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The Diagnostic Dilemma of Pathological Appearance and Performance Enhancing Drug Use

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Abstract

Appearance and performance enhancing drug (APED) use includes the use of a range of pharmacologically distinct substances and concurrent investment in outward appearance or achievement, dietary control, and frequent exercise. A number of existing reviews and conceptual papers have defined pathological forms of APED use within the APED class of anabolic-androgenic steroids (AASs) and using the framework of AAS dependence. We review published data on APED use including human studies of AAS users and identified three defining phenomenological features associated with increased health risk and pathology. These features included (1) polypharmacy or the concurrent use of several pharmacologically distinct substances used to change outward appearance or increase likelihood of personal achievement; (2) significant body image disturbance; (3) rigid practices and preoccupations with diet and exercise. Investigations into the latent structure of APED use suggest these features cluster together in a homogenous group of APED users who have the highest health risk and most psychopathology. These features are discussed in the context of AAS dependence and problems with defining classic tolerance-withdrawal symptoms among APED users. Suggestions for a resolution and outline for future research needed to determine the best system for identifying and diagnosing pathological APED use are discussed.

Keywords

Anabolic-androgenic steroids; appearance and performance enhancing drugs; substance use disorder; diagnosis; body image disturbance; compulsive exercise

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1. Introduction

Appearance and performance enhancing drugs (APEDs) are substances used for their effects on one's outward appearance (e.g., increased muscle, reduced fat) or for improving one's performance and likelihood for personal achievement (e.g., weightlifting, sports, fighting, sex, job performance). Anabolic-androgenic steroids (AASs) are a family of synthetic hormones derived from natural sex hormones such as testosterone and its derivatives or precursors [e.g., dihydrotestosterone (DHT); Shahidi, 2001] and are included under the umbrella of APEDs (Hildebrandt et al., 2007). AAS use is often discussed as a subset of APED use and the majority of scientific, clinical, and public attention has focused on this single drug class. AASs have obtained notable public interest due to scandals involving professional and Olympic athletes (Catlin et al., 2008; Tsitsimpikou, et al., 2009) as well as tragedies involving suicide/homicide, cardiac events, or other severe psychiatric or medical complications (Cowan, 1994; Dickerman et al., 1995; Hausmann et al., 1998; Huie, 1994; Patil et al., 2007; Peet and Peters, 1995; Santamarina et al., 2008; van Breda et al., 2003). Currently, there is no formal category of AAS or APED misuse in the *Diagnostic and Statistical Manual for Mental Disorders-4th edition* (*DSM-IV*; American Psychiatric Association, 1994), but AASs are listed as an "other" substance in the SUD subsection. The recognition of potential health risks and the sociopolitical environment perpetuated by cheating athletes has brought about a diagnostic dilemma—developing a set of criteria that captures both the drug-based psychopathology of APED use and the defining attitudinal and behavioral psychopathology of body image disturbance, rigid dieting, and compulsive exercise. Where these diagnostic criteria would place APED use in the larger landscape of psychopathology is yet unclear.

The purpose of this review is to critically examine the existing attempts to define and diagnose pathological APED use and delineate key elements needed for revision to the diagnostic system. To accomplish this goal, we (a) briefly describe the scope and risks associated with APED use, (b) review the most recent proposal to diagnose pathological APED use as a SUD, (c) describe the unique features of APED use that are most clearly associated with risk and pathology, and (d) offer a possible solution and outline for future research.

2. The Scope and Risks of Appearance and Performance Enhancing Drug Use

2.1 Scope of AASs and APED use?

The APEDs encompass a wide range of substances including AASs, non-steroidal anabolics, stimulants and other weight loss or endurance drugs, ancillary drugs, and nutritional supplements. Table 1 provides some common examples of APEDs. There are no population based prevalence estimates of many APEDs, but there are published data on the prevalence of AASs. Conservative estimates suggest that about 1–3% of young men in Western cultures have used AASs (Centers for Disease Control, 2008;Kanayama et al., 2009a) with higher estimates outside the United States (Baker et al., 2006;Galduroz et al., 2005). Estimates of adolescent AAS use are more variable, indicating use in 3–12% of males (Buckley et al., 1988;Kokkevi et al., 2008;Nilsson et al., 2001;Tanner et al., 1995). Legal APEDs, such as nutritional supplements, are used daily by about 33% of adults (Millen et al., 2004;Radimer et al., 2000), and they are contaminated with AASs in as much as 12.5% of samples (Martello et al., 2007) leading to significantly more exposure to AASs than is self-reported in population studies.

2.2 Risk and Impairment: The Physical and Psychiatric Consequences of AASs

Perhaps the most significant risk attributed to AASs is to the cardiac system; AAS users are at increased risk for negative cardiac effects including cardiomyopathy and ischemic stroke (Sullivan et al., 1998), and this risk might persist after discontinuation of AAS use (Urhausen et al., 2004), although this might also be due to the cardiac effects of strenuous exercise (Haykowsky et al., 2003). Liver toxicity is also well documented in animal models of AAS use (Noorafshan et al., 2005; Vieira et al., 2008) and supported by case studies (e.g., Socas et al., 2005). Other physical side effects have been difficult to document consistently, but are likely to include milder side effects such as acne or hair loss and more serious side effects such as gynecomastia, hypogonadism, or infertility (Hartgens and Kuipers, 2004; Evans, 2004).

A number of psychiatric side effects are also linked to AAS use, the most prominent being aggression and violence (Trenton and Courrier, 2005). AAS users are more likely to die from violence compared to other substance users (Petersson et al., 2006; Thiblin et al., 2000) and they are at increased risk for violent acts (Beaver et al., 2008), particularly for those with comorbid substance use problems (Klotz et al., 2007). Placebo controlled studies in healthy volunteers support these epidemiological data (e.g., Daly et al., 2003; Pope et al., 2000; Su et al., 1993), as does controlled observational research community-based APED using samples (Pagonis et al., 2006). Other mood related consequences include symptoms of hypomania, elevated mood, or impulsivity (Pope et al., 2000) or depressive symptoms (e.g., Pope and Katz, 1994) that occur especially in cases of hypogonadism related to chronic AAS use (Tan and Scally, 2009)

2.3 Addiction and AASs

In addition to aggression, much of existing psychiatric literature has focused on the classic abuse-dependence model of addiction (Brower, 1992, 1993; Brower et al., 1990; Lukas, 1996; Midgley et al., 1999) or recent variations of this model (Kanayama et al., 2009a, b). This literature indicates that about one-third of AAS users meet criteria for AAS dependence and that dependent AAS users experience higher levels of psychiatric comorbidity, particularly with SUDs (Kanayama et al., 2009c). The prevalence of these classic drug dependence symptoms varies widely from study to study (12.0—83.7%) and this may be related to difficulty in defining a unique withdrawal syndrome and methodological issues related to self-report (Kanayama et al., 2009a). There are no published studies considering the broader category of APEDs, although much of this research notes the tendency for AAS users to abuse other APEDs.

3. Describing and Defining the Psychopathology of APED use

AAS and APED use are currently orphaned in the greater landscape of psychopathology and their appropriate placement in future diagnostic systems is up for debate. Existing definitions of APED pathology have applied a “top-down” approach by forcing APED misuse into an AAS dependence model. The consequence of this approach is the assumption that AASs must work like other substances of abuse (Wood, 2008) where the underlying pathology involves an altered motivation-reward system (Koob, 1992), and the dependence syndrome focuses on the experience of AAS tolerance and withdrawal. However, the difficulties in defining a clear AAS tolerance-withdrawal syndrome indicate that APEDs may not be best conceptualized as a SUD. A “bottom-up” approach, rather, highlights three distinct features associated with health risk and impairment among APED users. These features include (a) polypharmacy, (b) body image disturbance, and (c) disturbances in diet and exercise. The primary role of all three features in APED risk and impairment suggests a need for a diagnostic system that weighs each element of psychopathology equally.

3.1 DSM and the AAS Addiction Model

The majority of efforts have sought to define pathological APED use as an addiction and used the *DSM-III-R* or *DSM-IV* dependence criteria. These basic dependence criteria have evolved tremendously over the past 50 years with the most recent models being heavily influenced by the description of the Alcohol Dependence Syndrome (ADS; Edwards and Gross, 1976). The ADS defined dependence as a dimensional construct with a focus on the psychobiological symptoms such as tolerance and withdrawal. Although this syndrome was based on the clinical presentation of alcoholics, subsequent versions of the *DSM* unified pathological forms of substance use by standardizing this symptom palette across substances. Early attempts to define pathological AAS use borrowed this symptom palette and rationalized this adaptation based on the potential for AAS tolerance and withdrawal (Kashkin and Kleber, 1989).

Alterations to these ADS-based symptoms have recently been proposed (Kanayama et al., 2009 a,b). These changes maintain the structure of the original ADS symptom palette, but offer alternative definitions of several key symptoms. For example, the definition of AAS tolerance is expanded to include body dissatisfaction. A similar change can be found in the D4 “unsuccessful efforts to cut down” and D6 “activities reduced or given up” criteria, where the pathology is evident by preoccupation and anxiety surrounding one’s appearance and the peripheral effects of AASs. The altered criteria also incorporate dietary restrictions and excessive exercise in the D5 “time spent on AAS effects and activities” and D6 criteria. These altered criteria represent a specific attempt to maintain the top-down approach which forces APED use into a SUD, but at the cost of fundamentally changing the meaning of the primary drug-based criteria.

As discussed by Kanayama et al. (2009a, b), AASs deviate from classic drugs of abuse in several ways. For instance, they argue that there is no evidence that AASs have an intoxication syndrome, immediate adverse effects, impairment in performance (e.g., driving, work activities), centrally mediated drug tolerance, or that the AAS use is time consuming. Inconsistencies not discussed include the lack of communal use, dependency of the desired drug effects on diet and exercise, and the magnitude of time, energy, and effort needed to achieve the desired effects. Most classic drugs of abuse are initiated and reinforced in a gregarious social context, interfere with the pursuit of health and wellbeing, and require little effort to achieve the desired effects. An APED user must use the drug for months in conjunction with a strict diet and exercise regimen in order to achieve the desired drug effects. Furthermore, SUDs share a primary source of psychopathology (i.e., dysregulation of the motivation-reward system), which is not apparent in the manifestations of APED tolerance and withdrawal.

3.2 Complexities of Anabolic-Androgenic Steroid and APED Tolerance and Withdrawal

One primary misfit between SUDs and APEDs misuse are the definitions and role of tolerance and withdrawal. Both features are linked to hedonic drives and the neurobiology of addiction is based off these opponent processes (O'Brien et al., 2006) and their translational counterparts of reward and anti-reward (Koob and Le Moal, 2008). However, the function of tolerance and withdrawal among APED users is more clearly linked to regulation and adaptation of the HPG axis and its influence over muscle mass. For instance, the main targets of AASs are not essential to the motivation-reward system (Hamson et al., 2004; McAbee and DonCarlos, 1998; Pfaff, 1968; Sarkey et al., 2008; Simerly et al., 1990) and AASs act only as mild reinforcers compared to other drugs (Wood, 2004). This distinction in primary dysregulation provides a degree of complexity to the definitions of tolerance and withdrawal not captured by hedonic-based drug tolerance-withdrawal.

3.2.1 Anabolic-Androgenic Steroid APED Tolerance—Drug tolerance occurs when an increase in drug amount is needed to achieve intoxication or there is a diminished effectiveness of the drug of over time (APA, 1994). Applied to APED use, drug tolerance would occur when large doses or duration of AASs no longer yield significant changes in muscle mass or the effect of APED use diminishes significantly (Kanayama et al., 2009a,b). There are several problems with retaining this definition. First, there is no easily quantifiable measure of AAS amount because of (a) the variability in drug potency, (b) the tendency to sequence different substances, and (c) the general lack of pharmacological data on many AASs. The second issue is that 'diminished effects' will vary greatly based on the goal of the APED user. APED use appears to be motivated by a range of distinct bodily ideals or performance goals (Hildebrandt et al., 2007; Hildebrandt et al., 2006a); drug patterns (including amount, frequency or duration) may increase due to the extremity of the ideal rather than the ineffectiveness of the drug. Third, age represents a potential confound, as with other drugs (Chen and Anthony, 2003; Chung et al., 2004; Chung et al., 2001). As men and women get older, their ability to build and retain muscle changes, so tolerance may represent a function of age as well as physical adaptation to the drug. Finally, there is no intoxication syndrome with AASs or APEDs, so drug tolerance loses its relevance to hedonic models of drug dependence. These problems suggest drug tolerance is unlikely to be a useful diagnostic marker of APED pathology.

3.2.2 Anabolic-Androgenic Steroid and APED Withdrawal—The construct of AAS withdrawal also has limitations that suggest a misfit with a SUD. The functional significance of withdrawal to addiction is that it describes a state where the individual is highly motivated to seek the drug in order to relieve distress. Thus, withdrawal for SUDs yields a drug specific craving and strong desire to resolve the physical and psychological discomfort of drug cessation. APED withdrawal, however, diverges from this pattern in several important ways. First, the majority of users do not report high levels of discomfort upon cessation from an APED cycle (Hildebrandt et al., 2006a). Second, APED users who experience distress will often use non-AAS medicines (e.g., human chorionic gonadotropin) to prevent withdrawal. Interestingly, many of these individuals purposefully seek a period of discontinuation to re-regulate their HPG axis, so drug cessation does not appear to increase AAS craving or specific drug seeking. Third, the distress associated with cessation from APEDs is more clearly linked to concerns with changes in appearance or strength than the opioid-based withdrawal described elsewhere (e.g., Brower, 2002; Wood, 2008). The traditional explanation for drug withdrawal involves a failure of the motivation-reward system to function properly without the drug (Koob and Le Moal, 2008). APED withdrawal, rather, involves the failure of the HPG axis to achieve or maintain desired levels of muscular hypertrophy or similar physical changes in the context of heavy exercise. Thus, the primary mechanisms of APED withdrawal appear to differ from those of other SUDs.

AAS withdrawal, and the neurobiological links to the motivation-reward system, is not without some support. An emerging line of evidence based on case studies, animal data, and comorbidity patterns indicates that AAS dependence shares basic mechanisms with opioid dependence (Kanayama et al., 2009a,b,c). Opioid withdrawal (agitation, anxiety, yawning, sweats, diarrhea, insomnia, and dilated pupils), however, has poor symptom overlap with the most frequently reported AAS withdrawal symptoms, which includes depressed mood, fatigue, and decreased libido (Brower, 2002; Brower et al., 1991; Brower et al., 1990). The poor overlap raises the possibility that AAS withdrawal may not be related to AASs. Rather, these symptoms could be tied to other commonly used APEDs. For instance, these symptoms are characteristic of stimulant withdrawal (Barr and Markou, 2005; Kitanaka et al., 2008; McGregor et al., 2005) as well as hypothyroidism (Roberts and Ladenson, 2004).

3.2.3 Anabolic Steroid-Induced Hypogonadism as a Medical Confound—

Anabolic steroid-induced hypogonadism (ASIH) is a medical consequence of illicit APED use and is not dependent on drug tolerance or withdrawal. Although the hedonic values and pharmacological properties of AASs are heterogeneous (Kicman, 2008), they share a common ability to cause suppression of natural androgen production, which persists after the cessation of AAS use (e.g., Jarow and Lipshultz, 1990). This neuroendocrine effect involves suppression of circulating gonadotropic hormones via negative feedback at the level of the hypothalamus. The psychological effects of this hypogonadism are similar to those described for AAS withdrawal (Tan and Scally, 2009) and this overlap offers the potential to equate drug withdrawal to ASIH. However, the two phenomena are distinct; drug withdrawal is believed to motivate an individual to seek greater amounts of the drug to relieve discomfort whereas ASIH can be resolved with an individual's natural return to normal levels of androgen production without the use of exogenous androgens. This latter goal is what most APED users pursue post-cycle. Thus, the distinction between ASIH and AAS withdrawal involves a shifting focus from the classic motivation-reward system to the functioning of the HPG axis. This shift is likely to lead to more appropriate medical treatments for post-cycle psychological symptoms, such as the use of clomiphene citrate to stimulate testosterone production (Tan and Vasudevan, 2003).

3.3 Core Features of APED use Associated with Pathology and Risk

The majority of what is known about pathological APED use originates from a handful of field studies conducted over the past 25 years with weightlifting men and women who were recruited from local gyms or more recently through online discussion boards dedicated to weightlifting, sport, or APEDs. A closer look at these studies, approaching the description and delineation of APED psychopathology from a "bottom-up" approach, reveals three major features of APED use that can be linked to risk and impairment including (a) polypharmacy, (b) body image disturbance, and (c) disturbances in dieting and exercise.

3.3.1 Polypharmacy as an Indicator of Problematic APED Use—

The case for polypharmacy as an indicator of problematic APED use is relatively clear from descriptive studies of AAS users. Table 2 summarizes the existing published data on APED use patterns from field studies with AAS users that reported descriptive data on the basic pattern of drug use. Comparative studies were excluded if these data were not available (e.g., Hildebrandt et al., 2006a;Kanayama et al., 2006). Averaging across studies, the typical APED user reported taking an average of 1304.52 mg/wk of AAS for an average of 11.65 weeks, but this dosage appears to be increasing over time. The use of more than one AAS was common (>90% where reported) and the majority (M = 60.07%) reported the use of non-steroidal APEDs. Although AASs remain a primary component of this polypharmacy, CNS stimulants, thyroid hormones, ancillary agents (e.g., anti-estrogens), and non-steroidal anabolics (e.g., insulin) were also regularly reported. Even when measured as part of a "typical" use pattern, 60% reported non-steroidal anabolic use (Hildebrandt et al., 2007). These data suggest that the mixture of pharmacologically distinct substances is common among APED users. This polypharmacy appears to be an important predictor of intentions for future APED use (Hildebrandt et al., 2006a) and of drug use severity among APED users (Hildebrandt et al., 2007). Specifically, polypharmacy is associated with increased quantity and frequency of APED exposure, psychiatric side effects, physical side effects, and intentions to continue using APEDs despite health risks.

A second issue raised by the use of such a wide range of substances is the increase in acute psychiatric and physical risk associated with non-AASs. For instance, the stimulants taken by APED users have independently documented acute and chronic cardiac and psychiatric side effects (Caplan et al., 2007; Samenuk et al., 2002), abuse potential (Tinsley and

Watkins, 1998), and reinforcing properties (Li et al., 2005; Stoops, 2008); thyroid hormones may contribute to elevated mood, irritability, and lead to hypothyroidism upon cessation (Snyder and Jaffy, 1997); and insulin and human growth hormone (hGH) may increase the likelihood of acute cardiac effects (Gilmore and Stead, 2006; Klein and Ojamaa, 1992). These latter substances are also highly correlated with other indicators of APED risk, including the use of higher doses, duration, and investment in prolonged APED use (Hildebrandt et al., 2007). Thus, impairment from APED use appears to be strongly related to the degree of polypharmacy.

3.4 Core Psychiatric and Behavioral Features of APED Use

3.4 Body Image Disturbance—Body image disturbance is perhaps the most robust and reliable psychiatric disturbance associated with APED use (Cafri et al., 2005; McCreary et al., 2007). The symptoms of this disturbance manifest in attitudes about the importance of outward appearance, preoccupations or obsessions about one's appearance, behavioral patterns of body evaluation and avoidance, or difficulty tolerating changes in appearance. Investigations into APED use and these symptoms suggest they are highly correlated and most clearly visible in their patterns of comorbidity. Furthermore, among adolescents, body image disturbance is theorized to be a specific risk factor (Cafri et al., 2005; Ricciardelli and McCabe, 2004) and predictive of intentions for future illicit APED use (Cafri et al., 2006; Dunn et al., 2009).

There have been several cross-sectional studies that suggest AAS users have higher rates of body image disturbance than non-AAS using controls. For instance, AAS users have been found to report higher rates of muscle dysmorphia (MD; a subtype of body dysmorphic disorder) compared to weightlifting controls (Kanayama et al., 2006), lower body esteem (Kanayama et al., 2003), and stronger desire to increase lean muscularity (Blouin and Goldfield, 1995; Brower et al., 1994). Consistent with these findings, APED use appears to be increased among those with MD (Cafri et al., 2008; Pope et al., 2005). This disorder is characterized by obsessive-compulsive appearance-evaluating behaviors such as body checking and avoidance (Olivardia, 2001; Pope et al., 1997) and the desire or investment in a high degree of lean muscularity (Grieve, 2007). Thus, comorbidity patterns and cross-sectional studies suggest higher rates of body image disturbance among APED users.

Specific features of body image disturbance appear to be related to APED use. Body checking appears to be an important behavioral indicator of body image disturbance more broadly, as it is predictive of quantity and frequency of exercise, degree of APED use, and positive attitudes about APEDs (Hildebrandt et al., 2009; Walker et al., 2009). Investment in appearance is also thought to be important and unique aspect of body image disturbance among weightlifting men (Pickett et al., 2005), akin to the construct of shape and weight preoccupation found among those with eating disorders (Grieve, 2007; Mosley, 2009). This investment may leave individuals emotionally vulnerable to changes in appearance (i.e., post-cycle losses in muscle) and precipitate recurrent APED use. Thus, the symptoms of strong desire for extreme lean muscularity (particularly when already lean and muscular), high investment in appearance, behavioral body checking and avoidance, and negative emotionality tied to appearance appear to be good indicators of body image disturbance severity, and among APED users appear to drive the pathological (i.e., chronic, high dose APED use) drug patterns.

There is also variability in body image disturbance among male weightlifters and APED using men. Hildebrandt et al. (2010) found evidence of a continuum of disturbance that correlates with quantity and duration of APED cycles and investment in future APED use. This severity continuum was also marked by certain types of heterogeneity related to the types of bodily change desired (i.e., leanness vs. muscle), with those engaged in the greatest

degree of polypharmacy and invested in leanness and muscularity reporting the most severe body image disturbance. Thus, the continuum of severity would appear to be anchored by this extreme disturbance in muscularity at one end and those who are relatively satisfied with their appearance on the less pathological end.

3.4.2 Disturbances in Dieting and Exercise—The diagnostic value of diet and exercise patterns among APED users remains underappreciated. Broadly, disturbances in these clinical features can be conceptualized by their potential to be obsessive-compulsive or of high reward value and thus likely prone to difficulty in limiting their use. Disturbances in diet and exercise may be present when diet and exercise are characterized by (a) endorsement and adherence to strict rules, (b) preoccupations or compulsive diet and exercise behaviors, (c) difficulty controlling these behaviors due to their pleasurable effects, (d) or feelings of guilt or loss of control associated with eating or exercise. For instance, APED users may feel extremely guilty if they deviate from a high protein diet and they often compensate with changes to their exercise pattern or intensity.

Several lines of evidence support a unique role for dietary practices and exercise patterns in problematic APED use. For example, diet and exercise patterns can include strict adherence to caloric or macronutrient regimens (Kleiner et al., 1990; Lambert et al., 2004) as well as intense and excessive exercise. This phenomenon is noted in discussions of APED use (Cafri et al., 2005; Evans, 2004; Hartgens and Kuipers, 2004; McCreary et al., 2007), and considered to be characteristic of APED users. The desired effects of APEDs (i.e., lean muscularity) are heavily dependent upon the effects of exercise and nutrition, making these domains strong candidates for a source of APED pathology. In fact, APEDs are extremely unlikely to be used or misused outside the context of dietary control and/or regular exercise, given the primary motivations for APED use (Copeland et al., 2000; Evans, 1997; Perry et al., 2005). As with body image disturbance, problematic forms of diet and exercise may be resistant to change and a primary source of impairment or distress.

In addition to their direct effects on lean muscularity, aspects of dieting and exercise may have a synergistic effect with APEDs on risk and impairment. For instance, increased caloric intake could contribute to increased lipid levels or hyperglycemia (Keith et al., 1996) and lifting heavy weights may exacerbate the potential for negative heart effects (Haykowsky et al., 2003). In addition, exercise has an independent potential for an addiction-like syndrome. There is a well established literature on the construct of exercise dependence (Bamber et al., 2003; Hamer and Karageorghis, 2007) or the related construct of compulsive exercise (Dalle et al., 2008) which have both been linked to bodybuilding (Hurst et al., 2000; Smith and Hale, 2005). Exercise in this form leads to impairment or distress because of its tendency towards preoccupation, time-consuming nature, continued practice despite physical injury, and difficulty regulating exercise frequency, duration, or intensity. It is in this type of environment where APED use provides the most functional significance; APEDs are likely to prevent overtraining and the hormonal or neuroendocrine effects of this state (Hildebrandt et al., in press).

Although there is no systematic research on these clinical features among APED users, there is some evolving animal research to suggest an important relationship between exercise and AASs. In particular, androgen administration appears to lead to increases in exercise behavior among hamsters (Wood, 2002). Interestingly, exercise shares some overlap with androgens in reinforcement mechanisms by increasing opioid release (Goldfarb and Jamurtas, 1997) and or testosterone production (Kraemer and Ratamess, 2005). Thus, it seems that there is validity for considering exercise disturbance as a foundation for APED pathology. Whether disturbances in exercise and dietary control constitute a severity continuum will need to be further explored. If exercise is necessary to promote the opioid

releasing effects of androgens, then APED misuse becomes a mixed substance-behavioral disorder whereby exercise is a necessary element of APED psychopathology.

3.5 Insights Derived from the Latent Structure of Problematic APED Use

There continues to be debate about the best approach to classification and conceptualization of psychiatric diagnosis, with some favoring purely dimensional models, others maintaining the parsimony of the existing categorical framework, and still others favoring an integration of categorical and dimensional models (Brown and Barlow, 2005). The *DSM-IV* and *ICD-10* SUD criteria represent diagnostic systems in which the underlying constructs and inherent structure (categorical, dimensional, or combination; Helzer et al., 2007; Helzer et al., 2006) are still evolving and subject to debate (Hasin et al., 2006). Combinations of categorical and dimensional approaches have distinct advantages, mainly in providing stronger predictive power, capturing heterogeneity in the diagnoses, and providing clinically relevant information about severity (Kuo et al., 2008; Muthen, 2006). In the case of APED use, similar advantages to integrated dimensional and categorical models are likely. For APED use, each domain (drug use, body image, and diet/exercise) can be conceptualized as having a unique continuum of severity. Consistent with other SUDs, drug dependence criteria appear to measure a single construct (Helzer et al., 2007; Krueger et al., 2004; Martin et al., 2006; Saha et al., 2006). There is some evidence that a single dimensional severity construct also underlies APED use phenomena, with more complex patterns and certain types of high risk drugs (e.g., hGH, insulin) being good indicators of greater drug use severity (Hildebrandt et al., 2007). Similar evidence exists for a single continuum of severity underlying the body image disturbance among APED users (Hildebrandt et al., 2010).

Categorical distinctions are also likely to be important for APED use. While drug use severity and body image disturbance have dimensional properties, the population of APED users is also characterized by certain subtypes (Hildebrand et al., 2010; Hildebrandt, et al., 2007). These subtypes are distinguishable by the APEDs used and the intensity of body image disturbance. The subgroup self-reporting the greatest risk and impairment (e.g., side effects, duration and intensity of APED use, or investment in future APED use) engages in the greatest degree of polypharmacy (i.e., using a higher number of drugs from a greater number of drug classes) with a pattern of body image disturbance characterized by desires for extreme leanness and simultaneous hyper-muscularity. This group is in contrast to a second group that uses primarily fat burning and weight loss drugs in order to be leaner (as opposed to more muscular). A third group uses primarily AASs with lower rates of fat burning or weight loss drugs in order to achieve hyper-muscularity. Finally, there is evidence of a large subgroup of APED users with low rates of polypharmacy and little evidence of body image disturbance. Interestingly, these patterns are consistent with the subgroups found among community samples of weightlifters that included APED users and non-users (Hildebrandt et al., 2006b), suggesting that these groups may be representative of different types of men more broadly engaged in shape and weight controlling behaviors.

5. Conclusions and Future Directions

5.1 Conclusions

The diagnostic dilemma of harmful APED use concerns the proper placement of APEDs in the greater landscape of psychopathology and the development of diagnostic criteria that are best suited for identifying this psychopathology. Currently, AASs are the only APED considered for a psychiatric diagnosis and most believe AAS misuse belongs to the SUDs (Kanayama et al., 2009a,b). This SUD classification comes with the challenge of applying the ADS symptom palette to the clinical phenomena of APED use. Unfortunately, this cluster of symptoms may not be an accurate or valid measure of pathological APED use,

failing to translate directly to the methods, motivations, or types of negative consequences experienced by APED users. Conservative attempts to reconcile this problem have led to a proposal to alter the existing criteria by incorporating body image disturbance, diet, and exercise into the drug dependence criteria. This alteration, however, represents a top-down approach in which the core features of APED use are obscured behind the continuity with the ADS symptom palette. This type of adaptation has also been used to classify a range of impulsive and compulsive behaviors as behavioral addictions (e.g., Allegre et al., 2006), it misses opportunities to identify the sources of dysregulation that cause the disorder, define the pathology, and provide the most clinically relevant information for a diagnostic system. In order for a diagnostic system to capture and define a valid diagnostic entity, a bottom-up approach must first identify key elements of risk and impairment. For APED use, these features include polypharmacy, body image disturbance, and disturbances in dieting and exercise. The identification of these core elements suggests that APED use is likely to be something other than a classic SUD.

5.2 Recommendations for Resolution to the Diagnostic Dilemma of APED Misuse

In order to resolve the misfit between APED use and classic drug dependence, there are at least three options. The first option includes the adjustments proposed by Kanayama et al., (2009, a, b), which position APED use as a SUD, but change the meaning and interpretation of the dependence criteria by referencing disturbances in body image, exercise, or dieting. This approach has some use of the key elements of APED pathology, but does not include polypharmacy, and remains committed to the ADS symptom palette. For this framework to remain valid the primary dysfunction for APED misuse has to be a dysregulation of the motivation-reward system and the data do not fully support this as the primary source of psychopathology. A second option would involve moving APED use into a section of *DSM* where body image disturbance, exercise, and dieting are central to the diagnosis; body dysmorphic disorder (BDD) and eating disorders are the best match. APED use has already been described in the context of BDD so this option has some appeal. For eating disorders, APED use could be considered a non-purging compensatory behavior. These options have the advantages of removing the focus from drug-based pathology and consequently eliminating the problems with defining drug tolerance, withdrawal, and the reliance on the hedonic properties of AASs to define dysfunction. However, neither diagnostic category provides for enough focus on the impairment that results from APED use and thus misses an opportunity to identify significant impairment. The most ambitious option includes separation of APED use from other diagnostic categories. As a unique disorder, APED misuse would have the flexibility to consider diagnostic criteria that are specific to the phenomenology of APED use and equally weigh the influence of drug use, body image disturbance, and problematic diet and exercise in making a diagnosis. Table 3 summarizes a proposed set of criteria using these three areas of impairment. The weighting of all three domains in the diagnostic framework provides a clear resolution to the diagnostic dilemma. Tolerance and withdrawal are eliminated, which leaves room for specific medical consequences such as ASIH to be considered a result of the disorder. The use of a broad APED diagnosis and inclusion of polypharmacy also allows for the diagnosis to remain stable as the drug market evolves. In addition, the formal introduction of body image, diet, and exercise allow for the identification of pathology even when an individual is between cycles or as his or her drug pattern changes. By not relying exclusively on drug-based impairment, the proposed criteria are more likely to capture pathology among individuals that use APEDs, and remain consistent with the empirical investigations into APED pathology.

5.3 Recommendations for Future Research

There are three methodological issues that must be addressed in order to resolve the diagnostic dilemma. First, the recruitment and sampling of APED users suffers from some logistical barriers. Many APED users find medical research to be stigmatizing and are distrustful of the academic and medical communities (Monaghan, 2002; Pope et al., 2004). These attitudes can prevent certain users from disclosing use when seeking treatment, and similarly prevent them from participating in APED research. Thus, there will likely be problems with sampling bias in most attempts to study human APED use unless these barriers are adequately addressed. Second, there is no standardization of assessment across research or clinical groups studying APED use. Without reliable and valid measures of APED use and related phenomena, it will be difficult to pool findings and ultimately understand APED use. Finally, the polypharmacy practiced by users introduces a significant amount of heterogeneity in terms of drug effects, risks, and impairment. These differences make it difficult to compare users to each other on relevant characteristics or to define syndromes or symptoms that rely heavily on a singular mechanism of action.

Beyond these methodological limitations there are three areas in which future research can provide the data necessary to improve diagnosis: (a) research for which human research is possible, (b) research for which human research is not possible, (c) research for which only human research can be used. The priorities for translational research that involves humans include the examination of neuropsychological, neuroendocrine, and behavioral outcomes as a function of APED use in controlled or observational research with APED users. This line of research should be able to identify whether internal mechanisms of dysregulation identified in pre-clinical studies are associated with risk and impairment. Pre-clinical research priorities include the examination of specific drug effects on internal mechanisms and the interaction between drug effects and behavior. For instance, delineating the role of exercise in the central effects of androgens would be a clear priority. This type of research should be able to explain why pathological APED use only occurs in the context of heavy exercise. Finally, human studies are needed to evaluate the psychometric properties of diagnostic criteria, predictive value of certain psychological features such as body image disturbance, and the role of psychiatric or personality comorbidity in longitudinal outcomes. This line of research should be able to provide a functional test of any diagnostic system developed. Furthermore, clinical response is often used in the validation of different diagnoses, and to date there are no published studies reporting on specific interventions developed for AAS dependence or other forms of APED misuse, although basic models for intervention have been suggested (Kanayama et al., 2010).

In conclusion, there are a number of research priorities for developing and validating a diagnostic system that captures those APED users with significant impairment and who suffer as a consequence of their APED use. These priorities span the resolution of existing methodological issues, the absence of certain types of human data, and animal models that can answer very specific questions about APED use. Significant progress in all three domains will be necessary as APED use continues to expand, evolve, and affect larger numbers of men and women. However, APED use remains a complex phenomenon that will require a specific set of diagnostic criteria to aid in the development of clinical interventions and understanding of the etiology, course, and outcome of APED use.

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Table 1

Examples of Appearance and Performance Enhancing Drugs

Drug Class	Primary Trade/Street Name(s)	Generic Name	Description and Function
Anabolic Androgenic Steroids	Anavar	Oxandrolone	Synthetic hormones derived from male teroids such as testosterone or nortestosterone designed to increase protein synthesis for muscle growth, along with enhancing the development and maintenance of male characteristics
	Androgel	Testosterone	
	Deca-Durabolin, “Deca”	Nandrolone Decanoate	
	Dianabol, “D-bol”	Methandrostenolone	
	Equipoise, “EQ”	Boldenone Undecylenate	
	Sustanon ‘250’	Testosterone propionate + testosterone phenylpropionate + testosterone isocaproate + testosterone decanoate	
	Testosterone cypionate	Testosterone cypionate	
	Trenbolone, “Tren-A,” “Fina”	Trenbalone acetate	
	Winstrol, “Winny,” “Win-V”	Stanozolol	
Non-Steroidal Anabolics	Human Growth Hormone, “HGH”	Somatropin	Pituitary (hGH) or pancreatic (insulin) hormones taken to increase muscle growth and restore youth
	Insulin, “Slin”	Insulin	
Cutting Drugs	Cytomel, “T-3”	Liothyronine	Synthetic thyroid hormones used to increase metabolism and reduce fat
	Synthroid, “T-4”	Levothyroxine	
Stimulants	Ephedrine	Ephedrine hydrochloride or Ephedrine sulfate	Central nervous system stimulants that increase metabolic rate through autonomic arousal
Ancillary Agents	Arimidex	Anastrozole	Function varies based on substance but sually targets some physiological process disrupted by training or concurrent drug use
	Clomid	Clomiphene citrate	
	Nolvadex, “Nolva”	Tamoxifen citrate	
	“HCG”	Human Chronionic Gonadatropin	
	Viagra	Sildenafil	
Supplements	Creatine	Creatine	Function varies based upon substance designed to increase an aspect of muscle development or recovery
	L-Carnitine	L-Carnitine	
	L-Glutamine	L-Glutamine	
	Protein powder (Whey, egg, soy rice)	Protein Powder	

Table 2

Summary of Descriptive Field Studies of Anabolic-Androgenic Steroid Use

Study	Sample	MS	AAS Amount in mg/week M (SD); Range	Cycle Length in weeks M (SD); Range	Co-Morbid Substance Use Disorder (%)	Non-steroidal APED use %[M (SD); Range]**
Pope and Katz (1988)	39 M, 2 W	IV	750‡ (n/a); n/a	n/a ;4–12	n/a	n/a
Pope et al. (1988)	17 M	AQ	n/a	18.7 (15.3); 5 –52	35% > 12 drinks/week 24% >100 times lifetime illicit drug use	n/a
Lindstrom et al. (1990)	53 M	AQ	n/a; 175–875	n/a; 4–12	n/a	28%*[n/a]
Lefavi et al. (1990)	31 M	AQ	550‡ (n/a); (n/a)	n/a	n/a	n/a
Perry et al. (1990)	20 M	IV	n/a†	n/a (n/a);2–68	45% Lifetime Achl Abuse/Depen 10% Lifetime Drug Abuse/Depen. 30.2% CAGE score positive (≥ 2)	n/a
Brower et al. (1991)	49 M	AQ	9.4–814.7 (4.0–1401); n/a	n/a	8.1% cocaine/amphetamine use	n/a [5.7(2.29); n/a]
Bahrke et al. (1992)	26 M	AQ	297.17 (61.74); 70–620	10.17 (2.15); n/a	n/a	n/a
Moss and Panzak, (1992)	25 M	AQ	436 ‡(n/a); n/a	n/a	n/a	n/a
Moss et al. (1993)	30 M	IV	459.67(n/a); n/a	n/a	n/a	n/a
Pope and Katz (1994)	88 M	IV	700 (n/a); (n/a)	n/a	33%	n/a
Malone et al. (1995)	77 M	IV	513‡ (n/a); (n/a)	n/a	1.3% Current Alchl Depen. 2.5% Current Drug Depen.* 10.4% Past Alchl Depen. 9% Past Drug Depen.*	n/a
Galligani et al. (1996)	30 M	IV	n/a; 175–1300	n/a	n/a	n/a
Evans (1997)	100 M	AQ	n/a (n/a);250–3200	n/a; 4–12	n/a	70%* [n/a]
Midgley et al. (2001)	50 M	IV	Avg. 103 doses/year	14.4 (n/a); n/a	n/a	n/a
Gruber and Pope (2000)	25 W	IV	n/a (n/a); n/a	n/a	24% Lifetime Alcohol/Drug Dependence	80%*[n/a]
Copeland et al. (2000)	94 M, 6 W	AQ	370.01 (n/a); n/a	n/a	n/a	n/a
Kanayama et al. (2003)	48 M	IV	n/a; n/a	n/a	44% Lifetime Alcohol/Drug Abuse/ Dependence	n/a
Perry et al. (2005)†	207 M	WS	825.70 (186.50);	5.9 oral, 9.1 injectible (n/a); 5–10	n/a	14.5%* [0.5 (0.9); 1–9] Non-Steroidal Ergogenic Agents

Study	Sample	MS	AAS Amount in mg/week M (SD); Range	Cycle Length in weeks M (SD); Range	Co-Morbid Substance Use Disorder (%)	Non-steroidal APED use %[M (SD); Range]**
						60.86%*[n/a] Dietary Supplements 25%[n/a] Ephedrine Products
Striegel et al. (2006)	84 M/W	AQ	n/a	n/a	n/a	44%[n/a]
Pagonis e al. (2006)	160 M/W	n/a	n/a†	9.4 (n/a); 6–12	n/a	n/a
Parkinson and Evans, (2006)	500 M	WS	n/a ;70–6000	n/a; 4–20	n/a	96%[n/a]
Cohen et al. (2007)	1955 M	WS	500–1000 (n/a); <200 – 10,000	11 median (n/a); 1–728	n/a	49.5%*[n/a] Non-steroidal Erogenic Agents 65.3%*[n/a] Ancillary agents
Hildebrandt et al. (2007)	400 M	WS	1250–1500 (n/a); 250–3000	13.9 (10.9); 7–48	n/a	62.6% [n/a]
**Kanayama et al., (2009)	62 M	IV	1101.68 (739.06); n/a	n/a	21% Lifetime Alchl Depen. 54.5% Lifetime Drug Depen.	33.9% [n/a]

Note.

*Denotes minimum possible percentage.

**Denotes descriptive statistics for number of non-steroidal APEDs endorsed by sample.

‡means taken from Pope et al, 1994.

†study reports information for each drug and overall means could not be calculated. M = mean. SD = standard deviation. % = percentage of individuals endorsing use of any substance in drug category. MS = Measure. IV = Interview. AQ = Anonymous Questionnaire. WS = Web based survey. n/a = not available from published article.

Table 3

Suggested Criteria for Defining an Appearance and Performance Enhancing Drug Use Disorder

A). Recurrent pattern of polydrug use aimed to alter one's appearance or affect one's performance that leads to significant harm or dysfunction marked by at least three of the following:

a1) Significant degree of polypharmacy (e.g., >5 substances) which includes substances from multiple drug classes including but not limited to:

- Anabolic-androgenic steroids
- Central Nervous Stimulants (ephedra, mau huang, caffeine, etc.)
- Metabolic Hormones (e.g., T3, T4, Insulin)
- Non-steroidal Anabolic Hormones (HGH, Insulin-like Growth factor, etc.)
- Eurethropotetics (e.g., EPO)
- Pain Killers/Anti-inflammatory (oxycodone, etc.).

a2) Recurrent problems in occupational or related areas of functioning brought on by APED use

-- Recurrent trouble maintaining employment or fulfilling expectations of work, school, or similar environment; may manifest by increased conflict with coworkers or ability to follow rules or keep deadlines.

a3) Recurrent impulsive behavior brought on or exacerbated by APED use

-- increases in unprotected sex, sexual assault, concurrent drug use, impulsive aggression, etc.

-- must occur only in the context of APED use or be significantly increased using the drug.

a4) Recurrent problems in interpersonal functioning brought on or exacerbated by APED use

-- Fights with spouses or partners caused by or exacerbated by APED use

a5) Use of ancillary drugs for the purpose(s) of

1. Increasing the amount, duration, or intensity of an APED cycle or
2. Pattern of APED use is unlikely to be tolerated without the use of ancillary drugs.

a6) Repeated unsuccessful attempts to cut down or quit APED use

-- Planned cycles persist past determined end date due to concerns about changes or dissatisfaction with cycle effects

a7) Pattern of continuous or almost continuous APED use.

-- APED use lasts > 8 months and/or cycles are "bridged" with lower doses of used between cycles.

-- Amounts must be intended to elevate levels of testosterone above normal body production for age, weight, and size.

a8) Continued use despite knowledge of recurrent or persistent physical or psychological problems that are brought about by APED use.

-- cardiomiopathy, dyslipidemia, excessive bone growth, gynecomastia

-- Depression, labile mood, irritability, aggressiveness, impulsivity

B). Significant Disturbance in the Experience of One's Outward Appearance or Ability to Perform marked by at least three of the following criteria

b1) Primary Investment in one's outward appearance, composition of one's body, or ability to perform in athletic and/or similar contexts (e.g., fighting, sex, school) at the expense of social, occupational, or educational functioning.

b2) Compulsive, ritualized, or critical body evaluation that leads to significant distress or takes up a significant amount of amount of time, energy, or effort in one's daily life.

b3) Behavioral avoidance or experience of significant distress in situations where one's body is exposed or performance is evaluated by others.

b4) Unrealistic standards for one's outward appearance or physical performance such that these goals are likely unattainable without use of APEDs.

b5) Primary distortions in the perception of one's own body such that the individual views him/herself significantly different than he/she actually appears. (e.g., perceived as very fat when at a low body fat percentage, perceived as very weak when hypermuscular).

b6) Post-cycle changes in appearance or performance lead to significant distress.

C). Pattern of Diet and/or Exercise that causes significant distress or leads to impairment in social, occupational, or physical functioning as evidenced at least two of the following

c1) Strict adherence to rigid rules around dieting or exercise leading to distress or impairment

-- Difficulty deviating from planned or expected patterns, type, or quality of exercise or dietary control

c2) Compulsive or ritualized exercise patterns resulting in significant distress or takes up a significant amount of time, energy, or effort in one's daily life.

-- Exercise used to reduce acute anxiety about one's appearance or ability to perform

-- Feeling compelled to exercise or control diet

c3) Continued exercise or dietary control despite physical or psychological problems

-- E.g., Lifting weights with torn tendon or muscle or extreme caloric restriction to cut weight resulting in increased anxiety, distress, or physical consequences such as severe dehydration

c4) Preoccupation with diet or exercise patterns leading to distress or impairment

-- unwanted, intrusive, or uncontrollable thinking about exercise and diet or their effects

c5) Changes to diet or reduction in intensity or duration of exercise lead to distress or impairment

-- Reduction in exercise results in depressed mood, irritability, or psychomotor agitation

-- Deviations from diet lead to significant distress, for example eating a candy bar

c6) Recurrent instances where exercise persists longer than intended or is experienced as difficult to control

-- Workouts regularly last longer than intended or one feels that once they start exercising they have difficult stopping on their own

Note. A diagnosis of an APED Disorder is made when two criteria (A + either B or C) are met.