

# Can the DSM-IV Be Salvaged for Individuals With Severe Intellectual Disabilities?

Jarrett Barnhill, M.D., DFAPA, FAACAP<sup>1</sup>

<sup>1</sup>University of North Carolina, School of Medicine

This paper outlines the rationale for an alternative to the DSM-IV for individuals with severe intellectual disabilities. The model departs from a purely descriptive and categorical approach to psychiatric diagnosis by integrating temperament, genetic risk, and new findings in the clinical neurosciences. Integrating etiology and dimensionality into the diagnostic process allows the clinician to use additional tools to increase the flexibility of our current nomenclature and minimize multiple Axis I and II disorders. This expanded approach may improve our current existing diagnostic tool kit by generating more developmentally appropriate diagnoses and hopefully more appropriate treatment strategies.

**Keywords:** *categorical diagnosis, developmental disability, dimensionality, genetic vulnerability, intellectual disability, mental retardation, neurobiology, psychiatric disorder, temperament*

Over the past decade, there have been challenges to the use of a categorical classification for psychiatric disorders. One group of dissenters challenges the idea that psychiatric disorders are discrete, well-demarcated entities. The basis for this position is the result of growing evidence that schizophrenia, autism, major depressive, and bipolar disorders are probably better described as spectrum disorders.<sup>9,35</sup> Another challenge comes from growing clinical research interest in the relationship between subsyndromal forms of severe psychiatric illnesses and a range of nonspecific emotional and behavioral disorders.<sup>29</sup> The ascendancy of these conceptual models also challenges the clinician to expand our conceptual models of psychiatric disorders to include dimensional as well as purely categorical phenomena.<sup>29</sup>

For people with intellectual disabilities (IDs), the range of emotional and behavioral disorder is affected by variations in tested intelligence and adaptive capacities. People with mild IDs generally present with less neuromedical comorbidity. As a result, there are relatively few adjustments needed in the psychiatric assessment and diagnosis. People with severe IDs, on the other hand, present a more complicated clinical picture. Underlying metabolic disorders, comorbid epilepsy or cerebral palsy<sup>32</sup> clouds diagnostic certainty.

Deficits in cognition and communication skills also frequently hamper the diagnosis of psychiatric disorders. They do so by limiting the accurate self-reporting of subjective mood and cognitive states essential to most psychiatric assessments.<sup>49</sup> In addition, severe cognitive

deficits and associated neurological disorders confound diagnostic classification by lowering threshold for stress-induced positive symptoms (hallucinations or bizarre behavior), thought and behavioral disorganization, and affective turmoil. These variables contribute to the frequently daunting task of making a reliable diagnosis using the current DSM-IV-TR nomenclature. As a result, there is a considerable degree of uncertainty about diagnosing major psychiatric syndromes such as schizophrenia, mood and anxiety disorders.<sup>27,43</sup>

Several weaknesses in the DSM format contribute to this difficulty. First, the DSM-IV is not designed for people with ID. Second, it may be difficult to translate individualized behavioral data (target behaviors) into psychiatric syndromes. Third, there are problems with the fundamental structure of the DSM-IV- reliance on descriptive criteria, exclusion of etiopathogenic models, and a categorical method of diagnosis. The categorical approach is based on symptoms that define specific syndromes, but unfortunately this methodology frequently results in cumbersome multi-Axis I diagnoses. This paper grapples with the problem of adapting existing diagnostic criteria to fit the needs of people with severe developmental disabilities.

## HETEROGENEITY AMONG DIAGNOSTIC CRITERIA

Descriptive or phenomenological models for diagnosis have made a substantial contribution to psychiatry. But there are weaknesses. One problem involves the etiological heterogeneity among the core symptoms of most psychiatric disorders. For example, there is a significant

heterogeneity of affective symptoms in mood disorders. Sadness, irritability and crying are key criteria affective symptoms for mood disorders. But sadness, irritability, and crying are not confined to primary mood disorders. They can be observed secondary to subcortical and prefrontal dysfunction,<sup>39</sup> intense distress over interpersonal loss, negative environmental events, or major depression. In the first instance, crying may occur independently of underlying mood in patients with frontal lobe disorders or pseudobulbar palsy. These individuals have spontaneous episodes of crying that are disconnected from the reported affective state.<sup>39,48</sup> This affective disinhibition may accompany other neuropsychiatric disorders such as stroke, seizure, dementia and other brain disorders.<sup>22</sup> Sadness, on the other hand, can result from transient reality-based reactions to chronic pain, loss, overwhelming stress, or demoralization from a chronic medical disorder. These affective states include feelings of depression but lack key neurovegetative symptoms or fail to meet duration or severity of criteria. Major Depressive Disorder, however, involves a mood state coupled with changes in sleep, appetite, energy level, capacity to experience pleasure, and feelings of guilt or hopelessness/helplessness. But guilt, hopelessness and helplessness follow a developmental course that depends on the emergence of future orientation and abstract thought. These cognitive abilities may not emerge in normal children until 10-12 years of age.<sup>11,20</sup> Unfortunately, people with severe ID may not display these development-sensitive cognitive symptoms.

Adaptability plays a crucial role in life adjustment. Like other executive functions adaptive skills follow a developmental course that parallels the ascendancy of prefrontal and other association networks.<sup>21,41</sup> These developmental changes in brain function also result in an expanding capacity to generate, implement, and assess the efficacy of novel behavioral response. Most developmental disorders affect this developmental trajectory. The severity of these cognitive impairments varies inversely with tested IQ or degree of neurological dysfunction. Severe ID reflects compromises in both domains, and the resulting lack of cognitive and behavioral flexibility contribute to higher rates of maladaptive responses such as perseverative behaviors, stereotypies, self-injurious behavior

(SIB), aggression, and attempts to escape demands.

Compromised behavioral flexibility may also increase the likelihood that stressors may trigger the onset of a severe mental illness in genetically vulnerable individuals.<sup>24,28</sup> But this relationship is more complicated than meets the eye. It is often difficult to tell where adaptive deficits associated with IDs end and those found in mental illness begin—hence problems with diagnostic overshadowing. Part of this confusion arises from the permeable borders between trait-related reductions in adaptive skills central to IDs and illness related (state-related) phenomena. In spite of these uncertainties, it appears that compromised adaptive skills play a major role in the etiology of psychiatric disorders in people with severe IDs.

These time-limited maladaptive behaviors are usually diagnosed as “Adjustment Disorders” or “Brief Psychotic Disorder” (DSM-IV). They can also be classified as phase-specific or state-related phenomena. In contrast, personality disorders represent long-standing maladaptive behaviors (“trait-related” phenomena). But these classifications are not mutually exclusive. In fact, people with personality disorders and organic brain syndromes are at increased risk for time-limited behavioral changes in reaction to periods of environmental stress.<sup>32</sup> Irritability provides a good example. Chronic irritability (trait) and periodic explosive behaviors are common in individuals with brain disorders. But these same individuals may also be genetically vulnerable to major psychiatric disorders. In these situations, phasic changes in irritability may characterize an exacerbation of their psychiatric illness (e.g., baseline exaggeration during a manic episode). Once in remission, the individual may return to baseline levels of irritability-trait-related behaviors.<sup>54</sup> Unfortunately, their baseline or residual irritability may compromise ongoing social relationships, access to and compliance with treatment, and prognosis.<sup>2</sup>

#### HETEROGENEITY WITHIN DIAGNOSTIC CATEGORIES

In addition to variability among syndrome specific symptoms, there is considerable variability within DSM-IV categories. For example, mood disorders may emerge from several sources. Major Depressive Disorder may result from a reaction to severe psychosocial stresses, as an expression of underlying brain dysfunction or a combination of these as well as other factors.<sup>39</sup>

For example, an individual who has a negative family history for mood disorders may experience transient depression after the sudden death of a parent or caretaker. A similar individual (no genetic risk) who has history of abuse or early parental death may present with similar symptoms but have a very different clinical course and prognosis.<sup>48</sup> A person with a positive family history of bipolar disorder, however, may develop severe depression or mania in response to such a loss. In each of these examples, the presenting symptoms are similar but the outcome and treatment needs vary considerably. For the genetically vulnerable individual, loss may not only trigger the emergence of depression but it may also reveal differences in severity of mood changes, duration of symptoms, polarity (bipolar or unipolar), and treatment response.<sup>20,51</sup> Intra-syndrome heterogeneity (mood disorder) of this type is complicated further by the multiple medical and neurological comorbidities that frequently accompany severe ID.<sup>32,48</sup>

#### IMPACT OF SEVERE ID

As noted previously, developmental brain disorders can also seriously limit behavioral flexibility, and contribute to increased vulnerability to a broad range of environmental disruptions. They may also lower individual threshold for experiencing environmental stressors as traumatic. Once exposed to such traumatic events, stress-induced changes in the frontal and temporal networks and the limbic system may further disrupt ongoing adaptive responses.<sup>33,52</sup> In this sense, psychological trauma may adversely affect the neurophysiological substrates organizing, planning, monitoring, and anticipating environmental events.<sup>56</sup> These disturbances may also limit the development of affect regulation and inhibition of socially inappropriate behaviors.<sup>24,41</sup> When combined, these factors create a vicious cycle of maladaptive behaviors and contribute to the high rates of psychopathology seen in this population.<sup>32,43</sup>

Behavioral disorders are the end result of a complex interaction between state and trait phenomena. People with severe ID have an increased prevalence of co-existing cerebral palsy (static encephalopathy), metabolic and systemic medical disorders, and epilepsy. The combination of ID and associated neurological complications increases the risk for disruptive behaviors such as SIB, aggression, hyperactivity, affective lability, and stereotypic behaviors.<sup>43</sup> For example, SIB is

often a trait-related hyperreactivity to a range of environmental stimuli, but also affected by state-related problems such as constipation, otitis media, and premenstrual discomfort. SIB can also occur as a trait phenomenon, either resulting from an irritable temperament or a specific behavioral phenotype. From this perspective, SIB has attributes of state-related (response to environmental events), trait-related (characteristic of a personality disorder) phenomenon, or a combination of the two (baseline exaggeration during the active phase of disorder). SIB also straddles the dimensional boundary between target behaviors and symptoms of psychiatric disorders—autism, bipolar and schizophrenia spectrum disorders.<sup>43</sup> The typology may be similar but the underlying “motivation” may differ, emphasizing the need to understand the etiology of SIB.<sup>3</sup>

#### MORE ABOUT GENES

Recent advances in molecular genetics, mapping of the human genome, and evolving microchip technologies will have a significant impact on our understanding of major mental illnesses. In spite of impressive knowledge, the actual translation of genes (genotype) into a human being (phenotype) is a complex and incompletely understood process. A large portion of the human genetic code is devoted to the CNS, reinforcing the complexity of the human nervous system. But the construction of a functioning brain is more than the sum of its genes. It is well established that environmental and other ecological factors have a profound effect on gene expression and eventual phenotype.<sup>26,38</sup>

There is a growing list of genetic disorders linked to severe IDs. Many of these disorders are associated with multiple developmental abnormalities and are incompatible with longevity. For example, phenylketonuria (PKU) is an autosomal recessive disorder that has profound effects on brain development. Diagnosed early, a phenylalanine-free diet is a highly effective intervention that can prevent severe cognitive and other developmental delays. But PKU is more complex than previously thought. A subgroup of people have abnormalities in biotin metabolism that differs from the phenylalanine hydroxylase abnormality. In addition, pregnant adult women successfully treated as children and no longer following a PKU diet, are exposing the developing fetus to high levels of phenylalanine metabolites. This exposure

may disrupt normal brain development even though these children have a functional gene for the crucial enzyme, phenylalanine hydroxylase.<sup>17</sup> There is also a line of research that reports adverse effects of ongoing elevations in phenylalanine metabolites on cognitive and behavioral functions of adults with this disorder. This research suggests that EEG and MRI changes are partially responsive to re-introduction of the phenylalanine free diet.<sup>37</sup>

The genetics of many developmental disorders are more complex than PKU and beyond the scope of this paper. The complexity and uncertainty is even greater for neuropsychiatric disorders since most involve polygenic inheritance (multiple genes) and it is unlikely that a single candidate gene or specific enzyme defect will be responsible. Behavioral phenotypes provide an example of gene-behavioral interactions at a more complex level. They represent shared patterns of behavior associated with specific genetic disorders. For example, Prader-Willi (hyperphagia), Fragile-X (anxiety),<sup>18,38</sup> and Lesch-Nyhan syndrome (LNS) illustrate the complex behavioral effects of particular genetic mistakes. Individuals with the genotype for LNS present with a pattern of severe self-injury as well as self-restraining behaviors. But the picture is not so cut and dry since there is individual variability of syndrome specific abnormal movements, mood, cognitive, and developmental delays. Yet in spite of the uncertainties, behavioral phenotypes do provide useful information about the effects of specific genes on some types of behaviors.<sup>4</sup>

There is also growing interest in the inheritance of certain core features of temperament.<sup>38</sup> Although temperament may involve a wider range of behaviors than behavioral phenotypes,<sup>15</sup> there may be a common genetic substrate that underlies both the neurobiology of some temperamental features and primary psychiatric disorders. This influence may be a risk factor, or modulate severity, clinical course or long-term prognosis.<sup>29</sup>

#### PSYCHOBIOLOGY OF TEMPERAMENT

The idea of temperament is an ancient one. Galen systematically described the adverse effects of imbalanced "humors" on personality and psychopathology. Fifteen hundred years later, Chess and Thomas<sup>13</sup> produced a 30-year long landmark study of temperament that culminated in the New York Longitudinal Survey (NYLS). To Chess and Thomas, temperament represents

"how" we behave. They characterized temperament based on complex patterns of behavior that included approach-avoidance, threshold for reaction, intensity of reaction, adaptability, rhythmicity, and activity levels. These trait phenomena are discernable during early infancy and serve as the basic building blocks of healthy development and psychological adjustment.<sup>25,33</sup>

Certain combinations of these traits, however, may present greater developmental challenges.<sup>25</sup> "Slow to adapt" children are characterized by low adaptability, withdrawal reactions to novel stimuli factors, and negative affective responses.<sup>13</sup> A subgroup of more intense "slow to adapt" children are troubled by an over-reactive sympathetic nervous system<sup>5,7,8</sup> and high levels of avoidance behaviors. Kagan used the term behavioral inhibition to describe this group of children. Later research suggested that behavioral inhibition is a precursor to social anxiety, panic disorders and mood disorders.<sup>4,30</sup> The children of parents with agoraphobia, social anxiety and mood disorders are more likely to display behavioral inhibition. These findings support a relationship between genetic risk, behavioral inhibition, and adult onset of internalizing disorders and support the idea of temperamental factors functioning as risk factors for primary psychiatric disorders.<sup>4</sup> These studies suggest that parents can help the child to adjust and master behavioral inhibition.<sup>42</sup> The process involves slowing the pace of new experiences—an example of matching their child's reactive style. Parents who disregard this temperamental style are likely to increase their child's distress, oppositional behavior and anxiety-related symptoms.<sup>12,13</sup>

Difficult children represent the other end of the temperament spectrum. These children present with avoidance behaviors, slow adaptability along with intense but negative affective responses to novel experiences, low stimulus threshold for arousal and affective response, and a greater risk for externalizing behaviors. Children with brain disorders are more likely to display a "difficult" temperament.<sup>13,43</sup> Helping these children negotiate their world requires a different skill set—pacing their exposure to novelty requires patience in the face of their intensely negative reactions to change. In the NYLS, children with difficult temperaments who were mismatched had the greatest risk for a range of disruptive or externalizing behavior disorders including adult borderline personality

disorder (BPD). In some settings, BPD may be evolving from an adverse psychosocial environment that does not allow the child to learn adaptive strategies for his/her intense response style. Genetic vulnerability to bipolar affective disorders (hyperthymic temperament), CNS dysfunction, history of traumatization, and parental inflexibility/psychopathology may contribute to this mismatch.<sup>1</sup>

Cloninger *et al.*<sup>14</sup> proposed another model of temperament. Their model grew out of attempts to associate specific temperamental traits with different subsets of addiction behavior. To Cloninger, temperament represents the expression of pre-wired automatic behavioral responses (unconscious) to external and internal events. Cloninger *et al.*<sup>14</sup> attempted to define the core neurobiological features of temperament by focusing on novelty seeking, harm avoidance and reward dependence. Novelty seeking involves the active pursuit of novel experiences, pleasurable arousal from novel experiences, and a tendency to seek out highly rewarding activities. Low novelty seekers tend to exercise caution and avoid risk taking situations or events. High novelty seekers are easily bored and may react negatively to frustration of their activities. High novelty seekers may also be extroverted "thrill seekers."<sup>44,45</sup> Among high novelty seekers, the urge for positive experiences, relative aversions to negative affective states, and low threshold for frustration-induced behaviors suggest an increased risk for externalizing behaviors. Cloninger suggests that high novelty seekers are driven by catecholaminergic dysregulation and highly attuned reward centers. High novelty seekers may also manifest the substrate for genetic vulnerability to addictions and antisocial personality disorders.<sup>45</sup> Interestingly, bipolar illness (hypomania) may represent a state-related change in novelty seeking behaviors.<sup>2,51</sup>

Harm avoidance is associated with a lower threshold for behavioral inhibition, diminished exploratory behavior, and sensitivity to punishment or negative consequences. High levels of harm avoidance appear associated with cautiousness, avoidance behaviors, and "neuroticism."<sup>19</sup> Low harm avoidance is linked to impulsivity and a reduced capacity to learn from negative consequences.<sup>15</sup> Harm avoidance is analogous to behavioral inhibition, especially overactive or under-regulated autonomic nervous system. Both factors contribute to internalizing psychiatric disorders.<sup>4,30</sup> Excessive harm

avoidance also represents an imbalance between behavioral facilitation and inhibition and suggests overactivity of serotonergic, cholinergic and peptidergic overactivity in the septo-hippocampal system.<sup>15,16,52</sup> Alcohol, benzodiazepines like Valium, beta-blockers, and SSRIs may reduce the activity in this region and explain their usefulness in social anxiety and other internalizing disorders.<sup>34</sup>

Reward dependence incorporates social-emotional attachment and patterns of motivation. Adrenergic activity plays a crucial role in reward dependence. Several studies suggest that asociality or social anhedonia is associated with low levels of dopamine b-hydroxylase (decreased synthesis) and developmental abnormalities in MAO activity (altered metabolism).<sup>12,44</sup> Oxytocin and other stress peptides may play a major role in attachment behaviors as well as behavioral inhibition.<sup>47</sup>

High rates of reward dependence are associated with increased externally directed motivation, dependence, and increased sensitivity to disruptions in emotional attachments. High reward dependence may also increase individual vulnerability to separation or loss experiences. From this perspective, the differences between separation anxiety and BPD reflect the effects of harm avoidance, impulsivity and intensity of affective response.<sup>1</sup> For individuals with BPD, severe abuse and neglect may also play a role in disturbed attachment behaviors as well as associated intense affective reactions to stressors.<sup>7,33,56</sup>

Individuals with low levels of reward dependence tend to be independent, goal rather than people oriented and relatively asocial.<sup>14</sup> At one extreme, social anhedonia and aloofness lead to isolation, disinterest, and disregard for others. Social anhedonia, high levels of avoidance behaviors and "psychoticism"<sup>19</sup> may represent the core substrate for schizoid personality or schizophrenia spectrum disorders.<sup>6,53</sup> In contrast to schizophrenia spectrum disorders, low reward dependence in antisocial personalities disorder is associated with extroversion, impulse dyscontrol, thrill seeking, and callous disregard for others. Low levels of anxiety, and avoidance conditioning may contribute to a failure to learn from negative consequences and a tendency towards criminal behaviors.<sup>8,15</sup>

#### TEMPERAMENT IN FLUX

Like Chess and Thomas, Cloninger proposes that the automatic temperamental responses are continuously modified by an interaction between brain maturation and life experiences.<sup>50</sup> As noted earlier in a discussion of executive functions, brain maturation brings on line cortical regions that moderate pre-wired response patterns by integrating memory, emotional responses, and temperament.<sup>14</sup> The development of the association networks plays a crucial regulatory role in social perception, autonomic or affective arousal, and impulse control. These developmental changes also allow for new learning and modification of automatic, conditioned emotional and behavioral responses.<sup>15</sup> Top-down regulation associated with prefrontal maturation is also crucial for working memory, cognitive flexibility and social adaptability.<sup>52</sup> Individual variations in personality development result from the ongoing interaction between temperament and prefrontal brain development.<sup>25,44,47</sup>

As previously noted, Chess and Thomas<sup>13</sup> suggest that the psychosocial environment affects the expression of temperament. Adaptive and attuned parents play a key role in healthy psychological development whereas ineffective parenting styles (mismatches) may contribute to the evolution of maladaptive behaviors and some forms of psychopathology. They also suggested that favorable psychosocial environments modify the pre-wired circuitry associated with temperament. Stated in another way, there is a dynamic lifelong transactional relationship between genes, temperament, and interpersonal environments.<sup>25,26,38,45</sup>

#### NEUROBIOLOGY, GENES AND PSYCHIATRIC DISORDERS

Teasing out genetic influences on Axis I psychiatric disorders is even more complicated. When compared to known behavioral phenotypes, most psychiatric disorders lack target genes, common biochemical abnormalities or definitive diagnostic laboratory tests. Psychiatric disorders also include a broader range of symptoms. Psychiatric symptoms can be trait-related (personality disorders, organic personality disorders), state-related (episodes of major depression, psychosis, or delirium), or a combination of both (periodic exacerbations of positive symptoms in chronic schizophrenia).<sup>3,10,56</sup>

There is a far greater level of heterogeneity among psychiatric disorders as witnessed by the emergence of major depressive disorder in individuals with Lesch-Nyhan syndrome. There is

an ongoing debate as to whether depression is related to existential factors, underlying basal ganglia dysfunction, or chance comorbidity—both LNS and family history positive mood disorder.<sup>3</sup>

There is increasing interest in neurobiological circles in chronic, maladaptive (trait) behaviors such as personality disorders. Recent findings suggest that personality disorders<sup>2,47</sup> may lie on an etiological continuum that include adverse psychosocial influences, and prodromal or subsyndromal forms of Axis I disorders.<sup>40</sup> For example, patients genetically at risk for schizophrenia may present with schizotypal personality disorder but never progress to the full syndrome.<sup>9</sup> For others, symptoms of schizotypal disorder may steadily progress towards chronic, treatment-resistant schizophrenia.<sup>46,53</sup>

BPD is even more complicated. Although commonly associated with traumatization,<sup>10</sup> recent studies suggest that BPD is also related to Bipolar II Disorder—an inherited form of mood disorder. These findings suggest that BPD is related to temperamental vulnerability (psychobiological response style), Bipolar II Disorder, and risk factors for substance use disorders.<sup>40</sup> In all probability, BPD is the result of the combined effects of trauma, temperament, and genetic vulnerability to mood disorders.<sup>1</sup>

There is considerable evidence that severe abuse and neglect during infancy can alter gene expression (phenotype), brain development, and increase the likelihood of significant behavioral and cognitive disorders.<sup>38</sup> Early studies demonstrated the adverse neurobiological and developmental effects of extreme environmental and social-emotional isolation on infant rhesus macaques. The studies concluded that primates raised under experimental conditions displayed severe persistent behavioral and social-emotional disturbances. Subsequent research has demonstrated the adverse effects of abuse on brain development, neuroendocrine function, neurotransmitter activity, and neuro-anatomy.<sup>16</sup> The toxic effects of abuse and neglect illustrate the role of socio-emotional factors in the development of brain dysfunction, impaired cognitive abilities and socialization.<sup>10,22</sup>

#### TEMPERAMENT, PERSONALITY AND PSYCHIATRIC DISORDERS

As noted earlier, genetic and neurobiological factors play an important role in temperament and indirectly set the stage for many nonspecific behavioral disorders, personality disorders, and

many primary psychiatric disorders.<sup>50</sup> From this perspective, there appears to be a degree of continuity between various healthy stress reactions and major psychiatric disorders.<sup>8</sup>

But there are also major discontinuities between major psychiatric disorders and normal day-to-day experience. One difference involves the severity of emotional and behavioral reactions. Another set of discontinuities reflects differing levels of functional impairment and the presence of additional neurovegetative or neurocognitive symptoms. In most clinical settings, functional impairment is determined by severity, age of onset, polarity (mood disorders), duration of symptoms, gender, associated neurocognitive problems, and genetic vulnerability.<sup>51</sup> Yet in spite of apparent discontinuities, there are areas of significant overlap. For example, there appears to be a continuum between paranoid ideation and obsessive thoughts without insight; and a complex permeable boundary between obsessive-compulsive disorder and schizophrenia.<sup>9</sup>

So what is the clinician to do? One approach compares continuous and discontinuous features and looks for nodal or intersecting boundary points. For example, there appears to be a degree of overlap between temperament, personality, and psychopathology. Irritability may be common to each but there are significant differences between this affect in children with difficult temperaments, conduct disorder, and bipolar disorder. In one situation, the presence of irritability may define a temperamental style, an affective state associated with a disruptive behavior disorder, or a subtype of mood disorder (mixed bipolar type). Splitters prefer this type of subtype analysis to maximize the homogeneity of diverse clinical populations for psychobiological research or genetic studies.

Most clinicians prefer a more flexible approach that may lump individuals who present with irritability, preferring a final common pathway conceptualization such as a dysfunctional serotonin system.<sup>44</sup> There is a practical side to this approach since most referrals present with a more complex array of symptoms and comorbidities but respond to similar treatments (SSRIs). Clinicians struggle with the permeable boundaries between psychiatric disorders and may not be attuned to subtle differences in neurological examination or molecular genetics.

As discussed earlier, Chess and Thomas and Cloninger define subgroups ("splitters") based on a distinct group of temperamental traits—reward dependence or adaptability. But they also "lump"

temperamental characteristics into several composite groups. This frame of reference is broadened further to include domains—internalizing/externalizing domains neuroticism, psychoticism, extroversion and introversion.<sup>19,25</sup> The lumpers also consider that certain combinations of temperamental traits play a major role in the development of primary psychiatric disorders.<sup>42</sup> From this perspective, there are continuities between some temperamental traits, clusters of personality disorders, and certain forms of Axis I psychopathology. The splitters challenge these assumptions and point out the discontinuities between temperament and personality, and personality disorders and Axis I disorders.

It is apparent that people with IDs present a special problem for both lumpers and splitters. Some of this confusion arises from the complex interaction between neurobiological facts associated with severe ID and the clinical presentation of psychiatric symptoms. For example, the clinician may find that the boundary between DSM categories for mood or anxiety disorders is difficult to determine in a nonverbal client. For these individuals it may be more useful to defer the diagnosis and search for evidence of broader diagnostic concepts such as internalization, externalization and psychoticism. These broad constructs allow room for exploration of a range of biopsychosocial phenomena—social/interpersonal interactions, cognitive organizational skills, degree of impulsive control, and affective reactivity.<sup>25</sup>

#### INTERNALIZING DISORDERS

Internalizing disorders represent internalized conflicts expressed through specific psychic mechanisms and pathways—neurosis in another time. These same features also fit nicely into the temperamental models outlined in this paper. Chess and Thomas proposed the idea of "slow to adapt" temperamental style that suggest difficulties with adaptation to novelty, and

avoidance behaviors. Cloninger *et al.*<sup>14</sup> included low novelty seeking and high harm avoidance, varying levels of interpersonal attachment behaviors and motivational states (reward dependence). Kagan *et al.*<sup>30</sup> expanded this concept to include behavioral inhibition and laid the groundwork for Cluster "C" personality disorders (DSM-IV). It is apparent from these studies that "behavioral inhibition" is the substrate for a wide

range of primary psychiatric disorders. Behavior inhibition is a risk factor for social anxiety disorder, agoraphobia, and mood disorders.<sup>36</sup>

Genetic studies have focused on the relationship between parental anxiety and mood disorders and behavioral inhibition.<sup>51</sup> Outcome studies also suggest continuity between high levels of behavioral inhibition in children and increased risk for mood and anxiety disorders during adulthood.<sup>4,42</sup> The behavioral phenotype for Fragile X syndrome<sup>18</sup> may also fall within the internalizing frame of reference. Individuals with FRAXA present with a similar pattern of autonomic hyper-reactivity and social avoidance, but differ in some respects due to gaze aversion, hyperactivity, and mild SIB. In each of these scenarios, dysregulation of adrenergic activity via serotonergic, hormonal, GABA-ergic, peptidergic, and catecholamine activity is central to internalizing disorders.<sup>16,34</sup>

Hypervigilence, misperception of social interactions, deficits in a range of social communications, and problems with adaptive behaviors suggest boundary problems between behavioral inhibition, some symptoms of Posttraumatic Stress Disorder (PTSD),<sup>5,7</sup> and bipolar spectrum disorders.<sup>40</sup> PTSD is an acquired anxiety disorder associated with overwhelming life events. But PTSD is not uniformly distributed among people exposed to the same event. Those individuals with greater pre-existing autonomic hyperactivity appear to be at greater risk for PTSD.<sup>7,33</sup> The potential relationship between chronic PTSD, BPD and Bipolar II Disorder is intriguing since they represent a mixture of internalizing and externalizing domains.<sup>40</sup> PTSD is frequently associated with externalizing behaviors and BPD. On the other hand, Bipolar Disorder is associated with phasic changes (state-related) in internalizing/externalizing domains. Hypomania may represent a phase shift from internalizing to externalizing during the switch from depression. These state-related changes may contribute to symptoms of BPD— affective instability, poor impulse control and disturbed attachment behaviors.<sup>40</sup> Hypomania is associated with increases in potentially dangerous social behaviors that may indirectly increase the risk for traumatization. A great deal of work is needed to tease out this complex issue in people with ID.

#### EXTERNALIZING DISORDERS

Externalizing disorders include disorders of impulse control, affect lability, and behavioral

disinhibition. In psychodynamic terms, externalization results in acting out of internal conflicts. Rather than suffering from intrapsychic conflicts, the externalizing patient targets his/her environment and blames others. Chess and Thomas noted that children with difficult temperaments were more likely to develop externalizing symptoms due to exaggerated responses to frustration and slowness of adaptation. Cloninger considers the substrate for externalizing disorders to be an imbalance between novelty seeking, levels of harm avoidance, and reward dependence.

On closer examination, this temperamental style may be a substrate for a subgroup of people with attention deficit/hyperactivity disorder (ADHD), oppositional defiant disorder and conduct disorder in young people.<sup>44</sup> Numerous studies support a relationship between persistent ADHD, Cluster "B" personality disorders, and antisocial personality disorder. Cloninger *et al.*<sup>14</sup> also argues that this temperamental style is a factor in the development of severe substance abuse disorders. He associates high novelty seeking/low harm avoidance/variable reward dependence with antisocial personality and a particularly malignant form of substance use disorders.

This temperamental style is also reported in young people with bipolar spectrum disorder.<sup>54</sup> Children with ADHD and comorbid Bipolar Disorder may express trait-related irritability, explosiveness, and impulsivity as well as state-related intensification during episodes of hypomania. Patients with brain disorders and ID who present with externalizing symptoms are frequently classified with impulse control disorders, intermittent explosive disorder, and personality or mood changes due to underlying neurological disorders—"organic mental syndromes."<sup>39,48</sup> Unfortunately, a systematic examination of externalizing behaviors is frequently derailed by a need to intervene because of severe behaviors. Given plenty of time the clinician could explore the relationship between externalizing behavioral domain, frontal lobe function, comorbid epilepsy, unrecognized delirium and adverse drug reactions. The goal of this differential diagnosis is to distinguish developmental forms of externalizing disorders from those that are secondary to neuromedical disorders. One clue is that acquired externalizing disorders commonly present with a rapid onset and escalation of disruptive behaviors. This temporal profile suggests delirium, substance use

or withdrawal, or changes in medical or neurological status.<sup>43</sup>

Among normocognitive patients these disorders are associated with disturbances in nondominant prefrontal and orbitofrontal networks—including limbic and temporal lobe structures such as the amygdala.<sup>52</sup> Decreased autonomic arousal, diminished hypothalamic-pituitary-adrenal (cortisol) responses to stress, and decreased fear responses may play a key role in this group of individuals.<sup>45</sup> These same structures are crucial to interpersonal attachments and pro-social behaviors. Cognitively, these individuals may be prone to limited adaptability, perseveration, diminished self-reflection and critical self-appraisal, and misperception of social cues.<sup>21</sup> The interpersonal disturbances may be key to borderline and narcissistic personality disorders while cognitive changes may be state-related (hypomania) or trait-related (paranoid personality disorder).<sup>40</sup>

Cloninger<sup>15</sup> also proposes a linkage between the core features of externalizing disorders and several neurotransmitter systems—low harm avoidance (decreased inhibitory effects of serotonin) and novelty seeking (disturbances in dopamine and adrenergic systems). Clinical research studies of aggression, ADHD, fearlessness and neurochemical changes associated with mania also support a shared neurochemical substrate for temperament, externalizing disorders, and mood disorders. Molecular genetic studies provide some support for this position. There may be a close relationship between the externalizing domain and allelic variation in dopamine transporter proteins (re-uptake), MAO/COMT (metabolism), postsynaptic receptors (DRD2 and 4), serotonin receptors and re-uptake proteins and selected neuropeptides.<sup>45,47</sup>

#### PSYCHOTICISM

Psychoticism implies instability of perception, behavior, cognition, and social behaviors. For people with high psychoticism scores, anxiety or emotional arousal may evoke distressing fragmentation of thought and behavior and disturbances in sensory perception (including hallucinations). People with high levels of psychoticism may also have disturbances in emotional attachment behaviors (reward dependence) that are manifest by interpersonal discomfort, anhedonia for social interactions, and withdrawal.<sup>6</sup> Emotional aloofness, dissociative

behaviors and declining work or academic performance may herald a malignant developmental course.<sup>9,53</sup> High psychoticism ratings are seen in Cluster "A" personality disorders. These individuals also share trait-related low novelty seeking/high harm avoidance/low reward dependence,<sup>15</sup> high levels of social anxiety, and proneness to cognitive disorganization.<sup>46</sup>

These deviations suggest a relationship between some temperamental-personality traits and the core substrate for some features of psychotic disorders—Schizotypal Personality Disorder. Schizophrenia, on the other hand, represents a worsening of these core features—deficits in social communication, hedonic drives, social attachments and conceptual organization.

Attempts to define homogeneous psychotic populations for genetic analysis are confounded by their considerable heterogeneity. For example, individuals who meet the strict DSM-IV criteria for schizophrenia present with significant levels of clinical variability. From a developmental perspective, the role of these genes in schizophrenia is related to disturbances in brain development—cell migration, maturation, impaired apoptosis, and malfunctioning fronto-temporal-limbic interconnections. These developmental abnormalities result in deficits in attention memory, complex language processes, social attachment behaviors, and the integration of higher order cognitive processes. The clinical picture is clouded further by significant differences in severity and course of schizophrenia spectrum disorders. The combination of these factors suggests that both multiple genes and a second developmental factor are involved. There appears to be a major role for viral, nutritional, and early developmental insults in the development of schizophrenia.<sup>39,53</sup>

Psychotic forms of mood disorders may be difficult to differentiate from prodromal symptoms of schizophrenia in young people. In general, however, most people vulnerable to mood disorders do not resemble those with Cluster "A" personality disorder. Age of onset, pattern of onset, hypersomnia, hyperphagia and psychomotor slowing are risk factors for psychotic mood disorders. Thought disorganization and asociality are less common. Age and pattern of onset, polarity, and severity of mood disturbance recurring, and comorbid neurological symptoms episodes are more commonly associated with

psychotic symptoms. Individuals with BPD may be prone to brief stress-induced psychotic episodes. This group of individuals may regress rapidly but recover quickly. Some BPD individuals have a bipolar spectrum disorder (Bipolar II) that may be associated with temperamental patterns of irritability, explosiveness, and exaggerated attachment behaviors—"soft-bipolarity."<sup>40</sup>

Genetic loading for Bipolar I Disorder<sup>51</sup> is a risk factor for psychotic mood disorders. It is apparent that the presence of psychotic symptoms depends on age of onset, the frequency of relapses, neuro-imaging findings, comorbid substance use disorders, and polarity of the mood disturbance. More severe forms of bipolar illness may follow a chronic, nonprogressive, and relapsing course characterized by episodes of florid psychosis. The diagnosis of schizoaffective disorder is more likely in this extreme end of the mood disorder spectrum. Schizoaffective disorder supports the idea of a less rigid boundary between mood and schizophrenic spectrum disorders.<sup>9</sup>

It is apparent that the border between psychosis and severe brain dysfunction can be fluid (mixture of state and trait phenomena). This dimensional aspect of psychosis is especially relevant for people with severe ID.<sup>43</sup> In this population, psychotic symptoms (positive symptoms) may occur in response to the effects of psychosocial stress (Brief Psychotic Disorder or PTSD), especially among those individuals with significant neurological and medical comorbidity. The vulnerable individuals manifest higher rates of "organic" psychoses due unrecognized delirium. Delirium is frequently underdiagnosed or misattributed to primary psychotic disorders. Although the symptoms of "organic psychoses" differ from primary psychiatric disorders, it is often difficult to differentiate an acute relapse of schizophrenia from systemic lupus, adverse drug reactions, or neurometabolic disorders.<sup>48</sup>

#### DIAGNOSTIC PROCESS

So once again, what is a clinician to do? The answer is a work in progress but here are several possible starting points:

1. Don't throw the baby away with the bath water. Any reasonable diagnostic assessment begins with a description of target behaviors or symptoms.
2. Inventory environmental factors that trigger the observable behaviors. The process concludes with a thorough but conventional

behavioral analysis, in addition to developing operationalized target behaviors.

3. Rule out delirium by carefully assessing for rapidly fluctuating symptoms, confusion and disorientation.<sup>39</sup>
4. Search for neurovegetative symptoms, and changes in patterns of behavior and emotional reactivity.
5. Search for the presence of hallucinations, delusions or bizarre behaviors. If found, the clinician should thoroughly investigate, and not accept at face value that "hallucinations" are not manifestations of schizophrenia or other psychoses.<sup>27</sup>

Up to this point we have not broken new ground, but the clinician is still lost in the woods and may still be unable to make a valid diagnosis other than "NOS" or intermittent explosive disorder. Proceed along these lines:

6. Carefully assess the balance between the tested levels of IDs and adaptive capacities. Autistic spectrum disorders may have a relatively greater impact on social attachment, behavioral flexibility, and adaptive behaviors than tested intelligence. These patterns may be reversed from many with nonautistic ID.<sup>55</sup>
7. Address the intra-categorical differences between the subtypes of ID/MR. People with severe ID are more likely to present with complicated neurological, metabolic, or multi-system medical disorders. In addition, many require multiple medications that further confound the differential diagnosis.
8. Review with caretakers or family members their observations of temperament—approach-avoidance to novelty, behavioral inhibition, social relatedness and attachment behaviors, intensity of baseline reactivity to changing situations, and general tendencies of internalization or externalization. It is important to establish significant changes in these established patterns of behavior that might help differentiate state-related versus trait-related symptoms.
9. Obtain a thorough family history that includes questions about neuromedical and psychiatric disorders. If possible, review previous medical records, neurodiagnostic test results (EEG or CT/MRI), and history of past treatments. We can learn a great deal from unsuccessful

treatments about psychopharmacological sensitivities and diagnostically relevant information from drugs that exacerbate symptoms rather than reduce them.

10. The traditional psychiatric interview is often ineffective but a great deal of information can be gleaned from secondary reports and direct observation. Data from functional behavioral analyses may be helpful in establishing specific trigger events, threshold for reaction as well as intensity and duration of reactions (temperamental factors). Naturalistic observations outside of laboratory or clinic settings may also add significant information about the social context of behaviors and patterns of mutual social behaviors with peers, staff, and family members—similar to family therapy approaches or at an even more basic level, ethological field study. This data may be quite helpful, especially if it includes specific environmental triggers, patterns of reciprocal social interactions, and naturalistic factors that regulate the behaviors.

Integrating this information is the next crucial step. Traditionally, mental health professionals move quickly to establish a psychiatric diagnosis (DSM-IV), develop a behavioral intervention plan, or begin pharmacotherapy based on an incomplete understanding of the etiology of the behavior and erroneous theories about neurotransmitter-behavior interactions. Rather than mentally leafing through the DSM-IV to find a fit, it may be more effective to begin with a careful review of comorbid risk factors (behavioral inhibition—harm avoidance), physiological factors (autonomic overarousal, intensity of affective responses) and neurobiological factors (endocrine response) for internalizing disorders. With this information in hand, the clinician begins the process of integrating temperamental data with ecological and biopsychosocial observations. This information is then combined with data on genetic risks, age of onset, gender, behavioral phenotypes, comorbid neurological or medical disorders, intellectual and adaptive abilities, and significant psychosocial factors.

#### DIAGNOSTIC MODEL

Diagnosis involves a series of hierarchical analyses and hypothesis testing. But there are problems posed by the heterogeneity of most psychiatric disorders. To cope with this variability, the clinician may find that genetic and

temperamental information is a helpful starting point. The rest of the assessment information is used to fine tune and test hypotheses. Once these steps are completed, the search for a DSM-IV diagnosis is replaced by a slightly different but more relevant multi-axial diagnostic format.

A rough outline includes:

**Axis I:** Level of intellectual disability and global assessment of function.

**Axis II:** Data on temperament is categorized into internalizing/externalizing/psychotic spectrum of disorders.

**Axis III:** Genetic data on risk for neuromedical and psychiatric disorders; co-existing neuromedical conditions; past and current treatment of these conditions; history of medication trials and adverse drug reactions (akathisia from neuroleptics).

**Axis IV:** Findings from behavioral analysis (target behaviors) and symptoms of psychiatric disorder are integrated with findings from the mental status examination. This data includes a description of naturalistic observations of reciprocal social-emotional-attachment behaviors across several settings. This data includes observations from settings associated with higher, neutral, and lower rates of behaviors of peak behaviors. In addition, the temporal profile of symptoms should include seasonal or periods of sustained changes in target behaviors (baseline exaggerations).

**Axis V:** Narrative of the interaction between Axes I-IV and both past and present psychosocial ecologies. Once this process is completed, the clinician can then grapple with a DSM-IV-TR diagnosis.

#### CONCLUSION

This paper has explored a range of issues that undermines the validity of our current diagnostic nomenclature. From this perspective, it is interesting that the most significant weakness of the DSM is an unfortunate outgrowth of its greatest strengths—multi-axial format, categorical or descriptive diagnostic categories and elimination of etiology from the criteria. The original impetus for eliminating etiology in the diagnosis grew out dissatisfaction with the inconsistencies and vagaries associated with psychodynamic models for diagnosis. The paradigm shift towards phenomenology was an

attempt to standardize diagnostic criteria and design effective pharmacological treatments. Descriptive psychiatry also set the stage for an explosion of psychobiological and psychopharmacological research.

But, unfortunately, the neuroscience revolution is progressing faster than the introduction of new DSM's. It was hoped that these new technologies would help in the search for specific subtypes of psychiatric disorders ("splitting"). Unfortunately these increasingly sophisticated neurodiagnostic procedures are producing more ambiguous results. Although helpful in defining subtypes, these neuro-imaging and neurophysiological studies have also paradoxically added to our uncertainty about categorical psychiatric disorders<sup>23,31</sup> by diffusing the boundary between "organic" and "functional" disorders as relative.<sup>57</sup>

The genetics revolution produced the same paradox. The more we learn about the relationship between genes, anatomy and physiology, the more uncertain we are about the development of brain-behavior relationships in general and psychiatric disorders in particular. The expansion of studies into specific behavioral phenotypes is promising but detailed studies run headlong into the complexity of well-defined gene-behavior interactions. Genetic researchers are frustrated even further in their attempts to find target genes for specific psychiatric disorders. As a result, these researchers continually grapple with the natural diversity and transactional nature of psychiatric disorders. Rather than defining discrete naturally occurring entities, these researchers have stumbled into the categorical-dimensional debate that haunts clinicians—most psychiatric disorders may have subsyndromal forms or exist on a continuum (spectrum disorders). These "soft" forms of severe psychiatric disorders suggest that disorders like schizophrenia or bipolar disorder may lie on a severity continuum with some personality disorders.<sup>35</sup>

No matter who wins these debates, clinicians will still face the daunting task of making psychiatric diagnoses on individuals with severe ID. The introduction of genetic and neurodiagnostic testing is encouraging. These procedures may enhance our capacity to define specific syndromes or aid in the subclassification of psychiatric disorder based on genetic risk. But they also add another layer of complexity by supporting the observation that many behavioral

and psychiatric disorders may represent the final common pathway for a range of underlying neuro-medical conditions.

Unfortunately these advances have not trickled down to the level of routine clinical assessment and psychiatric treatment of people with severe ID. We are still struggling with the inherent weaknesses in the DSM-IV-TR and we are grappling to avoid the diagnostic purgatory of multi-axial chaos. The author has made a feeble attempt to integrate categorical diagnostic model with dimensional and etiopathogenic frames of reference. Unfortunately, this effort suffers from an inescapable weakness—reductionism. The tragic flaw in any diagnostic nomenclature appears whenever anyone attempts to reduce the richness and diversity of human experience in a few symptoms and syndromes. Much more work is needed.

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- CORRESPONDENCE:** Jarrett Barnhill, M.D., DFAPA, AACAP, Dept. of Psychiatry, University of North Carolina School of Medicine, CB 7160, Chapel Hill, NC 27599; email: Jarrett\_Barnhill@med.unc.edu.