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Review

Sensation-seeking: Dopaminergic modulation and risk for psychopathology

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HIGHLIGHTS

- We examine evidence implicating midbrain dopamine in sensation-seeking (SS) trait.
- Both high tonic dopamine and exaggerated responses to rewards may be involved.
- Evidence from humans and animals suggests a particular role for D2-type dopamine receptors.
- This may relate to increased risk for substance and gambling addictions in high SS.
- But a possible protective factor for high SS in stress-related psychopathologies.

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ABSTRACT

Sensation-seeking (SS) is a personality trait that refers to individual differences in motivation for intense and unusual sensory experiences. It describes a facet of human behaviour that has direct relevance for several psychopathologies associated with high social cost. Here, we first review ways of measuring SS behaviour in both humans and animals. We then present convergent evidence that implicates dopaminergic neurotransmission (particularly via D2-type receptors) in individual differences in SS trait. Both high tonic dopamine levels and hyper-reactive midbrain dopaminergic responses to signals of forthcoming reward are evident in higher sensations-seekers. We propose that differences in the efficacy of striatal dopaminergic transmission may result in differential expression of *approach-avoidance reactions* to same intensity stimuli. This constitutes a quantitative trait of intensity preference for sensory stimulation that may underlie core features of the SS personality. We review the evidence that high trait SS is a vulnerability factor for psychopathologies related to changes in brain dopamine function, in particular substance and gambling addictions. Conversely, we consider the possibility that increased tolerance of high intensity stimulation may represent a protective mechanism against the development of trauma-related psychopathologies (e.g. post-traumatic stress disorder) in high sensation-seeking individuals.

Further understanding of the brain mechanisms underlying SS trait might not only to shed light on the aetiology of these disorders, but also aid in developing individualised therapies and prevention strategies for psychopathologies.

Contents

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1. Introduction

Is there a hedonic drive to seek out 'sensations', above and beyond more traditionally conceived rewards? For example, what is it that motivates some people to devote large amounts of time, money, and effort in search of such – often fleeting – experiences as sky-diving, a rollercoaster ride, the thrill of fast driving or really spicy food?

Sensation-seeking (SS) has been described as "a trait defined by the need for *varied, novel, complex* and *intense* sensations and experiences, and willingness to take physical and social risks for the sake of such experiences" [1,2]. Tendency to engage in these kind of behaviours has been found not to be modality-specific, but rather to cluster across the senses, various kinds of social behaviour, and other classes of risky activity [3]. Indeed, it has been shown that degree of engagement in various SS activities (particularly licit and illicit recreational drug consumption, risky driving or sexual behaviours) covaries in both adults and adolescents [4–8]. The study of this intriguing individual difference can be traced back from mid-century homeostatic theories regarding optimal levels of sensory stimulation [9] through to the rise of personality psychology in the 1970s [1,2]. Recently, it has been greatly advanced via the use of cognitive neuroscience techniques in both humans and animal models.

As well as describing an interesting dimension of behaviour in and of itself, SS trait has been shown to be significantly related to health outcomes across a variety of domains, and has been identified as a relevant individual difference for several psychopathologies with high social cost [10]. Specifically, high trait SS is considered to be both a vulnerability factor and predictor of poorer prognosis in substance and gambling addictions (e.g. [11–13]). Conversely, a putative role in stress-resiliency may explain preliminary findings of higher SS status being a protective factor against psychopathologies resulting from exposure to high-intensity stressors, e.g. post-traumatic stress disorder [14–16].

The brain basis of this personality trait therefore has high relevance for understanding both healthy human behaviour and several prevalent disease states. This review first discusses insights into differences in neurobiology underlying differences in SS behaviour derived from studies in both humans and animal models, particularly with respect to midbrain dopamine systems. Evidence for how these differences might relate to differential risk for addictive and gambling disorders is then considered, as well as the role high SS may play in more functionally adaptive behaviour involving exploration and stress resiliency. Finally, we briefly touch upon the importance of considering individual differences such as SS in personalising both treatment and targeted intervention programmes for relevant psychopathologies.

2. Measuring sensation-seeking in humans and animals

2.1. Self-report measures of SS in humans

SS personality has to date been measured in humans via self-report questionnaires. The most commonly used instrument is the Sensation-Seeking Scale form V (the SSS-V), originally developed in the 1970s by Zuckerman and colleagues [1,2]. The SSS-V has four subscales [2]:

1. *Thrill and adventure-seeking*: desire to participate in physically risky activities that involve novel sensations and experiences.
2. *Experience-seeking*: search for new experiences.
3. *Disinhibition*: interest in socially and sexually disinhibited activities.
4. *Boredom susceptibility*: intolerance of routines and repetitiveness.

These four subscales have been shown to exhibit high internal reliability across a large number of samples [17], including from non-English-speaking cultures [2]. Recently, a slightly updated version of this measure has been produced using factor analysis, which has increased contemporary internal validity via exclusion of several more dated-sounding items (referring to 'queers', 'swingers', etc.) [18]. Other less frequently used measures include Zuckerman's Impulsive Sensation Seeking (a subscale of the Zuckerman-Kulman Personality Questionnaire, [19]), and the Arnett Index of Sensation-Seeking [20]; scales which both deliberately omit reference to any specific sensation-seeking activities.

Evidence from self-report measures supports the assertion that SS trait is a robust and valid individual difference in humans. SS scores have moderate to high heritability estimates (40–80%; [21–24]), and rank order differences in scores are highly stable over time [25]. Moreover, SS scores from a variety of instruments have repeatedly been shown to predict propensity to engage in real-life 'sensation-seeking behaviours' including licit and illicit substance use, participation in high impact sports, and risky driving and sexual behaviours [2,10,26] (see Section 4). This is apparent even when the measure used (unlike the SSS-V) deliberately omits any reference to such behaviours [20,27]. Self-reported SS scores have also been linked to a variety of markers of individual difference in brain function (particularly in the dopamine system, see Section 3.1).

2.2. Relationship to other constructs: impulsivity and novelty-seeking

SS has previously been described as a component of *impulsive behaviour* [28]. However, analysis of both cross-sectional and longitudinal samples has demonstrated that the two constructs are

somewhat distinct, as self-report scores exhibit divergent developmental trajectories [29–31]. In addition, there are only modest or non-significant correlations between SS and (other) impulsivity scores in adults [30,32,33]. For example, on the factor-analysis derived UPPS measure of impulsivity (which indexes urgency, premeditation, perseverance and sensation seeking), SS subscale scores do not correlate well with other impulsivity subscores in either healthy volunteer or patient samples [28,32,34]. Thus, trait SS possesses the potential to provide separate explanatory capacity from other forms of impulsivity, e.g. with regard to propensity to develop psychopathological symptoms.

Novelty-seeking has been described as a key component of SS personality [35,36]—a fact often reflected in the structure of self-report SS measures (e.g. [20]). Thus, scores on questionnaire measures of novelty-seeking (e.g. the novelty-seeking subscale of Cloninger's Tridimensional Personality Questionnaire, [37]) and SS have been shown to be significantly correlated [38], and, on self-report instruments at least, the degree of overlap between constructs may be significant. However, the two traits are somewhat conceptually distinct. In theory, high SS individuals may be motivated to continue to sample a particular high intensity sensory stimulus across repeated episodes of exposure, whereas in high novelty-seeking individuals this tendency may habituate over time (for relevant examples from the animal literature see [39,40]). This distinction may be relevant to different behavioural models of SS in the animal literature (see Section 2.2), and is one reason why analogous behavioural paradigms are needed in order to dissect out different aspects of sensation-seeking personality in humans.

2.3. Operational measures of SS

In animal models, sensation-seeking trait has mainly been operationalized in terms of extent and vigour of interaction with novel objects or environments. For example, on one of the oldest measures, the hole-board test, the animal is placed in a novel environment, on a board with several viewing apertures or holes. The frequency of 'head-dip' responses below the surface of the board is then interpreted as an index of exploratory tendency or novelty-seeking [41,42]. It should be noted that in the animal literature, the terms novelty and sensation-seeking are often used somewhat interchangeably, although as noted in the previous section there are at least subtle distinctions between the two behaviours. An important distinction can also be drawn between paradigms probing individual differences in reaction to *free-choice* versus *forced* novelty exposure (see Section 2.2.2): as inescapable novelty may represent a stressful rather than positive incentive value experience, particularly in rodents [43].

Three of the most commonly-used approaches to operationalising SS trait in animals (primarily in rodent models) are outlined below and in Fig. 1A.

2.4. Locomotor reactivity to novelty (LRN)

Perhaps the most established animal model of SS is 'locomotor reactivity to novelty' (LRN), i.e. general exploratory motor activity exhibited when an animal is placed in a novel environment [44,45]. This has been proposed as a model of SS as rodents classed as having 'high reactivity to novelty' (HR animals, usually classified as such on the basis of median split of group scores) show several similarities to human high sensation-seekers (for a review see [36]). Specifically, they demonstrate increased sensitivity to the activating and rewarding effects of psychostimulants drugs, which might relate to common factors involving the dopamine D2 system function (see Section 3.2).

However, it is debatable how well this measure maps onto human trait SS, at least in terms of face validity. In particular, although part of the original definition of the phenotype, it is often not empirically demonstrated in studies utilising the LRN model that increased 'locomotor reactivity' is specific to novel contexts. Thus, it is somewhat unclear in these studies the extent to which HR grouping may be driven by general locomotor activity levels. A further concern is that LRN can also be viewed to some extent as simply the inverse of rodent models of 'anxiety'. The latter is commonly indexed as time spent exploring exposed ('potentially threatening') areas on the open field test or elevated plus maze (environments to which the animal is often naïve). Thus, it is not surprising that HR rats show lower 'anxiety-like' behaviour on a variety of tests [45,46].

2.5. Novelty preference (NP)

SS trait has also been operationalized in rodents in terms of measures of novelty-preference (NP). Most commonly this is indexed by novel object preference (relative time spent exploring a novel object in preference to a familiar one), and various forms of novelty-related environment preference (usually simple relative preference for a novel over a familiarised space [43,47–49]). It has been argued that *choice*-based measures of response to novelty may represent better models of SS than simple locomotor activity in an (unescapably) novel environment, on the basis that novelty is viewed in the rodent literature as activating contradictory approach-avoidance motivational systems (see Section 3.3) [43]. Thus, active approach of the novel option may constitute a better rodent model of the higher risk or intensity-preference exhibited by human higher sensation-seekers than simple locomotor response to a novel environment [50].

2.6. Operant sensation-seeking (OSS)

A range of animals have been observed to work to receive purely sensory rewards–in the absence of association (or history of association) with any other primary reinforcer [51–54]. In the 'operant sensation-seeking' (OSS) paradigm [54], animals are presented with a choice between two operant levers: one, termed the 'active' lever, which results in the display of sensory stimuli (often a simple light onset, but sometimes a more complex audio-visual stimulus), and one which has no consequences (the 'inactive' lever). The key dependent variable is the animal's relative preference for the stimulus-producing lever (i.e. ratio of active:inactive lever presses; although sometimes the somewhat less valid measure of total active lever presses is reported).

OSS behaviour has been shown, at least in some hands, to be fairly robust, persisting over extended sessions, in extinction (when the sensory reward is no longer presented) and on demanding schedules where a progressively increasing number of responses are required to gain a single presentation of the sensory stimulus [54]. Thus, despite evidence that response rate on the active lever is positively related to variation in (or novelty content of) the sensory stimulus [40], it is unlikely that behaviour on this task can be explained purely by appetitive responses to 'novelty' alone. Although currently less extensively explored, this paradigm may have the most face validity with respect to the human trait of SS.

The three behavioural measures discussed above have been inconsistently inter-related. Specifically, LRN may be associated with total lever responses on OSS paradigm (i.e. general levels of responding), but not with specific responses for the active (sensory-associated) lever [54–56]. While some studies have found that HR rats show greater preference for a novel environment [45,57], others find no relationship between LRN and indices of novel object preference (e.g. [43,47]). This suggests that these different behavioural operationalisations of SS trait may depend upon at least partially different neurobiological systems. Furthermore, this

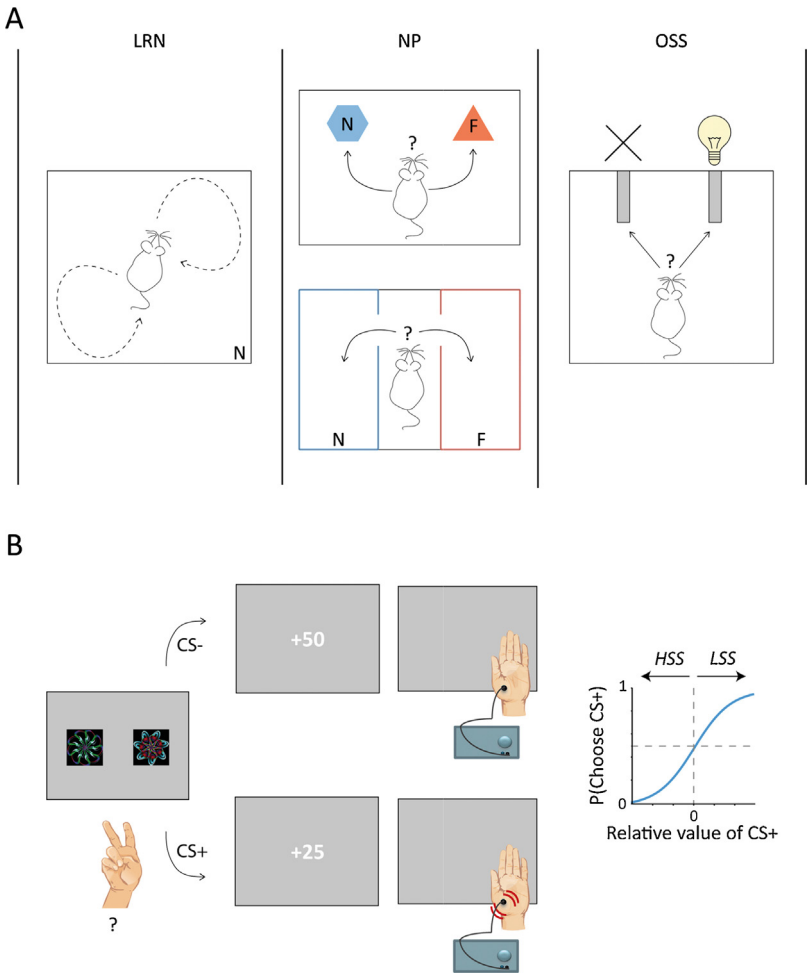

Fig. 1. Behavioural measures of sensation-seeking in rodents and humans. (A) Three commonly used behavioural measures of 'sensation-seeking' in rodents. (1) Locomotor response to novelty (LRN): general exploratory motor activity exhibited when an animal is placed in a novel environment for a set period of time. (2) Novelty preference (NP): commonly used choice measures of novelty preference include novel object preference (relative time spent exploring a novel object in preference to a familiar one), and novelty-induced place preference (relative preference for a novel over a previously familiarised environment). (3) The operant sensation-seeking (OSS) paradigm: animals are presented with two operant levers: an 'active' lever, which results in the display of sensory stimuli (e.g. a light onset), and an 'inactive' lever, which has no consequences. The ratio of active:inactive lever presses measures the animal's relative preference for the sensory stimulus. N = Novel; F = familiarised. (B) Operant 'sensation-seeking' paradigm developed for use in humans. In this task, participants first learn points values associated with different abstract choice stimuli or CSs (collected points are later converted into monetary winnings). Half the choice stimuli then become associated with the chance of receiving a mild electrical stimulation to the hand (become CS+s), whilst the others have no additional sensory consequences (become CS-s). Observing how the opportunity to receive this additional intense tactile stimulation affects participants' choice (previously based on economic value alone of the various CSs) allows derivation of the *value* individuals assign to opportunity to receive the extra sensory stimulation. A leftward shift in choice function (increased choice of CS+) is observed in higher sensation-seeking (HSS) individuals; whilst a rightward shift is observed in lower sensation-seeking (LSS) individuals.

might be reflected in differential relationship of these indices to different aspects of drug-related behaviour (see Section 4.1).

In addition to evidence from the behavioural assays described above, a further line of research has focused on characterisation of inbred rodent strains demonstrating SS-like traits. This approach enables the demonstration of significant heritability of the behaviours of interest, whilst decreasing genetic variability in the test population [58]. For example, selectively bred HR and LR animals have been extensively studied with respect to propensity for substance addiction [36] (see Section 5.1). Also of note from the animal literature are the Roman 'high avoidance' (RHA) and 'low avoidance' (RLA) rat lines.

These animals have been selectively bred over several decades from populations exhibiting high and low rates of avoidance conditioning on the shuttlebox paradigm (avoidance or escape responses observed when a conditioned light stimulus predictive of electrification of one area of the cage floor appears [59]). RHA rats have been described as 'high sensation-seeking' on the basis of observations of large differences from RLA animals in both avoidance of aversive stimuli and responsiveness for rewarding ones—including drugs of abuse (for reviews see [60,61]). RHA animals have further been shown to exhibit both increased locomotor responsivity in novel contexts and greater tendency to explore novel objects [62,63]—suggesting these constellation of behaviours may be under common genetic influence [58].

2.7. An operational measure of trait SS in humans?

Recently, we developed a behavioural task designed to be directly comparable to those used in animal studies (Fig. 1B). In this paradigm, human participants may choose to self-administer an additional 'intense' sensory stimulus (mild electrical stimulation) during performance of an economic decision-making task [64]. Across several samples, we found that some individuals choose to administer an above-chance proportion of stimuli associated with receiving this intense tactile stimulus—even when this involves the sacrifice of economic gain. This preference correlates with self-reported SS trait, but not other impulsivity scores, or other

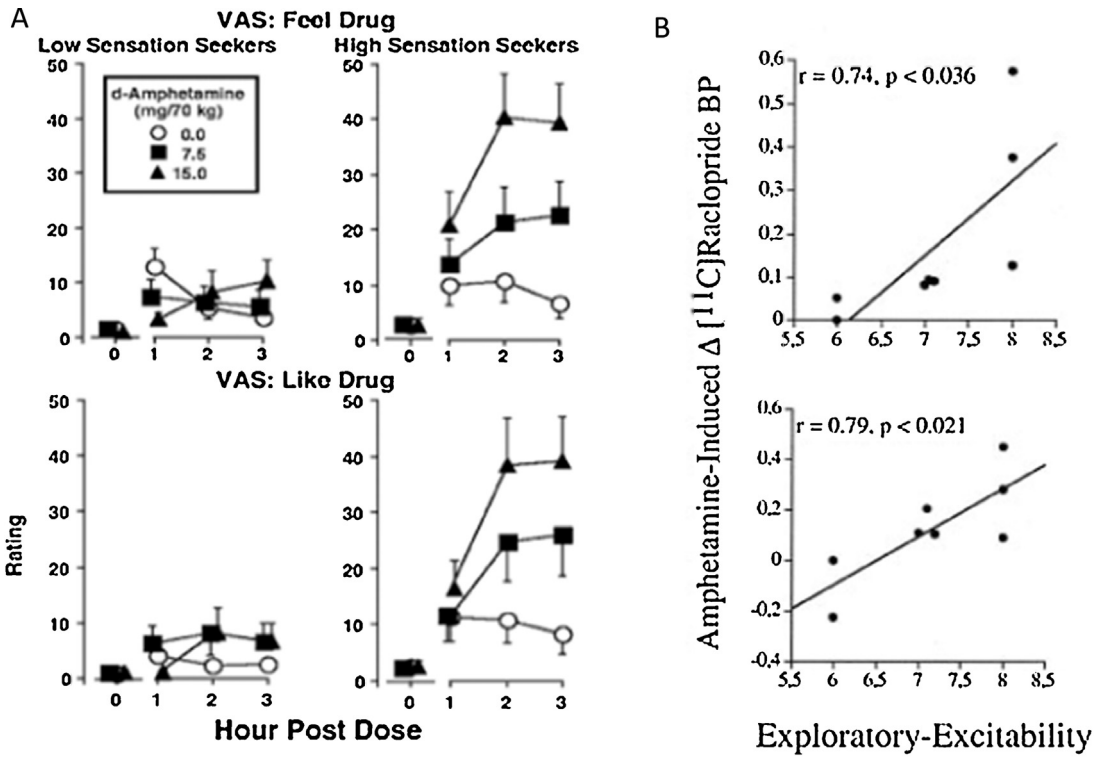

Fig. 2. (A) Time-course of the effects of d-amphetamine on visual analogue scale (VAS) ratings of 'feel drug' (top row) and 'like drug' (bottom row), for low and high self-reported sensation seekers. Error bars represent ±1SEM. *Reprinted with kind permission from Springer Science and Business Media* [76]. (B) Correlations between d-amphetamine-induced increases in extracellular dopamine levels (measured via change in binding potential, BP, of the dopamine D2/D3 receptor ligand [^{11}C]raclopride) and the scores on the Tridimensional Personality Questionnaire novelty-seeking subscale, "exploratory-excitability" (which has significant conceptual overlap with SS trait). Top panel; [^{11}C]raclopride BP values extracted from a manually drawn region of interest in the ventral; bottom panel the statistically generated parametric *t*-map across the whole brain.*Reprinted by permission from Macmillan Publishers Ltd: Neuropsychopharmacology (27:6), copyright 2002* [83].

psychological concepts such as trait anxiety and hedonic tone. Further study of behaviour on this paradigm may therefore provide a means to dissect out with greater precision in the lab neurobiological mechanisms underlying human SS behaviour.

3. Role of dopamine in individual differences in trait SS

3.1. Evidence from studies in humans

Previously research has identified a relatively strong relationship between polymorphisms at dopamine D4 receptor loci and individual differences in self-reported novelty-seeking personality (for a metaanalysis see [65]). Similarly, almost all data relating SS trait to neurotransmitter systems in humans concerns the dopamine system. Specifically, evidence from genetic and PET radioligand displacement studies suggests that individuals higher in SS personality may exhibit both higher endogenous dopamine (DA) levels and greater dopaminergic responses to cues of upcoming reward in striatal regions [66–70].

Higher sensation-seekers have been reported to show lower platelet levels and carry lower activity isoforms of monoamine oxidase (MAO), an enzyme responsible for the breakdown of DA [66,71,72]. They also exhibit relatively higher activity of dopa decarboxylase (DDC, a rate-limiting enzyme for DA synthesis) in the striatum, both via variation in the *DDC* gene itself [69] and the Taq1a polymorphism [73–75]. Thus, it might be expected that higher SS individuals have greater overall DAergic tone, particularly in striatal regions.

Individuals higher in SS trait also show *increased* physiological and subjective responses to dopaminergic stimulants such as amphetamine [76–78] (Fig. 2A). This also holds for drugs which may not directly target the DA system, such as oxycodone, diazepam and alcohol [76,79–81]. However, this may be the result of a final common pathway for these substances which results in increased DA levels in the ventral striatum [82]. Further, self-reported SS score correlates positively with both amphetamine-induced DA release in the striatum [67,83] (Fig. 2B), and the magnitude of dopaminergic response to cues of forthcoming rewards [70] (*nb* the former relationship has thus far only been observed in men).

SS trait has also been linked to variation in function in the D2 class of dopamine receptors (D2, D3, and D4 receptors) [74,84,85]. Gjedde and colleagues have recently argued on the basis of the above findings and PET evidence (Fig. 3) that higher sensation-seekers have both lower D2/D3 receptor density and higher endogenous DA levels than their high SS counterparts. Thus, the 'gain' (reactivity to the presence of dopamine) of the D2 system in the striatum might be inversely related to SS score [68].

Specifically, this hypothesis would predict greater amplification of the postsynaptic signalling cascade following DA binding in higher gain lower sensation-seekers, and a lower sensitivity post-binding cascade (due to higher tonic levels of synaptic DA) in lower gain higher sensation-seekers. In support of this, we previously found that the D2/D3 receptor *agonist* cabergoline has greater effects on performance on a probabilistic risky choice task in *lower* sensation-seekers [86], consistent with greater sensitivity of DAergic transmission in these individuals (Fig. 4A). Conversely, we recently found greater effects of a silent D2 receptor *antagonist* haloperidol in behaviourally defined *higher* sensation-seekers [64], suggesting a greater effect of disrupting signalling by endogenous ligand in these individuals (Fig. 4B).

3.2. Evidence from animal models

Data from the animal literature also supports the involvement of both a hyper-responsive striatal DA system and variation in D2-type receptor function in individual differences in SS-like

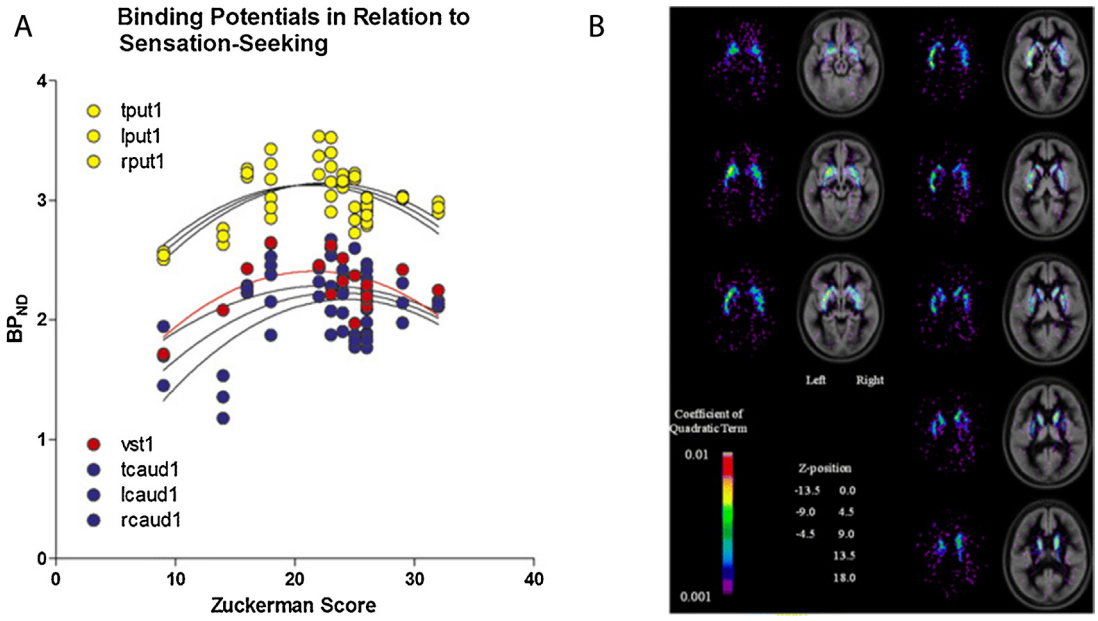

Fig. 3. (A) Binding potential (BP) of the dopamine D2/D3 receptor ligand [^{11}C]raclopride in the ventral striatum, total, right, and left caudate, and total, right, and left putamen of individuals with a range of self-reported sensation-seeking (Zuckerman) scores. *Adapted from* [68] ©the National Academy of Sciences. (B) Map representing the significance of the quadratic coefficient of Zuckerman's sensation-seeking score in predicting [^{11}C]raclopride binding potential at each voxel across the brain, highlighting striatal regions. *Adapted from* [68] ©the National Academy of Sciences.

behaviour. Performance on all three animal models of SS described in Section 2 above are sensitive to manipulation of brain DA function.

For example, rodents with higher than average locomotor reactivity to novelty (HR animals) have been shown to exhibit increased DA levels in the ventral striatum and a higher overall basal firing rate of midbrain DA neurones, in addition to decreased concentrations of D2 receptors overall in the striatum [36]. Selectively bred HR animals also have lower nucleus accumbens D2 mRNA levels than selectively bred low responders, and show a greater frequency of spontaneous dopaminergic transient currents in this brain region [87].

A different line of research has revealed that disruption of the dopamine transporter (DAT) *Dat1* gene attenuates novelty-related behaviour in mice [88]. High novelty-preferring rats may have reduced DAT affinity for DA [57], and therefore increased synaptic DA levels, due to decreased efficiency of synaptic clearance of DA [89]. In male minipigs, higher novel object exploration has been associated with greater dopaminergic response to amphetamine in the striatum, as measured using [^{11}C]raclopride PET [90]. Further, the D2 receptor antagonist haloperidol produces a dose-dependent attenuation of novelty-preference in free choice tests in rats [91]. D4 receptor knock-out mice exhibit reduced exploration of novel objects [92], and the association between individual differences in novelty-seeking and D4 receptor polymorphisms previously observed in humans has recently been replicated in non-human primates [93].

On the OSS paradigm, amphetamine injections to the ventral striatum increase relative responses on the active (sensory stimulus-associated) lever in a dose-dependent manner, an effect reduced by pre-application of the D2/D3 receptor antagonist sulpiride [94]. Mutant mice with disrupted function in particular dopamine D1 receptor-containing neurones fail to develop a preference for the active lever when it is associated with sensory

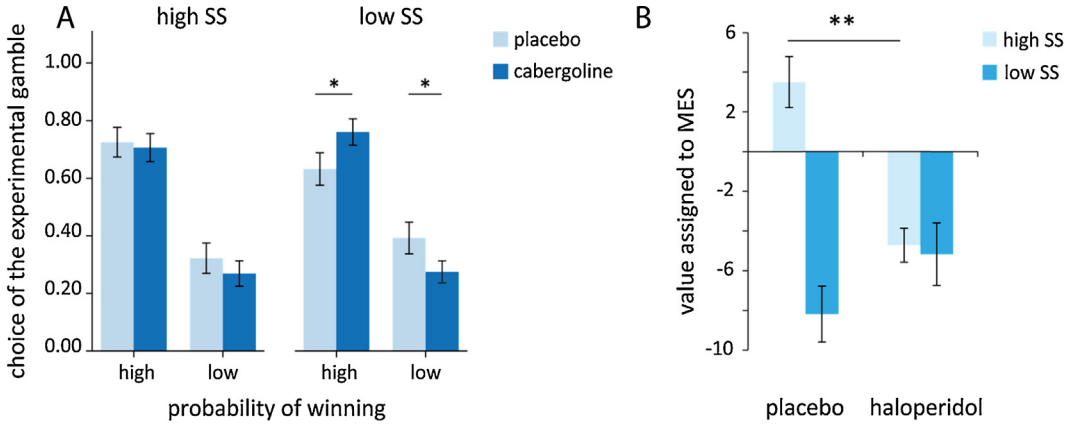

Fig. 4. (A) Data are depicted from a probabilistic gambling task where individuals chose between gambles that varied in the probability of winning (high vs low), amongst other dimensions. The D2/D3 agonist cabergoline was found to exert greater effects on risky choice within *lower* sensation-seeking (low SS) than high sensation-seeking (high SS) individuals, who varied their choice more accordingly to the gamble's probability of winning on drug vs placebo. *Adapted from* [86].*$p < 0.05$, drug vs placebo. (B) The D2 antagonist haloperidol was found to reduce the economic value assigned to the opportunity to receive intense tactile stimulation (mild electric stimulation, or MES) in individuals who showed speeding of responses (*approach* reactions) towards MES-associated stimuli under normal conditions ('high SSs'), but had no effect on this measure in individuals who showed slowed responses (avoidance reactions) to MES-associated stimuli ('low SSs'). *Adapted from* [64]. **$p < 0.01$, drug vs placebo.

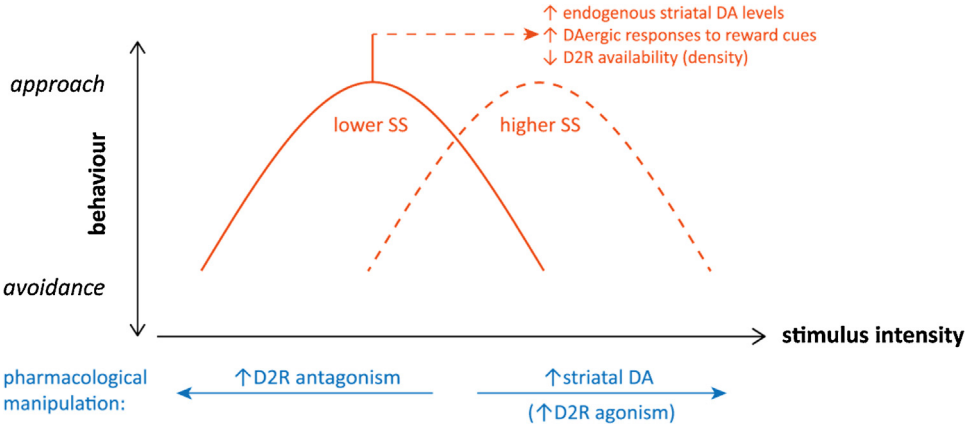

Fig. 5. Schematic of how differential activation of approach-avoidance tendencies in lower and higher sensation-seekers (SSs) may result in opposite behavioural reactions to the same intensity sensory stimulus. For example; a stimulus of an intensity that excites peak approach reactions in a lower sensation-seeker may be insufficient to elicit such a reaction in a higher sensation-seeker; whereas a stimulus of an intensity that elicits peak approach behaviour in higher SSs may be aversive and evoke an avoidance response in lower SSs. Higher SS trait is associated with differences in striatal dopamine (DA) function (*orange text*). Behavioural measures of SS preference are also affected by drugs which affect synaptic dopamine levels (e.g. amphetamine) or that target D2-type (D2/D3/D4) dopamine receptors (e.g. sulpiride), which are prevalent in the striatum (*blue text*). D2Rs = D2-type dopamine receptors (For interpretation of the color information in this figure legend, the reader is referred to the web version of the article.).

reward, but with ability to develop preference for a food reward intact [54]. By contrast, mice receiving low systemic doses of the DA antagonist flupenthixol (a mixed D1 and D2-type receptor antagonist) show *increased* responding on the active lever, an effect the authors argue is consistent with decreased sensory reward efficacy under these conditions [54].

Similar to human high sensation-seekers, RHA animals show increased midbrain dopaminergic responses to psychostimulants and other classes of drug (e.g. alcohol, morphine [61,95]), as well as increased amphetamine-induced striatal DA release [96]. There is some evidence of baseline differences in striatal DA function in RHA versus RLA animals, although the literature is rather inconsistent (see [97]). Recently, one study made use of a combination of PET and other techniques to suggest that RHA rats show both decreased availability of D2 receptors and hyper-DAergic tone in the striatum: a phenotype strikingly similar to that of human high sensation-seekers [96] (although see [98]).

The evidence presented above suggests that there may be at least partially shared neural pathways regulating behaviour across these three paradigms. In support of this interpretation, a mouse model with targeted inactivation of excitatory glutamate receptors in DA receptor-expressing neurones showed reduced instrumental responses on the OSS paradigm, reduced locomotor activity when placed in a novel environment, and decreased interaction with a novel object compared to control animals [99]. Importantly, there were no detectable behavioural deficits or abnormal learning abilities, suggesting these effects were not due to some generalised deficit.

3.3. *Do individual differences in dopaminergic approach-avoidance tendencies contribute to individual differences in trait SS?*

One influential theoretical account proposes that the core basis for individual differences in trait SS reflects the differential activation of *approach* versus *withdrawal* mechanisms in response to novel and intense stimuli [100,101] (Fig. 5). A candidate neural mechanism for this difference is variation in efficacy of striatal DA transmission, a pathway thought to be involved in the *vigour* of approach-type behaviours [102–105].

In favour of this hypothesis, there is some evidence to suggest that high sensation-seekers may show both increased appetitive responses and reduced defensive reactions to intense sensory stimuli [106–108]. For example, human high sensation-seekers have a greater response to intense auditory stimuli on EEG measures [109] and prefer both positive and negative affective stimuli to neutral ones, regardless of valence [110]. Conversely, low SS individuals exhibit greater affective startle potentiation, including during anticipation of aversive stimuli [108,111]. In the animal literature, rats selectively bred over many generations for low versus high expression of avoidance behaviour (RHA and RLA strains) also express marked differences in sensation-seeking-like behaviours (including novelty-preference and reactivity to drug rewards; see Section 2.2.3).

As outlined in the previous section, evidence from a variety of sources implicates individual variation in striatal dopamine function (particularly at D2-type receptors) in differences in SS personality in both humans and animals. Inconsequential, non-novel, but 'intense' or otherwise physically salient sensory stimuli have been shown to evoke robust responses in midbrain DA neurons in a variety of animal models [112–114]. Indeed, it has been argued that dopaminergic transmission in the ventral striatum may govern the vigour of approach-type behaviours in response to salient stimuli [103,104]. Individual differences in the efficacy of dopaminergic neurotransmission in this pathway might therefore contribute to interindividual variation in responsivity to these kinds of salient stimuli, constituting a quantitative trait of novelty or intensity preference.

Recently, direct evidence for involvement of DA-regulated approach-avoidance tendencies in human operant sensation-seeking-like behaviour has been presented [64]. Specifically, it was found that approach reactions to stimuli associated with intense tactile stimulation in higher sensation-seekers were selectively abolished under influence of the D2 receptor antagonist haloperidol (Fig. 4B).

Using this conceptual framework, it can be proposed that inappropriately high activation of *approach* tendencies towards intense stimuli may result in adverse outcomes, particularly where the 'intensity' of such experiences is inextricably bound up with or indeed derived from a risk of physical danger or damage to health. Conversely, inappropriately high activation of *avoidance* tendencies may hamper the ability to engage with potentially advantageous novel environments or experiences, and result in over-expression of anxiety-like responses to such stimuli. In the next section we consider the relationship of individual differences in trait SS to health and psychopathology.

4. Role of SS trait in general health outcomes and psychopathology

Links have been established in healthy individuals between high trait SS and increased engagement in various 'health risk' behaviours that may endanger the self or others [10,20,2,115–117]. Specifically, SS score exhibits medium effect sizes for predicting alcohol consumption and high effect sizes for illicit substance use, across many studies (for reviews and meta-analyses see [10,26,118,119]), including in non-Western cultures (e.g. [120]).

Higher SS score is also associated with greater likelihood of regular smoking [33,121], and increased rates of non-medical use of prescription stimulants [122]. Further, self-reported SS has been associated with increased frequency of risky driving and sexual practices [20,116,117,123], as well as increases in antisocial behaviour, shop-lifting, and truancy during adolescence [24]. However, it should be noted high SS score is also associated with increased incidence of 'pro-social' risk-taking among groups such as fire fighters, police, and bomb disposal experts, e.g. [124] (see Section 4.3). Finally, high trait SS has been also been specifically identified as a vulnerability factor for a variety of psychopathologies that have been associated with changes in brain DA function, in particular substance and gambling addictions.

4.1. High SS and substance use disorders

High SS scores have consistently been identified in people with substance use disorders (individuals with compulsive drug use, persisting in the face of recurrent adverse consequences [125]), across several classes of drug—including alcohol, psychostimulants, and opiates [12,33,32,126,127]. In particular, convincing data from longitudinal studies has shown that high trait SS in adolescence predicts substance use disorders later in life, especially for alcohol and tobacco [11,128].

Although there has been some debate about the primacy of SS in risk for *pathological* substance use [33] (e.g. heightened SS scores also occur in non-addicted recreational drug users [129]), it is likely that SS trait has at least moderate clinical relevance for drug-addicted populations. Among individuals with a diagnosis of substance use disorder, higher SS score is associated with earlier age of onset, increased polysubstance use, more severe functional impairment, poorer overall treatment outcome, and more greatly impaired decision-making [12,130–134]. Similarly, high SS trait may relate to increased risk for substance misuse problems comorbid in other psychopathological populations [135]. For example, amongst individuals with a diagnosis of unipolar or bipolar depression, high sensation seekers are more likely to be poorly compliant to prescribed medications or become demanding for drugs with perceived mood-elevating properties [136–138].

Interestingly, attempts to tease out the role of trait SS in addiction using animal models have revealed different relationships to aspects of substance addiction psychopathology, depending on the particular model of SS employed. Specifically, recent studies in rodents report that heightened novelty preference is associated with increased motivation to work for stimulant drug infusions, increased likelihood of progression to 'compulsive' drug use, and severity of 'addiction-like' behaviour (operationalized DSM-IV criteria for substance addiction, over several different measures), but not initial acquisition of drug self-administration behaviour [48,139,140].

Conversely, increased locomotor reactivity to a novel environment is associated with increased initial sensitivity to drugs – both ease of initiation of self-administration and range of dose supporting self-administered [36,44]) – but not with progression to an addiction-like state [141]. Thus, LRN has been linked to initial propensity to try out drugs of abuse, but not predisposition to 'addiction' *per se*, and *vice versa* for choice measures of novelty-preference [49]. Further confirmation for this dissociation comes from Meyer and colleagues who investigated novelty and drug-related behaviour across twelve different inbred rat strains (increasing genetic variability compared to previous studies carried out in single outbred strains). Across all strains, novelty preference, but not LRN, was associated with willingness to work for amphetamine injections on higher progressive ratio schedules (where many responses are required per drug infusion) [142]. Interestingly, it has recently been reported that preference for an environment established via pairing with cocaine administration (cocaine-induced conditioned place preference), which is subsequently allowed to extinguish in the absence of drug, is selectively reinstated after a priming dose of cocaine in high novelty-preferring mice [143]—possibly representing an increased risk of relapse in these animals.

The operant sensation-seeking (OSS) model has thus far been less well studied with respect to addiction vulnerability. Manipulations that fairly selectively affect OSS behaviour also affect drug self-administration, whilst leaving intact measures of learning and performance on operant tasks where food is the rewarding outcome. These findings, some have argued, suggest a common neural substrate of sensory and drug rewards [54,99,144]. In one recent study, mice with targeted inactivation of metabolic glutamate (mGluR5) receptors on D1 receptor-expressing neurons showed normal anxiety-like behaviour and learning abilities, but decreased SS-like behaviour on OSS, LRN *and* NP indices. Unlike control animals, these low SS mice did not escalate alcohol intake after enforced absence, perhaps indicating decreased risk of relapse upon drug re-exposure [99].

Evidence from the selectively bred Roman high/low avoidance animals also supports a role for SS-like traits in both initial sensitivity to the effects of drugs of abuse and maintenance of problematic use (including increased vulnerability to relapse). Specifically, RHA animals exhibit increased locomotor reactivity to stimulant drugs, prolonged responding for cocaine in extinction, and more robust drug-induced reinstatement of drug-seeking behaviour compared with LHA animals [61,145].

What underlies these findings? As described above, both human self-report and animal models of SS have been linked to variation in D2 receptor function. In particular high trait SS has often been associated with low striatal D2 receptor 'availability'—due to increased endogenous DA levels, low receptor density, or a combination of both these factors. In healthy humans, both high trait SS and low striatal D2 receptor availability have been linked to greater *'liking'* of stimulant drug effects [76,146] (e.g. Fig. 3A). This may therefore relate to increased likelihood of initial drug use or experimentation in high sensation-seekers, as paralleled by increased ease of acquisition of drug self-administration in by HR animals on the LRN model of SS.

Low striatal D2 receptor availability has consistently also been found in both individuals with *pathological* or compulsive substance use (including in withdrawal) [68,147,148], and in animals who exhibit elevated cocaine self-administration [149,150], and thus has been proposed as a vulnerability marker for progression to addiction. In human studies, it is usually unclear due to methodological limitations how much this is a cause and how much it is an effect of drug use [151]. Indeed, it is likely a combination of both [152–154].

Regarding evidence implicating high SS trait in *severity* of psychopathology in people with substance use disorders, one possible explanation is that these findings are all a legacy of earlier onset of drug use [155], i.e. during a period of heightened sensitivity to direct effects of substances of abuse on brain chemistry [156]. For example, it has been found that rates of adult alcohol dependence can be reduced by 10% for each year that drinking

is delayed in adolescence [157]. Intriguingly, a recent study in mice found that binge-like cocaine administration during adolescence induced a higher sensitivity to rewarding effects of both cocaine and MDMA (ecstasy) selectively in high novelty-seeking animals [158]. This suggests the existence of some kind of interactive effect between the sensitive period of adolescence and trait novelty and/or sensation-seeking. However, there may also be a role for heightened trait SS in increased susceptibility to progression from initial experimentation to *compulsive* substance use. In support of this, the animal evidence discussed above suggests a role of high SS trait (modelled as novelty preference across several different behavioural paradigms) in progression from sporadic use to an addiction-like phenotype. Furthermore, as we have seen, evidence from NP, OSS, and RHA models of SS also implicates a possible role of high trait SS in *susceptibility to relapse*—an integral feature of addiction psychopathology.

Thus, it is likely that individual differences in SS play a significant role in disease progression [159], although further work needs to be conducted to extract out exactly which components are the best predictors of different aspects of disease progression. As drug addiction is a multi-stage and multi-faceted disease, associated with numerous distinct behavioural traits, it will be important for future research to identify which dimensions of sensation and/or novelty-seeking in humans are modelled in rodent paradigms that embody vulnerability markers for progression to and maintenance of the addicted state [50]. This will be aided by development of similar operationalized paradigms for humans, which would be more directly comparable to animal findings than existing self-report measures.

4.2. High SS and pathological gambling

High SS is often cited as a risk factor for pathological gambling (PG; e.g. [10]), however, there are surprisingly inconsistent findings regarding the role of heightened SS in pathologically disordered gambling behaviour [160]. Laboratory studies have found medium to high effect sizes for SS scores on gambling and risky decision-making in healthy individuals, particularly when studied in more naturalistic settings such as mock or real casinos [10,161,162]. High SS individuals may also be more likely to engage in gambling activities in the real world [163]. Several studies report significantly higher SS scores in samples of pathological gamblers compared with controls [13,32,164,165]; however, others have found either a non-specific relationship [166] or no difference in SS score between problem gamblers and healthy controls [167–169]. This inconsistency may be due to heterogeneity within PG populations. Indeed there is some evidence that the role of heightened SS in PG may depend on the particular form of gambling engaged with [170], with high SS trait evident only in a subset of individuals with PG behaviour [171].

While there are links between brain systems associated with trait SS, risky decision-making, and PG – again, with transmission via D2-type dopamine receptors being commonly implicated [86,172] – it is currently unclear exactly what the nature of this relationship is. For example, a recent study found that rats more prone to an 'irrational' choice bias when choosing between risky reward options had lower striatal D2/D3 receptor density [173]. However, no evidence has so far been found for differences in striatal D2 receptor density in samples of human pathological gamblers compared to controls [168,174]. Some authors have argued that the high comorbidity between substance use disorders and PG [175], in addition to evidence for common genetic factors [176], implies that the two disorders have overlapping aetiologies [177]. It is possible that the role of trait SS in PG may be less clear than that observed in substance addiction due to a lack of involvement of substances of abuse that actively target brain systems, including dopaminergic ones, that are associated with SS trait [178].

The relationship between high trait SS and vulnerability to develop behavioural addictions may be more evident in disorders where prodopaminergic (predominantly D2 agonist) therapies have been linked to development of *de novo* compulsive behaviours. These are most commonly PG but also include compulsive shopping, hypersexual behaviour, and addiction to dopaminergic medication; collectively known as impulsive control disorders or ICDs [125]. This has been observed clinically in a variety of disorders treated with DA agonists (e.g. prolactinoma and restless legs syndrome), but has been most well studied in individuals with Parkinson's disease (PD), a disorder involving progressive loss of dopaminergic neurones [179–183].

PD patients have previously been reported to show relatively low self-reported SS scores [184,185]. Some researchers have developed this finding into the notion of the 'pre-Parkinsonian personality': a prodromal period of altered brain DA function, prior to the onset of signature motor symptoms, where individuals exhibit lowered sensation-seeking personality [184]. However, PD patients with ICDs may exhibit *heightened* impulsivity and novelty-seeking questionnaire scores, compared with non-ICD PD controls [186]. Although to date almost all studies of this relationship have been cross-sectional in design, one intriguing longitudinal study has shown evidence for decreased novelty-seeking in *de novo* PD, with *increased* novelty-seeking relative to healthy controls observed post commencement of pro-dopaminergic medication [187].

These findings may relate to increased reactivity of striatal DA observed in PD patients with ICDs. For example, greater radioligand displacement (interpreted as greater endogenous DA release) has been reported during gambling in PD patients with a diagnosis of PG [188]. Further, self-reported SS score has been found to be significantly positively correlated with striatal DA release to reward cues in PD patients with ICDs [70]. Similar to high SS healthy individuals, there is evidence of reduced D2/D3 receptor tracer binding in the ventral striatum of PD patients with a diagnosis of PG compared to PD controls [188] (although see [70]). This may be due to greater endogenous striatal DA levels in PD patients who go on to develop PG because these individuals exhibit both reduced binding of DA transporter ligands in the ventral striatum [189,190] and reduced concentration of midbrain dopamine autoreceptors [191].

These studies have recently been interpreted as providing converging evidence that both heightened striatal DA tone and increased DAergic response to reward cues is the underlying vulnerability in PD patients who develop ICDs such as PG after undergoing dopamine agonist treatment [177]. Strikingly, this is the same neurobiological signature that has been reported across several studies associated with high SS personality in the normal population.

4.3. Is high SS always a bad thing? Stress resiliency and the role of environment

Although so far we have presented evidence that high trait SS may be associated with increased levels of dysfunctional behaviour, there is also preliminary evidence that, under certain circumstances, high SS may be functionally useful.

From a developmental perspective, a general increase in SS in all individuals with onset of puberty [29,30] has been hypothesized to underpin an enhanced capacity to approach high-arousal, novel, or uncertain situations. Thus, would promote general exploration and learning of other 'independence-building' behaviours, in addition to underlying increases in potentially dangerous behavioural choices [192,193]. Thus, it has been suggested that one possible adaptive function for higher trait SS in both adolescence and

adulthood is to serve as a 'stress-buffer', allowing individuals to explore challenging and unpredictable environments laden with unknown risks [14].

In support of this hypothesis, higher SS status has been associated in humans with a general decrease in the tendency to view the world as 'threatening' [2]. There is a negative correlation between both participants' estimated probabilities of negative outcomes and their ratings of various real-world activities as being either risky or dangerous [194], and higher sensation-seekers show heightened thresholds for threat detection when viewing faces morphed between neutral and angry expressions [195]. Further, threatening images evoke potentiation of startle responses in low- but not high-SS individuals [108], and high sensation seekers display relatively decreased fear-potentiated startle to predictable aversive stimuli [111].

Animals inbred for low locomotor response to novelty also display enhanced anxiety-like behaviour on various measures [196] (although see Section 2.21 for a discussion of why this is perhaps somewhat unsurprising). Similarly, inbred Roman low avoidance animals show increased 'anxiety' on the same tests, compared to high avoidance strains [60]. When exposed to novel environment stress, RLA animals also show more pronounced 'emotional' responses such as more defecation and immobility, whereas RHA rats are more likely to exhibit exploratory behaviours. This has been interpreted by some researchers as evidence of a more 'active' coping style in RHA animals [197].

In support of a role of higher SS in coping with extreme stress in humans, several studies have reported that higher SS ex-prisoners of war report fewer symptoms of post-traumatic stress disorder (PTSD), and less severe psychiatric symptomatology in general, than low SS individuals [15,16]. SS scores were also significantly lower in those with compared to without PTSD in a sample of individuals with substance use disorders [198] and, under some circumstances, high SS status has been associated with higher physiological pain tolerance [199]. Evidence from the LRN model supports the idea that this may be due to increased stress resilience in high SS individuals. For example, inbred low response to novelty (bLR or 'low SS') adult rats who have undergone maternal separation stress when young show exaggerated stress responses in adulthood, while inbred high responders (bHR or 'high SS') animals are unaffected [200]. Exposure to chronic mild stress has been shown to result in increases in 'anhedonic' and anxiety-like behaviours in bLR animals, whereas stress-exposed bHR rats resemble non-stressed control animals on these measures [201].

This increase in stress tolerance may relate to differences in midbrain dopamine and D2 receptor function in high SS individuals [202]. Recent optogenetic studies have demonstrated a causal role of phasic firing of midbrain DA neurones in resilient versus susceptible phenotypes to repeated social defeat stress in mice [203]. Further, D2 receptor function has been implicated in successful resilience to chronic mild stress, in that changes in D2 receptor gene expression post stress-exposure have been shown to differentiate between stress-resilient and stress-reactive animals [204,205].

In some cases, it is possible that higher SS status itself may represent an active adaptation to chronic stress exposure. Possession of the *Taq1a* A1 allele (associated with lower rates of DA catabolism) plus a history of high intensity stress exposure (sexual abuse or overly strict parental disciplinary style) has been found to result in significantly higher sensation and novelty-seeking scores in adulthood, including in a longitudinal study [206,207]. Similarly, a recent longitudinal study found that an association between childhood sexual abuse and higher self-reported sensation-seeking score was moderated by *DRD4* (dopamine D4 receptor) genotype [208].

It is important to bear in mind that the environment plays a significant role in determining the form that SS behaviours may take. Families at higher socioeconomic levels may be able provide socially acceptable outlets such as adventure sports, travel and other stimulatory extra-curricular activities, whereas in many low socioeconomic environments the only readily available means of intense sensory experience may be higher risk, criminal or anti-social [209]. Recently, it has been argued that the expression of problematic behaviours associated with high trait SS is likely to depend on a complex interplay between environmental constraints (e.g. availability of satisfying behaviours), and other cognitive factors, such as impulse control [160]. Indeed, in animal models home-cage environmental enrichment decreases both rate of responding for unconditioned visual stimuli (OSS, [210]) and self-administration of amphetamine [211,212], an effect which may depend in part on changes to DAergic transmission [213].

Intriguingly, self-reported SS has been found to be somewhat positively related to IQ in samples of high school and college students [2]. Although the mechanism underlying this relationship is unclear, it is possible that a positive correlation between SS score and working memory performance during adolescence [214] may be due to a common relationship with striatal DA function [215]. It has also been reported in one longitudinal study that high 'stimulation-seeking' at age three predicts significantly higher IQ and school achievement at age 11 [216]. The authors argue that this is the result of young stimulation-seekers creating enriched environments for themselves that in turn stimulate further cognitive development.

5. Concluding remarks

Sensation-seeking is an intriguing trait, which appears to vary considerably across individuals in both humans and other animals. A growing body of evidence, reviewed above, has allowed us to start to understand some of the neurobiological differences underlying this variation. A combination of high dopaminergic tone and a lower density of D2-type receptors in the striatum appear to be potentially important contributors to higher SS trait—as reflected in an increased tendency to exhibit approach reactions towards intense and novel stimuli that may elicit aversive reactions in others [36,57,64,66,68,69,94,100]. This kind of neurobiological signature may constitute a vulnerability to the development of addictions when 'revealed' by the addition of drugs which increase striatal DA levels, both in the case of recreational substances (which tend to have a final common pathway in increasing ventral striatal DA levels) and prescription drugs that directly target D2-type receptors (abundant in striatal regions). In other circumstances, the relative under-activation of avoidance or withdrawal reactions towards intense stimuli may serve a protective role, e.g. in coping with situations of acute stress, which may have relevance for anxiety disorders such as PTSD [15,16,200].

The exact contribution of trait SS to the aetiology of these disorders is often difficult to parse out in human studies, and will be aided by development of analogous paradigms to the animal literature–a strategy which has previously proved fruitful with respect to increasing our understanding of other kinds of impulsive behaviour [159,217]. It is important to note that the psychopathologies mentioned here are heterogeneous and likely multi-causal. Better phenotyping of individuals with a diagnosis of these disorders, aided by a better understanding of neurobiological mechanisms underlying this heterogeneity, may support the development of more effective therapies tailored to specific individuals. For example, in the case of misuse of prescription drugs, it has been shown that the perceived harmfulness of such drugs lowers the likelihood of misuse in low, but not high SS individuals [218].

Such considerations are also highly relevant for targeted prevention therapies. Recently, clinical trials in adolescents at high risk for development of alcohol use disorders have found targeting different psycho-educational and cognitive behavioural strategies towards different 'high risk' personality types to be successful [219,220]. Interestingly, these interventions were found to be most effective in reducing risk in high SS individuals [219]. Furthermore, preliminary evidence indicates that there may be clinical utility in pre-emptively targeting interventions aimed at increasing stress resilience in *lower* sensation-seeking individuals in populations at increased risk of trauma-related psychopathology, e.g. military personnel and emergency service workers [15,16,200].

It is clear that we are still at a relatively early stage of translating knowledge about underlying neurobiology into the clinical arena. Nevertheless, the body of work reviewed here, across both animal models and humans, shows the potential power of using emerging neuroscience techniques to probe the mechanisms underlying sensation seeking. Further understanding of SS trait might not only to shed light on the aetiology of various psychopathologies, but also aid in developing individualised therapies and prevention strategies for these disorders.

References

[1] Zuckerman M. The sensation seeking motive. Prog Exp Pers Res 1974;7:79–148.
[2] Zuckerman M. Behavioral expressions and biosocial bases of sensation seeking. Cambridge University Press; 1994.
[3] Zuckerman M. Dimensions of sensation seeking. J Consult Clin Psychol 1971;36:45–52, http://dx.doi.org/10.1037/h0030478.
[4] Carmody TP, Brischetto CS, Matarazzo JD, O'Donnell RP, Connor WE. Co-occurrent use of cigarettes, alcohol, and coffee in healthy, community-living men and women. Health Psychol 1985;4:323–35, http://dx.doi.org/10.1037/0278-6133.4.4.323.
[5] King KM, Nguyen HV, Kosterman R, Bailey JA, Hawkins JD. Co-occurrence of sexual risk behaviors and substance use across emerging adulthood: evidence for state- and trait-level associations. Addiction 2012;107:1288–96, http://dx.doi.org/10.1111/j. 1360-0443.2012.03792.x.
[6] Caspi A, Begg D, Dickson N, Harrington H, Langley J, Moffitt TE, et al. Personality differences predict health-risk behaviors in young adulthood: evidence from a longitudinal study. J Pers 1997;73:1052–63.
[7] Miles DR, van den Bree MB, Gupman AE, Newlin DB, Glantz MD, Pickens RW. A twin study on sensation seeking, risk taking behavior and marijuana use. Drug Alcohol Depend 2001;62:57–68, http://dx.doi.org/10.1016/S0376-8716(00)00165-4.
[8] Terry-McElrath YM, O'Malley PM, Johnston LD. Energy drinks, soft drinks, and substance use among United States secondary school students. J Addict Med 2014;8:6–13, http://dx.doi.org/10.1097/01.ADM.0000435322.07020.53.
[9] Hebb DO. The organization of behavior: a neuropsychological theory. New York: Wiley; 1949.
[10] Roberti JW. A review of behavioral and biological correlates of sensation seeking. J Res Personal 2004;38:256–79, http://dx.doi.org/10.1016/S0092-6566(03)00067-9.
[11] Crawford AM, Pentz MA, Chou C-P, Li C, Dwyer JH. Parallel developmental trajectories of sensation seeking and regular substance use in adolescents. Psychol Addict Behav 2003;17:179–92, http://dx.doi.org/10.1037/0893-164X.17.3.179.
[12] Kosten TA, Ball SA, Rounsaville BJ. A sibling study of sensation seeking and opiate addiction. J Nerv Ment Dis 1994;182:284–9.
[13] Fortune EE, Goodie AS. The relationship between pathological gambling and sensation seeking: the role of subscale scores. J Gambl Stud 2009;26:331–46, http://dx.doi.org/10.1007/s10899-009-9162-8.
[14] Smith RE, Ptacek JT, Smoll FL. Sensation seeking, stress, and adolescent injuries: a test of stress-buffering, risk-taking, and coping skills hypotheses. J Pers Soc Psychol 1992;62:1016–24.
[15] Solomon Z, Ginzburg K, Neria Y, Ohry A. Coping with war captivity: the role of sensation seeking. Eur J Personal 1995;9:57–70, http://dx.doi.org/10.1002/per.2410090105.
[16] Neria Y, Solomon Z, Ginzburg K, Dekel R. Sensation seeking, wartime performance, and long-term adjustment among Israeli war veterans. Personal Individ Differ 2000;29:921–32, http://dx.doi.org/10.1016/S0191-8869(99)00243-3.
[17] Roberti JW, Storch EA, Bravata E. Further psychometric support for the sensation seeking scale-form V. J Pers Assess 2003;81:291–2, http://dx.doi.org/10.1207/S15327752JPA8103_12.
[18] Gray JM, Wilson MA. A detailed analysis of the reliability and validity of the sensation seeking scale in a UK sample. Personal Individ Differ 2007;42:641–51, http://dx.doi.org/10.1016/j.paid.2006.08.019.
[19] Zuckerman M. Zuckerman-Kuhlman personality questionnaire (ZKPQ): an alternative five-factorial model. In: de B, Perugini M, editors. Big five assess. Ashland, OH, US: Hogrefe & Huber Publishers; 2002. p. 376–92.
[20] Arnett J. Sensation seeking: a new conceptualization and a new scale. Personal Individ Differ 1994;16:289–96, http://dx.doi.org/10.1016/0191-8869(94)90165-1.
[21] Fulker DW, Eysenck SB, Zuckerman M. A genetic and environmental analysis of sensation seeking. J Res Personal 1980;14:261–81, http://dx.doi.org/10.1016/0092-6566(80)90033-1.
[22] Koopmans JR, Boomsma DI, Heath AC, Doornen LJP. A multivariate genetic analysis of sensation seeking. Behav Genet 1995;25:349–56, http://dx.doi.org/10.1007/BF02197284.
[23] Stoel RD, Geus EJC, Boomsma DI. Genetic analysis of sensation seeking with an extended twin design. Behav Genet 2006;36:229–37, http://dx.doi.org/10.1007/s10519-005-9028-5.
[24] Harden KP, Quinn PD, Tucker-Drob EM. Genetically influenced change in sensation seeking drives the rise of delinquent behavior during adolescence. Dev Sci 2012;15:150–63, http://dx.doi.org/10.1111/j. 1467-7687.2011.01115.x.
[25] Terracciano A, Esko T, Sutin AR, de Moor MHM, Meirelles O, Zhu G, et al. Meta-analysis of genome-wide association studies identifies common variants in CTNNA2 associated with excitement-seeking. Transl Psychiatry 2011;1:e49, http://dx.doi.org/10.1038/tp.2011.42.
[26] Perry JL, Joseph JE, Jiang Y, Zimmerman RS, Kelly TH, Darna M, et al. Prefrontal cortex and drug abuse vulnerability: translation to prevention and treatment interventions. Brain Res Rev 2011;65:124–49, http://dx.doi.org/10.1016/j.brainresrev.2010.09.001.
[27] Roth M, Hammelstein P. The need inventory of sensation seeking (NISS). Eur J Psychol Assess 2011;1:1–8, http://dx.doi.org/10.1027/1015-5759/a000085.
[28] Whiteside SP, Lynam DR. The Five Factor Model and impulsivity: using a structural model of personality to understand impulsivity. Personal Individ Differ 2001;30:669–89, http://dx.doi.org/10.1016/S0191-8869(00)00064-7.
[29] Steinberg L, Albert D, Cauffman E, Banich M, Graham S, Woolard J. Age differences in sensation seeking and impulsivity as indexed by behavior and self-report: evidence for a dual systems model. Dev Psychol 2008;44:1764–78.
[30] Harden KP, Tucker-Drob EM. Individual differences in the development of sensation seeking and impulsivity during adolescence: further evidence for a dual systems model. Dev Psychol 2011;47:739–46, http://dx.doi.org/10.1037/a0023279.
[31] Collado A, Felton JW, MacPherson L, Lejuez CW. Longitudinal trajectories of sensation seeking, risk taking propensity, and impulsivity across early to middle adolescence. Addict Behav 2014;39:1580–8, http://dx.doi.org/10.1016/j.addbeh.2014.01.024.
[32] Whiteside SP, Lynam DR, Miller JD, Reynolds SK. Validation of the UPPS impulsive behaviour scale: a four-factor model of impulsivity. Eur J Personal 2005;19:559–74, http://dx.doi.org/10.1002/per.556.
[33] Ersche KD, Turton AJ, Pradhan S, Bullmore ET, Robbins TW. Drug addiction endophenotypes: impulsive versus sensation-seeking personality traits. Biol Psychiatry 2010;68:770–3, http://dx.doi.org/10.1016/j.biopsych.2010.06.015.
[34] Smith GT, Fischer S, Cyders MA, Annus AM, Spillane NS, McCarthy DM. On the validity and utility of discriminating among impulsivity-like traits. Assessment 2007;14:155–70, http://dx.doi.org/10.1177/1073191106295527.
[35] Cloninger C, Svrakic DM, Przybeck TR. A psychobiological model of temperament and character. Arch Gen Psychiatry 1993;50:975–90, http://dx.doi.org/10.1001/archpsyc.1993.01820240059008.
[36] Blanchard MM, Mendelsohn D, Stamp JA. The HR/LR model: further evidence as an animal model of sensation seeking. Neurosci Biobehav Rev 2009;33:1145–54, http://dx.doi.org/10.1016/j.neubiorev.2009.05.009.
[37] Cloninger CR. A systematic method for clinical description and classification of personality variants: a proposal. Arch Gen Psychiatry 1987;44:573–88.
[38] Zuckerman M, Cloninger CR. Relationships between Cloninger's, Zuckerman's, and Eysenck's dimensions of personality. Personal Individ Differ 1996;21:283–5, http://dx.doi.org/10.1016/0191-8869(96)00042-6.
[39] Lloyd DR, Gancarz AM, Ashrafioun L, Kausch MA, Richards JB. Habituation and the reinforcing effectiveness of visual stimuli. Behav Processes 2012;91:184–91, http://dx.doi.org/10.1016/j.beproc.2012.07.007.
[40] Olsen CM, Winder DG. Stimulus dynamics increase the self-administration of compound visual and auditory stimuli. Neurosci Lett 2012;511:8–11, http://dx.doi.org/10.1016/j.neulet.2011.12.068.
[41] Boissier JR, Simon P. The exploration reaction in the mouse. Preliminary note. Thérapie 1962;17:1225–32.
[42] Boissier JR, Simon P, Lwoff JM. Use of a particular mouse reaction (Hold Board Method) for the study of psychotropic drugs. Thérapie 1964;19:571–83.
[43] Bardo MT, Donohew RL, Harrington NG. Psychobiology of novelty seeking and drug seeking behavior. Behav Brain Res 1996;77:23–43, http://dx.doi.org/10.1016/0166-4328(95)00203-0.

[44] Piazza PV, Deminiere J-M, Le Moal M, Simon H. Factors that predict individual vulnerability to amphetamine self-administration. Science 1989;245:1511–3.

[45] Dellu F, Piazza PV, Mayo W, Le Moal M, Simon H. Novelty-seeking in rats-biobehavioral characteristics and possible relationship with the sensation-seeking trait in man. Neuropsychobiology 1996;34:136–45, http://dx.doi.org/10.1159/000119305.

[46] Kabbaj M, Devine DP, Savage VR, Akil H. Neurobiological correlates of individual differences in novelty-seeking behavior in the rat: differential expression of stress-related molecules. J Neurosci 2000;20:6983–8.

[47] Cain ME, Saucier DA, Bardo MT. Novelty seeking and drug use contribution of an animal model. Exp Clin Psychopharmacol 2005;13:367–75.

[48] Belin D, Berson N, Balado E, Piazza PV, Deroche-Gamonet V. High-novelty-preference rats are predisposed to compulsive cocaine self-administration. Neuropsychopharmacology 2011;36:569–79, http://dx.doi.org/10.1038/npp.2010.188.

[49] Belin D, Deroche-Gamonet V. Responses to novelty and vulnerability to cocaine addiction: contribution of a multi-symptomatic animal model. Cold Spring Harb Perspect Med 2012:2, doi:10.1101/cshperspect.a011940.

[50] Deroche-Gamonet V, Piazza PV. Psychobiology of cocaine addiction: contribution of a multi-symptomatic animal model of loss of control. Neuropharmacology 2014;76(Part B):437–49, http://dx.doi.org/10.1016/j.neuropharm.2013.07.014.

[51] Stewart J. Reinforcing effects of light as a function of intensity and reinforcement schedule. J Comp Physiol Psychol 1960;53:187–93, http://dx.doi.org/10.1037/h0047315.

[52] Kish GB. Studies of sensory reinforcement. In: Honing WK, editor. Operant Behav. Areas Res. Appl. New York: Appleton-Century-Crofts; 1966. p. 109–59.

[53] Blatter K, Schultz W. Rewarding properties of visual stimuli. Exp Brain Res 2006;168:541–6, http://dx.doi.org/10.1007/s00221-005-0114-y.

[54] Olsen CM, Winder DG. Operant sensation seeking engages similar neural substrates to operant drug seeking in C57 mice. Neuropsychopharmacology 2009;34:1685–94, http://dx.doi.org/10.1038/npp.2008.226.

[55] Gancarz AM, Robble MA, Kausch MA, Lloyd DR, Richards JB. Association between locomotor response to novelty and light reinforcement: sensory reinforcement as a rodent model of sensation seeking. Behav Brain Res 2012;230:380–8, http://dx.doi.org/10.1016/j.bbr.2012.02.028.

[56] Gancarz AM, Robble MA, Kausch MA, Lloyd DR, Richards JB. Sensory reinforcement as a predictor of cocaine and water self-administration in rats. Psychopharmacology (Berlin) 2012;226:335–46, http://dx.doi.org/10.1007/s00213-012-2907-6.

[57] Marusich JA, Darna M, Charnigo RJ, Dwoskin LP, Bardo MT. A multivariate assessment of individual differences in sensation seeking and impulsivity as predictors of amphetamine self-administration and prefrontal dopamine function in rats. Exp Clin Psychopharmacol 2011;19:275–84, http://dx.doi.org/10.1037/a0023897.

[58] Crabbe JC, Belknap JK. Genetic approaches to drug dependence. Trends Pharmacol Sci 1992;13:212–9, http://dx.doi.org/10.1016/0165-6147(92)90066-F.

[59] Bignami G. Selection for high rates and low rates of avoidance conditioning in the rat. Anim Behav 1965;13:221–7, http://dx.doi.org/10.1016/0003-3472(65)90038-2.

[60] Steimer T, Driscoll P. Divergent stress responses and coping styles in psychogenetically selected Roman high-(RHA) and low-(RLA) avoidance rats: behavioural, neuroendocrine and developmental aspects. Stress 2003;6:87–100, http://dx.doi.org/10.1080/1025389031000111320.

[61] Giorgi O, Piras G, Corda MG. The psychogenetically selected Roman high- and low-avoidance rat lines: a model to study the individual vulnerability to drug addiction. Neurosci Biobehav Rev 2007;31:148–63, http://dx.doi.org/10.1016/j.neubiorev.2006.07.008.

[62] Escorihuela RM, Fernández-Teruel A, Gil L, Aguilar R, Tobeña A, Driscoll P. Inbred roman high- and low-avoidance rats: differences in anxiety, novelty-seeking, and shuttlebox behaviors. Physiol Behav 1999;67:19–26, http://dx.doi.org/10.1016/S0031-9384(99)00064-5.

[63] Pisula W. The Roman high- and low-avoidance rats respond differently to novelty in a familiarized environment. Behav Processes 2003;63:63–72, http://dx.doi.org/10.1016/S0376-6357(03)00032-9.

[64] Norbury A, Kurth-Nelson Z, Winston JS, Roiser JP, Husain M. Dopamine regulates approach-avoidance in human sensation-seeking. Int J Neuropsychopharmacol 2015, http://dx.doi.org/10.1093/ijnp/pyv041.

[65] Munafò MR, Yalcin B, Willis-Owen SA, Flint J. Association of the dopamine D4 receptor (DRD4) gene and approach-related personality traits: meta-analysis and new data. Biol Psychiatry 2008;63:197–206, http://dx.doi.org/10.1016/j.biopsych.2007.04.006.

[66] Zuckerman M. Sensation seeking, mania, and monoamines. Neuropsychobiology 1985;13:121–8, http://dx.doi.org/10.1159/000118174.

[67] Riccardi P, Zald D, Li R, Park S, Ansari MS, Dawant B, et al. Sex differences in amphetamine-induced displacement of [18F]fallypride in striatal and extrastriatal regions: a PET study. Am J Psychiatry 2006;163:1639–41, http://dx.doi.org/10.1176/appi.ajp.163.9.1639.

[68] Gjedde A, Kumakura Y, Cumming P, Linnet J, Møller A. Inverted-U-shaped correlation between dopamine receptor availability in striatum and sensation seeking. Proc Natl Acad Sci USA 2010;107:3870–5, http://dx.doi.org/10.1073/pnas.0912319107.

[69] Derringer J, Krueger RF, Dick DM, Saccone S, Grucza RA, Agrawal A, et al. Predicting sensation seeking from dopamine genes A candidate-system approach. Psychol Sci 2010;21:1282–90, http://dx.doi.org/10.1177/0956797610380699.

[70] O'Sullivan SS, Wu K, Politis M, Lawrence AD, Evans AH, Bose SK, et al. Cue-induced striatal dopamine release in Parkinson's disease-associated impulsive-compulsive behaviours. Brain 2011;134:969–78, http://dx.doi.org/10.1093/brain/awr003.

[71] Carrasco JL, Sáiz-Ruiz J, Díaz-Marsá M, César J, López-Ibor JJ. Low platelet monoamine oxidase activity in sensation-seeking bullfighters. CNS Spectr 1999;4:21–4.

[72] Verdejo-García A, Albein-Urios N, Molina E, Ching-López A, Martínez-González JM, Gutiérrez B. A MAOA gene × cocaine severity interaction on impulsivity and neuropsychological measures of orbitofrontal dysfunction: preliminary results. Drug Alcohol Depend 2013;133:287–90, http://dx.doi.org/10.1016/j.drugalcdep.2013.04.031.

[73] Ratsma J, van der Stelt O, Schoffelmeer A, Westerveld A, Gunning W. P3 event-related potential, dopamine D2 receptor A1 allele, and sensation-seeking in adult children of alcoholics. Alcohol-Clin Exp Res 2001;25:960–7, http://dx.doi.org/10.1111/j. 1530-0277.2001.tb02303.x.

[74] Eisenberg DTA, Campbell B, Mackillop J, Lum JK, Wilson DS. Season of birth and dopamine receptor gene associations with impulsivity, sensation seeking and reproductive behaviors. PLoS One 2007;2:e1216, http://dx.doi.org/10.1371/journal.pone.0001216.

[75] Laakso A, Pohjalainen T, Bergman J, Kajander J, Haaparanta M, Solin O, et al. The A1 allele of the human D2 dopamine receptor gene is associated with increased activity of striatal L-amino acid decarboxylase in healthy subjects. Pharmacogenet Genomics 2005;15:387–91.

[76] Kelly TH, Robbins G, Martin CA, Fillmore MT, Lane SD, Harrington NG, et al. Individual differences in drug abuse vulnerability: d-amphetamine and sensation-seeking status. Psychopharmacology (Berlin) 2006;189:17–25, http://dx.doi.org/10.1007/s00213-006-0487-z.

[77] Stoops WW, Lile JA, Robbins CG, Martin CA, Rush CR, Kelly TH. The reinforcing, subject-rated, performance, and cardiovascular effects of d-amphetamine: Influence of sensation-seeking status. Addict Behav 2007;32:1177–88, http://dx.doi.org/10.1016/j.addbeh.2006.08.006.

[78] Hutchison KE, Wood MD, Swift R. Personality factors moderate subjective and psychophysiological responses to d-amphetamine in humans. Exp Clin Psychopharmacol 1999;7:493–501.

[79] Zacny JP. A possible link between sensation-seeking status and positive subjective effects of oxycodone in healthy volunteers. Pharmacol Biochem Behav 2010;95:113–20, http://dx.doi.org/10.1016/j.pbb.2009.12.015.

[80] Fillmore MT, Ostling EW, Martin CA, Kelly TH. Acute effects of alcohol on inhibitory control and information processing in high and low sensation-seekers. Drug Alcohol Depend 2009;100:91–9, http://dx.doi.org/10.1016/j.drugalcdep.2008.09.007.

[81] Scott C, Corbin WR. Influence of sensation seeking on response to alcohol versus placebo: implications for the acquired preparedness model. J Stud Alcohol Drugs 2014;75:136.

[82] Pierce RC, Kumaresan V. The mesolimbic dopamine system: the final common pathway for the reinforcing effect of drugs of abuse? Neurosci Biobehav Rev 2006;30:215–38, http://dx.doi.org/10.1016/j.neubiorev.2005.04.016.

[83] Leyton M, Boileau I, Benkelfat C, Diksic M, Baker G, Dagher A. Amphetamine-induced increases in extracellular dopamine, drug wanting, and novelty seeking: a PET/[11C]Raclopride Study in healthy men. Neuropsychopharmacology 2002;27:1027–35, http://dx.doi.org/10.1016/S0893-133X(02)00366-4.

[84] Campbell BC, Dreber A, Apicella CL, Eisenberg DTA, Gray PB, Little AC, et al. Testosterone exposure, dopaminergic reward, and sensation-seeking in young men. Physiol Behav 2010;99:451–6, http://dx.doi.org/10.1016/j.physbeh.2009.12.011.

[85] Hamidovic A, Dlugos A, Skol A, Palmer AA, de Wit H. Evaluation of genetic variability in the dopamine receptor D2 in relation to behavioral inhibition and impulsivity/sensation seeking: an exploratory study with d-amphetamine in healthy participants. Exp Clin Psychopharmacol 2009;17:374–83, http://dx.doi.org/10.1037/a0017840.

[86] Norbury A, Manohar S, Rogers RD, Husain M. Dopamine modulates risk-taking as a function of baseline sensation-seeking trait. J Neurosci 2013;33:12982–6, http://dx.doi.org/10.1523/JNEUROSCI. 5587-12.2013.

[87] Flagel SB, Robinson TE, Clark JJ, Clinton SM, Watson SJ, Seeman P, et al. An animal model of genetic vulnerability to behavioral disinhibition and responsiveness to reward-related cues: implications for addiction. Neuropsychopharmacology 2010;35:388–400.

[88] Pogorelov VM, Rodriguiz RM, Insco ML, Caron MG, Wetsel WC. Novelty seeking and stereotypic activation of behavior in mice with disruption of the Dat1 gene. Neuropsychopharmacology 2005;30:1818–31, doi:10.1038/sj.npp.1300724.

[89] Jones SR, Gainetdinov RR, Jaber M, Giros B, Wightman RM, Caron MG. Profound neuronal plasticity in response to inactivation of the dopamine transporter. Proc Natl Acad Sci USA 1998;95:4029–34.

[90] Lind NM, Gjedde A, Moustgaard A, Olsen AK, Jensen SB, Jakobsen S, et al. Behavioral response to novelty correlates with dopamine receptor availability in striatum of Göttingen minipigs. Behav Brain Res 2005;164:172–7, http://dx.doi.org/10.1016/j.bbr.2005.06.008.

[91] Bardo MT, Neisewander JL, Pierce RC. Novelty-induced place preference behavior in rats: effects of opiate and dopaminergic drugs. Pharmacol Biochem Behav 1989;32:683–9, http://dx.doi.org/10.1016/0091-3057(89)90018-X.

[92] Dulawa SC, Grandy DK, Low MJ, Paulus MP, Geyer MA. Dopamine D4 receptor-knock-out mice exhibit reduced exploration of novel stimuli. J Neurosci 1999;19:9550–6.

[93] Bailey JN, Breidenthal SE, Jorgensen MJ, McCracken JT, Fairbanks LA. The association of DRD4 and novelty seeking is found in a nonhuman primate model. Psychiatr Genet 2007;17:23–7, doi:10.1097/YPG.0b013e32801140f2.

[94] Shin R, Cao J, Webb SM, Ikemoto S. Amphetamine administration into the ventral striatum facilitates behavioral interaction with unconditioned visual signals in rats. PLoS ONE 2010;5:e8741, http://dx.doi.org/10.1371/journal.pone.0008741.

[95] Corda MG, Piras G, Piludu MA, Giorgi O. Differential effects of voluntary ethanol consumption on dopamine output in the nucleus accumbens shell of roman high- and low-avoidance rats: a behavioral and brain microdialysis study. World J Neurosci 2014;04:279–92, http://dx.doi.org/10.4236/wjns.2014.43031.

[96] Tournier BB, Steimer T, Millet P, Moulin-Sallanon M, Vallet P, Ibañez V, et al. Innately low D2 receptor availability is associated with high novelty-seeking and enhanced behavioural sensitization to amphetamine. Int J Neuropsychopharmacol 2013;16:1819–34, http://dx.doi.org/10.1017/S1461145713000205.

[97] Moreno M, Cardona D, Gómez MJ, Sánchez-Santed F, Tobeña A, Fernández-Teruel A, et al. Impulsivity characterization in the roman high- and low-avoidance rat strains: behavioral and neurochemical differences. Neuropsychopharmacology 2010;35:1198–208, http://dx.doi.org/10.1038/npp.2009.224.

[98] Guitart-Masip M, Johansson B, Fernández-Teruel A, Cañete T, Tobeña A, Terenius L, et al. Divergent anatomical pattern of D1 and D3 binding and dopamine- and cyclic AMP-regulated phosphoprotein of 32 kDa mRNA expression in the Roman rat strains: implications for drug addiction. Neuroscience 2006;142:1231–43, http://dx.doi.org/10.1016/j.neuroscience.2006.07.041.

[99] Parkitna JR, Sikora M, Gołda S, Gołembiowska K, Bystrowska B, Engblom D, et al. Novelty-seeking behaviors and the escalation of alcohol drinking after abstinence in mice are controlled by metabotropic glutamate receptor 5 on neurons expressing dopamine D1 receptors. Biol Psychiatry 2013;73:263–70, http://dx.doi.org/10.1016/j.biopsych.2012.07.019.

[100] Zuckerman M. The psychophysiology of sensation seeking. J Pers 1990;58:313–45, http://dx.doi.org/10.1111/j. 1467-6494.1990.tb00918.x.

[101] Lang A, Shin M, Lee S. Sensation seeking, motivation, and substance use: a dual system approach. Media Psychol 2005;7:1–29, http://dx.doi.org/10.1207/S1532785XMEP0701_1.

[102] Salamone JD, Correa M. Motivational views of reinforcement: implications for understanding the behavioral functions of nucleus accumbens dopamine. Behav Brain Res 2002;137:3–25, http://dx.doi.org/10.1016/S0166-4328(02)00282-6.

[103] Robbins T, Everitt B. A role for mesencephalic dopamine in activation: commentary on Berridge (2006). Psychopharmacology (Berlin) 2007;191:433–7, http://dx.doi.org/10.1007/s00213-006-0528-7.

[104] Ikemoto S. Dopamine reward circuitry: two projection systems from the ventral midbrain to the nucleus accumbens–olfactory tubercle complex. Brain Res Rev 2007;56:27–78, http://dx.doi.org/10.1016/j.brainresrev.2007.05.004.

[105] Hoffmann Jdu, Nicola SM. Dopamine invigorates reward seeking by promoting cue-evoked excitation in the nucleus accumbens. J Neurosci 2014;34:14349–64, http://dx.doi.org/10.1523/JNEUROSCI. 3492-14.2014.

[106] De Pascalis V, Valerio E, Santoro M, Cacace I. Neuroticism-anxiety, impulsive-sensation seeking and autonomic responses to somatosensory stimuli. Int J Psychophysiol 2007;63:16–24, http://dx.doi.org/10.1016/j.ijpsycho.2006.06.004.

[107] Freeman HD, Beer JS. Frontal lobe activation mediates the relation between sensation seeking and cortisol increases. J Pers 2010;78:1497–528, http://dx.doi.org/10.1111/j. 1467-6494.2010.00659.x.

[108] Lissek S, Powers AS. Sensation seeking and startle modulation by physically threatening images. Biol Psychol 2003;63:179–97, http://dx.doi.org/10.1016/S0301-0511(03)00053-X.

[109] Brocke B, Beauducel A, Tasche KG. Biopsychological bases and behavioral correlates of sensation seeking: contributions to a multilevel validation. Personal Individ Differ 1999;26:1103–23.

[110] Zaleski Z. Sensation-seeking and preference for emotional visual stimuli. Personal Individ Differ 1984;5:609–11, http://dx.doi.org/10.1016/0191-8869(84)90040-0.

[111] Lissek S, Baas JMP, Pine DS, Orme K, Dvir S, Rosenberger E, et al. Sensation seeking and the aversive motivational system. Emotion 2005;5:396–407, http://dx.doi.org/10.1037/1528-3542.5.4.396.

[112] Freeman AS, Bunney BS. Activity of A9 and A10 dopaminergic neurons in unrestrained rats: further characterization and effects of apomorphine and cholecystokinin. Brain Res 1987;405:46–55, http://dx.doi.org/10.1016/0006-8993(87)90988-7.

[113] Horvitz JC. Mesolimbocortical and nigrostriatal dopamine responses to salient non-reward events. Neuroscience 2000;96:651–6, http://dx.doi.org/10.1016/S0306-4522(00)00019-1.

[114] Schultz W. Dopamine signals for reward value and risk: basic and recent data. Behav Brain Funct 2010;6:24, http://dx.doi.org/10.1186/1744-9081-6-24.

[115] Hoyle RH, Fejfar MC, Miller JD. Personality and sexual risk taking: a quantitative review. J Pers 2000;68:1203–31, http://dx.doi.org/10.1111/1467-6494.00132.

[116] Charnigo R, Noar SM, Garnett C, Crosby R, Palmgreen P, Zimmerman RS. Sensation seeking and impulsivity combined associations with risky sexual behavior in a large sample of young adults. J Sex Res 2013;50:480–8, http://dx.doi.org/10.1080/00224499.2011.652264.

[117] Oshri A, Tubman JG, Morgan-Lopez AA, Saavedra LM, Csizmadia A. Sexual sensation seeking, co-occurring sex and alcohol use, and sexual risk behavior among adolescents in treatment for substance use problems. Am J Addict 2013;22:197–205, http://dx.doi.org/10.1111/j. 1521-0391.2012.12027.x.

[118] Hittner JB, Swickert R. Sensation seeking and alcohol use: a meta-analytic review. Addict Behav 2006;31:1383–401, http://dx.doi.org/10.1016/j.addbeh.2005.11.004.

[119] Stautz K, Cooper A. Impulsivity-related personality traits and adolescent alcohol use: a meta-analytic review. Clin Psychol Rev 2013;33:574–92, http://dx.doi.org/10.1016/j.cpr.2013.03.003.

[120] Huang C-M, Lin L-F, Lee T-C, Guo J-L. Proximal to distal correlates of the patterns of illicit drug use among night school students in Taiwan. Addict Behav 2013;38:1481–4, http://dx.doi.org/10.1016/j.addbeh.2012.08.010.

[121] Doran N, Schweizer CA, Myers MG, Greenwood TA. A prospective study of the effects of the DRD2/ANKK1TaqIA polymorphism and impulsivity on smoking initiation. Subst Use Misuse 2013;48:106–16, http://dx.doi.org/10.3109/10826084.2012.733791.

[122] Lookatch SJ, Dunne EM, Katz EC. Predictors of nonmedical use of prescription stimulants. J Psychoactive Drugs 2012;44:86–91, http://dx.doi.org/10.1080/02791072.2012.662083.

[123] Jonah BA. Sensation seeking and risky driving: a review and synthesis of the literature. Accid Anal Prev 1997;29:651–65, http://dx.doi.org/10.1016/S0001-4575(97)00017-1.

[124] Gomà-i-Freixanet M. Prosocial and antisocial aspects of personality. Personal Individ Differ 1995;19:125–34, http://dx.doi.org/10.1016/0191-8869(95)00037-7.

[125] American Psychiatric Association. DSM-IV-TR: diagnostic and statistical manual of mental disorders. 4th revised edition Washington, DC: American Psychiatric Press Inc.; 1994.

[126] Adams ZW, Kaiser AJ, Lynam DR, Charnigo RJ, Milich R. Drinking motives as mediators of the impulsivity-substance use relation: pathways for negative urgency, lack of premeditation, and sensation seeking. Addict Behav 2012;37:848–55, http://dx.doi.org/10.1016/j.addbeh.2012.03.016.

[127] Franques P, Auriacombe M, Piquemal E, Verger M, Brisseau-Gimenez S, Grabot D, et al. Sensation seeking as a common factor in opioid dependent subjects and high risk sport practicing subjects. A cross sectional study. Drug Alcohol Depend 2003;69:121–6, http://dx.doi.org/10.1016/S0376-8716(02)00309-5.

[128] Sargent JD, Tanski S, Stoolmiller M, Hanewinkel R. Using sensation seeking to target adolescents for substance use interventions. Addiction 2010;105:506–14, http://dx.doi.org/10.1111/j. 1360-0443.2009.02782.x.

[129] Ersche KD, Jones PS, Williams GB, Smith DG, Bullmore ET, Robbins TW. Distinctive personality traits and neural correlates associated with stimulant drug use versus familial risk of stimulant dependence. Biol Psychiatry 2013;74:137–44, http://dx.doi.org/10.1016/j.biopsych.2012.11.016.

[130] Ball SA, Carroll KM, Rounsaville BJ. Sensation seeking, substance abuse, and psychopathology in treatment-seeking and community cocaine abusers. J Consult 1994;62:1053–7.

[131] Staiger PK, Kambouropoulos N, Dawe S. Should personality traits be considered when refining substance misuse treatment programs? Drug Alcohol Rev 2007;26:17–23, http://dx.doi.org/10.1080/09595230601036952.

[132] Noël X, Brevers D, Bechara A, Hanak C, Kornreich C, Verbanck P, et al. Neurocognitive determinants of novelty and sensation-seeking in individuals with alcoholism. Alcohol Alcohol 2011;46:407–15, http://dx.doi.org/10.1093/alcalc/agr048.

[133] Lackner N, Unterrainer H-F, Neubauer AC. Differences in big five personality traits between alcohol and polydrug abusers: implications for treatment in the therapeutic community. Int J Ment Health Addict 2013;11:682–92, http://dx.doi.org/10.1007/s11469-013-9445-2.

[134] Patkar AA, Murray HW, Mannelli P, Gottheil E, Weinstein SP, Vergare MJ. Pre-treatment measures of impulsivity, aggression and sensation seeking are associated with treatment outcome for African–American cocaine-dependent patients. J Addict Dis 2004;23:109–22, http://dx.doi.org/10.1300/J069v23n02_08.

[135] Fornaro M, Ventriglio A, De Pasquale C, Pistorio ML, De Berardis D, Cattaneo CI, et al. Sensation seeking in major depressive patients: relationship

to sub-threshold bipolarity and cyclothymic temperament. J Affect Disord 2013;148:375–83, http://dx.doi.org/10.1016/j.jad.2013.01.002.

[136] Ekselius L, Bengtsson F, Von Knorring L. Non-compliance with pharmacotherapy of depression is associated with a sensation seeking personality. Int Clin Psychopharmacol 2000;15:273–8.

[137] Liraud F, Verdoux H. Association between temperamental characteristics and medication adherence in subjects presenting with psychotic or mood disorders. Psychiatry Res 2001;102:91–5, http://dx.doi.org/10.1016/S0165-1781(01)00240-2.

[138] Åkerblad A-C, Bengtsson F, Holgersson M, von Knorring L, Ekselius L. Identification of primary care patients at risk of nonadherence to antidepressant treatment. Patient Prefer Adherence 2008;2:379–86, http://dx.doi.org/10.2147/PPA.S3511.

[139] Molander AC, Mar A, Norbury A, Steventon S, Moreno M, Caprioli D, et al. High impulsivity predicting vulnerability to cocaine addiction in rats: some relationship with novelty preference but not novelty reactivity, anxiety or stress. Psychopharmacology (Berlin) 2011;215:721–31, http://dx.doi.org/10.1007/s00213-011-2167-x.

[140] Dela Peña I, Gonzales EL, de la Peña JB, Kim B-N, Han DH, Shin CY, et al. Individual differences in novelty-seeking behavior in spontaneously hypertensive rats: enhanced sensitivity to the reinforcing effect of methylphenidate in the high novelty-preferring subpopulation. J Neurosci Methods 2014, http://dx.doi.org/10.1016/j.jneumeth.2014.08.019.

[141] Belin D, Mar AC, Dalley JW, Robbins TW, Everitt BJ. High impulsivity predicts the switch to compulsive cocaine-taking. Science 2008;320:1352–5, http://dx.doi.org/10.1126/science.1158136.

[142] Meyer AC, Rahman S, Charnigo RJ, Dwoskin LP, Crabbe JC, Bardo MT. Genetics of novelty seeking, amphetamine self-administration and reinstatement using inbred rats. Genes Brain Behav 2010;9:790–8, http://dx.doi.org/10.1111/j.1601-183X.2010.00616.x.

[143] Montagud-Romero S, Daza-Losada M, Vidal-Infer A, Maldonado C, Aguilar MA, Miñarro J, et al. The novelty-seeking phenotype modulates the long-lasting effects of intermittent ethanol administration during adolescence. PLoS ONE 2014;9:e92576, http://dx.doi.org/10.1371/journal.pone.0092576.

[144] Olsen CM, Childs DS, Stanwood GD, Winder DG. Operant sensation seeking requires metabotropic glutamate receptor 5 (mGluR5). PLoS One 2010:5.

[145] Fattore L, Piras G, Corda MG, Giorgi O. The Roman high- and low-avoidance rat lines differ in the acquisition, maintenance, extinction, and reinstatement of intravenous cocaine self-administration. Neuropsychopharmacology 2008;34:1091–101, http://dx.doi.org/10.1038/npp.2008.43.

[146] Volkow ND, Wang G-J, Fowler JS, Logan J, Gatley SJ, Gifford A, et al. Prediction of reinforcing responses to psychostimulants in humans by brain dopamine D2 receptor levels. Am J Psychiatry 1999;156:1440–3.

[147] Volkow ND, Fowler JS, Wang G-J, Hitzemann R, Logan J, Schlyer DJ, et al. Decreased dopamine D2 receptor availability is associated with reduced frontal metabolism in cocaine abusers. Synapse 1993;14:169–77, http://dx.doi.org/10.1002/syn.890140210.

[148] Volkow ND, Fowler JS, Wang G-J, Goldstein RZ. Role of dopamine, the frontal cortex and memory circuits in drug addiction: insight from imaging studies. Neurobiol Learn Mem 2002;78:610–24, http://dx.doi.org/10.1006/nlme.2002.4099.

[149] Caine SB, Negus SS, Mello NK, Patel S, Bristow L, Kulagowski J, et al. Role of dopamine D2-like receptors in cocaine self-administration: studies with D2 receptor mutant mice and novel D2 receptor antagonists. J Neurosci 2002;22:2977–88, doi:20026264.

[150] Nader MA, Morgan D, Gage HD, Nader SH, Calhoun TL, Buchheimer N, et al. PET imaging of dopamine D2 receptors during chronic cocaine self-administration in monkeys. Nat Neurosci 2006;9:1050–6, http://dx.doi.org/10.1038/nn1737.

[151] Neale MC, Aggen SH, Maes HH, Kubarych TS, Schmitt JE. Methodological issues in the assessment of substance use phenotypes. Addict Behav 2006;31:1010–34, http://dx.doi.org/10.1016/j.addbeh.2006.03.047.

[152] Simon NW, Mendez IA, Setlow B. Cocaine exposure causes long-term increases in impulsive choice. Behav Neurosci 2007;121:543–9, http://dx.doi.org/10.1037/0735-7044.121.3.543.

[153] Caprioli D, Hong YT, Sawiak SJ, Ferrari V, Williamson DJ, Jupp B, et al. Baseline-dependent effects of cocaine pre-exposure on impulsivity and D2/3 receptor availability in the rat striatum: possible relevance to the attention-deficit hyperactivity syndrome. Neuropsychopharmacology 2013;38:1460–71, http://dx.doi.org/10.1038/npp.2013.44.

[154] Jentsch JD, Ashenhurst JR, Cervantes MC, Groman SM, James AS, Pennington ZT. Dissecting impulsivity and its relationships to drug addictions. Ann NY Acad Sci 2014, http://dx.doi.org/10.1111/nyas.12388.

[155] Nees F, Tzschoppe J, Patrick CJ, Vollstädt-Klein S, Steiner S, Poustka L, et al. Determinants of early alcohol use in healthy adolescents: the differential contribution of neuroimaging and psychological factors. Neuropsychopharmacology 2012;37:986–95, http://dx.doi.org/10.1038/npp.2011.282.

[156] Suri D, Teixeira CM, Cagliostro MKC, Mahadevia D, Ansorge MS. Monoamine-sensitive developmental periods impacting adult emotional and cognitive behaviors. Neuropsychopharmacology 2015;40:88–112, http://dx.doi.org/10.1038/npp.2014.231.

[157] Grant BF, Stinson FS, Harford TC. Age at onset of alcohol use and DSM-IV alcohol abuse and dependence: a 12-year follow-up. J Subst Abuse 2001;13:493–504, http://dx.doi.org/10.1016/S0899-3289(01)00096-7.

[158] Mateos-Garcia A, Roger-Sanchez C, Rodriguez-Arias M, Minarro J, Aguilar MA, Manzanedo C, et al. Higher sensitivity to the conditioned rewarding effects of cocaine and MDMA in high-novelty-seekers mice exposed to a cocaine binge during adolescence. Psychopharmacology (Berlin) 2015;232:101–13, http://dx.doi.org/10.1007/s00213-014-3642-y.

[159] Jupp B, Dalley JW. Behavioral endophenotypes of drug addiction: etiological insights from neuroimaging studies. Neuropharmacology 2014;76(Part B):487–97, http://dx.doi.org/10.1016/j.neuropharm.2013.05.041.

[160] Hammelstein P. Faites vos jeux! Another look at sensation seeking and pathological gambling. Personal Indiv Differ 2004;37:917–31, http://dx.doi.org/10.1016/j.paid.2003.10.014.

[161] Anderson G, Brown RIF. Real and laboratory gambling, sensation-seeking and arousal. Br J Psychol 1984;75:401–10, http://dx.doi.org/10.1111/j. 2044-8295.1984.tb01910.x.

[162] Ashrafioun L, McCarthy A, Rosenberg H. Assessing the impact of cue exposure on craving to gamble in university students. J Gambl Stud 2012;28:363–75, http://dx.doi.org/10.1007/s10899-011-9262-0.

[163] McDaniel SR, Zuckerman M. The relationship of impulsive sensation seeking and gender to interest and participation in gambling activities. Personal Indiv Differ 2003;35:1385–400, http://dx.doi.org/10.1016/S0191-8869(02)00357-4.

[164] Blanco C, Orensanz-Muñoz L, Blanco-Jerez C, Saiz-Ruiz J. Pathological gambling and platelet MAO activity: a psychobiological study. Am J Psychiatry 1996;153:119.

[165] Hodgins DC, Schopflocher DP, Martin CR, el-Guebaly N, Casey DM, Currie SR, et al. Disordered gambling among higher-frequency gamblers: who is at risk? Psychol Med 2012;42:2433–44, http://dx.doi.org/10.1017/S0033291712000724.

[166] Grall-Bronnec M, Wainstein L, Feuillet F, Bouju G, Rocher B, Vénisse J-L, et al. Clinical profiles as a function of level and type of impulsivity in a sample group of at-risk and pathological gamblers seeking treatment. J Gambl Stud 2011;28:239–52, http://dx.doi.org/10.1007/s10899-011-9258-9.

[167] Michalczuk R, Bowden-Jones H, Verdejo-Garcia A, Clark L. Impulsivity and cognitive distortions in pathological gamblers attending the UK National Problem Gambling Clinic: a preliminary report. Psychol Med 2011;41:2625–35, http://dx.doi.org/10.1017/S003329171100095X.

[168] Clark L, Stokes PR, Wu K, Michalczuk R, Benecke A, Watson BJ, et al. Striatal dopamine D2/D3 receptor binding in pathological gambling is correlated with mood-related impulsivity. NeuroImage 2012;63:40–6, http://dx.doi.org/10.1016/j.neuroimage.2012.06.067.

[169] Lorains FK, Stout JC, Bradshaw JL, Dowling NA, Enticott PG. Self-reported impulsivity and inhibitory control in problem gamblers. J Clin Exp Neuropsychol 2014;36:144–57, http://dx.doi.org/10.1080/13803395.2013.873773.

[170] Coventry KR, Brown RIF. Sensation seeking, gambling and gambling addictions. Addiction 1993;88:541–54, http://dx.doi.org/10.1111/j. 1360-0443.1993.tb02061.x.

[171] Carver AB, McCarty JA. Personality and psychographics of three types of gamblers in the United States. Int Gambl Stud 2013;13:338–55, http://dx.doi.org/10.1080/14459795.2013.819933.

[172] Comings DE, Rosenthal RJ, Lesieur HR, Rugle LJ, Muhleman D, Chui C, et al. A study of the dopamine D2 receptor gene in pathological gambling. Pharmacogenetics 1996;6:223–34.

[173] Cocker PJ, Dinelle K, Kornelson R, Sossi V, Winstanley CA. Irrational choice under uncertainty correlates with lower striatal D2/3 receptor binding in rats. J Neurosci 2012;32:15450–7, http://dx.doi.org/10.1523/JNEUROSCI. 0626-12.2012.

[174] Boileau I, Payer D, Chugani B, Lobo D, Behzadi A, Rusjan PM, et al. The D2/3 dopamine receptor in pathological gambling: a positron emission tomography study with [11C]-(+)-propyl-hexahydro-naphtho-oxazin and [11C]raclopride. Addiction 2013;108:953–63, http://dx.doi.org/10.1111/add.12066.

[175] Petry NM, Stinson FS, Grant BF. Comorbidity of DSM-IV pathological gambling and other psychiatric disorders: Results from the national epidemiologic survey on alcohol and related conditions. J Clin Psychiatry 2005;66:564–74.

[176] Slutske WS, Eisen S, True WR, Lyons MJ, Goldberg J, Tsuang M. Common genetic vulnerability for pathological gambling and alcohol dependence in men. Arch Gen Psychiatry 2000;57:666–73, http://dx.doi.org/10.1001/archpsyc.57.7.666.

[177] Clark CA, Dagher A. The role of dopamine in risk taking: a specific look at Parkinson's disease and gambling. Front Behav Neurosci 2014:8, http://dx.doi.org/10.3389/fnbeh.2014.00196.

[178] Clark L, Averbeck B, Payer D, Sescousse G, Winstanley CA, Xue G. Pathological choice the neuroscience of gambling and gambling addiction. J Neurosci 2013;33:17617–23, http://dx.doi.org/10.1523/JNEUROSCI.3231-13.2013.

[179] Claassen DO, van den Wildenberg WPM, Ridderinkhof KR, Jessup CK, Harrison MB, Wooten GF, et al. The risky business of dopamine agonists in parkinson disease and impulse control disorders. Behav Neurosci 2011;125:492–500, http://dx.doi.org/10.1037/a0023795.

[180] Dang D, Cunnington D, Swieca J. The emergence of devastating impulse control disorders during dopamine agonist therapy of the restless legs syndrome. Clin Neuropharmacol 2011;34:66–70, http://dx.doi.org/10.1097/WNF.0b013e31820d6699.

[181] Djamshidian A, Cardoso F, Grosset D, Bowden-Jones H, Lees AJ. Pathological gambling in Parkinson's disease-a review of the literature. Mov Disord 2011;26:1976–84, http://dx.doi.org/10.1002/mds.23821.

[182] Martinkova J, Trejbalova L, Sasikova M, Benetin J, Valkovic P. Impulse control disorders associated with dopaminergic medication in patients with pituitary adenomas. Clin Neuropharmacol 2011;34:179–81, http://dx.doi.org/10.1097/WNF.0b013e3182281b2f.

[183] Weintraub D, Koester J, Potenza MN, Siderowf AD, Stacy M, Voon V, et al. Impulse control disorders in Parkinson disease: a cross-sectional study of 3090 patients. Arch Neurol 2010;67:589–95, http://dx.doi.org/10.1001/archneurol.2010.65.

[184] Evans AH, Lawrence AD, Potts J, MacGregor L, Katzenschlager R, Shaw K, et al. Relationship between impulsive sensation seeking traits, smoking, alcohol and caffeine intake, and Parkinson's disease. J Neurol Neurosurg Psychiatry 2006;77:317–21, http://dx.doi.org/10.1136/jnnp.2005.065417.

[185] Poletti M, Bonuccelli U. Impulse control disorders in Parkinson's disease: the role of personality and cognitive status. J Neurol 2012;259:2269–77, http://dx.doi.org/10.1007/s00415-012-6506-6.

[186] Voon V, Thomsen T, Miyasaki JM, de Souza M, Shafro A, Fox SH, et al. Factors associated with dopaminergic drug-related pathological gambling in parkinson disease. Arch Neurol 2007;64:212–6, http://dx.doi.org/10.1001/archneur.64.2.212.

[187] Bódi N, Kéri S, Nagy H, Moustafa A, Myers CE, Daw N, et al. Reward-learning and the novelty-seeking personality: a between- and within-subjects study of the effects of dopamine agonists on young Parkinson's patients. Brain 2009;132:2385–95, http://dx.doi.org/10.1093/brain/awp094.

[188] Steeves TDL, Miyasaki J, Zurowski M, Lang AE, Pellecchia G, Van Eimeren T, et al. Increased striatal dopamine release in Parkinsonian patients with pathological gambling: a [11C] raclopride PET study. Brain 2009;132:1376–85, http://dx.doi.org/10.1093/brain/awp054.

[189] Cilia R, Ko JH, Cho SS, van Eimeren T, Marotta G, Pellecchia G, et al. Reduced dopamine transporter density in the ventral striatum of patients with Parkinson's disease and pathological gambling. Neurobiol Dis 2010;39:98–104, http://dx.doi.org/10.1016/j.nbd.2010.03.013.

[190] Voon V, Rizos A, Chakravartty R, Mulholland N, Robinson S, Howell NA, et al. Impulse control disorders in Parkinson's disease: decreased striatal dopamine transporter levels. J Neurol Neurosurg Psychiatry 2014;85:148–52, http://dx.doi.org/10.1136/jnnp-2013-305395.

[191] Ray NJ, Miyasaki JM, Zurowski M, Ko JH, Cho SS, Pellecchia G, et al. Extrastriatal dopaminergic abnormalities of DA homeostasis in Parkinson's patients with medication-induced pathological gambling: A [11C] FLB-457 and PET study. Neurobiol Dis 2012;48:519–25, http://dx.doi.org/10.1016/j.nbd.2012.06.021.

[192] Crone EA, Dahl RE. Understanding adolescence as a period of social–affective engagement and goal flexibility. Nat Rev Neurosci 2012;13:636–50, http://dx.doi.org/10.1038/nrn3313.

[193] Spielberg JM, Olino TM, Forbes EE, Dahl RE. Exciting fear in adolescence: does pubertal development alter threat processing? Dev Cogn Neurosci 2014;8:86–95, http://dx.doi.org/10.1016/j.dcn.2014.01.004.

[194] Franken RE, Gibson KJ, Rowland GL. Sensation seeking and the tendency to view the world as threatening. Personal Indiv Differ 1992;13:31–8, http://dx.doi.org/10.1016/0191-8869(92)90214-A.

[195] Mujica-Parodi LR, Carlson JM, Cha J, Rubin D. The fine line between brave and reckless: amygdala reactivity and regulation predict recognition of risk. NeuroImage 2014;103:1–9, http://dx.doi.org/10.1016/j.neuroimage.2014.08.038.

[196] Stead JDH, Clinton S, Neal C, Schneider J, Jama A, Miller S, et al. Selective breeding for divergence in novelty-seeking traits: heritability and enrichment in spontaneous anxiety-related behaviors. Behav Genet 2006;36:697–712, http://dx.doi.org/10.1007/s10519-006-9058-7.

[197] Driscoll P, Escorihuela RM, Fernández-Teruel A, Giorgi O, Schwegler H, Steimer T, et al. Genetic selection and differential stress responses: the roman lines/strains of rats. Ann N Y Acad Sci 1998;851:501–10, http://dx.doi.org/10.1111/j. 1749-6632.1998.tb09029.x.

[198] Weiss NH, Tull MT, Anestis MD, Gratz KL. The relative and unique contributions of emotion dysregulation and impulsivity to posttraumatic stress disorder among substance dependent inpatients. Drug Alcohol Depend 2013;128:45–51, http://dx.doi.org/10.1016/j.drugalcdep.2012.07.017.

[199] Bender TW, Anestis MD, Anestis JC, Gordon KH. Affective and behavioral paths toward the acquired capacity for suicide. J Soc Clin Psychol 2012;31:81.

[200] Clinton SM, Watson SJ, Akil H. High novelty-seeking rats are resilient to negative physiological effects of the early life stress. Stress 2014;17:97–107, http://dx.doi.org/10.3109/10253890.2013.850670.

[201] Stedenfeld KA, Clinton SM, Kerman IA, Akil H, Watson SJ, Sved AF. Novelty-seeking behavior predicts vulnerability in a rodent model of depression. Physiol Behav 2011;103:210–6, http://dx.doi.org/10.1016/j.physbeh.2011.02.001.

[202] Cabib S, Puglisi-Allegra S. The mesoaccumbens dopamine in coping with stress. Neurosci Biobehav Rev 2012;36:79–89, http://dx.doi.org/10.1016/j.neubiorev.2011.04.012.

[203] Chaudhury D, Walsh JJ, Friedman AK, Juarez B, Ku SM, Koo JW, et al. Rapid regulation of depression-related behaviours by control of midbrain dopamine neurons. Nature 2013;493:532–6, http://dx.doi.org/10.1038/nature11713.

[204] Żurawek D, Faron-Górecka A, Kuśmider M, Kolasa M, Gruca P, Papp M, et al. Mesolimbic dopamine D2 receptor plasticity contributes to stress resilience in rats subjected to chronic mild stress. Psychopharmacology (Berlin) 2013;227:583–93, http://dx.doi.org/10.1007/s00213-013-2990-3.

[205] Faron-Górecka A, Kuśmider M, Kolasa M, Żurawek D, Gruca P, Papp M, et al. Prolactin and its receptors in the chronic mild stress rat model of depression. Brain Res 2014;1555:48–59, doi:10.1016/j.brainres.2014.01.031.

[206] Groleau P, Steiger H, Joober R, Bruce KR, Israel M, Badawi G, et al. Dopamine-system genes, childhood abuse, and clinical manifestations in women with Bulimia-spectrum Disorders. J Psychiatr Res 2012;46:1139–45, http://dx.doi.org/10.1016/j.jpsychires.2012.05.018.

[207] Keltikangas-Järvinen L, Pulkki-Råback L, Elovainio M, Raitakari OT, Viikari J, Lehtimäki T. DRD2 C32806 T modifies the effect of child-rearing environment on adulthood novelty seeking. Am J Med Genet B Neuropsychiatr Genet 2009;150B:389–94, http://dx.doi.org/10.1002/ajmg.b.30830.

[208] Harden KP, Carlson MD, Kretsch N, Corbin WR, Fromme K. Childhood sexual abuse and impulsive personality traits: mixed evidence for moderation by DRD4 genotype. J Res Personal 2014, doi:10.1016/j.jrp.2014.12.005.

[209] Farley FH. Basic process individual differences: a biologically based theory of individualization for cognitive, affective, and creative outcomes. In: Farley FH, Gordon NJ, editors. Psychol. educ. state union. Berkely, CA: McCutchon Publishing; 1981.

[210] Cain ME, Green TA, Bardo MT. Environmental enrichment decreases responding for visual novelty. Behav Processes 2006;73:360–6, http://dx.doi.org/10.1016/j.beproc.2006.08.007.

[211] Bardo MT, Klebaur JE, Valone JM, Deaton C. Environmental enrichment decreases intravenous self-administration of amphetamine in female and male rats. Psychopharmacology (Berlin) 2001;155:278–84, http://dx.doi.org/10.1007/s002130100720.

[212] Green TA, Gehrke BJ, Bardo MT. Environmental enrichment decreases intravenous amphetamine self-administration in rats: dose-response functions for fixed and progressive-ratio schedules. Psychopharmacology (Berlin) 2002;162:373–8, http://dx.doi.org/10.1007/s00213-002-1134-y.

[213] Zhu J, Apparsundaram S, Bardo MT, Dwoskin LP. Environmental enrichment decreases cell surface expression of the dopamine transporter in rat medial prefrontal cortex. J Neurochem 2005;93:1434–43, http://dx.doi.org/10.1111/j. 1471-4159.2005.03130.x.

[214] Romer D, Betancourt LM, Brodsky NL, Giannetta JM, Yang W, Hurt H. Does adolescent risk taking imply weak executive function? A prospective study of relations between working memory performance, impulsivity, and risk taking in early adolescence. Dev Sci 2011;14:1119–33, http://dx.doi.org/10.1111/j. 1467-7687.2011.01061.x.

[215] Cools R, Gibbs SE, Miyakawa A, Jagust W, D'Esposito M. Working memory capacity predicts dopamine synthesis capacity in the human striatum. J Neurosci 2008;28:1208–12, http://dx.doi.org/10.1523/JNEUROSCI. 4475-07.2008.

[216] Raine A, Reynolds C, Venables PH, Mednick SA. Stimulation seeking and intelligence a prospective longitudinal study. J Pers 2002;82:663–74.

[217] Winstanley CA. The utility of rat models of impulsivity in developing pharmacotherapies for impulse control disorders. Br J Pharmacol 2011;164:1301–21, http://dx.doi.org/10.1111/j. 1476-5381.2011.01323.x.

[218] Arria AM, Caldeira KM, Vincent KB, O'Grady KE, Wish ED. Perceived harmfulness predicts nonmedical use of prescription drugs among college students: interactions with sensation-seeking. Prev Sci 2008;9:191–201, http://dx.doi.org/10.1007/s11121-008-0095-8.

[219] Conrod PJ, Castellanos N, Mackie C. Personality-targeted interventions delay the growth of adolescent drinking and binge drinking. J Child Psychol Psychiatry 2008;49:181–90, http://dx.doi.org/10.1111/j. 1469-7610.2007.01826.x.

[220] Conrod PJ, O'Leary-Barrett M, Newton N, Topper L, Castellanos-Ryan N, Mackie C, et al. Effectiveness of a selective, personality-targeted prevention program for adolescent alcohol use and misuse: a cluster randomized controlled trial. JAMA Psychiatry 2013:1, http://dx.doi.org/10.1001/jamapsychiatry.2013.651.