

# Behavioral addictions: a novel challenge for psychopharmacology

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Although addictive syndromes have been traditionally related to substance-use disorders, during the last few decades a novel addictive group, including the so-called “behavioral or no-drug addictions,” has been recognized and has attracted increasing attention for its relevant social impact. This group includes pathological gambling, compulsive shopping, TV/Internet/social network/videogame addictions, workaholism, sex and relationship addictions, orthorexia, and overtraining syndrome. Substance and behavioral addictions show similar phenomenological features, such as craving, dependence, tolerance, and abstinence, and perhaps they share a common possible pathophysiology. It is, however, controversial whether all or at least some of them should be considered real disorders or just normal, albeit extreme, behaviors. The aim of this article is to review current data on pharmacological treatment of behavioral addictions. As no specific and validated treatment algorithms are currently available, only an improved knowledge on their psychopathological, clinical, and neurobiological features may have relevant implications for more focused preventive and therapeutic strategies.

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## Clinical Implications

- A novel addictive syndrome, the so-called ‘behavioral or no-drug addictions,’ is gaining attention and is becoming a social problem.
- The behavioral addictions share with classical substance-use disorders craving, dependence, tolerance, and abstinence, and perhaps a common pathophysiology.
- The pharmacological treatment of the majority of behavioral addictions is empirical, as no specific treatment guideline is available.
- A deeper understanding of their psychopathological and clinical characteristics should lead to more focused preventive and therapeutic strategies.

## Introduction

According to the World Health Organization,<sup>1</sup> pathological addiction is the psychic, and sometimes even physical, condition arising from the interaction between a living organism and an exogenous substance, characterized by behavioral responses and other reactions that always include a compulsive need to take the substance continuously or periodically, in order to get its psychic effects and/or to avoid the distress related to its withdrawal.

Although the different editions of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) and the *International Classification of Diseases*, 10th edition (ICD-10)<sup>1</sup> continue to propose a notion of “addiction” referred to exclusively to the intake of substances with psychotropic activity, this notion is increasingly used also in the classification of syndromic entities arising from the development of addictive behaviors developing in the absence of substance intake.

The DSM system has long avoided the term “addiction,” while preferring to apply the terms “substance use” and “dependence.” According to its 4th edition (DSM-IV),<sup>2</sup>

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substance abuse refers to a repeated drug use, with a significant impairment of work, school, and social life. On the other hand, the definition of “addiction” relates to that of “drug dependence”: a relevant amount of time spent to obtain the substance, increased tolerance to it, physical or psychological damage caused by its use, failed attempts to stop it, and withdrawal symptoms.

The 5th edition of the DSM (DSM-5) does not separate the diagnoses of substance abuse and dependence as in the previous editions, while eliminating the confusion between the two terms, and provides criteria for substance use disorder, accompanied by those for intoxication, withdrawal, substance/medication-induced disorders, and unspecified substance-induced disorders, where relevant.<sup>3</sup> Therefore, DSM-5 substance use disorder criteria are nearly identical to the DSM-IV substance abuse and dependence criteria combined into a single list, with two exceptions. In the DSM-5 draft, the American Psychiatric Association (APA) originally proposed the inclusion of a new chapter entitled “Behavioral Addictions,” but this chapter was not included in the final edition. Nevertheless, the DSM-5 chapter “Substance-Related and Addictive Disorders” includes gambling disorder, and, as such, it reflects the increasing and consistent evidence that brain reward system may be disturbed in both drug abuse and behavioral addictions. Another behavioral addiction, the “Internet addiction,” has been included in Section 3, which concerns conditions that require further research before they can be formally considered “full disorders.” By contrast, the proposed “hypersexuality category,” which some authors considered simply as a subtype of sex addiction, was rejected.

The terms “new addictive syndromes” or “no-drug addictions” refer to a wide range of abnormal behaviors including pathological gambling, compulsive shopping, the so-called “new technologies addiction” (addiction to TV, Internet, social networks, videogames), work addiction syndrome (workaholism), sex (sex addiction) and emotional relationships, orthorexia, and overtraining syndrome.

In 1999, Francisco Alonso-Fernandez<sup>4</sup> proposed a broad classification of the concept of “addiction” based on social regulators, while distinguishing social or legal dependencies, including legal drugs, namely those allowed for free sale (tobacco, alcohol, drugs), and socially accepted activities (such as eating, working, shopping, playing videogames, surfing the Internet), from anti-social or illegal dependencies.

Both classical and new addictions share several features that include the following:

- *Pleasure and relief*: Pleasant sensations, albeit restricted to initial periods of substance use (or of the implementation of behavior). It is the so-called “honeymoon” phase, during which a denial of the problem is always present.

- *Dominance*: The substance (or behavior) constantly dominates the thinking (main ideation); there is an inability to resist the impulse to take the drug (or perform the behavior), experienced in a compulsive manner.
- *Craving*: There is a feeling and the increasing sense of tension before taking the substance (or implementing the behavior).
- *Mood instability*: This is initially limited to the beginning of substance intake (or behavioral implementation), then increasingly generalized and extended to all aspects of existence.
- *Tolerance*: The need to increase the amount of substance (or the time dedicated to behavior) to get the “positive” effect, that otherwise lessens over time.
- *Loss of control*: The increasing feeling of loss of control on substance intake (or on implementation of behavior).
- *Abstinence*: A deep psychic and physical distress when substance intake (or the period dedicated to behavior) is stopped or reduced.
- *Conflict*: The consequence of chronic use of the substance (or behavior), which leads to great impairment of familial, social, educational, and work adjustment.
- *Persistence*: Substance use (or behavior) continues notwithstanding the progressive and clear association with increasingly severe and negative consequences.
- *Impact*: There is the frequent tendency to use substances (or behavior) again after a period of interruption.
- *Polydrug abuse and cross-addiction*: High-frequency of intake of more substances (or running multiple behaviors), and “jumping” from one dependency to another. It should be noted that there is an important phenomenon of cross-dependence between substance and no-drug addictions.
- *The similarity of the main risk factors*: Impulsivity, sensation-seeking, cognitive styles, inadequate and disturbed parental environment.

Currently, the pharmacological treatment of no-drug addictions is established only on empirical assessments and based on clinical characteristics, similar to those of obsessive-compulsive (OCD) and impulsive spectrum disorders, or substance use and mood disorders, especially those belonging to the bipolar spectrum.<sup>5</sup> Several treatment options have been investigated, including different antidepressants, mood stabilizers, opioid antagonists, glutamatergic modulators, and atypical antipsychotics, that showed a good effectiveness in symptoms reduction and craving control. In addition, according to our clinical experience, in most cases, it seems useful to combine psychopharmacological treatments with psychotherapeutic and psychosocial intervention, although controlled studies exploring the real effectiveness of this strategy are not

available. Further, generally speaking, all the data on treatment of behavioral addictions are limited, and no specific guidelines are available.

Therefore, the aim of this article is to present an exhaustive review of the pharmacological treatment of behavioral addictions, while highlighting, when possible, future directions for more targeted and focused interventions.

### Pathological Gambling

Pathological gambling (PG) is characterized by the persistent inability to control and resist the impulse to gamble. The intensification of these behaviors may provoke a significant impairment of familial, social, and work adaptation, and may lead to an irreversible decline, with heavy financial losses that, in the most severe cases, may fuel frauds or criminal acts.

Custer<sup>6</sup> has proposed 6 different types of players: (1) professionals (they live on gambling that represents for them a true work; they are not dependent, as they can control the amount of money wagered and time spent playing); (2) antisocial players (they obtain money illegally through gambling, eg, playing with marked cards or being involved in rigged races); (3) socially appropriate players (they play for fun and socializing, and gambling does not interfere too much with their lives); (4) socially serious players (they invest time in gambling, which is their main kind of relaxation and fun; they are able to maintain control over gambling activities and do not neglect work and/or family); (5) escape and relief players, without addiction (they use gambling to cope with feelings of anxiety, depression, loneliness, and boredom; therefore, gambling represents for them a powerful drug to forget other things); and (6) compulsive gamblers, with addiction (they no longer have control over gambling; it has become the most important thing in their lives, so that they cannot stop).

### Pharmacological Treatment of PG

The potential effectiveness of different psychotropic drugs has been investigated in several double-blind studies vs placebo. In addition, a thorough meta-analysis is available that includes 16 randomized trials published between 2000 and 2006, which confirmed a good effectiveness of antidepressants, mood stabilizers, opioid antagonists and glutamatergic agents. However, to date, no medication has received specific indication for PG. Indeed, the studies that investigated outcome to drug treatment were generally carried out on small and heterogeneous samples of PG patients.<sup>7</sup> Given the current empiricism of PG treatment, according to some authors, the therapeutic design would benefit from a sub-classification of this disorder into 3 clinically

relevant subtypes: obsessive-compulsive, impulsive, and addictive.<sup>7</sup>

Alteration of the serotonergic system represents an important element in the pathophysiology of the disorder with important therapeutic implications.<sup>8-11</sup> Similar to what is observed in OCD, in controlled studies and in clinical practice, selective serotonin reuptake inhibitors (SSRIs) seem to play a key role in the treatment of PG, but at higher doses than those used in the treatment of depression. Three studies (single and double-blind) on small PG samples, with no comorbidity with other psychiatric disorders, suggested the effectiveness of fluvoxamine (100–250 mg/day).<sup>12-14</sup> Paroxetine (10–60 mg/day) was evaluated in 2 double-blind controlled studies vs placebo.<sup>7,15</sup> In the first, paroxetine proved to be effective, while in the second, the improvement was not confirmed, although a positive modification of Clinical Global Impression (CGI) scores was noted. Two open-label studies investigated the effectiveness of citalopram<sup>16</sup> and escitalopram.<sup>17</sup> Citalopram was tested in a sample of 15 patients that showed both a decrease in symptoms (assessed on the basis of the reduction in number of days devoted to gambling, amount of money, and plan and desire to play) and improvement of quality of life. Escitalopram was investigated in 16 patients, 14 of whom showed a significantly reduced scores of both Yale-Brown Obsessive Compulsive Scale (Y-BOCS) modified for PG, used as the primary efficacy measure, and of other scales assessing secondary outcomes.<sup>18</sup>

Among other monoaminergic reuptake inhibitors, nefazodone<sup>19</sup> and bupropion seemed to be interesting, the latter particularly when ADHD was comorbid.<sup>20</sup>

There are just a few data on the effectiveness of mood stabilizers, in particular lithium salts, carbamazepine, valproate, topiramate, and gabapentin. The rationale of their use can be found in similarities between impulsive behaviors, PG, and some features of mixed and manic phases of bipolar disorder.<sup>21</sup> A single-blind randomized study demonstrated the effectiveness of lithium salts or valproic acid in pathological gamblers not suffering from bipolar disorder.<sup>22</sup> Even topiramate monotherapy showed a good effectiveness.<sup>23</sup>

Naltrexone, an opioid  $\mu$ -receptor antagonist that is effective in modulating dopaminergic transmission in the mesolimbic area, and is commonly used in the treatment of alcohol and opioid dependence, showed effectiveness at an average dose of 188 mg/day, mainly in PG patients characterized by more marked impulsive traits.<sup>24</sup> Its use, however, is limited by the high risk of liver toxicity. From this point of view, the new opioid antagonist nalmefene appears more interesting.<sup>25</sup>

Since the improved glutamatergic tone in the accumbens has been associated with a reduction in reward-seeking behavior in addiction, N-acetylcysteine, a glutamatergic modulator, showed a certain degree of efficacy on PG

craving.<sup>26</sup> Along this line, the use of other GABAergic modulators, such as acamprosate, d-cycloserine, gabapentin, pregabalin, lamotrigine, seems promising.<sup>27</sup>

A few data are available regarding the effectiveness of atypical antipsychotics, which are sometimes successfully used in enhancing the effects of SRI and SSRIs in treatment-resistant OCD. In particular, olanzapine, as compared with placebo, was reported to be useful in video-poker addiction.<sup>28</sup>

Modafinil, an atypical stimulant, has been tested in a group of impulsive gamblers.<sup>29</sup> While patients with high levels of impulsivity showed a reduction in gambling search, those with low levels had the opposite effect. These data would indicate potential future research directions for drug development, which should be designed to explore the possible changes in treatment effects based on clinical characteristics and comorbidity of individual patients.

### Compulsive Shopping

Media programs gradually developed with the onset of the Industrial Revolution to promote purchasing through advertising, based on building a winning behavioral model whereby the possession of an asset, and, more recently, the access to exclusive services, is synonymous with well-being and happiness. Compulsive shopping (or “oniomania,” from the Greek *onios*, “for sale”—a term coined by the German psychiatrist Emil Kraepelin who, together with Eugen Bleuler, described for the first time these symptoms around the turn of the 19th century) is a disorder characterized by the continuous focus and loss of control on compulsive buying activities, that are often useless.

A set of diagnostic criteria has been proposed to distinguish the normal activity of shopping vs pathology<sup>30</sup>: the need or the impulse to purchase are perceived as irresistible, intrusive, or foolish; purchasing is frequently beyond their means and/or for unnecessary items (or needs); the concern, the impulse, or the act of buying cause marked distress, significant loss of time, interference with social and/or occupational functioning, financial losses; excessive purchasing does not occur exclusively during periods of mania or hypomania.

It is possible to distinguish 2 subtypes of pathological purchasing: “abusive” consumopathy (the purchase represents a sort of involuntary “compensation” of a primary psychiatric disorder, such as depression, bipolar, or some anxiety disorders; in these cases, the excessive purchases follow a course parallel to that of the primary disorder and disappear at its remission), and “morbid” consumopathy (in this case, compulsive buying represents the main phenomenon; if during the initial stages each new purchase induces pleasant sensations, subsequently there is the onset of feelings of guilt and shame, together with a sense of growing

inner tension). In women, who are most frequently affected by the disorder, purchasing is mainly addressed towards clothing, undergarments, shoes, cosmetics, and jewelry, while men prefer electronic items and car accessories. Some buyers diversify purchases, while others focus exclusively on a particular item in a sort of compulsive hoarding. Purchased items are often put aside, discarded, or thrown away.

Even in this disorder, there are symptomatological and behavioral phenomena similar to addiction, such as craving, habituation, tolerance, and withdrawal symptoms.

### Pharmacological Treatment of Compulsive Shopping

Although specific guidelines for drug treatment of compulsive shopping are not currently available, the first report of a psychopharmacological intervention in this disorder dates back to 1991 when McElroy et al<sup>31</sup> described the response to some antidepressants (bupropione, nortriptyline, fluoxetine) in 3 cases of compulsive buyers.

Three years later, the same authors studied 20 compulsive shoppers with comorbid mood disorders (14 bipolar disorder and 5 major depressive disorder). Ten out of 13 patients treated with antidepressant monotherapy or with antidepressants plus mood stabilizers showed a complete or partial remission of compulsive shopping.<sup>30</sup> It should be noted that antidepressant treatment could produce both a specific effect on compulsive shopping and on the comorbid mood disorder.

Lejoyeux et al<sup>32</sup> reported 2 cases of depressed compulsive buyers who showed complete remission after clomipramine treatment. Two SSRIs (fluvoxamine, citalopram), one anticonvulsant (topiramate), and naltrexone have been also investigated, although in small samples, with preliminary good results.<sup>33,34</sup>

More recently, memantine, a N-methyl-D-aspartate receptor antagonist that inhibits glutamatergic excitatory activity, was shown to reduce impulsive behaviors in 9 subjects with pathological shopping.<sup>35</sup>

### New Technology Addictions (Internet, Social Networks, Videogames, Mobile Phones, TV)

In 1995, Goldberg<sup>36</sup> proposed the ironic and provocative introduction in DSM of a new addictive syndrome called “Internet addiction disorder.” In 1996, Young<sup>37</sup> published the first clinical research on a sample of 396 dependent Internet users (“dependents”) vs a control group of 100 nondependent Internet users (“nondependents”). Diagnosis was carried out by using a specific test (“Diagnostic Questionnaire”), published directly on the Web, which modified criteria for pathological gambling to provide a screening instrument for addictive Internet use; cut-off was reached when users answered affirmatively to at least 5–8 questions.<sup>37</sup>

The use of internet becomes pathological where it consumes too much time and the subjects–work, school and social relationships. Other unspecific and therefore under-recognized symptoms of new technology addiction can be alterations of sleep–wake rhythm, chronic fatigue (due to the common preference for nighttime Web connection), reduced efficiency of immune system, abnormal appetite, poor self-care, headache, visual problems, back pain, and carpal tunnel syndrome due to prolonged mouse utilization. Some patients may be predisposed to the onset of seizures elicited by the continuous visual stimulation due to the long stay in front of a computer screen.

Young<sup>37</sup> described 5 subtypes of Internet addiction: cyber-sexual addiction (a compulsive need to access virtual sex and pornographic Web sites), cyber-relational addiction (excessive involvement in relations arising in the network), Net-compulsion (compulsive behaviors related to online activities such as gambling, shopping, and e-trade), information overload (an obsessive search for news on the Web), and computer addiction (a tendency to excessive involvement in virtual games such as multi-user dimensions and role playing games).

Among the several Internet addiction variants, the so-called cyber-relational addiction is of particular interest. It is characterized by a tendency to establish friendly or even love relationships with people met online, mostly via chat, forum, or social networks. It is a form of relationship where anonymity plays a main role—that allows one to “create” specific physical and personologic profiles, often different from their real personalities. Virtual relations become progressively more important than real-life relationships, and the subject undergoes a progressive isolation, while living in a parallel world, full of idealized people, and where communication is often symbolized through a special linguistic, grammatical, and visual form called IRC (Internet relay chat) that includes well known emoticons.

It is possible to distinguish 2 subtypes of Internet-addicted people: those who have already suffered from other psychopathological disorders (most frequently mood, anxiety, eating, conduct, impulse control, but also personality and psychotic disorders), and those who have never presented, at least apparently, any psychopathological feature. In the first type of patients, the previous disorders would represent facilitating factors toward the onset of any type of addiction. In the second, by contrast, first contacts with the “substance” (ie, the Internet) would trigger the need to maintain and intensify its “intake” (ie, Web connection).

Mobile phones represent a technological tool that are increasingly widespread and sophisticated. In parallel with the substantial and rapid increase in communication services, availability of accessories, and multiplication of technical features (short message service (sms), multimedia messaging service (mms), video calling, e-mailing,

instant-messaging), psychosocial aspects of this tool rapidly transformed. Mobile phones partially cancelled the spatio-temporal, emotional, and relational distances, and promoted novel emotional experiences and relationships that may become progressively prominent. The risk, especially in young people, who are the major users of this tool, is developing a full-fledged addiction. Increased worsening of stress and generalized anxiety levels would be due to continuous Web access and sms and e-mail control, at any place and time. Addictive syndrome starts when most of a person’s time and energies are spent in instrument use or related activities, and provokes personal, relational, emotional, familial, or school maladjustment. Mobile phone addiction may develop rapidly and worsen, while showing similar phenomena to those of substance addiction, such as craving, tolerance, and habituation. Other features that might indicate a dependence risk are the intense attachment towards a mobile phone, the refusal to abandon it even for a short time, and its use as the main, or even only means of knowledge and interpersonal relationships. Excessive use of mobile phones may lead to the development of specific disorders, such as the so-called “disconnection syndrome” and “ring or phantom vibration syndrome.” Similar to most addictions, mobile phone addiction occurs more easily in individuals with low self-esteem, social difficulties, high anxiety levels, marked interpersonal sensitivity, obsessive thoughts, and compulsive behaviors.

Television addiction configures an excessive (“teleabuse,” or exaggerated stay in front of TV screen) and/or distorted (habit of TV watching alone, motionless, in strict silence, preventing contact with other people, or presenting violence if stopped during TV watching) TV use.

### Pharmacological Treatment of New Technology Addictions

No specific indications exist for drug treatment of Internet addiction. Recent data have suggested the potential effectiveness of bupropion and methylphenidate in reducing videogames craving<sup>38,39</sup> and of naltrexone in reducing the search for pornographic sites.<sup>40</sup> A case report suggested the possible effectiveness of escitalopram (10 mg/day/in internet addiction),<sup>41</sup> which was subsequently confirmed in an open-label trial.<sup>42</sup>

### Workaholism

Robinson<sup>43</sup> interpreted the phenomenon of work addiction as a form of OCD characterized by self-imposed demands, inability to regulate work habits, and overindulgence in work with the exclusion of other major life activities. Moreover, the workaholic subject was described as an individual whose need to work is so excessive that it creates significant interference with

personal health, happiness, family relationships, and social functioning.

Workaholic individuals show high levels of aggression, continuous inner tension, and inability to relax; they are always self-confident, arid, poorly emphatic, and severe; focused almost exclusively on professional success; cultivate feelings of invincibility; do not tolerate criticism or obstacles; tend to show an exaggerated control on every aspect of existence, without distinction between professional and personal life; spend spare time and holidays in activities that may have some usefulness for work and for their career, and if they cannot do that, unbearable feelings of unrest and boredom appear. Workaholics strongly contempt useless and pointless activities, such as music, theater shows, and sports, and do not cultivate any hobbies unless they are somehow connected with a business advantage.

### Pharmacological Treatment of Workaholism

There are no controlled studies for workaholism treatment, but in clinical practice, antidepressants (mainly SSRIs) and mood stabilizers (such as valproic acid) are often prescribed.

### Sex Addiction

Sex addiction is a pathological relationship with sex. It is possible to recognize 2 different subtypes: the orgasmic reaction addiction (ORG) and oversexed egosyntonic behavior (OEB).

In ORG, habituation with increasing tolerance to endorphinic substances would be no longer efficient to dampen the erotic desire, whereby subjects are prone to repeat increasingly more orgasms in order to avoid the onset of withdrawal syndrome. OEB is characterized by some key elements:

- **Centrality:** In sex-addicted persons, sexuality plays a prominent role, and most of a person's experiences are addressed to satisfy poorly controlled or completely uncontrolled sexual drives. There is a constant search for situations that can facilitate sexual approaches and stimulate desire. At the beginning, sexual conduct reduces discomfort associated with irritability, but then guilt, depression, shame occur. Shame pushes the person to stop and/or to hide his/her impulses and behaviors, while increasing isolation and deterioration of quality of life. This triggers, however, the cycle of shame that strengthens dependence.<sup>44</sup>
- **Pervasiveness:** Sexual lust tends to increase constantly and becomes the main life focus.
- **Relationships with consequences:** Patients make choices based on an altered hierarchy of values and priorities, because their focus is the fulfilment of sexual appetites

and they underestimate, or ignore the devastating consequences for themselves and/or for others.

- **Inability to stop:** This inability to stop happens despite harmful consequences that are minimized or ignored.
- **Compulsivity:** Sexual behaviors are not intended to give pleasure, but to reduce anxiety and inner suffering.<sup>45,46</sup>
- **Inability to control sexual impulse:** Sexual drive is present with high frequency and intensity, and patients cannot resist its satisfaction.
- **Tolerance:** Sexual urges increase in frequency.
- **Abstinence:** The person experiences withdrawal symptoms, such as mood and emotional lability, irritability, reactivity, when they cannot implement sexual behavior.<sup>47</sup>

In 1987, the American Psychiatric Association recognized "sexual addiction" in the 3rd revised edition of the DSM, and in 1992, ICD-10 included "excessive sexual drive" as a distinct nosological category, subdividing it into "satyriasis" in men and "nymphomania" in women. Nevertheless, despite a good specificity, in 2001 this diagnosis was removed from DSM categories.

### Pharmacological Treatment of Sex Addiction

To date, controlled studies on sex addiction are not yet available. The specific literature includes a series of open-label investigations and some case reports, which are mainly focused to analyze therapeutic options of some sexual deviations.

Lithium salts, tricyclic antidepressants (TCAs),<sup>48-50</sup> SSRIs,<sup>51-54</sup> buspirone,<sup>55,56</sup> nefazodone,<sup>57</sup> and naltrexone<sup>58</sup> showed a certain degree of effectiveness.

The first report regarding the possible effectiveness of pharmacological treatment of compulsive sexual behavior disorders was that of Renynghe de Voxvrie<sup>59</sup> in 1968, who reported a significant effectiveness of clomipramine. However, Ananth et al<sup>60</sup> observed that improvement during clomipramine treatment should be mainly referred to the effect on general anxiety features more than on specific compulsive behavior. It should be noted that the reduced libido represents one of the most frequent (and generally unpleasant) side effects of serotonergic stimulation. The therapeutic interventions would reduce sexual compulsivity without a complete suppression of libido. Therefore, pharmacotherapy should substantially reinforce GABAergic inhibitory activity in frontal lobes, which are probably not efficient in ORG. For this reason, mood stabilizers with specific GABAergic activity, such as valproate, lamotrigine, gabapentin, pregabalin, topiramate, and vigabatrin might be effective in ORG, but there is no—this suggestion.<sup>61,62</sup>

As 2-AG endocannabinoid inhibits the production of the inhibitory neurotransmitter GABA,<sup>63,64</sup> thereby reducing its inhibitory action, it has been hypothesized

that compounds that block the release of brain endocannabinoids may increase control on compulsive sexual behaviors. Similarly, intravenous naltrexone, which totally blocks oxytocin release,<sup>65</sup> greatly reduces orgasmic pleasure with a concomitant production of  $\beta$ -endorphin, with a resulting failure of post-orgasmic libido decrease. Therefore, it has been hypothesized that compounds that modulate oxytocinergic transmission should perhaps facilitate the reorganization of sexual desire.

In OEB, abnormal sexual drive seems to be effectively modulated by the administration of antiandrogens (medroxyprogesterone acetate or cyproterone acetate). However, the possibility of severe side effects, such as thrombophlebitis, pulmonary embolism, and liver dysfunctions,<sup>66</sup> suggests that their use should be limited to cases of resistance to other treatments, such as conventional antipsychotics (chlorpromazine, pimozide, thioridazine, and fluphenazine).<sup>67</sup> Among these, thioridazine, due to its greater selectivity for basal ganglia and limbic-proneocortical dopamine receptors, would be theoretically the most adequate.

### Love Addiction

The problem of emotional addiction has been for a long time investigated only within the psychoanalytic domain. In 1945, Fenichel in *The Psychoanalytic Theory of Neurosis*<sup>68</sup> introduced the term “love addicts” to indicate people “in whom the affection or the confirmation they receive from external objects plays the same role as food in the case of food addicted individuals.” In 1975, Peele and Brodsky’s book entitled *Love and Addiction*<sup>69</sup> underlined the problem of love addiction and promoted a debate among professional communities. In 1976, the first Sex and Love Addicts Anonymous (SLAA) group was founded in Boston by a member of Alcoholics Anonymous. During the 1980s, the problem became very popular in the U.S. when the American psychologist Robin Norwood published the bestseller *Women Who Love Too Much*.<sup>70</sup> A certain degree of dependence and desire to merge with the partner should be considered normal in a loving relationship, in particular during the early stages, but tends to disappear over time. On the contrary, in pathological emotional dependence, the merging drive continues or even increases.

Probably because of separation anxiety, the dependent individual is completely devoted to the partner, in order to pursue exclusively his/her well-being and not his/her own, as should be the rule in healthy relationships. The partner becomes the primary purpose for existence, and even his/her temporary absence provokes discomfort and anxiety as if nothing makes sense.

Love addiction often leads its sufferers to choose problematic partners, who may be affected by mood instability, addictions, or impulse control disorders.

This often occurs in an effort to deny the individual’s needs, because only the partner needs to be helped. However, this is a sort of “sick” help, in which not only do the partners become co-dependent, but their interdependence is strongly reinforced. Loss of respect, different or even opposite life projects, and non-shared needs and desires, are almost always present. During this phase, it is progressively much more complicated to get out of a relationship that he/she admits to be hopeless, humiliating, and often unsatisfactory and self-destructive.

Even in this condition, phenomena of “thrill” (the relationship gives a feeling of euphoria, which becomes increasingly indispensable for maintaining an inner balance), tolerance (search for increasing “affective dosage,” demonstrations of love, time spent together with the partner), and abstinence (the separation from or absence of the partner induces a deep state of prostration) are present. Increasing “substance” assumption often excludes the pair from the rest of the world.

Awareness of a vicious cycle is not always present, nor is it always envisaged. Anxiety, guilt feelings, and dystimic traits sometimes produce inner tension, reactivity, irritability, jealousy, possessiveness, and even paranoid ideation that can fuel aggressive reactions.

### Pharmacological Treatment of Love Addiction

To our knowledge, no data on pharmacological treatment of love addiction is currently available. Clinical impressions suggest that antidepressants and mood stabilizers should be useful to improve mood dysregulation that may sustain, at least partly, this psychopathological condition.

### Orthorexia

Orthorexia (from the Greek “orthos,” fixed and “orexis,” appetite) is characterized by the presence of a strict control on diet and food that is generally selected on the basis of its deemed healthy features. This condition is related not only to the fear of experiencing a weight gain, but, above all, to build a nutritional policy that will allow the achievement of “perfect health.”<sup>71,72</sup>

Individuals with orthorexia tend to progressively isolate themselves and to adopt a standardized and rigid life style, regulated by precise and essential rules almost exclusively connected to food monitoring, and to refuse contacts with people who cannot understand their choices. Although the disorder may be of different severity, a gradual thought distortion is possible, so that the subject may become increasingly inaccessible to criticism, and may even develop psychotic thinking.

### Pharmacological Treatment of Orthorexia

The presence of common psychopathological characteristics with anorexia nervosa suggests the possible

usefulness of SSRIs and TCAs, as well as typical and atypical antipsychotics, but, to our knowledge, no study has been published on this topic.

### Sport Addiction (or Overtraining Syndrome)

Overtraining syndrome defines an altered balance between quantity and quality of sport training and recovery time, with a progressive decrease of performance capacity for saturation. This condition of imbalance derives from intense, physical effort when it is carried out too often, so that there is no time for energetic or neurobiological recovery, nor the possibility to recover from the strain by recharging physically and psychologically. The obsessive quest to lose weight and/or define muscles at any cost can impair, even dangerously or irreversibly, neuroendocrine control systems.<sup>73</sup>

“Sport mania,” which is another term used incorrectly as a synonym for “sport addiction,” is an excessive behavioral tendency that causes an imbalance in one’s relationship with sport and which does not always manifest itself in the symptoms common to addictions. Sport mania can evolve into prolonged abuse of sporting activities and cause over-reaching, that is, a subtle form of overtraining that can require a resting period of a few weeks for psycho-physical rest, or even bring on a more stable state of overtraining that requires months of rest as well as a daily, physical correctional programme. However, sport dependency, or sport addiction, is not always a quantitative problem and does not simply involve the abuse of sport.

Once started, overtraining tends to be a chronic condition and needs long recovery periods, even several months. This duration differs from simple “fatigue” that lasts for one or two days after a workout, or from “over-reaching” that lasts approximately 2 weeks.

The main symptoms of this condition are represented by excessive fatigue caused by very little effort, resting bradycardia, abnormalities in pressure homeostasis and sleep-wake rhythm, weight loss, muscle aches, onset of food intolerances favored by stereotyped or forced feeding, and lower tolerance for workloads. Mood instability, lability, and reactivity; reduced motivation toward training; reduced self-confidence; hyporexia; headache; gastrointestinal disorders; and ease of contracting infections are frequent. From a biochemical point of view, increased catecholamines, cortisol, and urea serum levels; reduction of calcium and testosterone plasma levels; reduced resynthesis of glycogen; and menstrual irregularities may be detected.

### Pharmacological Treatment of Sport Addiction

Data regarding possible pharmacological treatments of overtraining syndrome are not currently available. The

presence of common psychopathological features with OC spectrum disorders, such as body dysmorphic disorder and anorexia nervosa, suggests the possible usefulness of SSRIs and some atypical antipsychotics.

### Conclusion

Despite the significant amount of clinical, genetic, biochemical, and neuropsychological data, the field of behavioral addiction is still largely unknown.<sup>74–76</sup> Epidemiological data are meager, and there is a wide heterogeneity of tools used for diagnostic assessment, treatment, and interventions. Similarly, the pathophysiology of behavioral addictions, which might lead to specific treatments, remains obscure and mainly hypothetical. However, it is interesting to mention that neuropsychological tests have revealed that behavioral and drug addictions share similar abnormalities in complex executive functions, such as planning, capacity modulation, attention, response inhibition, elaboration of problem-solving strategies with tendency to perseveration error, exaggerated reward sensitivity, maintenance of abnormal and increased levels of excitation, and deficit of self-control. The need to satisfy a drive is always present, with the increasing inability to postpone it.<sup>74</sup> Such deficits have been linked to disturbances of the reward system, so-called “reward deficiency syndrome,” and of frontal lobe modulation, particularly of the prefrontal cortex. Moreover, biochemical and genetic studies in drug addictions and PG have suggested the possible role of altered 5-HT, norepinephrine, and dopamine, as well as glutamate and beta-endorphin regulation.<sup>75,76</sup> Therefore, there is an urgent need for studies to explore patients with different behavioral addictions by brain imaging techniques of peripheral markers of CNS parameters.

In conclusion, it is not surprising that no specific prevention protocol is available, especially in vulnerable populations, nor standardized treatment and rehabilitation interventions. It is not yet possible to define the essential levels of assistance (LEA) that are scientifically oriented; in some cases (eg, gambling), a pushy, persuasive, incentive-based bearer of deceptive messages is legally permitted.<sup>77</sup>

Behavioral addictions, therefore, represent one of the most important challenges of contemporary psychiatry. Clinical data, neurobiological profiles, and response to specific therapeutic strategies would indicate their intimate connection with substance addiction. However, there is a current and increasing debate on whether all, or at least some of them, should be considered real disorders or just normal, albeit maladjusted, behaviors.<sup>78,79</sup> The hope is, in the near future, to build a standardized, comprehensive, and multidisciplinary approach that is able to coordinate biochemical and genetic



research, behavioral restructuring, social/environmental conditioning factors (risk and resiliency) analysis, programming and organization of social and health systems, political acts, and appropriate legislative changes leading to focused prevention and tailored pharmacological treatment, when necessary.

## Disclosures

The authors do not have any disclosures, and the authors do not have any affiliation with or financial interest in any organization that might pose a conflict of interest.

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