Pathological Gambling: An Impulse Control Disorder? Measurement of impulsivity Using Neurocognitive Tests

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ABSTRACT: Pathological gambling is classified in the DSM-IV-TR (Diagnostic and Statistical Manual of Mental Disorders) and in the ICD-10 (International Classification of Disease) as an impulse control disorder. The association between impulsivity and pathological gambling remains a matter of debate: some researchers find high levels of impulsivity within pathological gamblers, others report no difference compared to controls, and yet others even suggest that it is lower. In this review we examine the relationship between pathological gambling and impulsivity assessed by various neurocognitive tests. These tests – the Stroop task, the Stop Signal Task, the Matching Familiar Figures Task, the Iowa Gambling Task, the Wisconsin Card Sorting Test, the Tower of London test, and the Continuous Performance Test – demonstrated less impulsivity in gambling behavior. The differences in performance between pathological gamblers and healthy controls on the neurocognitive tasks could be due to addictive behavior features rather than impulsive behavior.

KEY WORDS: pathological gambling, impulsivity, neurocognitive tasks, Stroop task, Stop Signal Task, Matching Familiar Figures Task, Iowa Gambling Task, Tower of London test, Continuous Performance Test, Wisconsin card sorting test

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Gambling behavior is defined as placing something of value at risk with the hope of gaining something of greater value in return [1]. Pathological gambling is characterized by gambling behavior that significantly impairs occupational, interpersonal and financial functioning [2].

Pathological gambling is classified in the Diagnostic and Statistical Manual of Mental Disorders [3] and in the International Classification of Diseases [4] as a disorder of impulse control. However, this association between impulsivity and pathological gambling remains an ongoing issue within the literature: some researchers report high levels of impulsivity in pathological gamblers while others cite results implying no difference in impulsivity of pathological gamblers versus controls, and yet others suggest that impulsivity in these gamblers is lower than in controls [5].

Although the term “impulsivity” is widely used, research has traditionally encountered several difficulties in defining and exploring the construct of impulsivity. Factor analyses of neuropsychological measures revealed the existence of the “inhibitory control” factor; this includes measures derived from the Matching Familiar Figures Task, the Go/Stop-Go, and the Stop Signal Task [6-16].

The Stroop Task [6] is one of the most commonly used instruments for the evaluation of cognitive control [7]. This task tests cognitive processes associated with goal-oriented behavior that selects a weaker, task-relevant response or a potentially stronger, task-irrelevant response [8,9]. Difficulty with inhibitory processing is reflected by an increase in time in the non-congruent condition of the Stroop test relative to the neutral condition. Subjects with prefrontal impairment have difficulty with this task, suggesting that frontally mediated processes are involved in adhering to the goals or rules of the task in the face of a competing, stronger (i.e., more salient, habitual, or prepotent) response [7]. Previous studies that measured Stroop performance in pathological gamblers are inconsistent. Some authors have suggested that the presence of Stroop impairments is an important characteristic distinguishing pathological gamblers from healthy controls [10], but others reported that the Stroop performance in these gamblers is similar to that of healthy controls, and differences can only be related to different neural mechanisms of inhibition control during performance [11].

Stop Signal Task constitutes a laboratory analog of a situation that requires an individual to stop a planned or prepotent response [12]. The SST is an objective measure of the latency and efficiency of the inhibition process to break the “go” response when it becomes inappropriate [13,14]. In this test, the examinee is required to make rapid motor responses on “go” trials but to inhibit responses if a “stop” signal occurs. Response inhibition ability can be quantified by the “stop” signal reaction time, an estimation of the time taken to inhibit the wrong motor response [12]. For the calculation of latency, it is necessary to know the latencies of starting and finishing

SST = Stop Signal Task
the "stop" processes. The discrepancy between the two latencies is the SSRT. The stimulus onset asynchrony defines the start of the "stop" processes, and the end needs to be derived from other results. Inhibition needs to be investigated through a comparison between conditions with and without response execution. It becomes harder to suppress a response as the "stop" signal is presented closer to the moment of responding (in other words if SOA is longer). A profile of inhibitory efficiency is derived over time by manipulating the SOA between the response and "stop" signal. It is possible to estimate the efficiency of response inhibition capacity in the SST that measures the number of false responses [12]. The concept of reflection-impulsivity was introduced by Kagan in 1964 and refers to the tendency to gather and evaluate information before making a decision [15]. One of the most widely used behavioral measures of the reflection-impulsivity dimension is the MFFT.

Matching Familiar Figures Task [16] requires subjects to search a number of similar pictures for only one that matches a criterion picture exactly. A reflective person tends to consider various possibilities before making a choice, while an impulsive person tends to quickly choose an answer without thoroughly considering alternatives; impulsive behavior has therefore been associated with short latencies and many incorrect answers on the MFFT [16,17].

Iowa Gambling Task is a frequently used neuropsychological test of decision-making ability under initially ambiguous conditions. The test simulates real-life decision making by testing the ability of participants to learn to sacrifice immediate rewards in favor of long-term gain. On this task, patients with medial and orbitofrontal lesions, pathological gamblers, and a subset of substance-dependent individuals demonstrate preferences for short-term gains at the risk of larger net losses [17].

Wisconsin Card Sorting Test assesses abstract ability, namely the ability to shift cognitive strategies in response to changing environmental conditions, thereby assessing the kind of executive functioning that involves strategic planning, organized searching, and the ability to use environmental feedback to modify cognitive sets [18]. This task has a different neuropsychological profile as it is sensitive to damage of the dorsolateral portion of the prefrontal cortex, as well as damage to non-prefrontal cortical regions connected to the prefrontal cortex, e.g., parietal cortex.

Tower of London test measures planning ability [19]. Performance on this task reflects cold processes that are dependent on the dorsolateral prefrontal cortex. Cold processes are emotionally neutral decisions with no weighing of rewards and punishments. Cold processes govern real-life decisions such as planning the details involved in opening a new company branch, for example. Risky or hot decisions, on the other hand, involve an evaluation of reward and punishment, with emotional significance attached to both outcomes. For example, the decision between financing one of several potentially excellent but risky business opportunities is a hot decision; it is difficult to ignore emotions.

Continuous Performance Test provides measures of sustained attention and impulsiveness. This test is one of the most acceptable tests in the diagnosis of attention deficit hyperactivity disorder [20]. ADHD is commonly related to impulsive and aggressive behavior with a propensity to addictions. Some researchers claimed that up to 40% of people with ADHD will suffer from at least one psychiatric disorder in their lives. Also, the possibility of this population to become addicts is as high as 20% [21]. However, most pathological gamblers do not suffer from ADHD and they have a different behavioral pattern [22,23]. They respond the same as normal controls (unpublished data).

We conducted a Pubmed-Medline search by using the following words: pathological gambling, neuropsychological tests, cognitive tasks, impulsive control disorders, dry addictions, Stroop, Go Stop Go, MFFT, Iowa Gambling Test, and Continuous Performance Test. We analyzed the data, and summarized the up-to-date evidence and the correlation between pathological gamblers and each individual test from Pubmed and our patient/control sample. Our aim was to consolidate the indications, advantages and disadvantages for preliminary diagnosis.

**NEUROCOGNITIVE TESTS**

- **The Stroop Task**: This is one measure of selective attention that has featured prominently in recent studies of cognitive biases in addictive behaviors [6]. The original Stroop Task incorporated only words relating to color; however, subsequent modified formats have used emotionally salient words to examine cognitive processing associated with emotional disturbance and disorders. These modifications of the Stroop Task have been extended to studies of addictive behavior including eating disorders and alcoholism. The Stroop Task is widely regarded as a reliable measure of attention and the phenomenon is robust and always statistically reliable [24].

Participants begin by reading aloud as quickly as they can from a page with the names of colors written in black ink.
Next, participants are presented with trigrams (“XXX”) that are printed in colored ink, and they are asked to state the ink color. Finally, they are presented with a page of color names printed in ink of colors different from the names. They are required to inhibit the desire to read the word and are instead given credit for stating the ink color. Outcome variables include the number of correct words read in 45 seconds in the following tests: Congruent (Stroop Word), Congruent (Stroop Color), Incongruent (Stroop Color Word), and Stroop interference, and results are given as t-scores [22].

- **Stop Signal Task:** This is performed with a preliminary sample trial. Participants are instructed to respond to the “go” as quickly as possible and should immediately stop their response when they see the flash. There are no specific instructions to wait for the stop signal. They are also given a feedback at the end of the practice setting, and are shown their accuracy of performance. Thus, in the practice setting, subjects are trained and achieve the 100% correct performance level.

False alarm errors occur when the subject presses a button if the flash over the red square appears; such a response is considered a measure of impulsivity. Errors of misses occur when the subject omits pressing the button when a red square appears; such a response is considered a measure of inattention.

Inhibition ability requirement can be controlled experimentally by varying the interval between the onset of the “go” stimulus and the onset of the “stop” signal (termed the stop-signal delay).

The speed of the inhibition response cannot be observed directly but can be derived mathematically. The calculated inhibition time is the time used to wait at the “stop” signal (in the “go” trial) minus the response time after the “stop” signal (in each of three “stop” signal conditions separately) as measured in milliseconds. Response time is defined as the time between the appearance of a “go” stimulus and response. A false alarm error is defined as a response to the “stop” signal [23].

- **MFFT:** The subjects are instructed to perform “as accurately as possible.” Participants respond with a dominant index-finger button press to the figure using a computer mouse, which is externally attached for administration of the MFFT.

Errors occur when the subject incorrectly responds to variants of a similar figure, which is not identical to the sample figure. To ensure comprehension of the task instructions, subjects carry out two trial practices. In all MFFT sets, they are given feedback showing accuracy of performance. Therefore, in each of the trials, accuracy of decision is stressed, and subjects need to achieve the highest correct results (minimum number of errors is 0 and maximum is 12 x 5 = 60).

Six dependent variables are analyzed: i) the mean latency to the first response, ii) the mean time taken to make the correct response, iii) the total number of errors, iv) the mean time taken to make the erroneous response, v) the standard deviation of the mean response time taken to make the correct response, and vi) the standard deviation of the mean response time to make the incorrect response.

- **Continuous Performance Test:** The subject has to press a spacebar when any letter, except for the letter X, appears on the screen. An omission error occurs when the subject fails to press the spacebar when a letter (except for X) appears, thus reflecting an instance of failure of the subject to react to the target stimulus. A commission error occurs when the subject presses the spacebar when an X letter appears on the screen, thus reflecting failure to inhibit a prepotent motor response. These two measures are considered as corresponding to the concepts of attentional and motor impulsiveness, respectively, in Barratt’s model of impulsiveness. Omission and commission errors are used as dependent measures to evaluate attentional and motor impulsivity, respectively [25].

- **Wisconsin Card Sorting Test:** The purpose of this task is to sort test cards so that they match one of four stimulus cards, according to a concept that is not known to the subject (form, color or number). Feedback is given regarding correctness of the response. After 10 consecutive correct responses the concept shifts, and the subject has to shift strategy and learn to sort the cards according to a new sorting concept [19].

- **Tower of London task:** The subject has to move colored balls on pegs from a fixed starting configuration to a goal configuration in a limited number of steps. Two, three, four and five-move problems are presented to the subjects, and the required number of steps is indicated. When subjects fail an item, they would have up to two extra trials to attain the goal configuration. The correct score of each item ranges from 1 to 3 points, with a reduction of 1 point for each extra trial that was needed. A linear decrease is expected in the number of correct trials. Therefore, regression coefficients (standardized beta scores) are determined for each participant and beta weights are calculated, with the number of correct trials as the dependent variable and difficulty level (four levels) as the predictor. A lower beta score indicates a steeper decrease on correct trials and thus indicates a worse performance. The dependent measure of this task is the beta weight of the correct score [19].

- **Iowa Gambling Task:** The computerized version of the Iowa Gambling Task consists of 100 successive trials in
which subjects are required to choose a card from one of four decks. Decks differ with respect to the size and frequency of payoffs produced by each card selection [26]. The participants are instructed to try to gain as much money as possible by drawing cards from one of four decks (A, B, C, D). The decisions to choose from the decks are motivated by reward and punishment schedules inherent in the task. Two of the decks (A and B) are disadvantageous, producing immediate gains (large rewards), but these are accompanied by larger losses in the long run (larger punishments). The C and D decks are advantageous: here, gains are modest but more consistent and losses are smaller. A net score [(C+D)-(A+B)] was computed, with a higher score indicating that a subject is more often choosing advantageous decks [26].

**COMMENT**

**Stroop Task:** In the Stroop Task, a central measure of cognitive control is the performance on the incongruent condition. The successful performance of the incongruent condition requires inhibition of the interference introduced by the semantic meaning of the word during signal perception, and perhaps also inhibition of the tendency to respond to the semantic meaning during response selection [27]. As predicted, error rates in the incongruent condition of the Stroop Task were significantly higher in the pathological gamblers. These individuals could be characterized as 'slow and inaccurate' performers. Slow and inaccurate responses are an expression of the inability to quickly adapt performance to task-related changes. This type of performance may be related to impaired ability to switch motor responses [27] and repetitive behavior [28].

**Stop Signal Task:** In the Stop Signal Task, impulsivity was defined as the inability to inhibit an activated or pre-cued response leading to errors of false alarms.

Inhibition is essential for the performance of everyday tasks as it allows us to adapt our behavior in line with signals from the ever-changing environment and with our own internal directions. These problems have been overcome by using behavioral measures of impulsivity as defined by the inability to anticipate and reflect on the consequences of decision making or by the failure to inhibit a response in a rapid response task [10].

A pathological gambler should calculate how much he can lose, or how likely he is to be the victim of uncontrolled decision making. Thus, since gambling requires various levels of reflection and control, it may be wrong to oversimplify and label pathological gamblers as “impulsive” [29].

The studies that focused on animal races found that frequent bettors appeared to delay placing their bets until just before the start of the race. Additionally, people who follow horse racing events spend considerable amounts of time and energy trying to increase their odds of winning. Studying the history of horses, jockeys and tracks all figure into their calculations. Sport event gamblers mostly invest hours examining players, injuries, previous games and match-ups in the hope of increasing their knowledge and subsequently their odds [30]. This behavior could explain gamblers’ propensity for a wait-and-see strategy rather than impulsive acts.

**MFFT:** The MFFT received a great deal of attention [31,32] as this task measures the capacity to attend to details while considering alternative hypotheses in processing information [16]. The presence of attention deficit hyperactivity disorder during childhood was proposed as a risk factor for the development of pathological gambling in adulthood [33,34]. Previous studies demonstrated a significant association between ADHD and several performance variables such as errors rate and response time variability [35]. However, in our sample, the variability of correct response time in the MFFT performance was not significantly different in pathological gamblers compared to controls (Dannon et al., unpublished data). Our sample was based on 82 pathological gamblers versus age and gender-matched normal controls. In this sample the variability of error response time in MFFT was less in the gamblers than in the controls. It was previously found that pathological gamblers with retrospective childhood diagnoses of ADHD did not exhibit significantly more impaired CPT [21] or go/no-go [36] performance than the pathological gamblers without ADHD. Although our gamblers have a significantly higher rate of errors on MFFT than controls, it appears unlikely that this was related to the comorbid diagnosis of ADHD.

Impulsive behavior, the identifying feature, is a preference to avoid delay, which the individual finds aversive [37]. Impulsive subjects are less able to delay gratification or resist temptation and they preferred an automatic quick selection of stimuli for responses without monitoring. Therefore, impulsive behavior would be associated with the tradeoff of greater speed at the cost of less accuracy. The results of our study showed that pathological gamblers tend to make more errors but not quicker responses as compared to the control group. In addition, in MFFT performance, we found a similar power of negative correlation between the number of errors and response time in both gamblers and controls. We may conclude that the impaired performance of our pathological gamblers as compared to the controls on the MFFT cannot be explained by a tradeoff of greater speed at the cost of less accuracy.

**CPT:** according to Rodriguez-Jimenez et al. [21], the CPT scores for sustained attention were not significantly different.

CPT = Continuous Performance Test
regarding either omission or commission errors between gamblers and controls.

**IGT:** This task presented various results in pathological gamblers. Some authors found that pathological gamblers show impaired decision making on this task. According to Forbush et al. [38] and Cavedini et al. [39], pathological gamblers have elevated levels of impulsivity, novelty seeking, harm avoidance and lower levels of self-directedness and cooperativeness. However, a different study showed that the gamblers did significantly worse than controls toward the end of the task, but there were no significant differences in other parts of the task [40]. According to these mixed results it is impossible to connect impulsivity with pathological gambling.

**WCST:** In their study, Forbush et al. [38] found that gamblers scored higher than controls on the number of total errors, preservative responses, preservative errors, and lower on learning-to-learn scores. Controls learned to make more advantageous card selection over time than the gamblers. Thus, while initially controls selected more disadvantageous decks, they rapidly shifted their preference toward advantageous decks [38]. According to Goudriaan et al. [19] as well, pathological gamblers completed fewer WCST categories than controls. The gambling group named fewer correct words [19]. However, the findings are inconsistent with a study that reported no impairments on the WCST in a smaller gambling group [39]. In a different study using WCST, the gamblers showed different alterations on the WCST, as compared to healthy control subjects, particularly perseverant errors, failure to maintain the series, and difficulty in learning to learn. The patients fell into the moderate performance group. The authors suggest that pathological gamblers have tremendous difficulty in finding alternative methods of problem solving. In addition, efficiency decreased instead of increasing during the consecutive phases of the test, so they seemed unable to learn from their mistakes. However, the number of categories completed, that is, the number of 10 consecutive correct matching according to the criterion of each category, was not different between gamblers and controls [18].

**Tower of London task:** This task showed a strong decrease in scores with increasing difficulty level in the pathological gambling group than controls [19]. However, there was no connection between impulsivity and gambling. The decrease was reported to be related to demographic factors and/or cooperation of the gambling group compared to the controls.

**CONCLUSIONS**

Neurocognitive tasks, as described above, may be necessary for the future exploration of pathological gambling and other psychiatric diagnoses. After reviewing the literature and applying a variety of neurocognitive tasks to pathological gamblers, we conclude that in concordance with our initial hypothesis, impulsivity is less related to pathological gambling, except for the ADHD group. Indeed, there are certain differences in performance between pathological gamblers and healthy controls on the neurocognitive tasks; however, these could be a result of addictive behavior features rather than impulsive behavior. In that case, neurocognitive tasks that measure addictive behavior could assist in the future exploration of pathological gambling neuropathology.

**References**


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**TOWER OF LONDON**

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**IGT = Iowa Gambling Task**

**WCST = Wisconsin Card Sorting Test**
Adeno-associated virus type 5-mediated intraarticular administration of tumor necrosis factor siRNA improves collagen-induced arthritis

RNA interference (RNAi) is a powerful tool for sequence-specific gene silencing, and interest in its application in human diseases is growing. Khoury and team developed rAAV5 vectors expressing short hairpin small interfering RNA (shRNA) against tumor necrosis factor-alpha (TNFα) under H1 promoter, and carrying the enhanced green fluorescent protein (eGFP) reporter gene under cytomegalovirus promoter (rAAV5-shTNF). TNFα gene silencing was validated in vitro with mouse macrophages. Mice with collagen-induced arthritis were injected in the ankle and knee joints, at disease onset, with either rAAV5-shTNF or control rAAV5-eGFP vectors (5×109 particles). After a single injection of rAAV5-shTNF into inflamed joints, local TNFα gene silencing provided rapid and long-term suppression of arthritis progression and reduced joint damage compared with that observed in control groups. Treatment with rAAV5-shTNF was associated with decreased proliferation and interferon-gamma production by antigen-stimulated T cells from draining lymph nodes, and the potency of this treatment was similar to that observed with other treatment strategies targeting TNFα at the protein level, either locally or systemically. These data present the first proof-of-concept for the application of rAAV5-mediated RNAi-based gene therapy for local blockade of inflammation in experimental arthritis.

“Not everything that can be counted are counts, and not everything that counts can be counted”

Albert Einstein (1879-1955)

“Tis better to be silent and be thought a fool, than to speak and remove all doubt”

Attributed to both Abraham Lincoln and Mark Twain