

Computerized Neuropsychological Examination of Impulsiveness: A Selective Review

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Abstract: There is a rapidly accumulating body of knowledge related to the neurobiology of impulsiveness from multidisciplinary neuropsychological and neuroimaging studies. This paper reviews recent research on impulsiveness in the context of neuropsychological theory and research. It has been emphasized that the controversy regarding the results of neuropsychological studies is related to different aspects of impulsiveness. The term “impulsivity” is related to more than one anatomical network among several brain regions. Impaired inhibition control, which has cognitive and behavioral dimensions, has a heterogeneous nature. Analysis of performance suggests that impulsivity includes three cognitive mechanisms: “prepotent inhibition,” “interruptive inhibition” and “interference control,” each having separate neurological bases. Based on neuropsychological data it has been stated that both the orbitofrontal cortex, dorsolateral prefrontal cortex and anterior cingulate cortex are functionally disturbed among impulsive individuals. Bringing together knowledge from clinical experience, neuroimaging examination and neuropsychological assessment will lead to better and wider understanding of behavioral symptoms in clinical psychiatric practice.

Introduction

Self-harm and externally-directed impulsive behaviors are relatively common in psychiatric populations. Impulsiveness is an important clinical issue, related to various psychiatric diagnoses such as schizophrenia, mood disorders, impulse control disorders and alcohol/drug abuse (1). Impulsiveness was, until recently, typically assessed in the clinical setting with self-report scales and psychiatric examination. Self-assessment questionnaires are biased by low self-awareness and test-taking attitudes, which may lead to an inaccurate evaluation of impulsiveness (2). Moreover, these scales are designed to measure long-standing behavioral tendencies (trait) and they are less suited to repeated evaluation over short periods of time (state) (3). There has been much interest in obtaining objective measures of impulsiveness as state parameters using computerized neuropsychological tasks (4), which potentially promise to be sensitive to treatment manipulation, and provide a quantitative measure of the elemental behavioral tendencies that constitute this concept (5). However, most performance measures of impulsiveness have been developed based on differing theoretical assumptions, and vary in fundamental ways.

There are few studies that have related any one task to another (6). Recent neuropsychological studies provide support for the notion that impulsiveness is a multifaceted cognitive concept (7). This article will attempt to integrate different neuropsychological concepts into the complex clinical assessment of impulsivity.

Impulsiveness can be defined as a neuro-cognitively based inability to conform behavior to its context or consequences. It appears to be strongly related to the “rapid-response” model of “answering before thinking” (8). In order to examine the “rapid-response” concept, a neuropsychological battery should test the patient’s ability to inhibit motor responses to non-target stimuli in different cognitive situations (9). For these notions, two performance measures (reaction time and number of errors) are analyzed as a speed-accuracy tradeoff (10).

Response control

A key component of cognitive process is the ability to suppress or override competing behavioral responses. Response control is a cognitive process involved in decision-making in situations in which

non-relevant information should be inhibited. Inhibition includes different neuropsychological mechanisms (11): 1) the ability *to delay* appropriate responses *before* checking all alternatives (“prepotent inhibition”), 2) the ability *to stop* an inappropriate response *after* the context has changed (“interruptive inhibition”), 3) the ability *to protect* the period of delay (a certain amount of time, in which no decision is taken) from disruption of competing events (“interference inhibition”).

1. Prepotent inhibition

There are two main tasks used to examine prepotent inhibition: the Matching Familiar Figures Test (MFFT) and the Continuous Performance Test (CPT). Although they are used in different experimental situations, they both deal with the same mechanism of inhibition control. However, the MFFT performance requires several abilities in addition to response inhibition (e.g., visual search, hypothesis testing). Kagan and coauthors introduced the MFFT for examination of the “reflection-impulsivity” dimension (12). The MFFT presents situations with several alternatives available, but with only one correct answer. The “response time” and “amount of errors” are direct measures of the ability to delay response before examining and evaluating hypotheses carefully. Subjects who respond quickly and err are said to be impulsive. It was found that non-impulsive “reflective” subjects examined more variants, made more eye fixations per stimulus and scanned all alternatives before answering than did impulsive subjects. The relation between “response time” and accuracy raised the argument that there are four types of response: 1) fast and accurate; 2) slow and accurate (“reflective”); 3) fast and inaccurate (“impulsive”); 4) slow and inaccurate.

The CPT is a well-recognized measure of sustained attention and impulsiveness (inhibitory impairment as measured by Go/No-Go paradigm) (13). Most versions of the CPT randomly present on a computer screen stimuli for 100–200 ms each, at a rate of 1 per 2 seconds. The whole tests last for 10–30 minutes, continuing without pause (for review: see 14). Subjects respond to the target stimulus by pressing a button. In its “classical” concept CPT requires a maintenance of attention in order to detect and respond to periodically appearing rare targets. Errors

of commission occur when the subject incorrectly responds to non-target (false alarms) stimuli; such a response is considered to be a measure of impulsiveness. Errors of omission occur when the subject omits pressing the button when a target stimulus appears; such a response is considered to be a measure of inattention (14). A relatively new measure of impulsiveness is the post-commission reaction time — the ability to notice an error made in a previous response. Commission errors (false alarms) are increased in incarcerated psychopaths, juvenile delinquents, adults with disorders of impulse control, and children with attention-deficit hyperactivity disorder (ADHD) (14). Psychopaths were found to be less likely to slow down and respond more quickly after punishment (14). This tendency to speed up (short post-commission time) has been taken as further evidence for the failure of impulsive individuals to learn from punishment.

The impulsive examinee showed significantly slower response time than healthy subjects. First results in the field of impulsiveness were non-concordant with theoretical assumptions of their more rapid responses to stimuli. In order to understand this paradox, it should be taken into account that CPT is a complicated task, assuming “Go” and “No-Go” responses. When response complexity in performance is increased, requiring subjects to respond as quickly as possible, impulsive individuals appear to be slower, not faster (3, 15). More impulsive subjects showed a significantly slower response time in the decision stage of reaction (15). Based on the work of Logan et al. (16), the response model suggested a race between two independent processes: “Go” and “Stop.” The “Go” situation triggers the go process and the “Stop” situation initiates the stop process. The process that finishes first wins the race. If the go process finishes first, the response is executed. And vice versa: If the stop process finishes first, the response is inhibited. Slowness of impulsive subjects may be the result of impaired speed of inhibition in situations in which there is an inability to withhold responses to “stop” signal (16).

The psychomotor slowness and inattention on CPT are related to dopamine hypofunctioning (17), but the higher number of commissions is associated with lower 5-HT levels (18, see later).

2. Interruptive inhibition

The Stop Signal Tasks (SST) is a measure of the ability to stop quickly and to change behavior in relation to suddenly changing information. The SST challenges the capacity to inhibit an act in progress, which involves processes of response inhibition (16). The SST requires the participant to respond to a "Go" signal. In addition, periodically and randomly on some of the presentations, an imperative "Stop" signal will appear (always occurs shortly *after* presentation of Go stimuli). An inhibition of motor response after "Stop" signals appears is required for accurate performance.

The "Stop" signal requires participant to interrupt a response already started (16). Longer periods of delay intervals ("Stop" after "Go") are associated with diminished probability of inhibiting the response. The outcome of SST situation depends on the speed of "Go" process, the delay between "Go" stimulus and "Stop" signal, and the speed of the "Stop" process. There are two versions of the Stop Signal Task: one with "Stop" signals presented at fixed intervals and a second applying a tracking mechanism to vary the interval between the "Go" and the "Stop" signal. The ability to initiate and to change behavior in relation to changing information is believed to be under the control of a neural circuit involving the subgenual sector of the anterior cingulate cortex (ACC) which appears to be critical for this type of impulsivity (19).

3. Interference inhibition

Interference control is the ability to inhibit the response to information irrelevant to goal-directed behavior (11). The Stroop Color-Word Test is seen as the "gold standard" measure of interference control (20). The Stroop test requires patients to name the ink colors of words referring to colors in which the words themselves are printed with colored letters. In some cases (congruent condition), the color name is the same as the color's letters, e.g., the word "red" printed in red, while in other cases (incongruent condition), they are different, e.g., the word "red" printed in blue, green or yellow. When subjects are required to report the ink color of the word, more difficulties are experienced in the incongruent condition. This can be measured by an increased

amount of time required to complete the task (the Stroop interference effect). One explanation for the interference effect is that word reading and the naming of colors are conflicting. Word reading is an automatic, reflex-like practiced process. In contrast, color naming is relatively novel, and is susceptible to interference from other conflicting processes. Thus, when the two conflicting responses are queued the same stimulus, the response associated with the weaker process will require more resources. The measure of inhibition ability is the relative response delay in Stroop interference condition (as measured by RT incongruent condition — RT neutral condition). In contrast, the time required in the congruent condition is slightly less than that required in the neutral condition (facilitation effect). In a variation of the above paradigm, when subjects are asked to name the word rather than to report the ink color, interference is also observed in the incongruent condition (the reversed Stroop effect). Recent studies have adopted computerized presentation of stimuli, which enables a more precise measurement of reaction time for Stroop performance. In recent years, measuring of the vocalizing a verbal response RT has been replaced by more simple manual key-press measure of reaction time, and no difference was found between the two methods of measurement in control subjects. Studies of interference control usually support evidence for a difficulty in interference control in impulsive subjects (11, 21). Recently, the Stroop test was used for evaluation of the integrity of the prefrontal cortex (PFC) and anterior cingulate cortex (22). First, the damage of prefrontal cortex, which is critical for inhibitory ability, is associated with slowness in Stroop performance (23). Slowness of responses is more prominent in the non-congruent condition of Stroop task, in which an examinee makes intensive use of his working memory and requires the prefrontal cortex activation during interference control (7, 24). Second, solving of problems, while weighing alternate solutions, involves activation of the anterior cingulate gyrus, and the basal ganglia (25–27). Damage of the anterior cingulate gyrus is associated with lower accuracy in interference control in Stroop performance (28).

Neuro-imaging and neuropsychological association

“Inhibition” refers to mechanisms by which the nervous system suppresses information, restricts its use, or restrains its transmission from one area of the brain to another. Inhibitory control and error monitoring are critical functions of the human brain (17).

The ability to inhibit movement is critical for response selection processes, which in turn contribute to accurate performance. This inhibitory process does not simply stop the flow of movement but is an active process that can suppress already prepared activation of the motor cortex (17). Lesion and imaging studies have shown that the orbitofrontal cortex (OFC) plays an important role in inhibition of inappropriate responses. The orbitofrontal cortex is involved in representing the reward value of stimuli and in the rapid learning of associations between visual stimuli and rewarding or punishing outcomes. Patients with OFC impairment often failed to switch their choices after obvious “losses” and were not able to take correct action between risky decisions associated with reward expectations (29). This impairment has been associated with difficulty in responding correctly to punishments, which in turn influence difficulties in learning from experience (30). Difficulties in learning from experience may influence impulsive and socially inappropriate behavior.

Response inhibition was associated with activation of the orbito-frontal cortex, superior temporal gyrus, anterior cingulate cortex, inferior parietal lobule (31), and dorsolateral prefrontal cortex (32, 33) predominantly on the right side. Impulsive patients had less activation of prefrontal cortex during response inhibition than did non-impulsive subjects (31). The defective neural activity (“immature brain”) during response inhibition performance was found among patients with drug and alcohol addiction (34, 35).

Inhibitory control and performance monitoring (error processing) are critical for behavioral control. Research findings provide evidence for a distributed error processing system in the brain that overlaps partially, but not completely, with brain regions involved in response inhibition. In particular, the rostral anterior cingulate cortex and posterior

cingulate gyrus, anterior insular cortex were activated only during error-processing, but not during response inhibition (36, 37).

Pharmacological evidence of multifaceted concept of impulsivity

Impulsive behaviors have been associated with indices of low serotonin (or 5-hydroxytryptamine [5-HT]) neurotransmission: low CSF concentrations of 5-HT, blunted prolactin responses to 5-HT agonists, and disturbances to markers on platelets and in plasma. Acute tryptophan depletion, a procedure that transiently decreases 5-HT neurotransmission, has been reported to increase impulsive behaviors. Together, these studies support the hypothesis that low serotonergic tone plays an etiological role in the pathophysiology of impulsivity. Moreover, depletion of 5-HT was found to effect distinct aspects of impulsive behavior (38). Lifetime histories of impulsive acts have been reported to correlate negatively with glucose metabolism in the OFC and in the temporal cortex (39). This hypocortical activity in patients with borderline personality disorder is related to low 5-HT neurotransmission in the prefrontal cortex (PFC), anterior cingulate cortex (ACC) and orbitofrontal cortex (OFC) (40, 41). Impulsivity may be assumed to be a multifaceted construct with distinct neurochemical substrate. Dissociation was found between the effects of 5-HT 2A,C receptor antagonism, which decreased impulsivity in the choice reaction time task, but had no effect on the delayed reward task. And, 5-HT₆ receptor antagonism, which had no effect on the choice reaction time performance, decreased impulsive responding in the delayed reward task (42). The results suggest that the choice reaction time and the delayed reward tasks do in fact measure different types of impulsive behavior, which are at least partially neurochemically distinct (42).

In accordance with previous conclusions about multifaceted concept of inhibition, dopamine and norepinephrine systems are essential to impulse control (43, 44) and possession of the DRD4 7-repeat allele appears to be associated with impulsiveness on neuropsychological tasks (45). Treatment with methylphenidate enhanced a “prepotent inhibition” but not “interference control” (46–48).

Conclusion

Neurocognitive deficits may be involved in impaired behavioral control that can lead to lower ability for socially appropriate behavior. Development of neuropsychological batteries for objective measurement of impulsiveness may clarify the association between cognitive and behavioral aspects of impulsivity and can facilitate prediction of future dangerous behavior. Neuropsychological tasks developed to simulate real-life decision-making processes may help to detect the specific cognitive mechanisms which may characterize different types of impulsiveness. Further studies will be necessary to clarify diagnostic specificity of inhibitory impairments. Combined use of neuropsychological assessment with functional neuro-imaging will further help understanding the biological basis of impulsive behavior and may help differentiate the psychopharmacological intervention. It could be suggested that orbitofrontal cortex, dorsolateral prefrontal cortex and anterior cingulate gyrus dysfunction may be involved in impulsive behavior.

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