Review article

Neuropsychological assessment of decision-making prefrontal circuits in schizophrenia: a systematic review of the literature

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INTRODUCTION

This article aims at performing a critical review of the existing literature on neuropsychological assessment of decision making (DM) in schizophrenia. Two aspects were considered crucial in the present article: firstly, to analyze the contribution of neuropsychological instruments (specific to the prefrontal region) in the understanding of the neurobiology underlying changes in processing choices and their stages, i.e., in DM, regarding schizophrenia; secondly, to investigate, by means of comparing the different studies, the correlation between the results in DM tests and the clinical and epidemiological characteristics of the samples, discussing the relevance of the findings in diagnostic, prognostic and therapeutic terms.

DM can be generically defined as a process in which the individual tries to increase the potential of benefits through the selection of responses that lead to positive results in given circumstances.[1] This complex process plays a major role in our everyday choices and contributes to modulating short, medium and long-term decisions, establishing priorities and avoiding alternatives whose outcome may be harming. In neurobiological terms, the processes that represent the complex decisive mechanism involve distinct brain areas, whose common objective is filtrating and selecting several stimuli and expressing an appropriate behavior adjusted to the contingencies of the external environment.

The association between the lesion in specific brain areas and changes in social behavior and DM was initially established by Harlow,[2] when describing the "Phineas Gage case." However, only after the 1990's the interest on researching emotional changes resulting from neurological affections was resumed, through the studies by Damasio et al.[3] This author assessed, using the dermal conductance response (DCR), patients with lesions in the orbitofrontal prefrontal cortex (OFPC).[4] Although demonstrating preservation in the global intellective functioning, the OFPC group revealed an inability in applying the knowledge or experience they had in contexts that reproduced situations of deliberation and choice. For Damasio,[4] this pattern was attributed to a failure in using the so-called "somatic markers," i.e., positive or negative valences (measured by DCR), defined at

each previous experience and that acquired an internal representation, associated with emotional regulation and social behavior.

Concomitantly, one of Damasio's collaborators, Bechara,[5] developed, with his group, the study of neuropsychological tests sensitive to OFPC assessment, creating the Iowa Gambling Task (IGT), a game of cards known as "gambling test" that simulates decision-making situations based on the choice of cards considered as high or low risk. This instrument was also initially applied in patients with orbitofrontal neurological lesions, being observed[5] a persistent standard of disadvantageous choices, including in situations in which they were previously warned about the possible unfavorable consequences of their decisions. Such behavior became known as "insensitivity to future consequences" or "myopia for the future." Over the past 10 years, further studies carried out by the same author have confirmed the IGT sensitivity to orbital disorder.[5-11]

The other resources used to investigate the neural connections underlying DM, especially positron-emission tomography (PET) and magnetic resonance, have also added evidence to the involvement of orbital prefrontal regions (orbitofrontal, but also orbitomedial) in processes of choice, reward and punishment, corroborating the IGT findings and other neuropsychological instruments assessing DM.[12] PET[13,14] and functional resonance[15] studies showed activation of different OFPC areas, with tasks assessing DM processing. Methodologically similar studies investigating reward processing also found activation of orbitofrontal areas.[16] Despite the advances mentioned earlier, only for 10 years the research on decision-making mechanisms and their relation with cortical areas has been gradually advanced to the investigation of different primary psychiatric disorders.[17] Neuropsychological tests sensitive to OFPC disorder (IGT and others) have been used to assess patients with obsessive-compulsive disorder,[18] antisocial personality disorder,[19] pathological gambling,[20] alcohol and drug dependency and abuse[9,10,21,22] and attention deficit.[23]

The interest on the study of regions associated with DM in schizophrenia is considered recent. Most previous studies focused on the investigation of subcortical areas and other regions of the prefrontal cortex, such as the dorsolateral sector, whose anomalies have been widely

described.[24-27] However, recent evidence involving schizophrenic patients revealed structural and functional changes in OFPC as well, demonstrating that other cortical areas, besides the dorsolateral prefrontal cortex (DLPFC), may be associated with clinical and behavioral characteristics specific of schizophrenia.[28-31] Schizophrenic patients also showed worse performance in neurological tests sensitive to orbitofrontal disorder, but unrelated to DM, as in the study by Moburg et al.,[32] using tests of olfactory identification, and by Abbruzzese et al.,[18] using tasks assessing strategy alternation (Object Alternation Task – OAT).

The body of evidence involving neuroimaging studies assessing functioning specificity of prefrontal cortical areas in schizophrenics, the poor performance of those patients in neuropsychological tests sensitive to other abnormalities attributed to orbitofrontal disorder, and finally previous studies showing association of OFPC and DM have motivated the increasing interest in investigating the performance of schizophrenic patients in tasks assessing decision-making skills. The importance of studying DM in schizophrenia lies especially in a more detailed understanding of the processes or stages that regulate emotion and social behavior in these patients and that play a major role in everyday immediate decision-making and in terms of future.

METHODOLOGY

A review of the literature was performed through a search in the electronic databases MEDLINE, PubMed, LILACS, PsycINFO and COCHRANE, including articles from January 1994 to September 2005 and using the following terms as search strategies: neuropsychology, decision making, schizophrenia, prefrontal cortex, orbitofrontal cortex and gambling task. References of selected articles were also used, with the aim of including publications missed by the electronic search. As far as we know, there is no review article available in the literature on DM in schizophrenia.

Among the criteria of article selection, relevant studies were those that used neuropsychological instruments sensitive to orbitofrontal disorder in schizophrenic patients as

outcome measurements, and whose outcome variable was the performance on tests assessing decision-making skills. Irrelevant studies for this review were those that investigated noncognitive aspects of DM – for example, articles focusing on the ethical or humanistic aspect. We also excluded case reports, letters to the editor, expert reviews and articles using homogeneous samples of other psychiatric disorders, although studies on patients with other psychotic disorders (delusional, schizoaffective) among the sample of schizophrenics were also included.

The abstracts found by the electronic search were analyzed by two independent reviewers (G.S.A. and M.R.), who selected, according to the inclusion and exclusion criteria, all the studies relevant for this review. In case there was no agreement between both reviewers as to the selection of an article, a specific discussion was held until reaching a final consensus.

RESULTS

A total of 22 articles considered relevant were assessed by the reviewers. Of these, only nine met the criteria for description and analysis in the present study. Table 1 below summarizes the selected articles, their methodology and results.

Table 1 - Decision-making studies in schizophrenic patients

Authors/year	Patients	Methodology	Results	Comments
Wilder et al.[33]	11 schizophrenics 1 schizoaffective 30 controls	IGT CVLT WCST LNSP WAIS-R	There was no difference in IGT performance between groups	- Small and heterogeneous sample - Controls with higher schooling level - Absence of control for ATP use
Hutton et al.[34]	28 patients in their first schizophrenic episode 22 chronic patients healthy controls	NDMT premorbid IQ	Worse performance and longer deliberation time among schizophrenic patients	- Absence of control for ATP use - Absence of tests assessing executive functions
Beninger et al.[35]	76 schizophrenic patients 50 controls	PCL Task IGT: 18 typical, 18 atypical and 18 controls	Patients using atypicals had worse IGT performance	Large number of ATP used did not allow a correlation with IGT performance
Ludewig et al.[36]	24 hospitalized patients (12 with deficits and 12 with no deficits) 12 controls	Two-Choice Prediction Task ME and MI measurements	Deficit schizophrenics with worse ME and MI performance and loss in DM	- Reduced samples and heterogeneous as to treatment - Absence of control for ATP use - IQ was not measured
Shurman et	39 outpatients	IGT	- Schizophrenics	- Small sample of

al.[37]	10 controls	WCST DMST	with worse IGT performance - Positive association between negative symptoms and worse IGT performance	control group and of patients taking typical ATP - Absence of control for use of medication - IQ was not measured
Ritter et al.[38]	15 schizophrenics 5 schizoaffectives 15 controls	IGT verbal IQ WCST	Worse IGT performance among psychotic patients	Heterogeneous and reduced sample
Bark et al.[39]	8 catatonic patients 20 paranoid patients 26 controls	IGT Go/No-Go Task WCST SPM nonverbal IQ verbal IQ (estimate) Multiple Vocabulary Test-B	- Worse global and IGT performance among catatonic patients - Paranoid patients did not show IGT changes	- Sample was not much varied - Small number catatonic patients - Acute catatonic patients and those who did not respond to lorazepam were excluded
Evans et al.[40]	19 chronic patients 19 healthy controls	IGT SANS/SAPS WAIS WCST	Schizophrenics and controls presented normal IGT performance	- Variables such as clinical subtype of schizophrenia were not mentioned

		COWAT		- Control group was not described in detail
Rodriguez-Sanchez et al.[41]	80 patients in their first psychotic episode in the schizophreniform spectrum 22 controls	VC (WAIS III) IGT FAS TMT	Schizophrenics and controls presented normal IGT performance	- Absence of correlation between cognitive changes and subtype of psychotic disorder - Patients were not later confirmed as to disease diagnosis

ATP = antipsychotics; COWAT = Controlled Oral Word Association Test; CVLT = California Verbal Learning Test; DM = decision making; DMST = Delayed Match to Sample Task; FAS = Fluence Assessment Scale; IGT = Iowa Gambling Task; IQ = intelligence quotient; LNSP = Letter Number Span; ME = metric entropy; MI = mutual information; NDMT = Novel Decision Making Task; SANS = Schedule for the Assessment of Negative Symptoms; PCL = Probabilistic Classification Learning; SAPS = Schedule for the Assessment of Positive Symptoms; SPM = Standard Progressive Matrice; TMT = Trail Making Test; VC = verbal comprehension; WAIS-R = Wechsler Adult Intelligence Scale – Revised; WAIS = Wechsler Abbreviated Scale of Intelligence; WCST = Wisconsin Card Sorting Test.

Most studies (n = 6) included IGT in their methodology.[5] In this task, the measured outcome variable was the proportion of advantageous choices minus disadvantageous choices in four groups of cards. The other articles (n = 3) presented other instruments to assess decision-making skills, such as the Two-Choice Prediction Task[36] and the Novel Decision Making Task (NDMT).[34] In all studies, performance in DM tests was compared to the results of other cognitive variables, such as

executive functions and verbal intelligence quotient (IQ). Table 2 below summarizes the tests used and their variables.

Table 2 - Description of the neuropsychological tests mentioned in the review of the literature

Test	Description	Assessed variables
Bechara et al.[5]	Free choice between four decks: A, B, C and D; all cards have a symbolic monetary value, representing gains or penalties A and B: "high-risk" decks; they favor loss during the game (high mean of gains; even higher mean of losses) C and D: "low-risk" decks; profit during the game (modest, but constant gains; small mean of losses) B and D: frequent (low) rewards, infrequent penalties (high) A and C: rare rewards (high), frequent penalties (low)	- Standard of choices during the test or advantageous cards minus disadvantageous cards: [(C+D) – (A+B)]; - Final profit
Ludewig et al.[36]	House placed in the center of the screen The individual has to choose in which side of the picture a car will appear in 250 ms 4 sets of 64 attempts	- Presence of car in each side - Latency in hunches - Response standard during the test
Rogers et al.[13]	10 red or blue boxes, in varied proportions during the game Gift randomly hidden inside one box; the individual has to choose in which box the gift is	- Ability to estimate probabilities - Latency in responses - Risk adjustment due to

	8 blocks of 9 attempts Initial bonus of 100 points Points are also possible with a hunch on the probability (established in fixed percentages: 5, 25, 50, 75 and 95%) of making the correct choice	changes in success probabilities

The first article[33] was based on the study by Bechara et al.[8] on patients with ventromedial disorder and on preliminary data assessing orbitofrontal disorder through tasks of olfactory identification.[42] The sample was composed of healthy controls and patients with schizophrenic and schizoaffective disorder, taking different classes of antipsychotics (ATP). The hypothesis tested was whether the disorder in DM occurs in a primary form (supposedly, due to a deficiency in somatic markers) or whether it is a consequence of intellective deficits associated with schizophrenia. Instruments used were IGT (DM assessment), an instrument assessing long-term memory (California Learning Verbal Test), and two others assessing procedural memory (Letter Number Span and Wisconsin Card Sorting Test – WCST). Outcome variable was IGT performance and its relation with cognitive variables assessed by other instruments. The similar pattern of outcome shown by controls and patients was seen as atypical, since it was not characteristic neither of patients in OFPC nor of other control groups described in the literature. Controls and patients preferred cards with rarer penalties and higher frequency of rewards, i.e., decks B and D. Due to outcomes similar to those obtained by controls, the outcome of patients in IGT was interpreted as "normal." On the other hand, there was no correlation between performance in IGT and assessed cognitive variables (working memory and delayed recall).

In a replication of the study by Wilder,[33] Ritter et al.[38] compared the measurements between IGT and WCST (both in electronic version) in schizophrenic, schizoaffective (subtype depressive) patients and healthy controls and observed a more daring pattern of choices in schizophrenics in the DM test. An estimation of premorbid verbal IQ (using the North American Adult Reading Test) and

an assessment of negative symptoms were also performed, using the Schedule for the Assessment of Negative Symptoms (SANS), as well as the severity of psychiatric symptoms, using the Brief Psychiatric Rating Scale (BPRS). Results showed that the 20 patients diagnosed with schizophrenia or schizoaffective disorder "earned" less money throughout the IGT and more frequently selected the cards in decks A and B, but, in contrast with the pattern found in OFPC patients, showed some evidence of learning during the test, and started choosing the most advantageous cards, even if at a lower proportion than the one found in the control group. In both groups, there was no correlation between IGT performance and WCST measurements. Performance in IGT test was not influenced by the score in SANS or BPRS.

In 2003, Beninger et al.[35] assessed DM through IGT and investigated the correlation of that test with the type of ATP used. The sample included a group of 18 patients taking typical ATP, 18 taking atypicals and 18 controls. The hypothesis was that the atypical medication (but not the typical) affected ventromedial circuits. The dependent variable associated with IGT was the mean number of choices of the decks considered advantageous in five blocks of 20 attempts each. They found that all 18 patients taking atypical ATP showed changes similar to those of patients with OFPC lesion, making high-risk choices (that is, more frequently selecting less advantageous decks) and showing reduced learning curve in the selection of low-risk cards during the blocks of choice. In contrast, all 18 patients taking typical ATP did not show differences in relation to healthy controls. An important limitation of the study was the lack of instruments assessing premorbid IQ. However, according to the second author, this variable did not seem to influence the performance of the groups, since the patients taking typical ATP represent the group of less schooling level and, in spite of that, had a similar performance to the control group in the IGT.

Hutton et al.,[34] using another neuropsychological test, the NDMT,[13] found differences in performance between controls, chronic schizophrenic patients and patients having their first psychotic episode. Their study did not use tests sensitive to dorsolateral disorder. Three variables involved in the DM process were investigated: response speed (or latency), risk adjustment (which

represented changes in success probability) and the ability of estimating probabilities. In all measurements, a worse performance was seen in both groups of schizophrenic patients, except for the ability of estimating probabilities, whose results in patients having their first psychotic episode were compatible with the control group. Despite the poor performance in NDMT between both groups of schizophrenics, there was a larger difference in those with chronic evolution when compared with controls. According to the author, this group had a performance very similar to patients with lesions in orbitofrontal neurological circuits, since they showed longer DM times, made more disadvantageous choices (even when warned about associated risks) and adjusted less adequately their responses toward changes in the game.

Another article emphasizing the establishment of clinical markers via DM for the subtypes of schizophrenia was that by Ludewig et al.,[36] whose results showed DM deregulation, especially in patients classified as having "deficits" (due to global impairments in psychosocial functioning and preponderance of negative symptoms), compared to "non-deficit" patients and healthy controls. The instrument used to measure DM was the Two-Choice Prediction Task.[36] The other instruments included the measurement of negative symptoms (by SANS) and a specific scale for deficit syndrome, the Schedule for the Deficit Syndrome.[43] Innovative concepts, such as entropy and mutual information (MI), were used in result analysis. The former is defined as the ability of modulating the response in relation to previous stimuli. MI corresponds to the measurement of the immediate influence of a previous response over the current response. The worst performance in the deficit group compared to controls was characterized by a great oscillation between sequences of highly predictable responses and others of high unpredictability. For Ludewig,[36] this result reflected as main aspects the deficiency in continuous update of behavioral strategies (low entropy) and a high level of dependence in current decisions in relation to previous tests (high level of MI). The study shows methodological limitations common to their predecessors, such as absence of control for cognitive variables (IQ), schooling level and antipsychotic medication.

In 2005, four studies used the same instrument for assessing DM (IGT), but found different results among the samples of schizophrenics. The first study[37] assessed 39 schizophrenic outpatients and 10 healthy controls and aimed at correlating clinical parameters – such as medication being used – with DM performance. It found a positive correlation between IGT performance and presence of negative symptoms. On the other hand, other variables, such as time of disease and use of antipsychotic medication, were not correlated with poor IGT. Schizophrenic patients presented lower scores in choosing cards considered advantageous and showed more tendency to choose low-valued reward decks and cards with rare but higher punishments (decks A and B). However, the study used a small control group (n = 10) and few patients taking atypical ATP. The second study was carried out by Bark et al.,[39] who used samples of hospitalized patients diagnosed with catatonia (n = 8) and paranoid schizophrenia (n = 19) and compared them to health controls (n = 26). They found a performance standard in the first group similar to that of patients with OFPC lesion. Instruments specific to frontal disorder, such as OAT and Go/No-Go Task, besides WCST, were also used. Catatonic patients tended to make high-risk choices, with higher proportion of decks A and B, in opposition to the other groups (paranoid patients and controls), who presented a more conservative tendency (that is, an ascending curve in selecting decks C and D, more profitable in the long term). Catatonic patients also presented comparatively worse OAT performance, with a large number of perseverative errors. According to the authors, poor OAT performance was directly correlated to IGT results. For Bark et al.,[39] the association between those measurements (OAT and IGT) could be translated into clinical terms as an incapacity or rigidity in alternation of adaptive strategies of selection and would contribute to generate a set of psychopathological changes, such as perseveration, echolalia, negativism and automatic obedience. The aspect of nosological classification of the catatonic group was often not assessed, since only the syndromic diagnosis was considered. The possible diagnostic heterogeneity in this group (patients with neurological or systemic diseases, mood disorders, psychotic disorders, etc.) is a limiting factor to the conclusion about the performance of catatonic schizophrenics in DM.

In the study by Evans et al.,[40] the performance of the healthy control group (n = 19) and schizophrenic patients (n = 19) was considered normal, considering the final outcome in terms of number of advantageous cards. All schizophrenic patients were taking atypical ATP. There was no correlation of patients' performance with SANS measurements (negative symptoms), Schedule for the Assessment of Positive Symptoms (SAPS) (positive symptoms), educational level or age. The study presents major limitations as to methodology and results. Firstly, it did not mention the clinical subtypes of schizophrenic patients and the sociodemographic characteristics of the control group. In addition, there was no description of the number of cards chosen in each deck by both groups under investigation. The results of other instruments used, such as Wechsler Abbreviated Scale of Intelligence (WASI) and WCST, were not even presented.

Finally, the study by Rodriguez-Sanchez et al.[41] involved the highest number of patients in the scope of psychotic disorders (n = 80), all in their first episode (clinically established) and receiving outpatient care, and 22 controls. There were no differences in IGT performance between compared groups. On the other hand, the absence of changes in the DM test between the group with psychotic disorder contrasts with the deficits observed in the instruments assessing executive functions and working memory (Digit Span Backward and Trail Making Test, respectively), which seems to suggest a functional independence of those circuits. Curiously, there was a choice standard of cards similar to that found in the study by Shurman et al.[37] and Wilder et al.,[33] giving preference to decks with low frequency and high magnitude of punishments, i.e., B and D. As in Bark et al.,[39] the study by Rodriguez-Sanchez et al.[41] used a potentially heterogeneous group from the nosological perspective, whose scope can comprehend disorders with varied clinical characteristics (and possibly neuropsychological).

DISCUSSION

The heterogeneity of findings in the studies described above seems to correspond to methodological methods found and to some characteristics pertinent to the samples, such as time of

disease onset, type of ATP, clinical subtype of the disease, presence of negative symptoms, relation between performance in decision-making tests, measurements of intellective (IQ) and executive functioning and the characteristics of the control sample. The following topics discuss the relation between clinical/epidemiological aspects and the results in DM tests found in different studies.

Antipsychotics

The lack of consistent data about the role of ATP in the performance of DM-related tasks can be attributed (among other factors) to the sample selection criteria in most studies. Only one study[35] showed a correlation between the use of atypical drugs and worse IGT performance. The other articles assessing the influence of drugs on tests found a negative association, but only used typical ATP.[36-39] In spite of that, the interest on the effect of ATP drugs in orbitofrontal sectors has been growing, especially due to the results of studies using other samples with psychiatric disorders, such as drug dependency and abuse, whose extensive findings relating orbitomedial disorder to risk behavior may reflect dopaminergic changes in those sectors, possibly resulting from psychoactive drugs in D1 and D2 receptors.[44-47]

Negative symptoms

Of the nine studies selected in this review, only those by Ludewig[36] and Shurman[37] found an association between negative symptoms and OFPC disorder. Those data, however, seem to be preliminary, since an association between orbitofrontal disorder and deficit symptoms seem to have an impact on the social cognitive functioning.[48] Furthermore, the involvement of prefrontal areas contiguous to OFPC in samples of patients with prevalence of deficit symptoms has been demonstrated, especially in neuroimaging studies.[49,50] For example, studies suggest that those patients have a standard of prefrontal hypoactivation during memory retrieval.[51] Another study of the left and right medial prefrontal cortex, using proton magnetic resonance spectroscopy, found disorder in frontal regions in the deficit group.[52]

Clinical types of schizophrenia

Any study showed association between a specific type of schizophrenia and altered performance in DM. Bark et al.[39] noted a great involvement of IGT among catatonic patients, but this group did not consider the nosological diagnosis and the possibility of affective or organic disorders in the sample. In spite of that, at least one neuroimaging study mentions ventromedial changes in catatonic schizophrenic patients.[31] On the other hand, also in the study by Bark et al.,[39] the standard of choice of cards in IGT between the paranoid group was similar to the control, which would suggest a preservation, in these patients, of neuronal circuits underlying DM. The changes found in the paranoid subtype of schizophrenia have traditionally been related to DLPFC.[53-55]

Cognitive skills

Bearing in mind that cognitive deficits can be considered reliable predictors of prognosis and clinical symptoms of long-term schizophrenia,[23] it is essential to understand the relations between the areas related to DM and the other frontal cortical regions, among them the DLPFC, known to be related to executive and planning functions and to procedural memory. In addition, it is important to have a better understanding about the role of intellective functioning (IQ) in tasks assessing decision-making skills. Despite the inconsistencies between the studies mentioned so far, in almost all of them there was a weak correlation between performance and IGT and other aspects of the cognitive domain. In six studies, the WCST was used, which is a test known as "standard" for assessing the executive functions associated with DLPFC and in which schizophrenic patients frequently present some degree of impairment.[37] Four studies directly correlated the IGT performance with scores found in WCST, registering a weak correlation.[33,38,37,41] A fifth study[35] observed, in schizophrenic patients with abnormal IGT performance, lower indexes than in controls in different WCST measurements, but a correlation between both measurements was not performed. IGT performance was not significantly associated with the global intellectual functioning, in four

studies,[33,38,39,41] learning list[33] or verbal short-term memory.[35] Those results add consistent evidence about the independence of the orbitofrontal sector in relation to other areas and cognitive domains, such as DLPFC and executive functions. However, because it is a complex and important function in the everyday life and involves other cognitive aspects, such as attention, operational memory and executive functioning, DM can hardly be isolated from these processes.[36]

Time of disease

With regard to the influence of time of disease on the decision-making skills, only one article found positive association between schizophrenia onset time and performance in DM tests.[34] This finding could not be replicated by further studies.[37,39] The finding of DM changes in chronic patients, in the one hand,[34] and the absence of these deficits in patients having their first psychotic episode,[34,41] on the other hand, are, according to some authors, related to different times in the process of frontostriatal circuit disorder associated with schizophrenia.[56,57] According to the same hypothesis, the orbitofrontal functions are relatively preserved in young patients, but follow a different deteriorating course with chronicity. On the other hand, the dorsolateral cortex might suffer early changes, and its deficits might remain stable throughout time, as described by the neurodevelopment hypothesis.[25]

Control group selection and the influence of schooling in samples

The problem of selecting a control group also seems to serve as an intervenient variable in the analysis of tests sensitive to orbital disorder (IGT and others), and the performance of this group in tasks may account for the differences found, even changing the interpretation about patients.[41] In the study by Rodriguez-Sánchez et al.,[41] the control group IGT performance proved to be worse than in two other studies, by Ritter et al.[38] and by Shurman et al.,[37] whereas the patients' performance in the same test was similar in all three studies.[38,39,41] Rodriguez-Sánchez's patients, however, had normal IGT measurements, after comparison with a control group. On the other hand,

in the study by Beninger et al.,[35] low educational level in the group using typical ATP was not correlated with worse IGT learning. Curiously, patients taking atypical ATP and with more schooling years (similar to the control group) showed worse IGT performance. Further studies should consider confusion variables related to the control group and the role of schooling in tasks assessing DM.

Schizophrenics and patients with OFPC lesion: similarities and differences in DM tests

Whereas, at least in some studies, the performance of schizophrenic patients in DM tests is similar to that of patients with orbitofrontal lesions, other findings do not seem to correspond to the typical pattern observed in patients with that neurological lesion, whose changes in DM were extensively studied by Bechara et al.[6,11,58,59] The articles mentioned in this review used different hypotheses to describe the probable behavioral mechanisms underlying the performance of schizophrenic patients. At least some of them presented converging aspects. Bechara et al.[6,58] proposed that patients with OFPC lesion gave preference to decks A and B (higher risk) because they suffered of "myopia for the future," i.e., they ignored previous experiences and did not adjust their behavior to a higher possibility of punishment inherent to this strategy, persisting in disadvantageous choices. Curiously, Shurman et al.[37] and Wilder et al.[33] found higher preference of schizophrenics for decks B and D, characterized by frequent rewards (of low value, though) and rare (but higher) punishments. There is a similar, but partial, tendency in the study by Ritter et al.,[38] with prevalent preference given to deck B. Those patients would supposedly be attracted by the higher probability of rewards over punishments, showing a relative negligence to the magnitude of gains and losses. Other authors diverge on the role of previous experience on present decisions in schizophrenic patients: for Ludewig et al.,[36] current experiences are highly influenced and dependent on previous choices, despite the possible result of the present decision. According to that author, this pattern of decisions contribute to a behavior known as autistic (or self absorbed), characteristic of many patients, whose everyday preferences are rarely influenced by social

interaction. One year before (2002), Hutton et al.[34] made similar comments, concluding that chronic schizophrenic patients tended to make disadvantageous choices even when warned about associated risks. In addition, he observed that chronic patients, such as those having their first psychotic episode, presented higher latency in decision making and less adequately adjusted their decisions based on changes in the test (NDMT). Only the study by Bark et al.[39] defended a relation between IGT performance and neuropsychological mechanisms specific of catatonia. Deficits might be motivated by a disability, among the catatonic group, of recognizing and implementing a favorable behavioral strategy (which explains the rigidity during the game and preference for decks A and B – high risk). Therefore, those patients could have a curve similar to that of individuals with neurological OFPC lesion.

CONCLUSION

Existing studies reveal so far conflicting results regarding the association between DM and affected OFPC areas in schizophrenia. Differences found and difficulties in replicating studies should consider many related variables, especially about selected samples, such as age of disease onset, diagnostic subtype of schizophrenia, predominant symptoms, motor changes and the role of drugs on the neuronal systems involved in the selection of choices. The correlation of measurements obtained in tests assessing decision-making skills with the standard of psychosocial functioning is also important, since the latter is considered a reliable predictor of schizophrenia prognosis.

Most studies to date have not been able to establish a similarity as to performance pattern (at least in IGT) between schizophrenic patients and other victims of orbitofrontal neurological victims, assessed in the first studies by Bechara et al.[5] and Damasio et al.[4] It is possible that those differences are attributed not only to the clinical variables mentioned above, but also to anatomofunctional aspects that regulate the DM process and are not clearly understood yet. If, on the one hand, there is a likely involvement of other noncortical areas, such as the anterior cingulum

and amygdala in the DM system, on the other hand, it is necessary to perform a more detailed screening of orbital cortical sectors (besides the OFPC) that account for the specific processing and in different stages of the decision-making mechanism. In summary, it is possible that current neuropsychological instruments are not specific to assess the complex processing of decision-making skills.

Therefore, further studies using more homogeneous samples and better defined methodological criteria as to clinical and demographic variables are needed, both to clarify the neurological basis and clinical repercussions of existing deficits, and also to define the role of current neuropsychological instruments. A more detailed understanding of the mechanisms of emotional regulation and social judgment may have important consequences, especially in terms of clinical and psychosocial rehabilitation.

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ABSTRACT

Objectives: *A critical review of the literature was undertaken with articles assessing neuropsychological deficits in decision making (DM) in schizophrenic patients.*

Methods: *This review included all articles that performed neuropsychological assessments with tests sensitive to cortical areas associated with DM, especially the orbitofrontal cortex dysfunction. Methodological aspects of the selected studies were compared, as well as the correlation between measures in DM tasks with clinical, cognitive and functional characteristics of the samples.*

Results: *Eight articles between 1997 and 2005 were selected. With regard to the instrument used to assess DM, six used the Iowa Gambling Task (IGT), one used the Novel Decision Making Task (NDMT) and one used the Two Choice Prediction Task (TCPT). All the studies compared schizophrenic patients to healthy controls. In four articles using the IGT and the others using either the NDMT or the TCPT, schizophrenic patients showed low performance in DM tasks.*

Discussion and conclusion: *Current studies are inconclusive in assessing DM deficits in schizophrenia. Clinical characteristics such as diagnostic subtype, predominant symptoms, type of medication and psychosocial functioning can account for the results found. Further studies are required to better investigate the nature of DM deficits in schizophrenia and their relevance to clinical presentation and illness course.*

Keywords: *Schizophrenia, decision making, neuropsychology, prefrontal cortex.*

Title: *Neuropsychological assessment of decision-making prefrontal circuits in schizophrenia: a systematic review of the literature*

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