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Perspective Article

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Reward Deficiency Syndrome: Criteria Unspecified Mental Disorder

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Abstract

Reward Deficiency Syndrome (RDS) is a neurogenetically influenced phenotype marked by impaired dopaminergic signaling and mesocorticolimbic reward-circuit dysfunction, leading to reduced reward sensitivity, motivational anhedonia, heightened stress reactivity, and increased vulnerability to compulsive, impulsive, and addictive behaviors. Evidence from molecular genetics, neuroimaging, behavioral neuroscience, and clinical outcomes research supports reward dysregulation as a shared mechanism underlying substance use disorders (SUD), behavioral addictions, mood and anxiety disorders, trauma-related conditions, and pain amplification syndromes. Despite more than five decades of investigation, RDS is not recognized as a discrete diagnosis in diagnostic and statistical manual of mental disorders (DSM) or international classification of diseases (ICD) systems. As a result, affected individuals are dispersed across symptom-based categories, obscuring shared biological vulnerability, fragmenting care, and limiting effective risk stratification, particularly in high-risk settings such as chronic pain management, postoperative opioid exposure, and relapse prevention. This perspective proposes recognizing RDS as a mechanism-informed clinical construct for descriptive documentation under existing codes such as F09 or F99 until formal classification is established. We present descriptive criteria integrating genetic vulnerability, assessed by the genetic addiction risk score (GARS®), with core symptom domains of reward and motivational dysfunction, stress dysregulation, compulsive or addictive behaviors, and neuropsychiatric comorbidity. Acknowledging RDS within contemporary diagnostic frameworks may enhance clinical utility, support personalized treatment planning, and improve epidemiologic surveillance and outcomes research. Recognition of reward dysregulation as a unifying mechanism is consistent with ICD-11's emphasis on etiological coherence and dimensional models of psychopathology and represents an important step toward integrating neuroscience and precision medicine into

psychiatric nosology and advancing more durable approaches to mental health and addiction care.

Keywords

Reward deficiency syndrome, Neuroscience, Genetic addiction risk score, International classification of diseases, Dysregulation

Introduction

In this short perspective we are proposing herein that RDS should be included as a - F09 unspecified mental disorder due to known physiological condition or other specified mental disorder 300.9 (F99) or unspecified mental disorder 300.9 (F99).

RDS is a condition which in which there is difficulty experiencing pleasure, anticipation, and reward [1-219]. Also, stress or negative emotions are more readily and deeply experienced [220]. RDS connects addictive, compulsive, and impulsive behavioral disorders [4]. Many disorders are symptoms of or related to RDS.

This group of behaviors has been associated with genetic variants and epigenetic (environmental) changes that result in an inadequacy in the neurotransmission of reward or pleasure [221, 222]. RDS was identified and developed from animal and human research that explored behavioral genetics and the molecular biology of neurotransmission [223]. Unlike many psychiatric disorders, the genetic causes of RDS are identified and can be tested for genetic polymerase chain reaction testing [224]. The key genetic causative factors revolve around inhibited dopamine function in the brain [225].

RDS involves dopamine resistance, a form of sensory deprivation of the brain's reward or pleasure mechanisms [226]. The syndrome occurs because of an individual's inability to derive reward from ordinary, everyday activities. Reward deficiency can range from mild to profound [227]. Addictions are a manifestation or symptoms of RDS. The subject of extensive peer review RDS is a disorder of the neurochemistry of the brain and affects nearly all people with SUD. Dopamine is a principal component of brain function and RDS [228]. The healthy function of molecular neuroanatomy ultimately results in the release of neurotransmitter dopamine, which is the key to feelings of well-being, motivation, and happiness [229].

Dopamine regulates "pleasure, anticipation, and reward" and reduces "stress". This phenomenon, the neuronal release of dopamine at the reward site of the brain, the nucleus accumbens, involves a complicated cascade of neurotransmission called the "brain reward cascade" (BRC). Dopamine released into the synapse results in feelings of well-being and reduced stress [230].

RDS is diagnosed by GARS/System [231]. Other confirmatory evaluation is warranted using rejection sensitive dysphoria screening tools and/or by full psychiatric and/or medical evaluation including differential diagnosis. A GARS of 4 or more indicates RDS may be present. A score of 7 or more means RDS is present. Screening for co-occurring pathologies indicated by the RDS report are warranted [231].

RDS is defined in the SAGE encyclopedia of abnormal and clinical psychology. The SAGE encyclopedia is the standard medical text for psychiatric issues [232].

The standard of care for RDS is IV D-phenylalanine including other ingredients co-administered with prodopaminergic supplementation and psychotherapy/ counseling [230].

Descriptive criteria of RDS

RDS is conceptualized as a neurogenetically influenced reward-processing dysregulation phenotype characterized by impaired dopaminergic signaling and altered functional dynamics within mesocorticolimbic circuitry. Clinically, RDS manifests as reduced reward sensitivity, diminished motivation and pleasure (anhedonia and motivational anhedonia), heightened stress responsivity, and an increased propensity toward substance-related and non-substance-related compulsive or impulsive behaviors. Rather than representing a single categorical disorder, RDS is best understood as a dimensional construct existing on a spectrum of severity and intersecting with multiple psychiatric, behavioral, and pain-related conditions.

Because RDS is not currently represented as a formal DSM or ICD diagnosis, the criteria below are intended to support descriptive clinical formulation, documentation, risk stratification, and individualized treatment planning. These criteria integrate:

(i) genetic vulnerability, as assessed by GARS, with

(ii) observable clinical features consistent with reward-circuit dysfunction.

Importantly, these criteria are intended to function as an adjunctive formulation, complementing rather than replacing—established psychiatric, pain, or substance-related diagnoses.

Core symptom domains - clinical criteria

Clinical criteria may be drawn from one or more of the following domains:

A. Reward and motivation dysfunction

- Anhedonia or reduced capacity to experience pleasure.
- Motivational anhedonia, apathy, or diminished goal-directed behavior.
- Reduced reward salience from normally reinforcing stimuli.

B. Stress and affective dysregulation

- Heightened stress sensitivity or poor stress tolerance.
- Dysphoria, irritability, or predominance of negative effects.
- Stress-induced craving or behavioral escalation.

C. Compulsive, impulsive, or addictive behaviors (current or historical)

- SUD (e.g., opioids, alcohol, nicotine, stimulants, and cannabis).

- Behavioral addictions (e.g., gambling, overeating, hypersexuality, compulsive shopping, and excessive internet use).
- Impulse-control difficulties or novelty-seeking behaviors.

D. Pain and somatic amplification phenotypes

- Low pain tolerance or hyperalgesia.
- Suspected opioid-induced hyperalgesia or paradoxical pain escalation.
- Chronic pain with disproportionate functional impairment.

E. Neuropsychiatric comorbidity

- Depression, anxiety, post-traumatic stress disorder (PTSD), attention-deficit/hyperactivity disorder (ADHD), or related disorders.
- History of relapsing vulnerability or treatment resistance.

Symptom criteria

To meet descriptive RDS symptom criteria, the patient must have A (any one) and B (any two), consistent with the above domains.

A. Present or past diagnosis or history of at least one of the following:

1. SUD or process addiction (behavioral addiction)
2. Anxiety disorders
3. Depression or mood disorders
4. ADHD
5. Trauma history or PTSD
6. Oppositional defiant disorder (ODD) or conduct disorder (CD).

B. Reported history of at least two of the following reward/behavioral features:

1. Novelty seeking
2. Impulsivity
3. Difficulty feeling reward (anhedonia)
4. Motivational anhedonia (reduced drive/initiative despite intact "wanting" narratives)
5. Rumination or obsessive/intrusive negative thoughts (repetitive, intrusive cognitive negativity that worsens stress reactivity and maladaptive coping).

Clinical note (recommended language): RDS may be documented when the above pattern suggests a persistent reward-circuit vulnerability that helps explain relapse proneness, maladaptive reinforcement behaviors, stress intolerance, or disproportionate functional impairment—particularly in contexts where reward dysregulation commonly amplifies clinical risk, such as chronic pain management, postoperative opioid exposure, or prolonged opioid therapy.

Severity stratification of RDS (GARS + clinical criteria)

Although RDS is supported by an extensive neurobiological and behavioral genetics literature, it remains absent as a discrete DSM/ICD entity. In current practice, patients with clearly overlapping reward-circuit dysfunction are distributed across multiple symptom-based diagnoses (e.g., SUD, mood and anxiety disorders, ADHD, trauma-related disorders, and pain amplification phenotypes), which can obscure shared vulnerability, fragment care, and weaken risk stratification—particularly in high-stakes contexts such as postoperative opioid exposure, chronic pain management, and relapse prevention. Accordingly, operationalized descriptive criteria are needed now to (i) standardize clinical documentation and research sampling, (ii) improve identification of individuals with heightened relapse and iatrogenic harm risk, and (iii) provide a mechanism-informed framework that complements (rather than replaces) established DSM/ICD diagnoses. The criteria below therefore integrate genetic vulnerability (GARS®) with clinically observable features of reward-circuit dysfunction to support consistent formulation and severity stratification (Table 1 and table 2).

Table 1: Descriptive criteria and severity stratification of RDS.

RDS severity	Genetic vulnerability (GARS®)	Clinical symptom burden	Typical clinical phenotype/descriptor
Mild RDS	GARS = 4	1 - 2 clinical criteria (from A/B)	Low–moderate genetic vulnerability with limited phenotypic expression. Subtle reward insensitivity, mild stress reactivity, or early impulsive/compulsive traits. Often latent; may emerge under stress, injury, postoperative opioid exposure, or psychosocial strain.
Moderate RDS	GARS ≥ 4	≥ 3 clinical criteria	Measurable reward-circuit dysfunction with clinically apparent affective, behavioral, and/or pain-related manifestations. Diminished reward responsiveness, stress-induced behavioral escalation, increased susceptibility to maladaptive coping. Intermittent but meaningful functional impairment, especially in chronic pain or postoperative settings.
Severe RDS	GARS ≥ 7 OR GARS ≥ 5	≥ 4 clinical criteria	High genetic vulnerability with multi-domain expression. Persistent anhedonia and motivational deficits, compulsive/addictive behaviors, relapse proneness, and/or pain amplification (e.g., suspected opioid-induced hyperalgesia). Stress-driven anti-reward states with escalating medication use and reduced treatment response.
Profound RDS	GARS ≥ 10	Typically, multi-domain and pervasive	Extreme reward-deficiency phenotype with extensive reward-pathway genetic risk. Early-onset, recurrent, or treatment-refractory addictive behaviors; severe anhedonia; marked stress intolerance; high relapse, and iatrogenic harm risk (e.g., chronic opioid dependence/hyperalgesia). Often requires highly individualized, multidisciplinary management.

Table 2: Symptom criteria for descriptive diagnosis of RDS.

Category	Criterion
A. Present or past diagnosis/history (any one required)	1. SUD or process/behavioral addiction 2. Anxiety disorders 3. Depression or mood disorders 4. ADHD 5. Trauma history or PTSD 6. ODD or CD
B. Reported reward/ behavioral features (any two required)	7. Novelty seeking 8. Impulsivity 9. Difficulty feeling reward (anhedonia) 10. Motivational anhedonia (reduced drive/initiative) 11. Rumination or obsessive/intrusive negative thoughts

Clinical use and documentation considerations

These descriptive criteria are intended to:

- Support mechanism-informed clinical formulation.
- Aid in risk stratification (e.g., relapse risk, opioid-harm risk, and pain amplification risk).
- Guide personalized intervention strategies, including behavioral, pharmacologic, and—where appropriate genetically informed adjunctive approaches.

RDS severity should be documented in conjunction with, not in place of, primary DSM/ICD diagnoses, where administrative coding is required, clinicians should prioritize coding established conditions and document RDS as a descriptive neurobehavioral construct that contextualizes the patient's vulnerability and treatment needs.

Policy

Contemporary psychiatric classification systems remain predominantly symptom-based, resulting in fragmentation of clinically similar patients across multiple diagnostic categories despite shared neurobiological mechanisms. This limitation is particularly evident in disorders characterized by recurrent relapse, cross-addiction, and persistent vulnerability to maladaptive reward-seeking behaviors, contributing to diagnostic instability, treatment failure, and escalating healthcare costs.

A growing body of evidence accumulated over more than five decades of molecular genetics, neuroimaging, pharmacogenomics, and clinical outcomes research supports reward dysregulation as a common underlying mechanism contributing to a spectrum of substance-related, behavioral, and affective disorders. Genetic polymorphisms affecting dopaminergic signaling, epigenetic modification of reward pathways, and measurable disruption within the BRC together constitute a reproducible pathophysiological substrate associated with diminished reward responsivity and heightened reinforcement-seeking behavior.

Within an ICD-11 framework, RDS may be understood as a mechanism-based clinical umbrella constructing describing impaired reward processing that contributes to multiple diagnostic presentations, rather than as a replacement for existing disorder categories. This formulation aligns with ICD-11's emphasis on clinical utility, etiological coherence, and dimensional understanding of mental and behavioral disorders.

At present, RDS does not have a unique diagnostic classification within ICD-10-current mandate (CM) (ICD-10-CM) or ICD-11. Accordingly, its application remains descriptive and complementary, supporting clinical formulation, research stratification, and hypothesis-driven treatment planning alongside established diagnoses. Until formal classification is established, clinicians must rely on existing diagnostic codes for documentation and coverage purposes, most commonly broad or non-specific categories such as mental disorders due to known physiological conditions (F09) or unspecified mental disorders (F99), when clinically appropriate. The necessity of using such non-granular codes underscores the current limitations of psychiatric nosology in capturing reward-based pathophysiology and highlights the unmet need for more precise, mechanism-informed classification.

The reliance on such non-specific diagnostic categories limits epidemiologic accuracy, obscures true disease prevalence, and constrains health-system planning, reimbursement modeling, and outcomes research for reward-related disorders.

Importantly, genetic tools such as the GARS® are not proposed as diagnostic instruments but as adjunctive biological risk-stratification measures analogous to genomic predictors used elsewhere in medicine. When integrated with comprehensive clinical assessment and differential diagnosis, such tools may assist in identifying individuals with heightened vulnerability to reward dysregulation prior to progression toward severe addiction, relapse, or poly-diagnostic psychiatric illness.

Formal efforts are currently underway to evaluate RDS for potential inclusion within the ICD classification system. This process reflects increasing recognition of reward dysregulation as a clinically relevant phenomenon and highlights the need for diagnostic frameworks capable of incorporating biological vulnerability, developmental trajectory, and environmental modulation within mental and behavioral disorders.

Recognition of reward dysregulation within future ICD revisions would enable standardized case definitions, facilitate epidemiologic surveillance, support outcomes-based research, and enhance alignment with global precision-medicine initiatives. Until such recognition occurs, the use of RDS as a descriptive construct provides a pragmatic bridge between advancing neurobiological science and existing diagnostic infrastructure, while reinforcing the need for greater diagnostic granularity within psychiatric classification systems.

Conclusion

As neuroscience, genomics, and systems biology continue to advance, psychiatric classification must evolve beyond purely symptom-based constructs toward frameworks that reflect shared biological vulnerability and clinical reality. Reward dysregulation represents one of the most consistently observed yet insufficiently defined mechanisms underlying addiction, relapse, and treatment resistance across diagnostic boundaries. The absence of granular classification for reward-based pathol-

ogy limits research precision, public-health surveillance, and health-system planning. Establishing mechanism-informed diagnostic language—through careful, evidence-driven refinement of existing classification systems—offers a necessary step toward aligning psychiatric nosology with contemporary neuroscience and advancing more effective, durable approaches to mental health and addiction care.

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Conflict of Interest

Kenneth Blum owns all rights and titles to GARS and KB220.

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