as has been demonstrated in other tasks, e.g. refs. [14,15]). The lack of task acquisition by normal luck-oriented subjects further suggests that attempts to solve the task using non-procedural strategies may interfere with task acquisition.

OCD patients also failed to acquire the card betting task. Of the 18 OCD patients, only 3 performed above chance level at the last training block. These three patients were not different from the other OCD patients in any of the other variables assessed (including, medication, age, years of education, luck score, BDI score, WISPI score, Y-BOCS score and response times).

The MDD group performed similarly to the control groups in terms of acquisition curves and the proportion of “Learners”. However, Chance–Luck orientation did not divide the MDD group into “Learners” and “Non-learners”, as it did for normal subjects (ref. [19] and the present study). As there were no significant differences between MDD “Learners” and “Non-learners” in none of the measures obtained in the present study (including, medication, luck score, age, years of education, BDI score, WISPI score and response times, all Fs < 1), the factor(s) that differentiates MDD patients into “Learners” and “Non-learners” is yet to be found.

The finding that MDD patients could learn the task suggests that the failure of OCD and PD patients to acquire the task is not a result of co-morbid depression. Lack of task acquisition in the OCD and PD groups was also not related to differences in Chance–Luck orientation, as the OCD and PD groups were not different from the other groups on this measure. Nor was it a result of response perseveration, as none of the patients chose one of the other three decks more than expected by chance.

The present results demonstrate that OCD and PD patients are impaired on a procedural learning task for which explicit processing probably impairs, rather than assists, acquisition. With regards to PD patients, their deficit likely reflects a dysfunctional procedural learning mechanism following the degeneration of the nigrostriatal dopaminergic pathway (e.g. [26,34,54,55]). Dysfunctional procedural learning following striatal dysfunction may also account for the impaired performance of OCD patients in the card betting task. Indeed, on the basis of their finding of lack of striatal activation in a group of OCD patients performing a procedural task, Rauch et al. [39] concluded that the striatal system is dysfunctional in OCD. These authors have attributed the successful performance of the patients on the procedural task to the abnormal hippocampal activation found in these patients. Interestingly, hippocampal, rather than striatal, activation was also observed in PD patients while they were successfully performing a procedural learning task [14,15]. Because the hippocampal system is known to be involved in explicit processing (for review see [51]), these patterns of activation were taken to suggest that OCD [39] and PD patients [14,15] overcame their dysfunctional striatal system by recruiting the hippocampal explicit processing system.

As noted in Introduction, however, performance at chance level on the card betting task does not necessarily reflect a general inability to acquire procedural knowledge (as evident in the failure of normal luck-oriented subjects to acquire the task), but can also result from the inappropriate use of a non-procedural strategy. An alternative interpretation of the lack of task acquisition by OCD patients is therefore that it is a result of exaggerated explicit processing which interfered with the functioning of the procedural system. This possibility fits well the cognitive-behavioral analysis of OCD provided by Salkovskis [44,45], according to which misinterpretation of normal intrusive thoughts is likely to result in an increase in deliberate efforts to exert control, which may lead OCD patients to “attempt to monitor closely and take control over processes that would otherwise operate in automatic and well-practiced ways. In many situations, this would result in poorer perceived performance, which would sometimes be accompanied by actual performance impairments as well as increased preoccupation” ([44], p. 40).

In line with the possibility that the impaired performance of the OCD patients was a results of exaggerated explicit processing, is evidence suggesting that under some conditions activation of the hippocampal system may interfere with striatal-mediated procedural learning. Thus, in normal humans, deactivation of the hippocampus and activation of the striatum has been reported during the acquisition of procedural tasks [15,35–37], and has been taken to suggest that hippocampal suppression is necessary for optimum performance of these tasks [15]. In animals, lesions to the hippocampal system have been shown to result in improved performance in procedural tasks known to depend on the striatal system [17,32,49,52]. It is therefore possible that OCD patients failed to deactivate the hippocampal system, and that this has led to a dysfunction of the striatal system, and therefore to impaired performance on the card betting task.

We would like to note that the two interpretations of our results, that is, that the striatal system is dysfunctional and that an inappropriate processing in the hippocampal system interferes with the functioning of the striatal system, are not necessarily mutually exclusive. It is also possible that they interact, so that as a result of a primary deficit in the striatal system there is an imbalance between the two systems so that the hippocampal system is overactive. Hippocampal recruitment may serve to partially overcome striatal dysfunction under some conditions, but may further contribute to impaired performance under other conditions.

Appendix A. Instructions for the card betting game (translated from Hebrew)

Shortly a betting card game will begin. On each trial, you will be asked to choose a sum between 10 and 100 points and to wage it on one of four card decks. The residual points out of the initial 100 points, which you choose not to bet on will be credited to your account. At each trial, the max amount you can wage on is 100 points. After placing your bet, you will be required to choose, using the computer mouse, one out of four decks of cards in order to turn over its uppermost card.

The winning card in this game is red. If the uppermost card in the deck you have chosen turns out to be red, the betting sum you chose for that trial will be doubled. If it turns out to be blue, the betting sum of that trial will be lost. During this game you are required to choose a betting sum and right afterwards to choose a deck. Your goal is to earn as much points as possible.

Appendix B. The Chance–Luck questionnaire (translated from Hebrew)

Instructions: In this questionnaire you will find short portrayals of several events. You are asked to account for the outcome of each event in terms of luck and chance, by splitting 100 points between these two factors (luck and chance), according to their relative influence over the outcome (the greater the effect any factor has over the outcome the larger number of points out of the 100 will be allotted to it). You are asked to divide the entire amount of 100 points between these two factors.

1. You were about to take a trip abroad. Upon arrival at the airport you realized that the time of departure indicated on your ticket was incorrect, and that your flight had departed already. You took the next scheduled flight. After landing you found out that your original flight had been hijacked en route.
   Please divide 100 points between chance and luck to indicate the weight of the two factors in accounting for the outcome:
   $\underset{\text{Chance}}{\underline{\qquad}} + \underset{\text{Luck}}{\underline{\qquad}} = 100$
2. You were working in a certain military office during your army service. You have asked to be transferred to another office due to personal reasons and your request was approved. A day after your transfer, a large bomb exploded in your old building, resulting in many casualties and damage to property.
   Please divide 100 points between chance and luck to indicate the weight of the two factors in accounting for the outcome:
   $\underset{\text{Chance}}{\underline{\qquad}} + \underset{\text{Luck}}{\underline{\qquad}} = 100$
3. You were driving your car while a truck driver who is moving towards you in the opposite lane fell asleep. His truck crossed into your lane and hit the car in front of you. Had it crossed a few milliseconds later, it would have been you. . .
   Please divide 100 points between chance and luck to indicate the weight of the two factors in accounting for the outcome:
   $\underset{\text{Chance}}{\underline{\qquad}} + \underset{\text{Luck}}{\underline{\qquad}} = 100$
4. You live in the Tel-Aviv area. During the Gulf War, a neighboring building was hit by a direct attack of a SCAD missile.
   Please divide 100 points between chance and luck to indicate the weight of the two factors in accounting for the outcome:
   $\underset{\text{Chance}}{\underline{\qquad}} + \underset{\text{Luck}}{\underline{\qquad}} = 100$

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