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1 **Executive functioning and risk-taking behavior in Parkinson's disease patients**
2 **with impulse control disorders**

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32
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35

36

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56

57

58

59 **ABSTRACT**

60 Background: Impulse control disorders (ICD) are common in Parkinson's disease (PD) and are
61 associated with dopaminergic medication. The purpose of this study was to investigate executive
62 function and risk-taking behavior in PD patients with ICD.

63 Methods: 17 PD patients with ICD (ICD-PD) were compared to 20 PD patients without ICD
64 (CTRL-PD) using neuropsychological and experimental tasks. Executive functions were assessed
65 using standard executive testing (Conner's Performance Test, Modified Wisconsin Card Sorting
66 Test, Trail Making Test and phonological verbal fluency). Subjects were also submitted to an
67 experimental gambling task consisted of three decks of money cards: neutral deck (equal
68 opportunity for gains as losses), winning deck (small amount of money with a positive balance) and
69 loser deck (high amount of money with a negative balance), evaluating risk-taking behavior
70 (number of cards picked in each deck) and valuation of the reward (subjective appreciation of the
71 value of each deck).

72 Results: There was no significant difference in executive functioning between groups. Both groups
73 selected more cards in the losing deck (high amount of money) as compared to the neutral deck
74 (Mann-Whitney test, ICD-PD, $p=0,02$; CTRL-PD, $p=0,003$) and to the winning deck (Mann-
75 Whitney test, ICD-PD $p=0,0001$; CTRL-PD $p=0,003$), suggesting an increased risk-taking behavior.
76 Interestingly, we found that ICD-PD patients estimated the value of decks differently from CTRL-
77 PD patients, taking into account mainly the positive reinforced value of the decks (Mann Whitney
78 test, $p=0,04$).

79 Discussion: This study showed that executive pattern and risk-taking behavior are similar between
80 ICD-PD and CTRL-PD patients. However, ICD-PD patients showed a specific deficit of the
81 subjective estimation of the reward. Links between this deficit and metacognitive skills are
82 discussed.

83

84 INTRODUCTION

85

86 Impulse control disorders (ICD) are behavioral disorders characterized by the failure to
87 resist an impulse, inability to cut down and unsuccessful attempts to control a specific behavior
88 (Evans et al. 2009). In Parkinson's disease (PD), the lifetime prevalence of ICD is about 14%
89 (Weintraub et al. 2010). The most frequent ICD in PD are pathological gambling (PG),
90 hypersexuality (HS), compulsive shopping (CS) and compulsive eating (CE) (Evans et al. 2009;
91 Weintraub et al. 2010). The high prevalence of ICD in PD has been associated to the dopaminergic
92 treatment, particularly to dopamine agonists (DA) (Weintraub et al. 2010). A possible hypothesis for
93 the association between DA treatment and ICD involves their relative selectivity of D2-D3
94 dopamine-receptor. Those receptors are particularly abundant in the ventral striatum known to play
95 a role in behavioral addiction and substance use disorders (Gurevich et al. 1999). In addition to DA
96 exposure, clinical risk factors associated with ICD in PD are male gender, younger age, younger age
97 at onset of PD and longer disease duration, personal or family history of alcohol or psychiatric
98 disorders, high novelty seeking personalities, impulsivity and alexithymia traits (Weintraub et al.
99 2010; Voon et al. 2011a; Goerlich-Dobre et al. 2014). Although the pathological mechanisms
100 remain largely unknown, the level of dopamine denervation of the fronto-striatal circuitry, involved
101 in executive as well as decision-making functions, has been associated to ICD in PD (Cilia et al.
102 2011; Vriend et al. 2014). Especially, Cilia et al. (2011) found decreased prefrontal cortex,
103 cingulate, insula, parahippocampal gyrus and striatal resting perfusion with increasing gambling
104 severity in PG patients. These regions are involved in reward and risk processing, error detection,
105 learning, decision-making and impulse control. Furthermore, the authors showed an anterior
106 cingulate cortex-striatum disconnection, which could underline a specific impairment in ability to
107 shift behavior after negative outcomes, leading patients to continue their behavior despite dramatic
108 consequences.

109 A growing amount of studies attempted to investigate the cognitive characteristics associated
110 with ICD in PD. Some studies found preserved cognitive functions (Siri et al. 2010; Djamshidian et
111 al. 2011a; Mack et al. 2013). By contrast, a significant association between executive dysfunction
112 and ICD has been demonstrated in few studies (Djamshidian et al. 2010; Vitale et al. 2011; Poletti et
113 al. 2012). Especially, PD patients with PG had more severe impairments in retrieval of verbal and
114 visuo-spatial information and cognitive flexibility (Santangelo et al. 2009). However, there were
115 several limitations in these studies including materials used to explore cognitive functioning, often
116 limited to working memory or global executive assessment.

117 Decision-making, connoting the process of choosing under ambiguous or risky situations the
118 optimal selection in terms of rewarding or punishing outcomes between several alternative course

119 of actions (Paulus 2005), has been well documented in PD patients (Delazer et al. 2009) and has
120 been specifically involved in PD patients with ICD (Djamshidian et al. 2010; Rao et al. 2010; Rossi
121 et al. 2010; Steeves et al. 2009). Especially, Rossi et al. (2010) found that PD patients with PG
122 obtained poorer performances in a risk-taking under ambiguity task than PD without PG. Using
123 delay-discounting tasks, several studies showed that altered impulsivity in PD with ICD can
124 contribute to risk-taking (Voon et al. 2010a; Housden et al. 2010). The pathophysiology underlying
125 risk-taking behavior in PD with ICD has been explored and involved dysfunction in the reward
126 system including ventral striatum (Rao et al. 2010; Steeves et al. 2009). For example, using
127 functional magnetic resonance imaging to quantify resting cerebral blood flow (CBF) and blood
128 oxygenation level dependent (BOLD), Rao et al. (2010) showed that compared with non-ICD PD
129 patients, PD patients with ICD demonstrated significantly reduced resting CBF in the right ventral
130 striatum and significantly diminished BOLD activity in the right striatum during risk-taking. The
131 influence of pharmacological status on risk taking and impulsivity in PD with ICD has also been
132 explored (Voon et al. 2010b; Housden et al. 2010; Djamshidian et al. 2011a; Leroi et al. 2013).
133 These studies broadly concluded that PD patients with ICD tend to make more impulsive and risky
134 choices while ON dopamine agonist relative to those OFF dopamine agonists or without ICD.

135 Self-awareness, metacognitive skills and their links to ICD have also been recently explored
136 (Brevers et al. 2013; Mack et al. 2013; Brevers et al. 2014). Self-awareness is usually evaluated by
137 questionnaire as the Beck Cognitive Insight Scale (BCIS), assessing the understanding of patients'
138 perspective about their anomalous experiences, their attribution and their aberrant interpretation of
139 specific life events. Impaired self-awareness or insight has been recognized as a feature of a large
140 number of neuropsychiatric disorders, including PD (Gilleen et al. 2010). Using the BCIS, Mack et
141 al. (2013) compared self-awareness of cognitive and behavioral issues in PD patients with and
142 without ICD and showed that PD patients with ICD are aware of their PD-related problems
143 including impulsivity. In a different perspective, Brevers et al. (2013; 2014) studied how
144 metacognitive sensitivity may influence gamblers without PD's decision-making. Metacognition
145 was assessed by asking participants to wager on their own decision. They found that gamblers tend
146 to wager high while performing poorly on the Iowa Gambling Task and in a non gambling task,
147 suggesting that pathological gamblers exhibit impaired metacognition in both gambling like and
148 more 'neutral' situations of decision-making.

149 The aim of the present study was to investigate executive functions with classical tasks and
150 risk-taking behavior using a task developed to assess behavioral response and valuation of the
151 reward in PD patients with ICD (ICD-PD) compared to PD control patients without ICD (CTRL-
152 PD).

153

154 **PATIENTS AND METHODS**

155 **Subjects**

156 Patients were selected from among those attending the movement disorders unit of the Pitié-
157 Salpêtrière Hospital (Paris, France). All patients met the following inclusion criteria: idiopathic PD
158 according to the United Kingdom Parkinson's Disease Society Brain Bank and absence of dementia,
159 according to the MDS task-force criteria (Dubois et al. 2007). All patients obtained score higher
160 than 130 on the MDRS. Exclusion criteria were a history of ICD prior to PD-onset and treatment by
161 deep brain stimulation (DBS) before the ICD onset. Between January 2007 and January 2008, all
162 patients suspected to have ICD in the interview with the neurologist received a specific evaluation
163 of their ICD by a neuropsychologist. Presence and severity of active ICD were assessed with a
164 semi-structured interview assessing behavior and mood in PD, the 'Ardouin Scale of Behavior in
165 Parkinson's Disease' (ASBPD) (Ardouin et al. 2009; Rieu et al. 2015). Inclusion criteria for ICD-
166 PD patients was a score ≥ 2 (moderate to severe) in at least one item in the ASBPD scale of
167 pathological gambling, compulsive eating, compulsive shopping and hypersexuality. The ASBPD
168 scale also evaluates compulsive DA and others hyperdopaminergic symptoms such as punding or
169 any form of hobbyism. Patients who presented punding or form of hobbyism without ICD were not
170 included in the study. CTRL-PD group was constituted of PD patients, matched with ICD-PD
171 patients for age, sex, educational level, disease's severity and duration, and who were candidate for
172 Deep Brain Stimulation (DBS) between the same period, without history of ICD. The CTRL-PD
173 patients were, therefore, at risks for ICD; their absence was confirmed by a score ≤ 1 (none or mild)
174 in all ICD's items of the ASBPD scale, described below. Informed consent was obtained from all
175 individual participants included in the study.

176

177 **Procedure**

178 The two groups of patients underwent a comprehensive assessment of clinical,
179 neuropsychiatric and neuropsychological functioning. Assessment was performed in a single
180 session that lasted approximately 3 hours and when patients were in the 'on' state. Breaks were
181 introduced to avoid fatigue.

182

183 ***Neurological assessment***

184 Patients underwent a neurological examination consisting of the motor section of the
185 Unified Parkinson's disease Rating Scale (UPDRS, section III) to measure the severity of motor
186 symptoms in the 'on' state. Most of patients in both groups were at the motor fluctuations stage of
187 the disease. The demographic data (age, educational level), neurological details (age at PD onset
188 and PD duration) and treatments (medication type, total L-dopa equivalent daily dose (LEDD) and

189 total L-dopa equivalent daily dose (LEDD) of dopamine agonists) of each patient enrolled were
190 recorded.

191

192 ***Psychological assessment***

193 All patients underwent a psychological assessment consisting of the following:

194 1. the Montgomery and Asberg Depression Scale (MADRS) to evaluate depression, using only
195 the dysphoria factor defined by Suzuki et al. 2005, naming items of reported sadness, pessimistic
196 thoughts and suicidal thoughts to avoid confounding symptoms related to PD as 'lassitude', 'inability
197 to feel' or 'concentration difficulties;

198 2. the Starkstein scale (Starkstein et al. 1992) to identify apathy state and the severity of
199 apathetic symptom;

200 3. the Barrat Impulsiveness Scale (BIS-11) (Fossati et al. 2001), a global self-report scale of
201 impulsivity;

202 4. the 'Ardouin Scale of Behavior in Parkinson's Disease' (ASBPD) (Ardouin et al. 2009; Rieu
203 et al. 2015). The ASBPD consist of 21 items, grouped into four parts: general psychological
204 evaluation (part I), apathy (part II), non-motor fluctuations (part III) and hyperdopaminergic
205 behavior (part IV). Part I successively evaluates depressive mood, hypomanic mood, anxiety,
206 irritability and aggressiveness, hyperemotionality, and psychotic symptoms. Part II evaluates apathy
207 in behavioral terms, that is, activity level, cognitive level, and emotional level. Part III evaluates the
208 psychological state associated with the motor symptoms in the OFF and ON states in fluctuating
209 patients. Part IV assesses the presence and the intensity of behavioral disorders induced by
210 dopaminergic treatment, including nocturnal hyperactivity, diurnal somnolence, eating behavior,
211 creativity, hobbyism, punding, risk-taking behavior, compulsive shopping, pathological gambling,
212 hypersexuality, dopaminergic addiction, and excess in motivation. The timeframe of the assessment
213 is the preceding month. Each item is rated on a five-point scale (severe disorder, 4; marked disorder,
214 3; moderate disorder, 2; mild disorder, 1; absence of disorder, 0), by taking into account the severity
215 and the frequency of the disorder and its impact. The interview is completed by a psychiatrist, a
216 neuropsychologist, or a clinical psychologist familiar with PD and neuropsychiatric disorders in
217 movement disorders. Total completion time is approximately 1 hour.

218

219 ***Neuropsychological assessment***

220 All PD patients underwent neuropsychological tasks to assess executive functioning and
221 risk-taking behavior. The Conner's Performance Test (CPT-II) (Connors 2004), a 15 minutes
222 computerized test, was used to evaluate attention and inhibition. The subject had to press the space
223 bar of the computer as soon as he sees any letter on the screen, except the letter X, that he has to

224 hold back and press nothing. Variability in reaction time (expressed in millisecond) was used to
225 assess attention capacity. Percentage of commission error (press when the letter is X) referred to
226 inhibition abilities. The executive functioning was also assessed using : 1) conceptualization
227 capacities measured by the reached number of criterion (range from 0 to 6) in the Modified
228 Wisconsin Card Sorting Test (MCST) (Milner 1963); 2) shifting and reactive flexibility evaluated
229 by the difference between the time scores of TMT-B and TMT-A in the Trail Making Test (TMT)
230 (Reitan et al. 1985); 3) spontaneous flexibility and cognitive auto-activation skills using the
231 phonological verbal fluency R with the total number of correct words given in 2 minutes (Cardebat
232 et al. 1990).

233 To assess risk-taking behavior, we used a gambling task adapted from the Iowa Gambling
234 Task (IGT) (Bechara et al. 1994). The subject saw on a screen 3 decks of cards labeled A, B, and C.
235 Every time the subject picked a card, a message was displayed on the screen indicating the amount
236 of money he immediately won or lost. At the same time, on the top of the screen, the total amount
237 of money was displayed. The subject was asked to choose 50 cards and to win as much money as
238 possible. Contrary to the IGT, subject was notified that some decks were more advantageous than
239 others in order to avoid ambiguity and facilitate the comprehension of the rule. At the end of the
240 task, subject was asked to appreciate if each deck was a winning, a losing or a neutral deck (called
241 subjective variables). Subject can evaluate several decks as winning, losing or neutral. Decks had
242 been constructed so that deck A was a neutral deck (equal opportunity for gains as losses). Deck B
243 (small amount of money with a positive balance) was the winning deck with small gains but smaller
244 losses. Deck C can be considered as the losing deck (high amount of money with a negative
245 balance) as the subject won big gains but lost even more. Objective variables were the number of
246 cards chosen in each deck. The score for each objective variable ranges from 0 to 50. The score for
247 each subjective variable (valuation of the reward by appreciation of each deck) ranged from 0 to 2
248 (0: loser deck; 1: neutral deck; 2: winner deck). This adaptation of the IGT was proposed to avoid
249 ambiguity and to focus on the ability to resist to a big risky reward for the benefit of a smaller but
250 safer reward rather than the capacity to detect and understand the rule. Especially, risk-taking
251 behavior is evaluated by comparing the number of cards picked in each deck, subjects being aware
252 of the advantageous/disadvantageous characteristic of the decks and constantly informed of his
253 immediate reward and the total amount of money. Moreover, due to subjective variables, this task
254 takes into account the valuation of the reward.

255

256 **Statistical Analysis**

257 For demographic characteristics and neuropsychological data a Mann-Whitney U-test or a
258 Fisher exact test were used to compare CTRL-PD and ICD-PD groups. For risk-taking task,

259 comparison between the 3 groups (HV, CTRL-PD, ICD-PD) and between the three decks (A, B, and
260 C) were performed by using a Kruskal Wallis test, followed when significant by a comparison of
261 each group by a Mann-Whitney U-test. All results were considered significant if the p-value was
262 less than 0.05 with no correction for multiple comparisons. Data were expressed as median +/-
263 upper and lower quartiles. Statistical analysis was performed using Statistica 9.1 software (StatSoft
264 France, F-94700, Maisons-Alfort).

265

266 **RESULTS**

267 **Patients' characteristics**

268 Thirty-seven patients (age range 33-69 years, men/women = 27/10) participated in this
269 study. Seventeen patients were diagnosed as having one or more active ICD as the time of
270 assessment. In ICD-PD group, specific criteria of the ASBPD confirmed presence of PG in 6
271 patients, HS in 1 patient, CS in 2 patients, CE in 2 patients and 6 patients had multiple ICD (i.e.
272 hypersexuality and pathological gambling or compulsive shopping and pathological gambling).
273 Twenty patients without history of ICD were included in the CTRL-PD group (score \leq 1 in all
274 ICD's items of the ASBPD scale).

275 The two groups did not differ in gender, age, educational level, age at PD onset, PD
276 duration, LEDD dopamine agonist dose, UPDRS-III while "on" state and MDRS score (see results
277 in table 1). However, the 2 groups differed in total LEDD ($p = 0,003$), possibly because CTRL-PD
278 patients were recruited among those candidate for DBS and therefore needed more dopaminergic
279 treatment to control the disease.

280 For neuropsychiatric characteristics, the two groups differed in MADRS dysphoria score (p
281 = 0,01), in Starkstein score ($p = 0,01$) and in the BIS-11 score ($p = 0,003$).

282

283 *[Insert Table 1]*

284

285 **Executive functions**

286 The two groups did not differ in attention capacities, conceptualization abilities, reactive
287 flexibility, spontaneous flexibility and inhibition capacities.

288

289 *[Insert Table 2]*

290

291 **Risk-taking behavior results**

292 For the risk-taking task, the two groups of PD patients were compared to fifteen healthy
293 volunteers (HV) matched in age, sex and educational level on the objective variables (number of

294 cards chosen in each deck) and the subjective variables (appreciation of each deck: winning, neutral
295 or losing deck).

296 For each selection, all patients were able to clearly identify the feedback they received.

297 First, we analyzed the pattern of performances inside each group. For HV, there was no
298 significant difference between decks for both objective and subjective variables (Kruskall-Wallis
299 test, $p = 0.61$ and $p = 0.13$ respectively). On the contrary, ICD-PD patients and CTRL-PD patients
300 both showed significant differences of the number of cards in each deck (Kruskall Wallis, $p = 0.004$
301 for CTRL-PD, $p = 0.007$ for ICD-PD). For both groups, the number of cards chosen in the losing
302 deck C (high amount of money) was higher as compared to the neutral deck A (Mann-Whitney test,
303 ICD-PD, $p=0,02$; CTRL-PD, $p=0,003$) and to the winning deck B (small amount of money) (Mann-
304 Whitney test, ICD-PD $p=0,0001$; CTRL-PD $p=0,003$). In addition, in the ICD-PD group, the
305 number of card chosen in winning deck B was significantly lower than in neutral deck A (Mann-
306 Whitney test, $p = 0.04$). Subjective variables were not significantly different in the HV or the
307 CTRL-PD groups (Kruskall-Wallis test, $p = 0.13$ and $p = 0.45$ respectively) whereas they were
308 significantly different in the ICD-PD group (Kruskall-Wallis test, $p = 0.01$). ICD-PD patients
309 evaluated the wining deck B (small amount of money) loser as compared to neutral deck A (Mann-
310 Whitney, $p = 0.04$) and losing deck C (Mann-Whitney, $p=0,01$).

311 Then, we compared the performances between the three different groups. When comparing
312 PD patients to HV, we found no significant difference between HV and CTRL-PD groups for both
313 objective and subjective variables. Furthermore, the ICD-PD group was significantly different from
314 the HV for both variables: ICD-PD patients chose significantly less frequently the winning deck B
315 (Mann Whitney, $p=0,04$) and evaluated this deck more frequently as a losing one (Mann Whitney,
316 $p=0,02$) as compared to HV. Moreover, ICD-PD patients evaluated the losing deck C more
317 frequently as a winner than HV (Mann Whitney, $p=0,02$). ICD-PD patients and CTRL-PD patients
318 did not significantly differ for any deck for objective variables. Furthermore, for subjective
319 variables, ICD-PD patients evaluated the winning deck B more frequently as a loser one than the
320 CTRL-PD patients (Mann Whitney test, $p=0,04$).

321

322 *[Insert Table 3]*

323

324 **DISCUSSION**

325 This study examined executive functioning and risk-taking in PD patients with ICD. As
326 previously observed by Weintraub et al. (2010) and Voon et al. (2011a), we found that ICD-PD
327 patients showed greater impulsivity, more depressive elements and lack of motivation than PD-
328 CTRL patients.

329 Concerning the executive functioning, we found that ICD-PD patients performed similarly
330 than CTL-PD patients, as supported by other studies, which showed no executive dysfunction
331 including set shifting, inhibitory process and reactive flexibility in ICD patients compared to CTRL
332 PD patients (Siri et al. 2010; Djamshidian et al. 2011a; Mack et al. 2013). This is against previous
333 reports showing a positive association between ICD and cognitive dysfunction (Santangelo et al.
334 2009; Vitale et al. 2011). Methodological and PD population's differences as well as small size of
335 groups can highlight those discrepancies.

336 In this study, we addressed to the patients an experimental task to investigate risk-taking
337 behavior and valuation of the reward. Our results showed that contrary to HV, both groups of PD
338 patients behave similarly, choosing more frequently cards in the loser deck (high amount of money)
339 compared to the other decks. These results confirm risk-taking behavior in PD with or without ICD
340 (Delazer et al. 2009; Djamshidian et al. 2010; Rossi et al. 2010). Risk-taking behavior in PD
341 probably involved dopamine replacement therapy's influence on mesolimbic spared circuit. For
342 example, Steeves et al. (2009) in a PET neuroimaging study in PD patients with PG demonstrated
343 decreased ventral striatal D2/D3 binding potential at baseline and a relatively greater decrease in
344 binding potential in the ventral striatum during performance of a gambling task. Consistent with our
345 results, Rao et al. (2010) found that both ICD-PD and CTL-PD groups behave similarly in a risk-
346 taking task. Interestingly, in that functional magnetic resonance imaging, the authors showed that
347 contrary to CTL-PD patients, ICD-PD patients demonstrated relatively diminished activity in the
348 ventral striatum during risk-taking.

349 Our results suggested also that ICD-PD patients showed a specific deficit of the subjective
350 estimation of the reward compared to patients without ICD, taking into account mainly the positive
351 reinforced value of the decks, and less considering the value of the loss. These results are in line
352 with studies exploring reinforcement sensitivity, demonstrating that via action on ventral striatal
353 dopamine function, dopamine replacement therapy could potentially alter reward responsiveness
354 and abilities to learn from negative decision outcomes (Franck et al. 2004; Pessiglione et al. 2006;
355 Piray et al. 2014). For example, Franck et al. (2004) showed that PD patients without ICD have
356 different learning and reward-seeking behaviors from healthy controls. PD patients showed exactly
357 opposite learning patterns during their medication ON and OFF states: PD patients achieved more
358 efficient learning by positive reinforcement during their ON medication state, whereas they
359 performed better through negative feedback during their medication OFF state. In ICD-PD patients,
360 it seems that dopamine agonist enhance the deviated learning pattern. Voon et al. (2010b) showed
361 that dopamine agonist enhance the rate of a gain-specific learning and increase striatal prediction
362 error activity observed in patient with ICD. Thus, ICD-PD patients can experiment a persistent
363 "better than expected" outcome while taking dopamine agonist. Dopamine agonists also enhance

364 risk-taking behavior in ICD-PD patients (Voon et al. 2011b). While taking dopamine agonists, these
365 patients seem to have a bias towards risky choice independent of the effect of loss aversion.
366 Especially, Voon et al. (2011b) showed that neural activity in brain areas associated with risk
367 representation, such as the ventral striatum, orbitofrontal cortex and anterior cingulate cortex, are
368 decreased in these patients.

369 In our study, both PD groups presented risk-taking behavior during the task but only ICD-
370 PD patients presented deficit in subjective appreciation of the reward. Especially, despite risk-taking
371 behavior, when they were asked about their perception of deck's value at the end of the task, CTL-
372 PD patients were able to correctly appreciate the reward. In contrary, ICD-PD patients presented a
373 specific deficit of the subjective estimation of the value of stimuli. Recent studies focusing on
374 influence of metacognitive skills on risk-taking process can probably contribute to understand this
375 specific deficit presented by our ICD-PD patients. Metacognition is the ability to cognizant and
376 have insight about the quality of the decision and to accurately judge whether the decision is surely
377 a good one or not. Brevers et al. (2013) studied how metacognitive sensitivity may influence
378 gamblers without PD's decision-making during the Iowa Gambling Task. Metacognition was
379 assessed by asking participants to wager on their own decision. They found that gamblers tend to
380 wager high while performing poorly on the Iowa Gambling Task and that the difference was not due
381 to reward/loss sensitivity, current clinical or cognitive status. The same authors in a more recent
382 study (Brevers et al. 2014) replicated these results with a non gambling task (grammatical
383 paradigm). They found that compared to healthy volunteers, pathological gamblers without PD also
384 erroneously think that they are performing much better than they actually are. Both studies
385 suggested that pathological gamblers exhibit impaired metacognition in both gambling like and
386 more 'neutral' situations of decision-making. In our study, the erroneous appreciation of deck's
387 values specifically presented by ICD-PD patients could be linked to deficit in metacognitive skills.
388 Indeed, in these patients, introspection's abilities are possibly based on the under-optimal behavior
389 and lead to focus on the positive reinforcement value. In that perspective, Djamshidian et al.
390 (2011b) showed that PD patients with ICD learn little of their mistakes, compared to ICD patients
391 without PD. On the contrary, a recent study evaluating self-awareness in PD patients with ICD
392 showed that presence of ICD was associated with awareness of impulsive behaviors, as indexed by
393 greater cognitive insight into thoughts and behaviors on the BCIS (Mack et al. 2013). In the
394 different studies cited above, different levels of awareness are probably involved and might explain
395 the discrepancies of the results. All together, these results showed that ICD-PD patients are
396 probably aware of ICD, but exhibit a fundamental impairment in their perception of winning or
397 losing behaviors among various situation of decision-making and provide an interesting perspective
398 to explain how metacognitive skills can contribute to the deficit of subjective estimation of the

399 reward presented by our ICD-PD patients.

400 There are however some limitations to our study. First, our sample size was small and may
401 not have provided adequate power to detect smaller differences across variables. Second, this study
402 focused on risk-taking behavior using an adapted task of the IGT to avoid fatigue, involvement of
403 working memory and ambiguity in order to focus on the ability to resist a big risky reward for the
404 benefit of a smaller but safer reward. This adaptation provides interesting results concerning risk-
405 taking behavior in line with other studies (Rossi et al. 2010; Rao et al. 2010). Nevertheless, this
406 experimental task is limited to the optimal selection in terms of rewarding or punishing outcomes
407 under risky situations. The absence of ambiguity in our task reduces the interpretation in terms of
408 decision-making process. Finally, a valuation of the reward was explored by an indirect measure
409 (appreciation of each deck at the end of the risk-taking task) limiting the interpretation in terms of
410 reward sensitivity. Despite these limitations, our study provides interesting findings on subjective
411 perception of the reward, showing that subjective valuation of the reward is specifically impaired in
412 PD patients with ICD compared to CTRL-PD patients.

413

414 In summary, our results show that executive pattern and risk-taking behavior are similar
415 between ICD-PD patients and CTRL-PD patients, but patients with ICD present a specific deficit of
416 the subjective estimation of the reward compared to CTRL-PD patients. Studies focusing on
417 metacognitive skills provide an interesting perspective to explain our results. In that perspective,
418 introspection's abilities of ICD-PD patients, possibly based on the under-optimal behavior, lead
419 ICD-PD patients to focus on the positive reinforcement value. Others studies exploring subjective
420 estimation of the reward and metacognitive skills are necessary to better understand their link and
421 their influence on risk-taking behavior in PD patient with ICD.

422

423

424

425 **Ethical approval:** All procedures performed in studies involving human participants were in
426 accordance with the ethical standards of the institutional and/or national research committee and
427 with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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TABLES

Table 1: Demographic and clinical aspects of PD patients with and without ICD

Values are median (lower-upper quartile). P-value: Mann-Whitney test between groups.

Characteristics	ICD-PD n = 17	CTL-PD n = 20	p
Men/Women, No	14/3	13/7	0,24
Age (Yr)	55 (37-69)	55 (40-62)	0,52
Education (Yr)	7 (3-7)	7 (3-7)	0,45
Age at PD onset (Yr)	48 (32-65)	48 (35-55)	0,57
PD duration (Yr)	7 (2-10)	5,5 (4-12)	0,60
LEDD (mg/dose)	897,5 (299,88-1247,33)	1049,89 (527,05-1549,84)	0,003
LEDD dopamine agonist (mg/dose)	299,94 (77-718)	340,23 (66,68-700)	0,78
UPDRS-III score while on state	7 (0-23)	8,5 (0-34)	0,62
Dysphoria specific MADRS score	6 (0-13)	1,5 (0-7)	0,01
Starkstein scale score	7 (3-14)	4 (0-10)	0,01
MDRS score	140 (133-144)	139 (131-143)	0,07

Table 2: Neuropsychological compares between patients with PD with and without ICD.

Values are median (lower-upper quartile). P-value: Mann-Whitney test between groups.

	ICD-PD n = 17	CTL-PD n = 20	p
Impulsivity			
Global BIS-11	63 (48-81)	52 (36-70)	0,003
Attention			
RT variability CPT	88,5 (4,74-202,2)	82,9 (3,05-193,4)	0,68
Executive functioning			
criterion number MSCT	6 (5-6)	6 (3-6)	0,23
TMT B-A	34 (6-149)	45,2 (10-78)	0,56
fluency R	26 (6-43)	20 (8-38)	0,08
% commission CPT	22,2 (4,7-38,9)	20,8 (5,6-70,8)	0,67

Table3: Compares between the two PD groups and the healthy volunteers on the risk-taking task

Values are median (lower-upper quartile). P-value: Kruskal-Wallis test for each deck between groups.

^aSignificantly different from HV ; ^bSignificantly different from CTL-PD ; ^cSignificantly different from deck B ;

^dSignificantly different from deck C, Mann Whitney test.

	ICD-PD n = 17	CTL-PD n = 20	HV n = 15	p
<i>Objective variables</i>				
Number of cards neutral deck A	17 (7-14) ^d	15 (8-23) ^d	15 (6-24)	0,58
Number of cards winning deck B	14 (5-18) ^{a, d}	15 (5-26) ^d	17 (10-33)	0,01
Number of cards losing deck C	19 (12-33)	20 (12-34)	16 (10-30)	0,21
<i>Subjective variables</i>				
Appreciation neutral deck A	2 (0-2) ^c	1 (0-2)	1 (0-2)	0,24
Appreciation winning deck B	0 (0-2) ^{a, b, d}	1,5 (0-2)	2 (0-2)	0,04
Appreciation losing deck C	2 (0-2) ^a	1,5 (0-2)	0 (0-2)	0,06