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# Decision Making and Executive Functions in REM Sleep Behavior Disorder

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**Study Objectives:** This study was designed to assess decision making and executive functions in patients with idiopathic REM sleep behavior disorder (iRBD). IRBD is often seen as an early sign of later evolving neurodegenerative disease, most importantly Parkinson disease (PD) and Lewy body dementia (DLB). It has been proposed that iRBD patients show a cognitive profile similar to patients with PD.

**Design:** All participants performed an extensive test battery tapping executive functions as well as the IOWA gambling task, which measures decision making under ambiguity.

**Setting:** University hospital sleep disorders center.

**Participants:** 16 iRBD patients and 45 age- and education-matched controls.

**Intervention**: N.A.

**Measurements and Results:** Compared with controls, iRBD patients showed disadvantageous decision making under ambiguity and did not learn by feedback over the task. IRBD patients' decision pattern was characterized by the lack of a consistent strategy, as indicated by frequent shifts between the single choices. A high proportion of iRBD patients (75%) showed random performance or worse even at the end of the task. No group differences were found in tasks assessing information sampling, flexibility and categorization, problem solving, and impulsivity.

**Conclusions:** As suggested by the present investigation, iRBD patients may show difficulties in decision making under ambiguity in a stage when other cognitive functions are relatively well preserved. Whether this is driven by subgroups of patients prone to develop PD or DLB has to be assessed by follow-up investigations.

**Keywords:** iRBD, IOWA gambling task, decision making, executive functions

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## INTRODUCTION

REM sleep behavior disorder (RBD) is a parasomnia characterized by loss of normal skeletal muscle atonia during REM sleep with prominent motor activity and dreaming.[1] Typically, RBD patients show dream-enacting behaviors (e.g., shouting, punching) related to unpleasant and sometimes violent dreams. Clinical and pathological data suggest that iRBD may be the earliest manifestation of neurodegenerative disorders such as Parkinson disease (PD),[2,3] Lewy body dementia (DLB),[4] or multiple system atrophy (MSA),[5] which may evolve in iRBD patients at a variable delay.[6-8] Since both PD and DLB are associated with cognitive dysfunction, subtle cognitive changes might also be expected in subjects with iRBD.

So far, a few studies have assessed neuropsychological functions of iRBD patients. Ferini-Strambi et al.[9] found impairments in tasks of visuo-constructive abilities and visuo-spatial learning in a group of 17 iRBD patients. A 2-year follow-up study in 24 cognitively asymptomatic iRBD patients revealed worsening in memory and visuo-constructive functions over time.[10] Terzaghi et al.[11] reported low performance of 23 iRBD patients in working memory, complex figure recall, and logical memory. Gagnon et al.[12] found a high incidence of mild cognitive impairment (MCI) in 32 iRBD patients and 22 PD patients with RBD. The main subtype of MCI in iRBD patients was non-amnestic with impaired executive functions. As a group, iRBD patients performed lower than controls in tasks of working memory, set shifting, verbal fluency, and verbal memory.[12,13] Massicotte-Marquez et al.[14] reported reduced executive functions, attention, and verbal memory, as well as EEG slowing during wakefulness in 14 iRBD patients. A recent investigation[15] found marked EEG slowing in iRBD patients with MCI and suggested that slowing of cortical EEG may indicate the short-term development of cognitive dysfunction. Summing up, neuropsychological investigations yielded only partially consistent results as regards a specific pattern of dysfunction. While three studies emphasized impairments in visuo-constructive abilities, visuo-spatial learning, or visuo-spatial memory,[9-11] other investigations stressed deficits in executive functions.[12-14] Despite these differences, all neuropsychological studies so far point to the similarities between the neuropsychological profile of RBD patients and the cognitive deficits typically associated with PD or DLB. They also agree that cognitive deficits might serve as early markers and could lead to presymptomatic identification of an underlying neurodegenerative disease in the future.[9,12]

Decision making is often found to be impaired in PD.[16-21] Deficits in decision making under ambiguity have been attributed to a dysfunction of the limbic fronto-striatal loop,[22] which is involved in risk and reward processing, learning from feedback, emotional regulation, and control. It is important to note, however, that performance in decision making is influenced by several factors including the stage of the disease, basal levels of dopamine function,[23] dopaminergic treatment,[23,24] as well as the presence or absence of executive function deficits.[25] Moreover, the nature of the decision situation (decision under ambiguity

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versus decision under known risk) and the complexity of the given task may account for differences in performance.[20,26]

Based on reported similarities between iRBD and PD patients' cognitive profiles,[9-12] we comprehensively assessed executive functions and decision making under ambiguity in iRBD patients.

## METHODS

### Participants

The study included 16 iRBD patients (13 men, 3 women) with a mean age of 65.2 ± 7.6 years. Mean RBD duration was 8.9 ± 7.1 years. Mean duration of education was 11.3 ± 2.8 years (range 8-17 years). Patients were compared to 45 healthy participants (22 men, 23 women) with a mean age of 63.9 ± 9.6 years and a mean duration of education of 11.8 ± 3.4 years (range 8-17 years). All iRBD patients and healthy controls > 60 years performed the Mini-Mental state examination (iRBD patients: 28.4 ± 1.4; controls: 28.7 ± 1.3). Groups were comparable in terms of age, education, and Mini-Mental state examination score (P values > 0.1). In all iRBD subjects, the diagnosis of RBD required (i) history of dream-enacting behaviors and (ii) nocturnal video-polysomnographic demonstration of prominent tonic and/or phasic EMG activity in the SINBAR EMG montage[27,28] associated with abnormal behaviors and absence of electroencephalographic epileptiform activity during REM sleep.[29] None of the patients fulfilled the criteria for dementia from *Diagnostic and Statistical Manual of Mental Disorders, 4th edition* or the UK Brain Bank criteria for Parkinson disease. Exclusion criteria were evidence of central nervous system comorbidities revealed by history (e.g., history of stroke) or clinical neurological examination, evidence of psychiatric comorbidity or untreated sleep apnea syndrome. Six patients received low doses of clonazepam (0.25-0.75 mg/day). No other medication possibly influencing cognitive processes was given.

In order to exclude major cognitive impairment, iRBD patients performed a short battery of neuropsychological background tests assessing naming to confrontation, verbal and figural episodic memory, visuo-constructive abilities, executive functions (CERAD Plus Battery [www.memoryclinic.ch],[30] Frontal Assessment Battery,[31,32] clock drawing) and a vocabulary test allowing the estimation of verbal intelligence.[33] Patients also responded to a questionnaire on anxiety and depression (HADS-D).[34] All median scores were in the average range of standardized norms, and no patient fulfilled the criteria of dementia.

The study was approved by the ethics committee of Innsbruck Medical University. Subjects' written informed consent was obtained according to the Declaration of Helsinki.

### Experimental Tasks

#### *Iowa Gambling Task computerized version (IGT)[35]*

The IGT measures decision making under initial ambiguity. In the IGT, 4 decks of cards are presented, which are labelled in a row A, B, C, and D. Participants are required to select one card at the time through mouse click for a total of 100 card selections. The selection of a card from decks A and B results in large gains of money. These gains are, however, followed by a large penalty at certain unpredictable times, so that the accumulated penalties are larger than the accumulated gains. Decks A and B are therefore disadvantageous in the long run. The selection of a card from decks C and D produces small immediate gains of money. The unpredictable losses are also small for them, so that the accumulated penalties are smaller than the accumulated gains. Decks C and D are the advantageous decks in the long run. Following convention, performance is analyzed by dividing the 100 trials into 5 blocks of 20 card selections and calculating the difference (*net score*) between the number of selections from advantageous decks (C+D) and the number of selections from disadvantageous decks (A+B). For each block, we also calculate the number of shifts made between decks. An analysis by individual compares the distribution of advantageous and disadvantageous selections with a random distribution by means of binomial test. Since learning over the task is essential, we included only the last 2 blocks (i.e., 40 card selections) in this analysis. On the basis of this analysis, participants' performance in the last 2 blocks was classified as advantageous if they had a net score ≥ 14 ((C+D)-(A+B) ≥ +14)) in the last 2 blocks; as disadvantageous if they had a net score of -14 or less ((C+D)-(A+B) ≤ -14)); or as random (net score between -14 and +14).

#### *Information Sampling Task (IST)[36]*

The IST assesses information sampling before making a decision and reflection impulsivity. The task is described in detail in Clark et al.[37] (for descriptions of all CANTAB tasks and interactive demos see also http://www.cantab.com/cantab-tests.asp). On each trial, participants are presented with a 5 × 5 matrix of gray boxes, with 2 larger colored panels below at the foot of the screen. Touching a gray box causes the box to reveal one of the 2 colors. Participants are instructed to decide the box color in the majority of boxes. There are 2 conditions (each 10 trials), with condition order counterbalanced across subjects. In the fixed win (FW) condition, the subject wins or loses 100 points on each trial, irrespective of the number of boxes opened. In the decreasing win (DW) condition, the win decreases from 250 points in 10 point steps with every box opened. In case of an incorrect decision, participants lose 100 points, regardless of the number of boxes opened. Performance on the IST is indexed by the number of boxes opened in each condition and by the probability (P) of the subject being correct at the point of decision. In the present study we also analyzed the number of discrimination errors. Discrimination errors are those trials in which the subject chooses a color that was not in the majority of boxes at the point of decision.

#### *Intra/Extra Dimensional Shift (IED)*

The IED taps mental flexibility, categorization, and set-shifting. The IED[36,38,39] requires the participants to learn a series of 2 alternative forced-choice discriminations using feedback provided by the computer. After 6 correct responses, the stimuli and/or rules are changed. There are 9 stages in fixed order, requiring intra- and extra-dimensional set shifting as well as reversal learning. We analyze the number of total errors adjusted for the number of stages completed, the number of Pre-ED errors (errors made prior to the extra-dimensional shift), of EDS errors (errors in the extra-dimensional stage), and of reversal errors (sum of errors committed in reversal stages 2, 5, 7, and 9).

#### *One Touch Stockings of Cambridge (OTS)[36,40]*

The OTS is a variant of the Tower of London task and measures complex problem solving. In the OTS subjects are not

asked to execute the appropriate moves in order to achieve a solution, but to solve the problem mentally and to indicate the number of necessary moves. Performance in the OTS is indexed by problems solved on first choice, by the mean number of choices to a correct response, the mean latency to the first choice, and the mean latency to the correct choice.

#### *Go-NoGo Task*

The task measures response inhibition (adapted from Fox et al.[41]). In this task, different colored letters are presented on the screen (N, J, W, O, and E). Go stimuli consist of letters N, J, and W presented in blue or the letter O presented in red, green, or yellow. The NoGo stimuli include O presented in blue and E presented in pink. Subjects are instructed to press as fast as possible a button following the Go stimuli and to withhold a response to the NoGo stimuli. In the present study we analyzed the proportion of correctly answered Go trials and the proportion of correctly answered NoGo trials. We also analyzed the proportion of participants in each group scoring below a cutoff of 90% correct responses in the Go trials and the NoGo trials.

### Statistical Analysis

Data were analyzed with parametric statistics where normality assumptions were met. Otherwise, nonparametric tests were used. Mean scores and standard deviations are reported for the tasks where parametric statistics were applied; median scores and interquartile ranges are reported for the tasks where nonparametric statistics were used. Greenhouse-Geisser correction was applied for repeated-measures ANOVA where assumption of sphericity was violated. One-way ANOVA was corrected where a violation of the assumption of homogeneity of variance in the data was detected. Frequency distributions were investigated by binomial test or Pearson $\chi^2$ test where appropriate. A Spearman rank-order correlation analysis between decision making tasks (net score in block 5 of the IGT, mean P(correct) in FW condition of the IST, mean P(correct) in DW condition of the IST), and executive function tasks (accuracy rate with NoGo stimuli, reversal errors in the IED, ED errors in the IED, number of problems solved on first choice in the OTS) was carried out for the iRBD patient group. Applying Bonferroni correction, significance level was set at P = 0.004.

## RESULTS

### Decisions under Ambiguity: Iowa Gambling Task (IGT)

Overall, healthy controls showed learning over the task, while iRBD patients remained at random level. A mixed ANOVA of the net score indicated a significant main effect of block, $F_{3.0,175.9} = 15.55$, MSE = 867.54, P < 0.001, and a significant interaction of block with group, $F_{3.0,175.9} = 2.66$, MSE = 148.52, P = 0.05. The main effect of group was not significant, though iRBD patients had lower scores (iRBD patients: mean net score 6.38 ± 25.06; healthy controls: mean net score 18.36 ± 27.54). As shown in Figure 1A, healthy controls made significantly more advantageous choices than iRBD patients in the last block of the task (block 5, $F_{1,59} = 4.00$, MSE = 340.65, P = 0.050), but not in the first block (P = 0.601) (see footnote 1 following article).

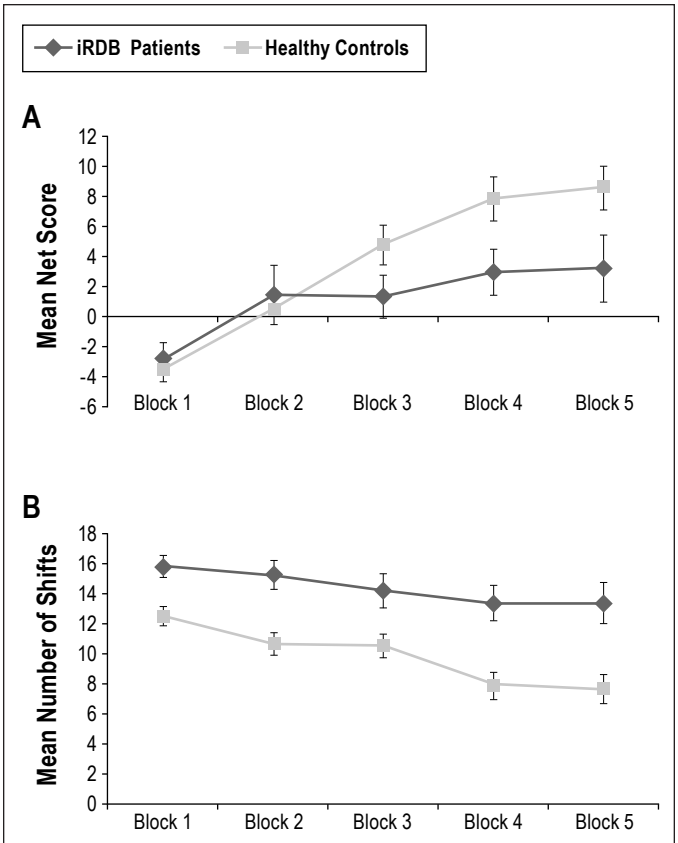


**Figure 1**—Mean net score **(A)** and mean number of shifts **(B)** as a function of group (healthy controls, iRBD patients) and block. Bars indicate the standard error of the mean.

We also analyzed the number of shifts between the 4 different decks. iRBD patients shifted overall more frequently between decks than healthy controls, thus showing less consistent behavior (iRBD patients: mean number of shifts 71.69 ± 17.80; healthy controls: mean number of shifts 48.87 ± 21.70). A mixed ANOVA revealed significant main effects of block, $F_{3.2,188.7} = 10.77$, MSE = 143.33, P < 0.001, and group, $F_{1,59} = 14.24$, MSE = 1229.41, P < 0.001, but no significant interaction, P = 0.282 (Figure 1B).

An analysis at the single subject level revealed significantly better performance of the control group. In the last 2 blocks of the task, the frequency of advantageous and disadvantageous selections did not differ from a random distribution for 10 iRBD patients (62.50%) and for 16 controls (35.56%). Four iRBD patients (25.00%) and 27 controls (60.00%) showed an advantageous decision pattern, while 2 iRBD patients (12.50%) and 2 controls (4.40%) showed a markedly disadvantageous decision pattern. The distribution of advantageous, disadvantageous and random performance significantly differed between iRBD patients and healthy controls, $\chi^2 = 6.02$, P = 0.049.

### Information Sampling and Reflection Impulsivity: Information Sampling Task (IST)

In this task we analyzed the probability of making a correct choice at the point of decision and did not find differences between iRBD and control group. A mixed ANOVA (see footnote 2 following article) on the mean P(correct) value indicated a

significant main effect of condition (fixed win, decreasing win), $F_{1,59} = 12.67$, MSE = 0.05, P = 0.001, whereas the main effect of group and the 2-way interaction were not significant, P values > 0.1. The probability of making a correct choice at the point of decision was higher in the FW condition than in the DW condition (Table 1). The analysis of the mean number of open boxes per trial revealed the same pattern as the analysis of the mean P(correct) variable. Groups were also comparable in the number of discrimination errors (Mann-Whitney U-test, P values > 0.1; Table 2) and in terms of mean response latencies.

### Flexibility and Categorization: Intra/Extra Dimensional Set Shift (IED)

In summary, iRBD patients and healthy controls performed the IED task comparably accurately. Results indicated that 12 iRBD patients (75.0%) and 35 controls (77.8%) completed all stages of the task ($\chi^2$ test, P > 0.1). There were no significant group differences in the number of trials needed to complete each single stage of the task, Mann-Whitney U-tests, Ps > 0.1. No significant group differences were found in the number of errors (Table 2), Mann-Whitney U-tests, Ps > 0.1.

### Problem Solving: One Touch Stockings of Cambridge (OTS)

iRBD patients and healthy controls performed comparably on this task (number of problems solved on first choice, mean number of choices to correct, mean latency to first choice, mean latency to correct; Mann-Whitney U-tests, Ps > 0.1; Table 2).

### Impulsivity: Go-NoGo Task

Groups' performance was comparable in this task.

**Table 1**—Means and standard deviations for healthy controls and iRBD patients in the IGT and the IST

| | Healthy Controls | | iRBD Patients | |
|---|---|---|---|---|
| | M | SD | M | SD |
| **IOWA Gambling Task (IGT)** | | | | |
| Total Net Score | 18.36 | 27.54 | 6.38 | 25.06 |
| Shifts between decks ABCD | 48.87 | 21.70 | 71.69 | 17.80 |
| **Information Sampling Task (IST)** | | | | |
| FW Condition | | | | |
| Mean P (correct) | 0.80 | 0.10 | 0.79 | 0.11 |
| Mean number of boxes opened / trial | 13.57 | 4.70 | 13.99 | 5.34 |
| DW Condition | | | | |
| Mean P (correct) | 0.76 | 0.07 | 0.74 | 0.08 |
| Mean number of boxes opened / trial | 11.12 | 4.10 | 10.82 | 4.25 |

#### *Go stimuli*

The proportion of iRBD patients performing without errors (8/15 (see footnote 3 following article), 53.3%) was comparable to that of healthy controls (30/44, 68.18%), $\chi^2$ test, P > 0.1. Only one iRBD patient and two controls obtained an accuracy rate < 90%.

#### *NoGo stimuli*

Two healthy participants and 2 iRBD patients performed without errors. Thirty controls (68.18%) and 12 iRBD patients (80.0%) obtained a score < 90%. The proportion of iRBD patients obtaining a score < 90% was comparable to that of healthy controls, $\chi^2$ test, P > 0.1. Analysis of accuracy scores by Mann-Whitney

**Table 2**—Medians and interquartile ranges for healthy controls and iRBD patients in the IST, IED, OTS, and Go-NoGo Task

| | Healthy Controls | | | iRBD Patients | | |
|---|---|---|---|---|---|---|
| | Mnd | Q.25 | Q.75 | Mnd | Q.25 | Q.75 |
| **Information Sampling Task (IST)** | | | | | | |
| FW Condition | | | | | | |
| Discrimination errors | 0.00 | 0.00 | 1.00 | 1.00 | 0.00 | 1.00 |
| Mean box opening latency (ms) | 1,269.67 | 886.91 | 1,837.71 | 1,157.86 | 967.93 | 2,180.53 |
| DW Condition | | | | | | |
| Discrimination errors | 0.00 | 0.00 | 1.00 | 0.50 | 0.00 | 1.00 |
| Mean box opening latency (ms) | 1,711.66 | 1,358.15 | 2,901.25 | 2,262.94 | 1,422.98 | 2,675.37 |
| **Intra/Extra Dimensional Set Shifts (IED)** | | | | | | |
| Total errors (adjusted) | 16.00 | 11.00 | 45.00 | 17.50 | 11.00 | 42.50 |
| Pre-ED errors | 6.00 | 5.00 | 10.00 | 5.50 | 4.00 | 7.00 |
| EDS errors | 4.00 | 2.50 | 17.50 | 7.00 | 2.50 | 20.50 |
| Reversal errors | 6.00 | 4.00 | 7.00 | 4.00 | 4.00 | 5.50 |
| **One Touch Stockings of Cambridge (OTS)** | | | | | | |
| Number of problems solved on first choice | 18.00 | 15.50 | 18.50 | 18.00 | 16.00 | 18.00 |
| Mean number of choices to correct | 1.15 | 1.10 | 1.25 | 1.13 | 1.10 | 1.25 |
| Mean latency to first choice (ms) | 13,277.50 | 9,637.80 | 18,330.23 | 16,181.50 | 13,359.28 | 23,708.25 |
| Mean latency to correct (ms) | 17,118.75 | 11,022.85 | 23,837.53 | 21,469.10 | 14,832.08 | 27,810.88 |
| **Go-NoGo task** | | | | | | |
| Go stimuli (% correct) | 100.00 | 98.89 | 100.00 | 100.00 | 97.78 | 100.00 |
| NoGo stimuli (% correct) | 83.33 | 73.33 | 90.00 | 83.33 | 70.00 | 86.67 |

U-test confirmed comparable performance of the 2 groups (Table 2).

### Correlation Analysis

A Spearman rank-order correlation analysis indicated no significant correlation between the measures of decision making and the executive function measures in the iRBD group. However, this result may be biased by the small sample size.

## DISCUSSION

To the best of our knowledge, this is the first study investigating decision making under initial ambiguity in iRBD. A high proportion of iRBD patients did not show learning over the task as healthy controls did and showed random performance even at the end of the task. IRBD patients' disadvantageous decision pattern was characterized by the lack of a consistent strategy as indicated by frequent shifts between the single choices. This result suggests that deficits in learning from feedback and in maintaining an advantageous strategy, rather than perseveration of risky choices, caused the disadvantageous outcome. Good performance in the information sampling task also suggests adequate risk processing in the iRBD group. Patients gathered information to the same extent as healthy controls and tolerated comparable levels of uncertainty when making a decision. That means simple risk processing was comparable between the iRBD and control group.

In line with previous studies emphasizing similarities between cognitive profiles in iRBD and PD,[9-12] decision making under ambiguity as seen in iRBD patients in this study was comparable to what we observed in cognitively well-functioning PD patients.[20] In PD patients, deficits in decision making under ambiguity have mostly been attributed to a dysfunction of the limbic fronto-striatal loop.[22] The dopaminergic system is critically involved in reward experience and reward prediction[42] and regulates learning from feedback as well as reversal learning.[43,44] Both types of learning are essential in the Iowa Gambling Task—subjects have to adapt their choices to losses and gains and have to switch between choices in order to maximize their reward. Indeed, subtle structural or functional alterations of the dopaminergic system have been demonstrated even in the idiopathic form of RBD.[45-52] Hypothetically, these alterations might account for iRBD patients' deficits in decision making. However, we in no way suggest that difficulties in decision making under ambiguity are specific for iRBD or PD. Decision making under ambiguity relies on several cognitive components and involves an extended network of fronto-striatal and limbic structures as well as neurotransmitter systems.

The present investigation suggests that iRBD patients may show difficulties in decision making under ambiguity in a stage when other cognitive functions are well preserved. The neuropsychological background testing evidenced no major cognitive impairment and the iRBD group overall performed well in the battery of computerized tasks (CANTAB)[36] assessing several executive functions (information sampling and reflection impulsivity, set-shifting, working memory, and problem solving). We thus assume that the present patient sample indeed was cognitively relatively well performing. Whether difficulties in decision making have a predictive value for developing more pervasive cognitive deficits in the context of PD or DLB in later years has to be assessed by longitudinal investigations. Furthermore, it is open for investigation whether these difficulties have an impact on everyday decision making. Possibly, overall good cognitive functioning, intact reasoning, adequate information seeking, as well as risk processing allow patients to compensate for their deficits in implicit learning from feedback and in making decisions under ambiguous conditions.

## FOOTNOTES

1. In order to exclude gender effects, an analysis comparing only male iRBD patients (n = 13) with age- and education-matched male subjects from the control group (n = 20) was performed. While the net scores did not differ between groups in block 1 (Mann-Whitney U-test, $P > 0.1$; median scores: controls -4, iRBD -2), controls performed significantly better in block 5 (Mann-Whitney U-test, $P = 0.043$; median scores: controls 11, iRBD 2). A further analysis on medication effects compared IGT performance between patients with clonazepam (n = 6) and patients without medication (n = 10). Net scores did not differ in any block (Mann-Whitney U-tests, $Ps > 0.1$; median scores in block 5: group with medication 4, group without medication 2).
2. A first analysis indicated that the effect of the presentation order (FW condition first, DW condition first) was not significant. Therefore, we did not further take into account this factor in the following analysis.
3. One control and one iRBD participant did not perform the Go-Nogo task.

## ABBREVIATIONS

DLB, dementia with Lewy bodies
DW, decreasing win
ED, extra-dimensional
EDS, extra-dimensional stage
FAB, frontal assessment battery
FW, fixed win
iRBD, idiopathic REM sleep behavior disorder
IED, Intra/Extra Dimensional Set Shift
IGT, IOWA gambling task
IST, information sampling task
MCI, mild cognitive impairment
MSA, multiple system atrophy
OTS, One Touch Stockings of Cambridge
PD, Parkinson disease
RBD, REM sleep behavior disorder

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## DISCLOSURE STATEMENT

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