

Managing Prader-Willi Syndrome: A Primer for Psychiatrists

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I Heterogeneity of PWS

PWS results from the deletion of paternally derived genetic material from the region of chromosome 15q11-q13. Selected genes in the PWS region are *imprinted*, that is they carry a marker indicating the parental chromosome of origin. Imprinted genes are always switched on; the corresponding genes from the other parent are switched off. In the majority of cases, PWS genotype results from the loss of paternally imprinted genes either through *deletion*, *maternal uniparental disomy*, or *imprinting center mutation*. Among the genotypes, the deletion condition is roughly three times more common than the disomy condition and a deletion of the imprinting center or other mutations are much less common. Although the fundamental defect is not known, all individuals with PWS experience variable degrees of hypothalamic dysfunction resulting in dysregulation of growth, muscle tone, sexual maturation, temperature, appetite/satiety, respiratory drive, sleep/wake cycle, pain awareness (sensitivity/localization), and stress response. However, CNS dysfunction is not limited to the hypothalamus; both research and symptoms point to a more diffuse cerebral localization.

II Developmental Manifestations

Neonates with PWS display marked hypotonia; they have a weak cry and poor suck. Feeding disturbances leading to failure to thrive are common among infants. As toddlers, they display global developmental delays. In the preschool years or later, interest in food increases and weight gain begins. Temper tantrums emerge later than in typical children and can be severe and sustained. Learning problems become evident at school age; phonological abnormalities, arithmetic disability and motor coordination problems are common. Most children display mild intellectual deficiency. Deficits in social adaptation become apparent by middle school. Supervision is needed for even the brightest individuals with PWS. Prospects for gainful employment and independent living are poor. The goal in adulthood is maximal function with support. A major cause of psychiatric/behavioral crises in adulthood is the withdrawal of supports from an adult with PWS who has been functioning well with support. Because judgment is impaired at any age regardless of intellectual potential, guardianship is recommended for all matters related to food, medical care, money management, hygiene, and living arrangements.

III The PWS PERSONALITY

Among individuals with PWS, some temperamental and behavioral characteristics are so commonly present that they are considered to be part of the **behavioral phenotype**. These features are the “background noise” when considering psychiatric diagnoses in patients with PWS; changes in the severity of these symptoms are clues to changes in mental status, mood, and/or behavior. All of *the characteristics of this phenotype can become exaggerated with stress*.

The behavioral phenotype of PWS defines the PWS PERSONALITY; it corresponds to the DSM IV Axis I Diagnosis of *Personality Change Due To A Medical Condition (310.1)*. There are five domains of psychiatric/behavioral symptoms in the PWS PERSONALITY: food related behaviors, oppositional defiant behaviors, cognitive rigidity/inflexibility, anxiety/insecurity, and skin picking.

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PWS PERSONALITY: FIVE DOMAINS of PSYCHIATRIC/BEHAVIORAL SYMPTOMS

Food related behaviors:

- overeating of typical food
- eating atypical food (frozen, raw, spoiled food or pet food)
- sneaking food in the home
- night time foraging in the home
- arguing or manipulating to get food
- tantrumming to get food
- opportunistic food theft (shoplifting from a store or stealing food from school or work)
- planned food foraging expeditions in the neighborhood or community
- nonconfrontational, invasive food access (breaking locks on cabinets, refrigerator or freezer, trespassing)
- confrontational food access (using verbal or physical threats or actual aggression to access food)

Oppositional defiance:

- noncompliance
- argumentativeness
- tantrums/shut downs
- manipulation
- lying/confabulation

Anxiety/insecurity:

- stress sensitivity
- inability to tolerate uncertainty
- somatic complaints
- dependency
- constant need for reassurance
- collecting and hoarding
- affective reactivity

Skin picking (common, but not universal):

- habit behavior
 - opportunistic typography:
 - arms, face and scalp
 - nasal septum
 - pulling out toenails, teeth
 - peeling skin from soles of feet
- Intense, severe, reactive
 - gouging
- related to chronic stress
 - rectum and/or vagina

Cognitive rigidity/inflexibility:

- perseveration, "sticky thinking"
- difficulty with transitions or changes
- rituals
- selective interests (jig saw puzzles, word searches)
- impaired judgment
- single mindedness, difficulty taking multiple view points
- egocentrism

IV Psychiatric Evaluation

Obtaining an adequate database: Because psychiatric evaluation is most likely to occur after a behavioral crisis, much of the history of the presenting problem will be obtained from other informants. Past medical and psychiatric history should be obtained from a family member or designee; group home, workshop or school personnel accompanying the individual may not have the breadth of information essential for a thorough assessment.

Taking a transactional history: Because of the patient's dependence on the environment, a transactional history is optimal for elucidating the nature, severity and duration of psychiatric symptoms juxtaposed with environmental changes or responses. This provides the best opportunity to explore the precipitating and perpetuating factors essential to the case formulation. Predisposing medical factors (genotype, complications of obesity, status of hormone therapy or other medical interventions) and familial factors (family psychiatric history or history of family dysfunction) are essential. Protective factors

are equally as important; knowing the conditions under which the patient has displayed the highest level of functioning will help to determine the amount of structure needed to achieve maximal function with support.

Using a semi-structured interview format: The patient interview can be a rich source of clinical information if the following limitations are understood: 1) The individual with PWS may present with a language disorder limiting receptive ability or expressive ability; 2) Intellectual deficiency, concrete thinking, and cognitive inflexibility will affect the response to the questions asked; 3) Numerical reasoning, time concepts and spatial reasoning abilities may be poorer than expected by the verbal ability demonstrated; 4) Recall of a situation will be from the point of view of the individual only; and 5) Insight is variable, but judgment and problem solving are always impaired. 6) Lying and confabulation are commonly observed [See page 5, Factitious disorder]. Because of these factors, individuals with PWS are considered to be poor historians and they are rarely competent to consent for medical treatment, regardless of level of intellectual ability.

The style of the patient interview determines the validity of the clinical data obtained. An overly structured interview is likely to lead to false positives or false negatives. An open-ended interview will not obtain the breadth of information required. A semi-structured format works optimally because it provides contextual cues together with the opportunity to pursue pertinent responses. When possible, questions should be asked in a developmentally appropriate way. Individuals with PWS tend to be suggestible, so assessing both the internal validity of the symptoms presented and obtaining external validation is necessary. Ascertaining level of impairment caused by symptoms is essential to making an accurate diagnosis. Inquiry about mood state is essential in the PWS patient, but vegetative symptoms pertaining to sleep and appetite are less reliable than changes in interest or personal care. Use of quantitative scales to assess symptom severity should be avoided unless the scales are behaviorally defined and other qualified informants verify the responses.

V Psychiatric Co-morbidity

The following psychiatric disorders appear to occur with increased frequency in persons with PWS:

- **Sleep Disorders**

PWS predisposes to sleep abnormalities including sleep disordered breathing, daytime somnolence and narcolepsy. Obstructive sleep apnea emerging during the developmental years may require consultation. Untreated, obesity-related breathing abnormalities are the primary cause of death. Evaluation of obesity-hypoventilation requires sleep studies, and external positive ventilation during sleep may be prescribed. Exercise and weight loss are the definitive treatment.

Daytime somnolence is fairly common across all ages; it is present among individuals of normal weight as well as the obese. Occasionally, individuals with PWS present with the classic narcolepsy triad of daytime sleepiness, cataplexy and sleep paralysis (including hypnagogic and hypnopompic hallucinations); it responds to the typical pharmacological treatment interventions.

- **Disorders of Elimination**

Bedwetting and fecal incontinence occur while awake and appear to be related to an indifference to being wet or soiled; this is a common occurrence *at any age* and may be worsened by obesity.

- **ADD and ADHD**

Inattention, distractibility and impulsivity can emerge during the developmental period. Standard assessment tools may miss these symptoms because of low motor activity due to hypotonia and morbid obesity. Nocturnal hypoxia due to sleep related hypoventilation with or without obstructive sleep apnea must be considered in the differential when ADD symptoms present in the obese child or adolescent.

ADD and ADHD occurring in individuals with PWS respond to the typical treatment package of behavioral, educational, and psychostimulant interventions.

- **Disruptive Behavior Disorders**

Although argumentativeness, noncompliance and tantrums are part of the PWS PERSONALITY profile, the intensity may warrant a separate diagnosis, especially during the developmental period. Symptoms of theft, predatory aggression, property destruction, running away, fire setting and cruelty to animals indicate the presence of a conduct disorder. Behavioral and eco-environmental interventions are essential, and placement in a facility specializing in the management of PWS may be the only way to achieve the environmental control required to manage these symptoms. Psychotropic medications may be useful to alter the threshold for expression of symptoms of impulsivity and anger.

- **Anxiety Disorders**

Generalized anxiety, separation anxiety and social anxiety can occur and respond to typical psychological behavioral and psychopharmacological interventions.

- **Obsessive Compulsive Disorder**

Although cognitive rigidity, need for structure and routine, collecting and hoarding, and rituals commonly occur, individuals with PWS are rarely bothered by these traits and clinical experience suggests that they don't experience disgust. OCD symptoms of ordering, counting and hygiene compulsions are infrequent. If symptoms are severe enough to warrant a diagnosis of OCD, environmental interventions are likely to be required to augment cognitive behavioral treatment. Pharmacological management with SRIs can be considered, but the possibility of behavioral disinhibition and mood activation must be kept in mind.

- **Dysthymia and Depression**

Dysthymia and depression occur in response to life stress such as separation events occurring across the developmental years. Low self-esteem may occur as the individual reaches adolescence. Short stature, obesity, delayed puberty, social skills deficits, and continual conflicts over food and exercise create stress and conflict with little opportunity for mastery. Separation/individuation issues are again challenged as the individual with PWS enters young adulthood when job/workshop opportunities and degrees of freedom in the community are limited due to the constant need for structure, supervision and control over food access. Psychological interventions can improve the quality of life experience of high functioning individuals with the syndrome. Antidepressant medications can be very helpful, but the dose must be titrated slowly and well monitored due to the risk of mood activation.

- **Bipolar Mood Disorder**

The incidence of all types of this disorder appears to be higher than expected and may indicate a predisposition among persons with PWS. Individuals with the disomy condition may be more vulnerable to bipolar I disorder, and the incidence may increase with advancing age. As previously noted depression is fairly common, and mood activation with antidepressants may be the first indication of a cycling disorder. Bipolar I and Bipolar II disorders have been identified across the developmental spectrum. Onset may be as early as the first decade. Symptoms have ranged from frank bipolar illness with psychotic depression or mania to nonpsychotic manifestations with chronic irritability and mood lability. Some patients demonstrate rapid cycling. Younger children may present with intense disruptive behavior and mood irritability. Juvenile mania should also be suspected if there is a poor therapeutic response to environmental or behavioral interventions, or if behavioral disinhibition occurs with stimulants. Psychotic symptoms are frequent and must be evaluated with the developmental age of the individual in mind. Mood stabilizers can be very helpful at standard doses. Atypical neuroleptics may augment therapeutic efficacy especially if psychotic symptoms are present.

- **Psychosis**

There is an increased incidence of psychosis in PWS. However most cases appear to be a manifestation of an underlying cyclic mood disorder. Onset may occur in childhood and is usually recognized in the context of a major stressor precipitating a behavioral change. Some patients may not be able to articulate delusional thinking nor report hallucinations. Stress appears to play a role in the etiology of these symptoms; some patients have been psychotic during a grief reaction or other major stressor, and symptoms have subsequently remitted when the environment has stabilized.

The incidence of this schizophrenia does not appear to be increased in PWS.

- **Developmental Learning Disorders**

Although the distribution of intellectual ability follows a normal curve, the majority of individuals with PWS have mild mental retardation. A wide variability has been noted in learning styles, language skills, visual perceptual skills and nonverbal problem solving ability. Articulation disorder and verbal dysfluencies are common in children and often persist into adulthood. Although puzzle-solving abilities tend to be well developed among many children with PWS, nonverbal learning deficits are seen such as pragmatic language deficits, dysgraphia and dyscalculia. Difficulties “reading” social situations may be a source of behavioral problems in otherwise high functioning individuals.

- **Autistic Spectrum Disorders**

To the inexperienced clinician, individuals with PWS may appear to meet criteria for pervasive developmental disorders because of restricted interests (at times reaching savant skills), social communication problems, and cognitive rigidity. Hypotonia may result in motor clumsiness. Although they may have pragmatic language deficits, perseverative thinking, and even stereotypies, they possess social interest, a desire to “fit in” and preserved theory of mind capacity that is essential to the ability to be clever at food acquisition, manipulation and lying.

- **Impulse Control Disorder**

Serious assault and destructive acts perpetrated by individuals with PWS are the exception. As defined, the degree of aggression is out of proportion to the precipitating event. The event can be followed by the appearance of fatigue and contrition, or the individual might argue adamantly that the behavior was justified.

- **Impulse Control Disorder, NOS**

This is the appropriate diagnosis for patients in whom the skin picking behavior is severe and has resulted in medical complications. Specially designed behavioral programs may be required to interrupt the cycle of picking, and mechanical barriers as well as topical medicinal treatment may be required.

- **Factitious Disorder**

Patients with PWS typically lie to get out of trouble. They lie to manipulate others (for food) and some are creative prevaricators. They are capable of confabulating allegations of abuse, claims of romantic entanglements, and calling 911 with false reports with astounding believability! Some individuals have fabricated circumstances in order to obtain admission to hospital. Despite general noncompliance, they derive satisfaction from being the subject of medical procedures. Similarly they have medication seeking behaviors that are not related to drug abuse. Persons with PWS can also be very resistant to changes in medication regimen. They may complain of pain to avoid work or exercise; at the same injuries can be missed because of abnormal pain awareness. Any review of systems for medical differential must be

conducted in an indirect fashion with corroboration by outside sources to maximize accuracy and to minimize false positives on exam. Massive denial about personal limitations and responsibility for one's actions sometimes borders on the delusional.

VI Management

• Environmental Control

The core symptoms of PWS Personality are managed through an environmental program called *The Basic Plan* that consists of *The Daily Schedule*, *Food Security*, and *Mandatory Exercise*. Oppositional defiant behaviors are managed through the use of behavioral interventions that are added to The Basic Plan in a gradient of intensity to address the level of severity of disruptive behaviors.

The Daily Schedule is a linear arrangement of daily activities including ADLs, mealtimes, exercise, work/school activities, chores, rest and leisure time. It addresses many of the syndromic behaviors related to cognitive rigidity and stress sensitivity. The Daily Schedule is always posted; this helps to achieve the process of *flow* through the day.

FOOD SECURITY is the other essential ingredient for managing the food related behaviors associated with the syndrome. FOOD SECURITY has been defined as *the ready availability of nutritionally adequate and safe foods with an assured ability to acquire acceptable foods in socially acceptable ways*. In PWS, FOOD SECURITY provides **no doubt** when meals will occur and what will be served; **no hope** of getting anything different from what has been planned, and **no disappointment** related to false expectations. FOOD SECURITY is achieved by securing food access across all environments, supervising food access across all environments, posting mealtimes and menus, and training all team members. When the individual with PWS is experiencing FOOD SECURITY, that is, **no doubt**, **no hope** and **no disappointment** related to food, a generalized behavioral improvement typically occurs. For this reason, FOOD SECURITY *is the mainstay of PWS management before considering the implementation of behavioral interventions and pharmacotherapy*.

• Behavioral Interventions

Behavioral management strategies are an essential tool for a successful treatment plan. Non-contingent reinforcement (NCR) is the delivery of reinforcement independent of an individual's response. It is a powerful tool for establishing rapport. Contingent reinforcement is the delivery of reinforcement dependent upon the individual's response. It is a powerful tool for shaping appropriate behaviors. Extinction, selective attention, praise, and differential reinforcement of other behaviors are examples of contingent reinforcement. Praise is afforded to all appropriate behaviors, especially those facilitating daily transitions such as the timely completion of ADLs, grooming, exercise effort, social skills, following rules and directives, and working toward treatment goals. A token economy works well as a structured system for delivering contingent response. For symptoms of disruptive behavior disorder in PWS, a response cost intervention is recommended. It will be necessary to post the rules and expectations; delineate rewards (tokens) for achieving expectations, and define the cost or loss of rewards (tokens) for not achieving the desired results.

Skin picking is not a manifestation of OCD and does not respond to SRIs. Topiramate and naltrexone have been reported to be useful in some cases. Even when picking is severe, the behavior has been known to resolve spontaneously; in other cases it may last for years with or without serious medical complications. Behavioral programs can "backfire" if they draw increased attention to the behavior. Rewards for "not picking" are generally ineffective. Patients have been motivated to allow a picked lesion to heal when a special reward has been negotiated. Extinction is used to manage stereotypic skin picking through two venues: 1) low attention, and 2) mechanical barriers that interrupt the behavior. Low attention is directed to skin picking behavior unless clean up is required; even medical attention should be provided with minimal emotional response. For persistent open wounds requiring medical attention, mechanical barriers (bandages) or chemical barriers (polysporin ointment) work well to interrupt the behavior so that

healing can occur. Some patients require mechanical barriers and the frequent (hourly if necessary) application of a greasy antibiotic ointment that reduces the ability to pick effectively. Fingernails should be kept short. Patients also respond to rewards contingent upon cooperating with protective bandages or wearing nighttime mittens. One patient achieved rapid healing by wearing support pantyhose to protect lower leg lesions. Other patients have torn through plaster casts in order to pick. Supervision and environmental controls are essential to reduce the amount of tissue damage even though the behavior is likely to continue. Sensory integration programs have been tried with a favorable response if the stimulus can be delivered with high frequency.

Rectal or vaginal picking is a nonspecific stress symptom; it is not a symptom of hypersexual behavior or sexual abuse. It improves with management of environmental stress, treatment of other psychiatric symptoms or decreased interpersonal conflict. Unnecessary medical procedures investigating the cause of rectal or vaginal bleeding can result when this behavior is not recognized.

- **Psychological Therapies:**

The utility and effectiveness of psychological interventions is based entirely upon the individual's verbal and intellectual abilities. High functioning individuals with PWS grieve the loss of a "normal" life. They realize that their potential for independence is limited, and that many life goals shared with typical peers may never be actualized. Social and family situations which are usually joyful such as graduations, marriages and births, may be reminders of unachievable milestones for the high functioning individual with PWS and precipitate dysphoric responses. These situational crises can be addressed through psychotherapy with the individual and family.

For lower functioning individuals who have minimal insight, individual therapy should be supportive and focused on "here and now" issues e.g. how to minimize stress, enhance coping abilities, and improve participation and compliance with daily programming. Strategies and modalities for relaxation (progressive muscle relaxation, deep breathing, and visual imaging), anger management, social problem solving and social skills training may be prescribed, taught to the individual with repetition and drill, woven into the fabric of The Basic Plan, and implemented with prompts, cues and supervision.

- **Psychotropic Medications:**

Medication management in the absence of environmental interventions is likely to be ineffective. The choice of psychotropic medication is the same as in typical patients; it is *driven by psychiatric diagnosis not by PWS diagnosis*. There is no "Prader-Willi pill." As in the general population, medication response is individually based. Because many individuals with PWS never achieve pubertal status, their metabolism may remain at prepubertal levels. Consider this fact when prescribing doses and schedule of administration.

Attempts to suppress appetite with medication have been unsuccessful. Iatrogenic appetite stimulation from medication is not a problem for PWS patients living in a setting where food is controlled. When The Basic Plan is implemented, the neuroleptics, atypical neuroleptics, valproic acid, and lithium have all been used effectively without a discernible change in food-seeking behavior.

SRI have induced mood activation in a number of patients causing worsening of behavioral dyscontrol and even psychosis in vulnerable patients. These adverse effects may appear after an initial good response to the SRI causing physicians to *increase* the dose rather than recognize a treatment emergent effect. Other patients have had depression or true OCD symptoms effectively treated by this class of medication without complication.

Mood stabilizers have been used successfully for treating mood disorders and severe impulse control disorders. Valproate and lithium are well tolerated at typical doses. Carbamazepine and oxcarbazepine must be used with care because of the increased risk for hyponatremia. Patients with PWS will sometimes ingest large amounts of flavored beverages (including non calorie beverages) or even water;

they are more susceptible to hyponatremia than non-PWS individuals. Low dose topiramate has been used for skin picking. Higher doses that are typically used for mood and impulse control disorders have been associated with renal tubular acidosis which leaches calcium, further exacerbating a predilection for osteoporosis among persons with PWS. Atypical neuroleptics must be used with caution. They have been used effectively to manage psychosis, severe impulse control problems and manifestations of bipolar mood disorder. However, the low muscle mass and hypotonia in PWS makes EPS symptoms subtler to detect. Shuffling gait, loss of associated arm swing and decreased affective modulation are frequently observed EPS symptoms without signs of increased tone, cogwheeling or tremor. Although neuroleptic malignant syndrome has not been reported to date, body temperature is not a reliable assessment tool in PWS due to hypothalamic abnormalities. The increased risk for hyponatremia has already been noted.

Global Assessment of Functioning (GAF) Scale for PWS

Code

- 100 Superior functioning in a wide range of activities; life's problems never get out of hand;
 I sought out by others because of many positive qualities; no symptoms.
 91
- 90 Absent or minimal symptoms; good functioning in all areas; interested and involved in
 I a wide range of activities; socially effective; satisfied with life; no more than everyday
 81 problems or concerns.
- 80 If symptoms are present, they are transient and expectable reactions to psychosocial
 I stress; no more than slight impairment in social, occupational or school function.
 71
- 70 Some mild symptoms (e.g., depressed mood, mild insomnia, daytime sleepiness) OR
 I some difficulty in social, occupational, or school function (e.g., difficulty with transitions;
 61 argumentative, theft within the household), but has meaningful interests and activities.
- 60 Moderate symptoms (e.g., labile affect, circumstantial speech, temper tantrums) OR
 I moderate difficulty in social, occupational or school function (e.g., noncompliance,
 51 shutdowns, bully or victim, collects and hoards, lies or barter for food).
- 50 Serious symptoms (e.g., suicidal ideas, cognitive rigidity and tantrums, steals food
 I outside the home) OR serious impairment in social, occupational or school function
 41 (e.g., low intensity picks, tantrums with aggressive and destructive behavior).
- 40 Some impairment in reality testing or communication (e.g., tells whoppers, grandiose
 I ideas, dials 911) OR major impairment in several areas such as school, family, work
 31 (e.g., injures small animals, picks require medical attention, constant supervision).
- 30 Behavior is influenced by delusions or hallucinations or serious impairment in
 I communication or judgment (e.g., erotomanic attachments, outrageous behavior,
 21 stays in bed all day, runs away, takes car for joy ride, suspended from school).
- 20 Some danger to self or others (e.g., attacks self or others with knives or scissors,
 I rectal picking, confrontational food theft, foraging causes massive weight gain) OR
 11 poor hygiene (e.g., smears feces, soils and urinates inappropriately) OR confusion.
- 10 Persistent danger of hurting self or others (e.g., severe skin picks, property destruction,
 I arrest, suicidal behavior, homicidal behavior, fire setting) OR inability to care for self
 1 (e.g., stays in bed, urinates and soils bed, refuses meals, requires constant care.)

FOOD SECURITY for PWS

Food insecurity contributes to over eating, poor nutrition and obesity. **FOOD SECURITY** is defined as *the ready availability of nutritionally adequate and safe foods with an assured ability to acquire acceptable foods in socially acceptable ways*. The principles of **FOOD SECURITY** are:

- **No doubt** when meals will occur and what foods will be served.
- **No hope** of getting anything different from what is planned.
- **No disappointment** related to false expectations.

Here are some ways to achieve FOOD SECURITY:

1) Secure food accessibility across *all* settings by:

- a) Controlled access to:
 - i) Refrigerator, freezer and pantry
 - ii) Vending machines
 - iii) Money

- b) Avoiding any spontaneity related to food
- c) No snacks on demand
- d) No food left out
- e) No “free” foods or beverages
- f) Absolute portion control
- g) Pre-packaged condiments

Have a Plan

A person who needs food security should never enter a “food situation” without knowing what the plan is for maintaining his or her dietary needs.

Some individuals need all of these measures; others only some.

2) Supervise food exposure:

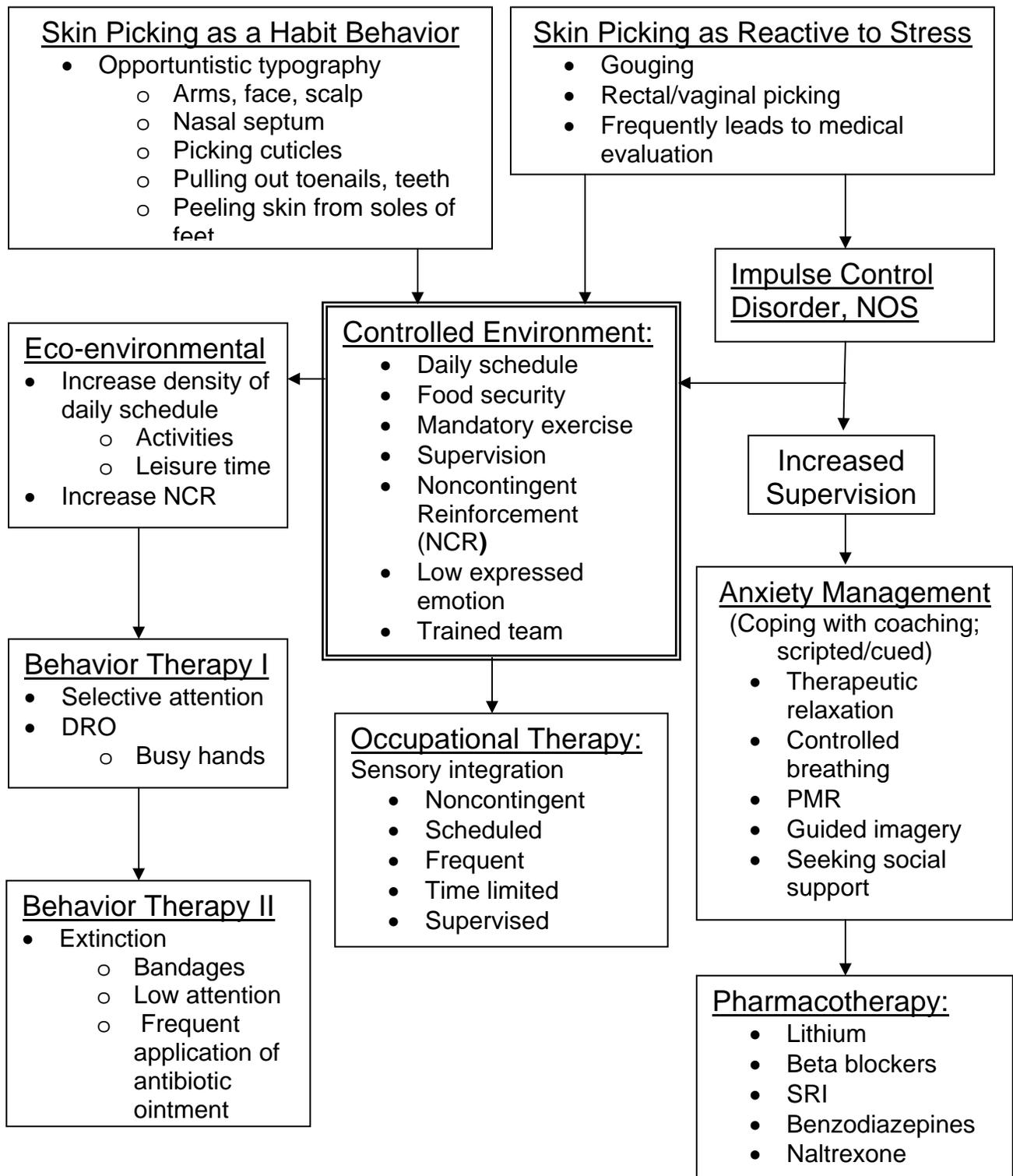
- a) At stores
- b) During food preparation and mealtime
- c) During special occasions (birthday parties, seasonal celebrations, etc.)
- d) When dining out in the community...
 - i) Access menus from restaurants in advance and decide what will be ordered.
 - ii) In general, buffets are understood to be “off limits?” Or, if unavoidable, it is understood that the plate will be prepared by someone else.

3) Post the schedule for mealtimes and snacks.

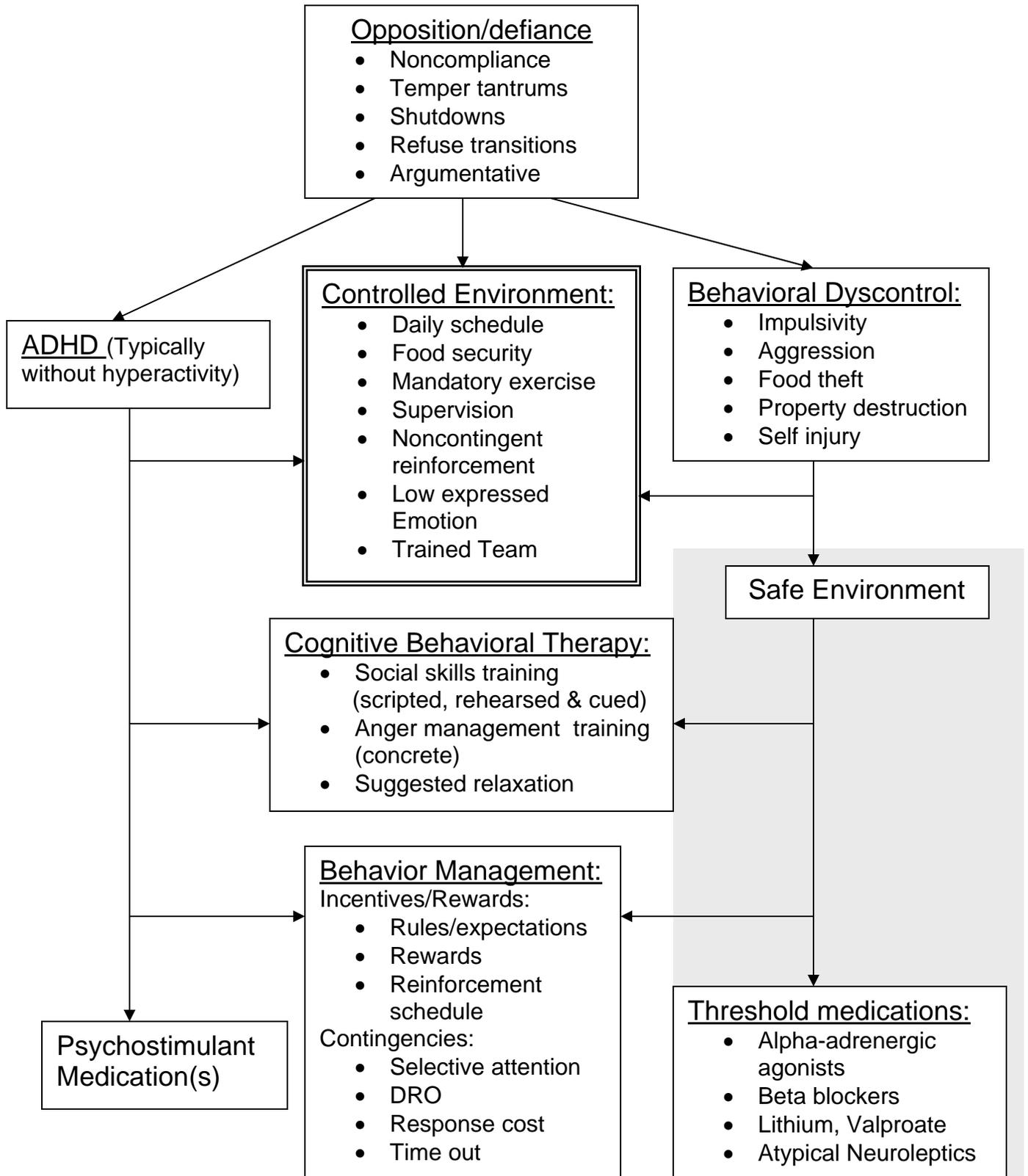
4) Post the schedule and the menus for meals and snacks.

5) If necessary, because of raised expectations or anxiety, avoid places and social situations associated with excess food

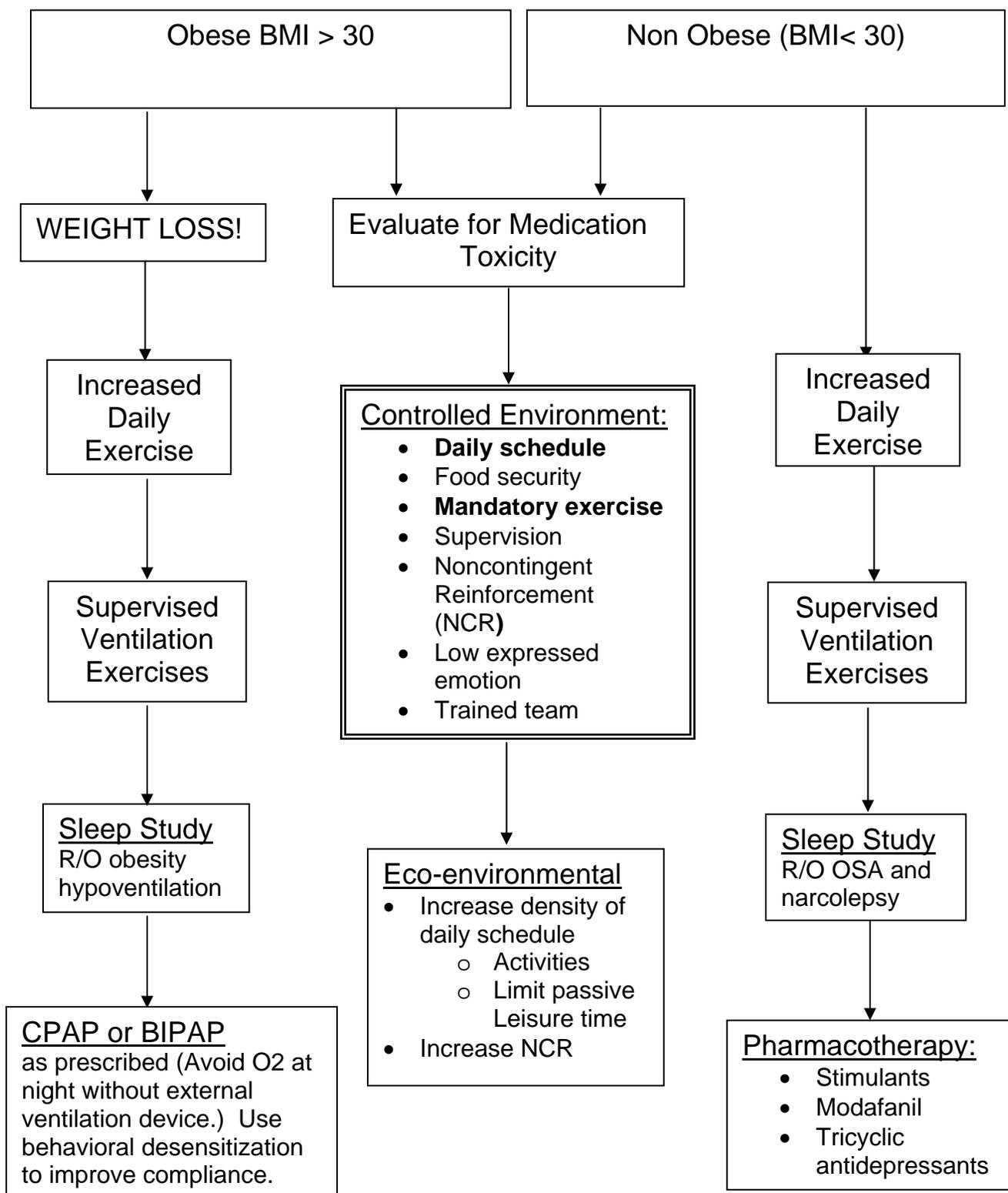
PWS CORE Symptoms: Skin Picking



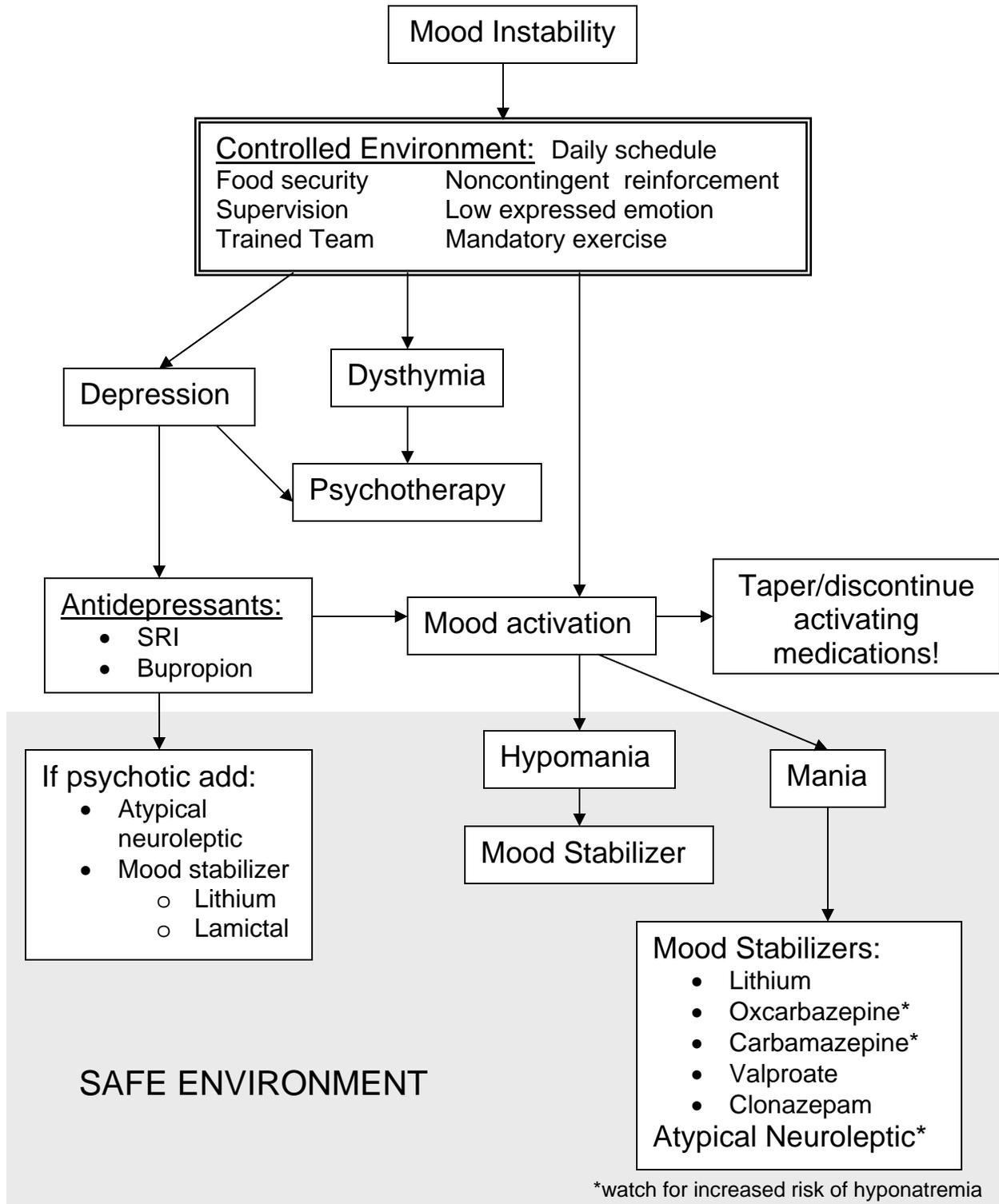
PWS CORE Symptom: Disruptive Behavior



PWS CORE Symptom: Excessive Daytime Sleepiness



PWS CORE Symptom: Mood Instability



PWS CORE Symptoms: Cognitive Rigidity & Anxiety

