Recent Insights into the Neurobiology of Impulsivity

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Abstract Impulsivity is associated with various psychopathologies, and elevated impulsivity is typically disadvantageous. This manuscript reviews recent investigations into the neurobiology of impulsivity using human imaging techniques and animal models. Both human imaging and preclinical pharmacological manipulations have yielded important insights into the neurobiological underpinnings of impulsivity. A more thorough understanding of the complex neurobiology underlying aspects of impulsivity may provide insight into new treatment options that target elevated impulsivity and psychopathologies such as addictions.

Keywords Impulsivity · Neuroimaging · Translational · Human · Rodent · Delay discounting

Introduction

Impulsivity can be described as “swift action without forethought or conscious judgment” [1, 2], and it can be conceptually divided into multiple forms that may include self-report, response, and choice impulsivity. Self-report impulsivity refers to a more general impulsivity measure, or impulsivity as a personality trait, whereas response impulsivity is the inability to withhold a proponent response, and choice impulsivity

reflects an inability to delay gratification for a larger payout [1, 3]. Different forms of impulsivity may factor separately from one another, raising questions regarding whether they form a unitary or distinct constructs. For example, choice and action impulsivity in both rats and healthy humans were not related to each other in either species [4•]. Multiple forms of impulsivity may be elevated within specific diagnostic groups [5–9]. For example, addictions are associated with elevated trait, action, and choice impulsivity [10–16]. Therefore, determining the underlying neurobiologies of specific domains of impulsivity may help understand the etiology, prevention, and treatment of addictions and other disorders. This review focusses on recent studies of impulsivity, particularly as related to addictions.

Measures of Impulsivity

Human Measures of Impulsivity

Self-report measures may be used to assess impulsive tendencies. A common assessment is the Barratt Impulsiveness Scale (BIS-11), which has been found to factor into three subscales, including attentional, motor, and non-planning impulsivity [17], although recent studies have identified different subscale patterns within different diagnostic groups (see Reid et al. [18]). The UPPS-P is another self-report measure that has been found to factor into five subscales (negative urgency, positive urgency, lack of premeditation, lack of perseverance, and sensation seeking) [19]. Some other measures of impulsivity may fall across several domains. For example, the Monetary Choice Questionnaire (MCQ or Kirby) measure assesses delay discounting by asking individuals to make choices between two hypothetical outcomes and may reflect trait/self-reported tendencies as well as choice impulsivity [14]. For example, would you rather have \$50 today or \$75

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next month? Similar to behavioral delay-discounting tasks, discounting curves can be calculated, with steeper curves reflecting greater self-reported choice impulsivity.

In addition to measures that rely on self-report, computerized tasks have been developed to measure response impulsivity. Response impulsivity may be described as diminished control over action cancellation, although this definition may be more closely aligned with the stopping of an ongoing action (as assessed with the Stop Signal Task [SST]) than with the withholding of an initial response (as assessed with the Go/NoGo Task [GNG]). In the SST, participants are instructed to make a rapid response (e.g., button press) to a given cue (e.g., plus sign). After learning this requirement, participants are randomly and without warning given a ‘stop’ signal, which indicates that they should inhibit the rapid response [20]. The ability of participants to successfully cancel an action and the latency to do so are measured. Those who are considered impulsive tend to make more errors or have an increased latency in action cancellation. Similar to the SST, GNG participants are given two cues: a ‘go’ cue that signals they should perform a specified action (e.g., button press) and a ‘no go’ cue that signals they must inhibit the action [21]. Again, both reaction time and successful inhibition are measured. Individuals who have difficulty successfully inhibiting their response after the stop signal is presented display greater response impulsivity. There are several variations of the continuous performance task, which tax individuals’ sustained attention [22], that have been associated with measures of impulsivity as task participants must respond or withhold responding to stimuli.

A third form of impulsivity is impulsive choice, which reflects a preference for smaller, sooner over larger, later rewards. The main measurement of impulsive choice employs delay-discounting tasks, during which individuals choose between two different rewards. Delay discounting describes the phenomena wherein the subjective value of a reward decreases (or is discounted) as the time to reward receipt becomes farther into the future [23, 24].

Animal Measures of Impulsivity

Response impulsivity is commonly measured in rodents using the five-choice serial reaction-time task (5CSRTT). In this task, rodents are placed into operant chambers and are required to scan five apertures on one wall of the chamber for the presentation of a brief target visual stimulus (e.g., light) in one of them. Immediately following stimulus presentation, the rodent is required to make a nosepoke response at that aperture to obtain a food reward. Rodents can commit several types of errors during the 5CSRTT, with ‘premature errors’ specifically linked with response impulsivity. These premature errors occur when the rodent responds in an aperture before the target stimulus has been presented, i.e., the rodent has failed to wait

for the appropriate signal before making a response (for review see Dalley et al. [25]). More impulsive animals display a greater number of premature response errors.

Delay-discounting tasks, similar to those used in humans, have been developed to measure impulsivity in rodents. In these tasks, rodents are placed in operant chambers and presented with choices between a smaller, sooner reward or a larger, later reward. While human delay-discounting tasks typically use money as a tangible reward, rodent tasks typically use food or water as the reward. Greater discounting of the large reward (e.g. steeper discounting) is indicative of a more impulsive animal [26, 27].

Underlying Neurocircuitry of Impulsivities

Both clinical and animal studies investigating the neurobiological and psychopharmacological basis of impulsivity have focused on and heavily implicated monoaminergic corticostriatal systems [28]. Brain imaging studies in humans have identified structural and functional alterations in corticostriatal circuitry in impulsive individuals. In particular, dysfunctional or dysregulated monoaminergic signaling (most notably within the dopaminergic [DA] and serotonergic [5HT] systems) has been suggested to underlie both response impulsivity and impulsive choice.

Self-Report

In healthy humans, gray- and white-matter volumes have been found to correlate with scores on the BIS-11 and MCQ. Positive correlations were observed between total BIS-11 scores and volumes of the left anterior cingulate gyrus, left medial frontal gyrus, and left middle frontal gyrus (within the dorsolateral prefrontal cortex [dlPFC]) [29]. In the same study, non-planning impulsivity on the BIS-11 correlated positively with volumes of the left anterior cingulate gyrus, right middle cingulate gyrus, left middle cingulate gyrus, left middle frontal gyrus (within dlPFC), and right orbitofrontal gyrus. BIS-11 attentional impulsivity scores correlated positively with volumes of the left medial frontal gyrus, right medial frontal gyrus, and left middle frontal gyrus (within dlPFC). Positive correlations were observed between MCQ scores and volumes of the right medial frontal gyrus, right orbitofrontal gyrus, left medial frontal gyrus, left anterior cingulate gyrus, and left middle cingulate gyrus; negative correlations were observed between MCQ scores and bilateral ventral putaminal volumes. Taken together, these results suggest regional specificity in the relationships between facets of self-reported impulsivity and gray-matter brain volumes and overlap between the regions linked to BIS-11-assessed and MCQ-assessed impulsivity. A separate study identified negative correlations between left middle frontal gyrus cortical thickness and scores on the BIS-11 and its attentional, motor, and non-planning subscales

[30]. Negative correlations were also observed between cortical thickness in the orbitofrontal cortex (OFC) and superior frontal gyrus with both overall BIS score and motor impulsivity. The only positive correlation was between the right inferior temporal lobe and non-planning impulsivity. The different results from these two studies could reflect procedural, analytical, or other differences. More studies are needed to investigate the potentially contrasting findings noted above.

Investigations of impulsivity and brain structures have also been conducted in individuals with addictions. Cocaine-dependent individuals have been reported to display lower gray-matter volumes in the OFC, right inferior frontal gyrus (IFG), right insula, left amygdala, left parahippocampal gyrus, temporal gyrus, and bilateral caudate, and lower white-matter volumes in the left inferior and middle frontal gyri, superior temporal gyrus, right anterior cingulate cortex (ACC), insula, and caudate [31]. “Lack of premeditation” scores on the UPPS-P in cocaine-dependent individuals was negatively correlated with gray-matter volumes in the insula and putamen, and positive correlations were observed between self-report impulsivity on the UPPS-P and gray-matter volumes in the left inferior and middle frontal gyri [31].

Functional brain activity has also been linked to impulsivity in addictions. Decreased resting-state connectivity within the putamen and posterior insula has been related to elevated BIS-11 scores in cocaine-dependent, but not healthy comparison, individuals [32]. In a cocaine-craving functional magnetic resonance imaging (fMRI) task, an association between motor impulsivity scores on the BIS-11 and inhibition-related activations in the right IFG and pre-supplementary motor area was observed in abstinent cocaine users [32]. More research is needed to examine the extent to which such findings might relate to clinically relevant measures like vulnerability to relapse.

Response Impulsivity

Human Studies

Regions implicated in response impulsivity include the PFC, OFC, anterior insula, ACC, striatum, and frontal gyri [28], with functional connectivity between these regions also contributing importantly. On the GNG, connectivity between the dlPFC and gray matter around the bilateral intraparietal sulcus positively modulated mean go-reaction times and connectivity between the medial PFC and posterior cingulate cortex (PCC) negatively modulated mean go-reaction times [33]. Another study reported that the right anterior insula and right superior frontal gyrus were involved in action restraint, and the right anterior insula and right middle frontal gyrus were involved in action cancellation [34•]. In the latter study, investigators used

transcranial theta-burst stimulation in healthy control individuals to selectively disrupt the right anterior insula, right superior frontal gyrus, or right middle frontal gyrus independently. Disruption of the right anterior insula resulted in decreased restraint and cancellation, disruption of the right superior frontal gyrus resulted in decreased restraint, and disruption of the right middle frontal gyrus had no effect on task performance [34•]. In a separate study, Steele et al. [35] compared correctly inhibited no-go trials in the go/no-go task to correct go trials. During response inhibition, regions particularly implicated in successfully inhibiting the response included the fronto-parietal regions, specifically the bilateral ACC and insula, right OFC, right dlPFC, and right supplementary motor areas. During GNG performance, response inhibition was related to increased activation in bilateral subgenual cingulate, bilateral occipital gyrus, right inferior parietal lobe, right precuneus, and right putamen [36]. Error processing activated over 30 regions, including the ACC, superior and medial frontal gyri, IFG, superior and middle temporal gyrus, insula, inferior parietal lobule, and precuneus.

Serotonin (5HT) function has been linked to GNG performance. Activation of the left IFG during no-go was greater with citalopram administrations than with acute tryptophan depletion [37]. The IFG during no-go trials displayed an interaction between type of 5HT challenge and neocortical 5HT_{2A} receptor binding, such that acute tryptophan depletion produced an increase in response during no-go trials in right IFG in subjects with low 5HT_{2A} binding potential and a decrease in no-go response in those with high 5HT_{2A} binding potential as measured by positron emission tomography (PET) [37]. Taken together, findings suggest that there may be an optimal level of serotonin, or activation of the 5HT_{2A} receptor subtype, which allows for successful no-go responses. These findings suggest avenues for pursuit of personalized treatment options relating to impulsivity and 5HT_{2A} receptor function.

Recently, a human four-choice serial reaction time task has been developed as a novel translational analog to the rodent 5CSRTT [38, 39]. During this task, the participant is required to press a button for cue onset, when a green target will appear on the screen. The participant is then required to respond to the green target within an allotted time. Similarly to 5CSRTT, reaction time and premature responding are measured. Interestingly, Worbe et al. [38] found that tryptophan depletion significantly increased premature responding, a finding similar to that in the rodent 5CSRTT. The increase in premature responding was correlated with motor impulsivity on the BIS-11. These results suggest that the 4CSRTT in humans is a valuable new tool that can be used for cross-species translational studies. In addition, these results are also consistent with those from a previous study investigating tryptophan depletion in humans while performing the continuous performance task [40]. Voon et al. [39] found that, compared with healthy volunteers,

cannabis users, tobacco smokers, and those dependent on either alcohol or methamphetamine showed increased premature responding, consistent with other studies that investigated impulsive action using GNG tasks in groups abusing heroin [41], cocaine [42–44], and tobacco [45], particularly during deprivation [46].

Additionally, GNG performance has been studied with respect to familial alcoholism. Relatively increased activation was observed in the left anterior insula and IFG during successful inhibitions in the family-history-positive group, and these same regions were implicated in greater impulsivity when scans were compared with out of scanner self-reported impulsivity (on the BIS-11) and greater discounting in an experiential discounting task [47•]. Smokers show activation in similar regions when performing a monetary incentive GNG task, such as hyperactivation in the right insula, inferior and middle frontal gyri, dlPFC, and the inferior parietal lobe during inhibition [48]. However, when smokers performed a more standard GNG task, they demonstrated hypoactivity in the left IFG, right medial frontal gyrus, and ACC [48]. Administration of the D2/D3 antagonist haloperidol in smokers during a GNG task resulted in reduced accuracy and reduced activation in the ACC, right superior frontal gyrus, and left IFG [45]. Interestingly, this effect was more pronounced in non-smokers than in smokers, which supports the idea that dopamine is implicated in impulsive action and altered in smokers.

Dopamine also appears relevant to impulsivity in cocaine dependence. In cocaine-dependent individuals, administration of the pro-dopaminergic agent methylphenidate resulted in the restoration of activation in precuneus/posterior cingulate and ventromedial (vmPFC) regions prior to stop errors [49], regions that had been previously implicated in error processing [50, 51]. Curiously, activation patterns in former cocaine users differed more from those in control individuals performing a GNG task than current users, showing greater activation in the right middle frontal/precentral gyri, right inferior parietal lobe, and left angular/supramarginal gyri [51]. Another study found significantly greater activation within the prefrontal, cingulate, and inferior frontal gyri in abstinent cocaine users for both successful response inhibition and error processing [52]. Taken together, these studies suggest that former cocaine users have greater recruitment of frontal systems while performing inhibitory tasks than both current users and healthy controls. The greater activation may be a compensatory mechanism that may help reduce impulsive actions and assist in maintaining abstinence, particularly as regional activation during inhibitory control has been related to successful abstinence [53, 54].

Animal Studies

Animal studies use analogs to human response impulsivity tasks, including the 5CSRTT, the SST, and the GNG. For

example, in rats, inactivation of the vmPFC resulted in impaired inhibition in the 5CSRTT, indicating vmPFC involvement in controlling premature responding [55]. Decreased gray matter in the left accumbens core has been associated with high impulsivity in the 5CSRTT [56•]. Decreased levels of the GABA receptor GAD65/67 in the accumbens core was related to both decreased gray matter in the accumbens core and higher impulsivity, and experimentally reducing GAD65/67 receptors in the accumbens core bilaterally in low impulsive animals increased impulsivity [56•]. In line with these findings, inactivation of the accumbens core by the GABA_A agonist muscimol resulted in global impairments in 5CSRTT performance, and inactivation of the shell induced specific impulse-control deficits [57]. GABAergic projections have been less well investigated in the context of addiction, although GABAergic mechanisms influence function of the mesolimbic pathway [58]. While GABAergic manipulation was successful in modulating response impulsivity in rodents, in humans, GABAergic function has been arguably linked more closely to self-report impulsivity and impulsive choice [59–61] than to response impulsivity (although see Silveri et al. [62]). Within the mesolimbic pathway, dopamine and serotonin have been the two most heavily studied neurotransmitters with regard to impulsivity.

Administration of d-amphetamine, which influences dopaminergic and noradrenergic function, may increase response impulsivity in rodents [63, 64]. D2-like receptor agonism has been reported to reduce response impulsivity in rats during the 5CSRTT [65], regardless of pre-existing high or low impulsivity levels. Additionally, antagonism of D2-like receptors within the dorsal striatum during SST performance or within the ventral striatum during 5CSRTT performance results in ‘normalized’ behavior [66, 67], such that D2-like receptor antagonism may stabilize or improve impulsive responding when antagonists are infused directly into those regions; however, there are no alterations in response impulsivity if D2-like receptors are blocked within the PFC [68–71]. Highly impulsive animals, as measured by the 5CSRTT, display low D2-like receptor availability in the mesolimbic pathway [72]. Rats with high impulsivity in the 5CSRTT have low D2/D3 expression in the striatum as measured by PET. A relationship between D2/D3 receptor expression and impulsivity was recently reported in humans using PET while participants performed the SST, such that D2/D3 availability was negatively correlated with speed of response inhibition and positively correlated with inhibition-related fMRI activation in frontostriatal circuitry [73•]. Moreover, administration of the D2-like agonist cabergoline in healthy human controls resulted in an increase in stop signal reaction time (decreased response impulsivity) in the SST [74]. Administration of the D2/D3 receptor antagonist nafadotride into the accumbens shell in rats enhanced premature responding in high impulsive rats [75], and rats with lower D2/D3 receptor availability in

the ventral striatum display greater response impulsivity on the 5CSRTT [76]. These findings further implicate the ventral striatum (more specifically, the nucleus accumbens) in regulating impulsivity, but they additionally highlight the importance of D2-like receptor activation within this region.

Similar to the dopamine system, alterations on impulsivity via the 5HT system can be regionally dependent [77–80]. Global reductions in 5HT (including lesion studies) increase response impulsivity [81, 82]. Mice lacking *Tph2* (a manipulation that depletes the brain of serotonin) show impulsive, compulsive, and aggressive behaviors [83] (note that Dambacher et al. [84] found an overlap in motor impulsivity as measured by GNG and aggression in the anterior insula). The elevation in response impulsivity was notably not related to anxiety, and reversal learning was intact. Restoration of 5HT by treatment with the *Tph2* precursor 5-hydroxytryptophan resulted in attenuation of increased impulsivity and aggression [83]. Specific 5HT receptors have been related to response impulsivity. In particular, 5HT_{1A} and 5HT_{2A/C} agonists increase response impulsivity [85, 86], whereas the 5HT_{2A} and 5HT_{2A/2C} receptor antagonists decrease response impulsivity during 5CSRTT performance [87, 88]. In contrast, the 5HT_{2C} agonist decreases response impulsivity, whereas the 5HT_{2C} antagonist increases response impulsivity [89, 90]. Increased 5HT_{2C}R levels in the OFC have been observed in the brains of high-impulsive animals [72]. However, 5HT manipulations have not been particularly beneficial in humans [91–98] (although, see Booij et al. [99], Dougherty et al. [100], LeMarquand et al. [101], Walderhaug et al. [102, 103], and Crean et al. [104], as tryptophan depletion can increase impulsivity), which may be a result of the limitation of serotonergic drugs currently approved for administration in humans. For example, many of the drugs available for administration are selective serotonin reuptake inhibitors that lack specificity for individual receptors, and certain 5HT receptors are currently not targeted in humans in the context of impulsivity. The divergent actions of specific serotonergic receptors highlight the need for more research investigating the roles of different 5HT receptors and their relationship to different forms of impulsivity.

In addition to dopaminergic and serotonergic contributions to impulsivity, other systems have been implicated. For example, the alpha2-adrenoceptor agonist guanfacine slows SST performance and impairs accuracy, particularly when administered in the dorsomedial (dmPFC) [68, 69, 105]. The norepinephrine inhibitor atomoxetine increases stop-signal reaction times in both rats and humans [69]. While both norepinephrine and dopamine appear important for both error monitoring and performance adjustment, norepinephrine may be more critical in the inhibition of already initiated responses, whereas dopamine may be more important for motor readiness [106].

Impulsive Choice

Human Studies

Mesocorticolimbic dopamine pathways within the medial PFC (mPFC), OFC, and ventral striatal projections are involved in impulsive choice [107–122]. For example, decreases in white matter in the prefrontal cortex, and increases in the right parahippocampus and hippocampus, have been found in impulsive individuals [123]. The mPFC has been linked to varying degrees to impulsive choice [25, 124–133]. In humans, the subjective value of monetary rewards has been associated with activation of the ventral striatum (VS), mPFC, and PCC. During in-scanner delay-discounting performance, the vmPFC was active during the delay period and during choice, which is consistent with a role for the vmPFC in time coding and subjective value. The VS showed a similar pattern, particularly in impulsive participants. The anterior PFC (aPFC) showed a decrease of delay-related choice activation, but it was selective in impulsive individuals. Additionally, functional connectivity analyses indicated that both vmPFC and aPFC moderated VS activation in different fashions, such that vmPFC activation resulted in an increase in VS activation whereas the aPFC activation results in a deactivation of the VS [134].

Monetary delay discounting studies have found that drug addiction is associated with elevations in impulsive choice [12, 135–139]. Such patterns of impulsive choice have been observed well into abstinence; for example, cocaine users who were abstinent at least 30 days did not discount rewards differently from those currently using cocaine [140], and heroin users who were abstinent at least 16 months were also indistinguishable on this measure from current users [141]. Interestingly, modafinil administration improved delay discounting in alcohol-dependent individuals by enhancing recruitment of frontoparietal regions, reducing recruitment of the vmPFC and enhancing functional connectivity between the superior frontal gyrus and VS [142]. While different drugs of abuse may differentially alter brain functioning and ultimately impulsive choice in individuals with addictions, pharmacological manipulation of the same brain regions implicated in impulsive choice in both healthy and addicted individuals (e.g., vmPFC, frontoparietal, and striatal regions) may provide assistance in reversing (potentially) drug-induced elevations in impulsivity.

Work investigating relationships between cannabis use and impulsive choice has not found differences between users and nonusers [143] in discounting rates; however, those seeking treatment for cannabis dependence tend to increase impulsivity over time in the absence of contingency management [142]. It is difficult to determine whether the increase in

impulsive choice is related to cigarette use (instead of cannabis, particularly since nearly all of the cannabis users studied were also tobacco smokers). Additionally, as reported earlier, tobacco-smoking deprivation may exacerbate impulsive action [46], and perhaps the same is true for impulsive action and cannabis use. Studies have begun to investigate cross-commodity discounting of rewards in relationship to addictions. While smokers did not show differences in discounting between monetary and cigarette rewards, the different commodities activated different circuitry. The choice of smaller versus larger rewards, regardless of reward type, activated the mPFC, anterior insula, middle temporal gyrus, middle frontal gyrus, and cingulate gyrus in smokers. The choice of monetary over cigarette rewards was associated with lateralized activation patterns, with cigarette choices primarily involving activation of the PCC, medial and middle frontal gyri, and the precentral gyrus in the left hemisphere, and monetary choices involving activation of VS, temporoparietal cortex, and angular gyrus in the right hemisphere [144•]. These findings resonate with others suggesting lateralization of reward processing networks [145, 146]. Additionally, it appears that contingency management might provide some sort of protection toward elevations in impulsivity and may provide assistance in maintaining abstinence.

Animal Studies

Alterations in delay discounting are often studied after acute drug exposure; however, cocaine administration may cause long-lasting elevations in impulsive choice as measured by delay discounting [27, 147, 148], a finding consistent with the human literature mentioned above. Perhaps the most compelling evidence for long-term alterations in impulsive choice as a result of cocaine exposure is in rhesus monkeys. Hamilton et al. [149] investigated monkeys that had been exposed to cocaine in utero and found that the males displayed elevated impulsive choice in delay discounting 14–15 years later; however, it is still unclear how cocaine may alter brain functioning to result in such long-term alterations in impulsive choice.

In rodents, d-amphetamine-induced elevations in dopamine signaling decrease impulsive choice [150]. Rats with high levels of impulsive choice show low levels of D2 dopamine receptor messenger RNA (mRNA) expression in the mPFC [64]. 5HT appears particularly relevant to the ‘waiting’ aspect of impulsive choice, as depletion of 5HT results in increases in impulsive choice, and the extracellular content in the dorsal raphe increases when animals are waiting. 5HT may also signal proximity or likelihood of rewards, especially in the OFC given data linking OFC function to subjective value determination [106, 151–153]. Global reductions in

5HT have mixed results on impulsive choice, with some studies reporting increases and others reporting decreases in impulsive choice [154–158]. Mixed results may reflect contributions from different 5HT receptors, with possible different contributions from 5HT_{1A} [154], 5HT_{1B} [159], and 5HT_{2B/C} [160] receptors.

Noradrenergic contributions to impulsive choice have been suggested. The alpha2-adrenoceptor agonist guanfacine, when injected into the ventral hippocampus, decreased delay discounting, while the dopamine D1-like agonist SCH23390 had no effect (although administration of this agonist may alter impulsivity when administered elsewhere in the brain [161, 162]), and the GABA receptor agonists muscimol and baclofen increased delay discounting. Given projections from the hippocampus to the amygdala [163, 164], these findings may have implications for context-induced emotional influences on decision making.

Summary and Conclusions

Multiple brain regions have been associated with impulsivity across self-report, response, and choice domains. Other regions show stronger associations with specific facets of impulsivity. Therefore, a basic underlying ‘core’ circuit may underlie the drive and/or inhibition of basic motivated behaviors, with additional regions influencing this circuitry and leading to specific forms of impulsivity.

Although the current review focuses on self-reported, choice, and response impulsivity, other domains may exist that relate to reflection and decision making [28]. Additionally, impulsivity may be context and emotion dependent, and use of instruments like the UPPS-P scale (which can assess both positive and negative urgency) and the Difficulties in Emotion Regulation Scale may provide insights into such tendencies [165, 166].

While brain imaging has facilitated an understanding of the brain biology underlying impulsivity, one should be cognizant of limitations of each approach. That being said, improvements in image acquisition and analysis continue to be made and should be integrated into research as they become available. Of particular importance will be the integration of multiple forms of imaging that offer complementary information with clinically relevant measures. Translational research (from pre-clinical research to clinical research and from research settings into community clinics) will be important with respect to using the information gained about impulsivity to generate improved policy, prevention efforts, and treatments.

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Compliance with Ethics Guidelines

Conflict of Interest Marci R. Mitchell does not have any conflicts of interest to declare. The authors report no conflicts of interest. Dr. Potenza has consulted for and advised Boehringer Ingelheim, Lundbeck, Ironwood, INSYS and Shire; has financial interests in Somaxon; has received research support from the National Institutes of Health, Veteran's Administration, Mohegan Sun Casino, the National Center for Responsible Gaming and its affiliated Institute for Research on Gambling Disorders, and Forest Laboratories pharmaceuticals; has participated in surveys, mailings, or telephone consultations related to drug addiction, impulse control disorders, or other health topics; has consulted for gambling and legal entities on issues related to addictions or impulse control disorders; has provided clinical care in the Connecticut Department of Mental Health and Addiction Services Problem Gambling Services Program; has performed grant reviews for the National Institutes of Health and other agencies; has guest-edited journal sections; has given academic lectures in grand rounds, CME events, and other clinical or scientific venues; and has generated books or book chapters for publishers of mental health texts. The manuscript was generated independently of these efforts and while some of the thematic content (relating to impulsivity and addictions) may be shared, they represent independent endeavors.

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