Chapter 7
Autonomic Nervous System and Brain Circuitry for Internet Addiction

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Abstract The autonomic nervous system can be divided into sympathetic and parasympathetic divisions. The activation of the sympathetic and parasympathetic autonomic nervous systems in Internet addiction is similar to that in drug addiction. The sympathetic division is more strongly reactive, with responses in internal glands and bodily organs and acceleration of heart rate (or blood volume pulse) and respiratory response rate as well as a reduction of temperature, while surfing the Internet. However, contradictory data have also been obtained. Decelerations of skin conductance have also been observed in Internet addiction, showing activity of the parasympathetic division, but not the sympathetic division. Drug addiction produces greater activation of the sympathetic nervous system, but less activation of the parasympathetic system. The autonomic nervous system reciprocally connects to neural circuitry in the brain to modulate both systems, reflecting specific features of Internet addiction. Moreover, Internet addiction induces numerous behavioral and psychopathological symptoms related to pathogenesis, including depression, anxiety, hostility, psychoticism, interpersonal sensitivity, attention-deficit/hyperactivity disorder, obsessive-compulsive disorder, novelty seeking, and social anxiety disorder. Therapeutic interventions for Internet addiction, including pharmacological and non-pharmacological treatments, need to be linked to psychopathological symptoms. The autonomic nervous system, brain circuitry pathogenesis, and specific interventions targeting Internet addiction are discussed in the present review article.

7.1 Introduction

Internet addiction is a newly emerging and increasing prevalent addictive disorder. In contrast to drug addiction, Internet addiction does not directly act via substance consumption on receptors of neural substrates to induce compulsive and impulsive

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Table 7.1 The neural mechanisms, pathogenesis, and interventions of Internet addiction

Internet addiction		
Neural mechanisms	Pathogenesis	Interventions
1. Central nervous system: neural substrates	Psychopathological behaviors/symptoms	1. Pharmacological treatments
2. Peripheral nervous system: autonomic nervous system (1) Sympathetic nervous system (2) Parasympathetic nervous system	1. Before Internet addiction: Obsessive-compulsive disorder	2. Non-pharmacological treatments
	2. After Internet addiction: Depression, anxiety, hostility, interpersonal sensitivity, and psychoticism	

behavior. Thus, while Internet addiction may partially share neural substrates with drug addiction, it also involves some different brain mechanisms to drug addiction. Comparisons of neural substrates in the peripheral autonomic and central nervous systems of the brain between Internet addiction and drug addiction allows a better understanding of the behavioral and neural mechanisms of Internet addiction.

Internet addiction has been linked to many psychopathological and behavioral symptoms, such as depression, anxiety, hostility, psychoticism, interpersonal sensitivity, attention-deficit/hyperactivity disorder, obsessive-compulsive disorder, novelty seeking, and social anxiety disorder. The pathogenesis of Internet addiction is discussed in the present article, and the current discussion may provide some novel viewpoints into therapeutic interventions for Internet addiction.

To enable a better understanding of Internet addiction, it is important to combine our knowledge of the activity of the autonomic nervous system and neural circuitry in the brain, as the pathogenesis of Internet addiction presumably results from behavioral and neural activity arising from these systems. Accordingly, interventions for Internet addiction may be based on the pathogenesis of Internet addiction. Therefore, three components of Internet addition—pathogenesis, neural mechanisms, and interventions—are interconnected, and their relationship is shown in Table 7.1. The present review article discusses these three aspects of Internet addiction.

7.2 Internet Addiction and the Peripheral Nervous System

7.2.1 Internet Addiction Impacts the Autonomic Nervous System

To our knowledge, little research has investigated how Internet addiction affects the autonomic nervous system with regard to the sympathetic and parasympathetic divisions. Our 2010 study was the first to delve into this interesting issue. The study used the Chen Internet Addiction Scale (CIAS) to assess the magnitude of Internet addiction and to screen participants for allocation into low- and high-risk Internet abuse groups.

Table 7.2 Spearman correlations among BVP, SC, TEMP, RESPR, and CIAS score

	BVP	SC	TEMP	RESPR	CIAS score
BVP (%) (Mean = 0.024, SE = 0.011)	1.000				
SC (%) (Mean = 0.649, SE = 0.223)	−0.101 0.239	**1.000**			
TEMP (%) (Mean = 0.002, SE = 0.009)	−0.056 0.346	**−0.461**** **0.000**	1.000		
RESPR (%) (Mean = 0.202, SE = 0.039)	−0.044 0.379	**−0.238*** **0.045**	0.001 0.497	1.000	
CIAS score (Mean = 56.221, SE = 1.605)	0.188 0.091	**−0.065** **0.323**	−0.312* 0.012	0.336** 0.007	1.000

$^{**}p < 0.01$, $^{*}p < 0.05$, significant α value of Spearman correlation

Four psychophysiological assessments of autonomic nervous activity, including blood volume pulse (BVP), skin conductance (SC), peripheral temperature (TEMP), and respiratory response (RESPR), were recorded while the participants spent 6 min browsing the Internet. Some important findings were obtained in this study. First, RESPR and TEMP were sensitive psychophysiological indices of Internet addiction that were positively and negatively correlated with CIAS score, respectively. Blood volume pulse and SC were unrelated to CIAS score (Table 7.2). Blood volume pulse and RESPR in high-risk Internet abusers were significantly increased compared with low-risk Internet abusers. Skin conductance and TEMP were lower in high-risk abusers compared with low-risk abusers (Figs. 7.1, 7.2, 7.3 and 7.4). This means that greater activation of the sympathetic nervous system, reflected in the increased BVP and RESPR together with decreased TEMP, was observed in the high-risk Internet abusers. However, the SC results showed paradoxical responses in comparison to the other psychophysiological indices. Lower skin conductance activation was observed among high-risk abusers, suggesting that the parasympathetic nervous system was simultaneously activated in this group. Based on these observations, the autonomic activity hypothesis of Internet addiction is suggested to explain how the sympathetic and parasympathetic divisions of the autonomic nervous system are activated in Internet abusers.

The autonomic nervous system is composed of sympathetic and parasympathetic divisions (Fig. 7.5). With regard to structure, the sympathetic and parasympathetic nervous systems can be divided into preganglionic and postganglionic neurons. The dissociation between the sympathetic and parasympathetic divisions involves preganglionic fibers in the sympathetic nervous system that are shorter than those in the parasympathetic nervous system. Similarly, preganglionic fibers in the parasympathetic nervous system are longer than those in the sympathetic nervous system. With regard to functional aspects, the sympathetic nervous system has been shown to govern and enhance the activation of internal glands and bodily organs. The parasympathetic nervous system plays an inhibitory role to attenuate the activity of glands and organs. The sympathetic/parasympathetic divisions are activated within the same internal glands and bodily organs in a complementary way. When the sympathetic division is

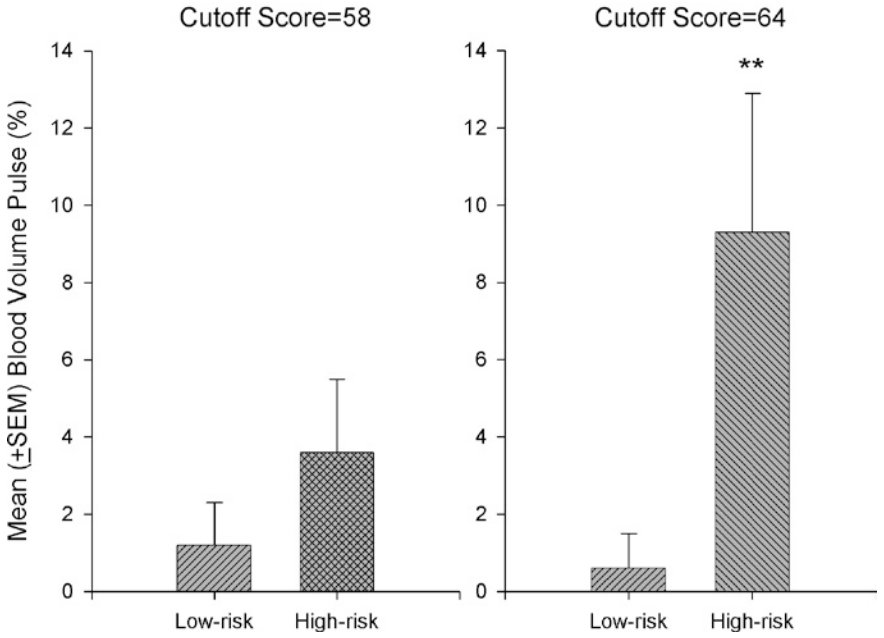

Fig. 7.1 Mean (± SEM) BVP (%) in high- and low-risk Internet abusers, with cutoff scores of 58 or 64 in the CIAS screening of Internet addiction. $^{**}p < 0.01$, versus low-risk group with the same cutoff score

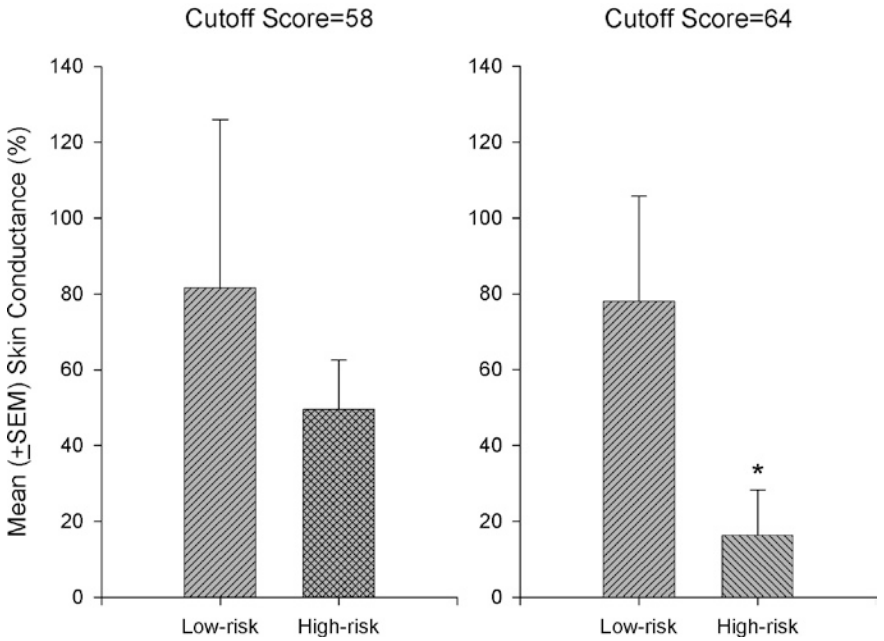

Fig. 7.2 Mean (± SEM) SC (%) in high- and low-risk Internet abusers, with cutoff scores of 58 or 64 in the CIAS screening of Internet addiction. $^{*}p < 0.05$, versus low-risk group with the same cutoff score

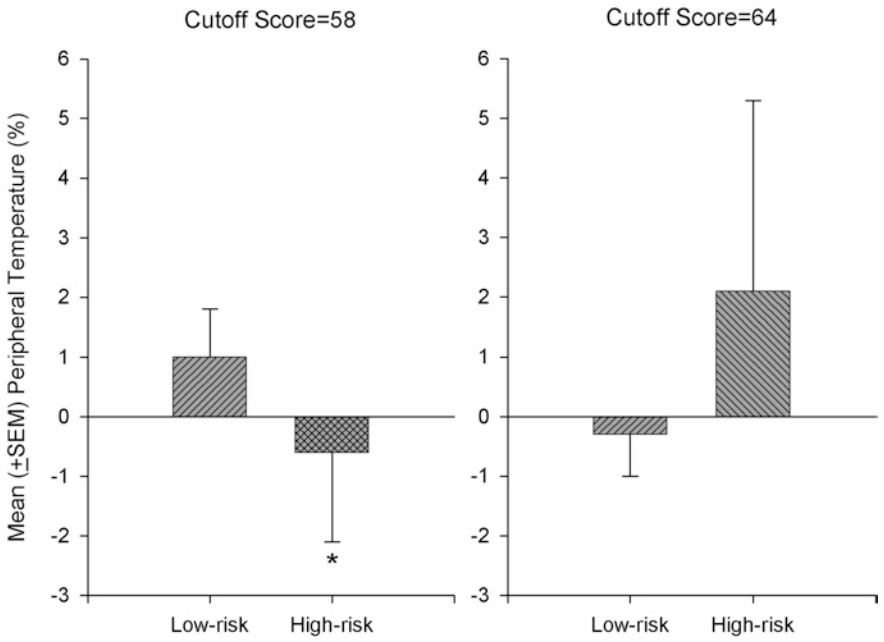

Fig. 7.3 Mean (± SEM) TEMP (%) in high- and low-risk Internet abusers, with cutoff scores of 58 or 64 in the CIAS screening of Internet addiction. *$p < 0.05$, versus low-risk group with the same cutoff score

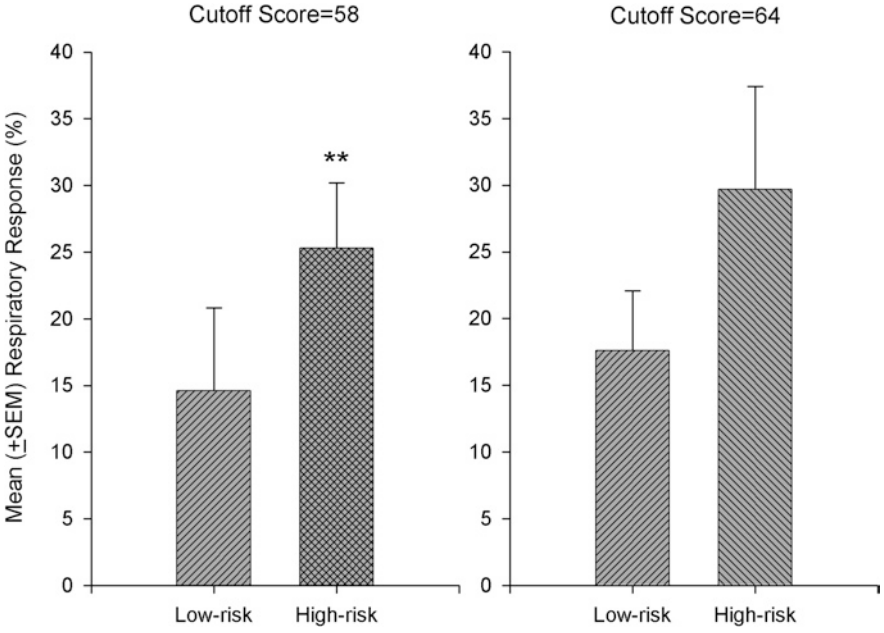

Fig. 7.4 Mean (± SEM) RESPR (%) in high- and low-risk Internet abusers, with cutoff scores of 58 or 64 in the CIAS screening of Internet addiction. **$p < 0.01$, versus low-risk group with the same cutoff score

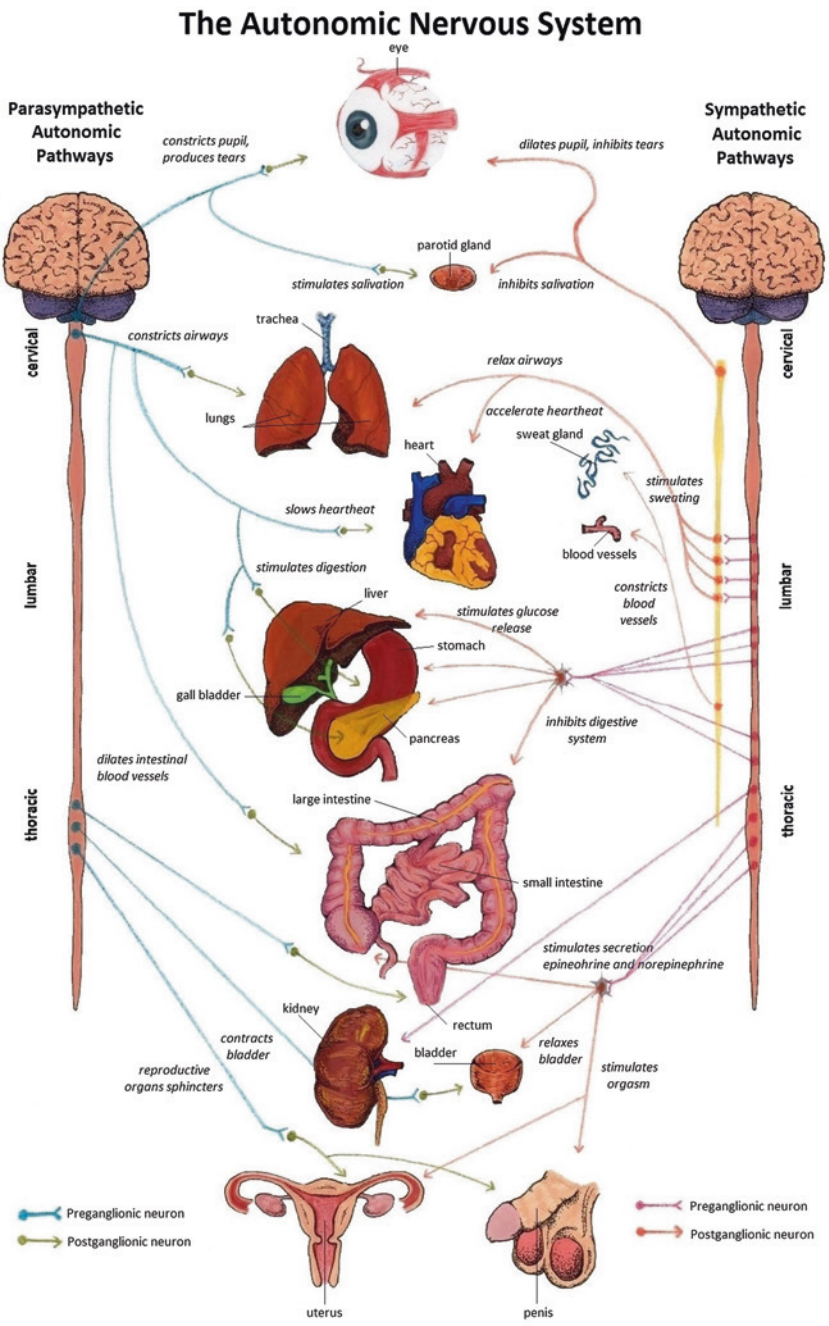

Fig. 7.5 The autonomic nervous system. The schematic figure depicts the target organs and functions served by the sympathetic and parasympathetic fibers of the autonomic nervous system

activated, the parasympathetic division is antagonized, and vice versa. This is referred to as sympathetic-parasympathetic antagonism (Carlson 2007). However, our previous data seemingly contradict the notion of sympathetic-parasympathetic antagonism. One question is why the sympathetic division is activated with regard to BVP, TEMP, and RESPR, and the parasympathetic division responds with changes in SC at the same time. This issue warrants further investigations.

Similarly paradoxical findings related to sympathetic-parasympathetic antagonism have been reported in a number of studies. For example, a study of voluntary control of physiological feedback affecting autonomic activity, found that heart rate feedback training reduced heart rate, and the deceleration in heart rate was linked to an increase in SC magnitude. The results showed a contradiction between the sympathetic division (i.e., SC responses) and parasympathetic division (i.e., heart rate activity; Gatchel 1976). Another study investigated how pathological worry affects heart rate variability arising from the sympathetic-parasympathetic nervous system. Their results indicated that threat stimuli (e.g., worrisome events) inhibited heart rate variability, and this effect was likely attributable to the inhibition of parasympathetic activity and simultaneous suppression of the sympathetic response (Weng and Teng 2005). A critical review reported that the activity arising from the sympathetic-parasympathetic divisions of the autonomic nervous system cannot be understood in terms of an antagonism of sympathetic and parasympathetic nervous activities on the level of each single internal gland or bodily organ, because some glands and organs are controlled by the single sympathetic or the single parasympathetic division of autonomic nervous system activity (Meyers 1959). For illustrative purposes; sympathetic but not parasympathetic nerves innervate nictitating membranes, most blood vessels, and sweat glands. On the other hand, the lacrimal gland, ciliary body, and iridal muscle are controlled by parasympathetic nerves, but not sympathetic nerves. Vascular smooth muscles are governed by alterations of activity in parasympathetic fibers. Although salivary glands are mediated by the sympathetic-parasympathetic divisions, two different types of cells within the salivary gland receive either sympathetic or parasympathetic innervations. In conclusion, internal glands and bodily organs may synergize but not antagonize each other through the sympathetic-parasympathetic divisions (Meyers 1959). Therefore, our previous contradictory data showing sympathetic and parasympathetic activity with regard to BV, TEMP, RESPR, and SC, are consistent with the idea that sympathetic and parasympathetic nervous system do not necessarily antagonize each other.

7.2.2 Explanations for Contradictory Data in Four Psychophysiological Measurements in Internet Addiction: Rewarding and Aversive Properties of Addiction

Our contradictory findings indicate that the observed differences in BV, TEMP, and RESPR in Internet addicts may be attributable to reactivation of the sympathetic division, and that alterations in SC in Internet addicts may result from

parasympathetic activity. The hypothesis of the rewarding and aversive properties of addiction may help to explain this contradictory data.

According to this hypothesis, addictive stimuli and their associated cues result in both rewarding and aversive effects, which influence the sympathetic-parasympathetic divisions of autonomic nervous system activity. Two lines of research have elucidated the activity of the sympathetic-parasympathetic divisions of the autonomic nervous system in humans and animals when individuals are confronted with rewarding and aversive events (Bradley et al. 2008; Ettenberg and McFarland 2003; Firestone and Douglas 1975; Inagaki et al. 2005). For example, a recent animal study investigated the relationship between reward conditioning and activity of the autonomic nervous system. This study showed that both conditioned stimuli (i.e., cue) and unconditioned stimuli (i.e., reward) significantly increased heart rates (Inagaki et al. 2005). Additionally, a previous animal study examined the effect of the dopamine D2 receptor antagonist haloperidol on heroin consumption-related automatic activity and behavioral performance (in terms of reward and motivation). This study found that haloperidol attenuated heart rate and running speed following heroin injections. These results demonstrate that the blocking of the dopamine D2 receptor decreased the rewarding effect of heroin and reduced heart rate (Ettenberg and McFarland 2003). A prior human study assessed SC and heart rate under reward, punishment, and reward + punishment conditions. The results indicated that SC was not significantly different between these three groups, but the heart rate response was stronger in the reward condition than in the other two conditions (Firestone and Douglas 1975). Another human study examined how arousal in response to pleasant, unpleasant, and neutral pictures influenced autonomic activation. The subjects' pupil diameters and SC responses were increased when encountering pleasant and unpleasant pictures, but heart rate was decreased in relation to the occurrence of the unpleasant picture (Bradley et al. 2008).

On the other hand, the way in which aversive stimuli induce sympathetic-parasympathetic activity of the autonomic nervous system remains unclear (Campbell and Ampuero 1985; Ditto et al. 1987; Marsh et al. 2008; Miller and Ditto 1988, 1989, 1991; Olafsdottir et al. 2001; Palomba et al. 2000; Sirota and Schwartz 1976; Weng and Teng 2005). One study tested cardiac performance while watching an unpleasant film and showed that sympathetic nervous system activity was enhanced when subjects encountered the unpleasant film, including an increase in heart rate and electrodermal activation (Palomba et al. 2000). A facial expression study demonstrated that sad facial expressions (i.e., aversive stimuli) facilitated parasympathetic activity and reduced sympathetic responses, with lower SC (Marsh et al. 2008). An animal study examined how conditioned heart rate was activated in response to aversive classical conditioning with conditioned stimuli (e.g., light or tone) and unconditioned stimuli (e.g., electric shock). The authors reported that the presentation of the conditioned stimulus, which was associated with an aversive unconditioned stimulus, produced a prolonged deceleration in heart rate (Campbell and Ampuero 1985). The team of Miller and Ditto has found that subjects who were exposed to an aversive stimulus in a video-game avoidance task exhibited an increase in heart rate and peripheral vascular responses

(Miller and Ditto 1988, 1989). Moreover, they have also shown that aversive psychological stress could elicit strong sympathetic activity, such as an increase in cardiovascular responses (Miller and Ditto 1991). A previous human study trained female subjects to voluntarily control their heart rate under aversive conditions using a biofeedback device, and reported that all of the subjects could voluntarily decelerate their heart rate to relieve anxiety and fear reactions (Sirota and Schwartz 1976). Their evidence suggests that aversive stimuli increase the activity of the sympathetic nervous system through enhanced heart rate.

An old hypothesis developed by Silvestrini (1990) to explain how aversive stress activates the autonomic nervous system suggests that a stress-related stimulus may elicit both orthodox and paradoxical stress reactions. These two stress reactions are reflected in the response of the sympathetic system when individuals encounter emergency situations. The orthodox responses consist of pupil dilatation, increased blood pressure or heart rate, the concentration of blood flow at specific organs (e.g., the heart and muscles), the facilitation of blood coagulation, an increase in the metabolism of glycogen to glucose, the inhibition of some instinctual drives (e.g., hunger and sex), increases in alertness, mental activity, and muscle strength. These orthodox responses result in the effects of analgesia in physical and mental conditions. On the other hand, paradoxical stress responses are thought to be a common basis for some abnormal conditions including depression, panic attack, obesity, sexual deviation, alcoholism, and drug addiction. The paradoxical stress response produces an effect opposite to the orthodox response. For example, the orthodox stress response is speculated to decrease hunger and sex, but the paradoxical stress response excessively increases hunger and sex drives, eventually resulting in obesity and impotence. Silverstrini explained the paradoxical stress responses induced by some abnormal conditions and said, “On the basis of my empirical clinical experience, I have proposed that depression is associated with a state in which stress produces mental pain, rather than analgesia” (Silvestrini 1990, p. 7). Internet addiction also involves these abnormal and psychopathological domains (e.g., depression, obesity, alcoholism, and drug addiction) and therefore is expected to induce a paradoxical stress response, resulting in the effect of mental pain but not analgesia.

Based on the prior data, we suggest that a rewarding event (or the anticipation) may trigger sympathetic nervous system activity (e.g., an increase in heart rate and SC), whereas an aversive event may elicit parasympathetic nervous system activity (e.g., a decrease in heart rate and SC). Nevertheless, it is of importance to remember some of the aforementioned inconsistencies of sympathetic-parasympathetic divisions of the autonomic nervous system, in the context of rewarding and aversive events.

In summary, individuals with Internet addiction are suggested to expose to these two contradictory rewarding and aversive processes. When surfing the Internet, Internet abusers may encounter a rewarding process. However, when they do not use the Internet, Internet abusers may experience aversive feelings that may be related to withdrawal symptoms (Young 1996). The autonomic activity hypothesis of Internet addiction is proposed in this regard; suggesting that the sympathetic nervous system is activated by the rewarding properties of Internet addiction. However, we found that SC did not follow this viewpoint because

Internet abusers exhibited lower SC than normal subjects. Therefore, the SC response is likely related to parasympathetic activity.

7.2.3 *Drug Addiction Reflected in the Autonomic Nervous System: Comparison with Internet Addiction*

In contrast to Internet addiction, most addictive drugs exert their effects in the sympathetic-parasympathetic divisions of the autonomic nervous system with apparent consistency, indicating that the sympathetic nervous system, but not parasympathetic activity, is more active in drug addiction (Table 7.3; Brunelle et al. 2006; Fishbein et al. 2005; Henry et al. 2012). For example, some addiction studies related to betel chewing found that consumption of a small amount of a betel nut can induce more cardiovascular responses, suggesting that it results from sympathetic nervous activity, whereas large amounts of consumption cause hyperactivity of the parasympathetic nervous system (Chu 1995, 2001, 2002). Abusers with methamphetamine

Table 7.3 Comparisons of heart rate/blood volume pulse, skin conductance, finger temperature, and respiratory rate of the autonomic nervous system for Internet addiction and drug addiction

Autonomic nervous system activity					
Type	Characteristic				Note
	HR/BVP	SC	TEMP	RESPR	
Internet addiction	+(S)	−(Para)	−(S)	+(S)	
Betel chewing	+(S)	+(S)	N/A	N/A	Small amount →Sympathetic activity (↑) Large amount →Parasympathetic activity (↑)
Methamphetamine	+(S)	N/A	N/A	N/A	
Stimulant user (alcohol challenge)	+(S)	N/A	N/A	N/A	
Marijuana user	None	N/A	N/A	N/A	
Hallucinogen user	None	N/A	N/A	N/A	
Polydrug abuse (cocaine, heroin, alcohol, marijuana, and methamphetamine)	N/A	+(S)	N/A	N/A	
Alcohol (withdrawal state)	+(S)	N/A	N/A	+(S)	
Alcohol user	+(S)	N/A	−(S)	N/A	
Opiate user (heroin, morphine)	−(Para)	N/A	N/A	−(Para)	
Naltrexone therapy (+) or Methadone therapy (−)	+(S)	N/A	N/A	N/A	

HR heart rate; *BVP* blood volume pulse; *TEMP* peripheral temperature; *RESPR* respiratory response; *S* sympathetic nervous system; *Para* parasympathetic nervous system; *N/A* not applicable

dependence have been shown to have decreased heart rate variability, reduced parasympathetic activity, and attenuated heartbeat variability, while they also show increased sympathetic activity with heart rate facilitation (Henry et al. 2012). A comparative investigation of drug addiction among psychostimulant, marijuana, and hallucinogen abusers that assessed the activity of the autonomic nervous system found that psychostimulants abusers had significantly higher ethanol-induced heart rate increases than non-abusers. However, alcohol-induced heart rate in marijuana abusers and hallucinogen abusers was not significantly different compared to controls. This suggests that psychostimulant addiction can elicit hyperactivity of the sympathetic nervous system (Brunelle et al. 2006). A recent study of polydrug abuse, including cocaine, heroin, alcohol, marijuana, and amphetamine, indicated that drug abusers had a stronger SC response and worse performance on Gambling and Rogers Decision Making Tasks, suggestive of hyperactivity of the sympathetic nervous system in drug addiction (Fishbein et al. 2005). A review article related to alcohol addiction suggested that animals with alcohol withdrawal symptoms had increased heart rate and RESPR (Becker 2000). However, acute and chronic alcohol administration has been shown to enhance heart rate and inhibit TEMP (Boschloo et al. 2011; Johnson et al. 1986), indicating sympathetic nervous system activity, regardless of withdrawal and administration phases.

Opiate addiction exerts effects on the sympathetic-parasympathetic divisions of the autonomic nervous system through different means. Some studies of opiate abusers, such as heroin and morphine, demonstrate that dogs that receive chronic injections of morphine exhibit decreased heart rate and RESPR, indicative of parasympathetic nervous system activity (Napier et al. 1998). The opioid receptor antagonist naltrexone has been used for opiate detoxification and was shown to have an inverse effect, in which subjects had increased heart rate (Hoffman et al. 1998). Methadone, an opioid receptor agonist, activated sympathetic activity, with heart rate acceleration (Chang et al. 2012; Huang et al. 2012). Altogether, opiate abusers exhibit activation of the parasympathetic system rather than the sympathetic system. This is very different from other drug addictions (Table 7.3).

Internet addiction studies have reported contradictory data, in which the sympathetic nervous system is more highly active, with increases in heart rate and RESPR and a decrease in TEMP. Simultaneously, the parasympathetic nervous system is active, with a decrease in SC. These autonomic activity data are slightly different from those on drug addiction.

7.3 The Connections: Autonomic Nervous System and the Brain

To our knowledge, few studies have investigated how neural activity in the brain connects and governs the activity of the sympathetic-parasympathetic divisions of the autonomic nervous system (Hosoya et al. 1991; Leone et al. 2006; McAllen and May 1996; Montenegro et al. 2011; Okano et al. 2013). For example,

a recent study used transcranial direct-current stimulation to assess the relationship between the temporal and insular cortices and autonomic nervous system, reflected by exercise performance. These authors suggested that stimulation of the temporal and insular cortices by transcranial direct-current stimulation modulated the activity of the autonomic nervous system and the perception of exertion and performance during maximal exercise (Okano et al. 2013). Moreover, another study showed that the application of transcranial direct-current stimulation in the left temporal lobe in athletes modulated heart rate variability. Additionally, it increased parasympathetic activity but decreased sympathetic activity and sympatho-vagal balance (Montenegro et al. 2011). Furthermore, an electrical recording study in an animal model found that the activity of medullary premotor neurons in the brainstem was correlated with the contraction of cutaneous vasoconstrictor postganglionic fibers. This suggests that brainstem neurons govern postganglionic sympathetic nerves (McAllen and May 1996). A previous review of neuroimaging and pain in humans reported that many of the brain areas related to pain functions directly mediate the activity of the sympathetic-parasympathetic divisions of the autonomic nervous system. A neuroanatomical study showed that the brain pain system is highly associated with the autonomic nervous system, and lamina 1 neurons in the brain receive pain and visceral information from relevant visceral organs that is then transmitted to the spinothalamocortical pathway in central brain structures. Interoceptive visceral messages project to the viscerosensory cortex, including the right anterior insula and orbitofrontal cortices and nociception structures, such as the anterior cingulate cortex (Leone et al. 2006). Alternatively, an afferent axon tracing study investigated the neural pathways between the hypothalamic paraventricular nucleus and peripheral sympathetic preganglionic neurons. The results indicated that the hypothalamic paraventricular nucleus projects descending inputs to sympathetic preganglionic neurons, indicated by the labeling of the anterograde transport of *Phaseolus vulgaris* leukoagglutinin (i.e., a protein derived from kidney beans and used as an anterograde tracer). Sympathetic preganglionic neurons retrogradely project ascending fibers to the hypothalamic paraventricular nucleus, revealed by cholera toxin subunit B (i.e., a retrograde tracer). Therefore, the hypothalamus paraventricular nucleus interacts with peripheral sympathetic preganglionic neurons in the autonomic nervous system (Hosoya et al. 1991).

In summary, some neural substrates of the brain indeed connect to the autonomic nervous system. The hypothalamic paraventricular nucleus reciprocally projects to sympathetic preganglionic neurons. Medullary premotor neurons in the brainstem might control the activity of postganglionic sympathetic nerves. Numerous neural substrates of pain in the brain, including the right anterior insula, orbitofrontal cortex, and anterior cingulate cortex, govern autonomic nervous activity. The temporal and insular cortices can modulate autonomic nervous system cardiac activity and the perception of exertion and performance during strenuous exercise. How central brain substrates control the peripheral sympathetic-parasympathetic divisions of the autonomic nervous system remains uncertain and needs to be scrutinized in future studies.

7.4 Internet Addiction and the Neural Circuits of Brain Reward

The neural circuitry of reward has long been demonstrated in animal models, indicating the existence of dopamine reward systems, including the mesolimbic and mesocortical dopamine systems (Di Chiara 1998; Wise 1988, 2008; Wise and Rompre 1989). The mesolimbic dopamine system is defined as the neural projection from the ventral tegmental area to many brain areas of the limbic system, such as the amygdala, nucleus accumbens, hippocampus, and olfactory cortex. The mesocortical dopamine system projects from the ventral tegmental area to the prefrontal cortex (Oades and Halliday 1987). The function of the mesolimbic dopamine system is proposed as the governance of rewarding and hedonic effects (Koob and Swerdlow 1988). However, the mesocortical dopamine system plays a crucial role in high-level cognitive functions, such as logical thinking, reasoning, and planning, although some reports have shown that its function may also incorporate rewarding and hedonic effects, similar to the mesolimbic dopamine system (Fibiger and Phillips 1988). To review the literature of Internet addiction related to neural circuitry in the brain, evidence of Internet addiction in humans has been inconsistent with drug addiction data in animals (Dong et al. 2012a, b; Han et al. 2010; Ko et al. 2009; Liu et al. 2010; Lin et al. 2012; Lorenz et al. 2013; Sun et al. 2012; Weng et al. 2013). For example, a diffusion tensor imaging study indicated that subjects with Internet gaming addiction showed greater fractional anisotropy (i.e., a value that is calculated from a marker of diffusion along the axon and diffusion perpendicular to the axon) due to an increase in white matter integrity in the thalamus and left posterior cingulate cortex compared with normal subjects. Moreover, greater volume of white matter in the thalamus was associated with the severity of Internet addiction (Dong et al. 2012a). A similar study that used a diffusion tensor imaging approach related to Internet addiction showed that subjects with Internet addiction had significantly decreased fractional anisotropy in orbitofrontal white matter, corpus callosum, cingulum, inferior fronto-occipital fasciculus, and corona radiation internal and external capsules (Lin et al. 2012). A recent study of online gaming addiction suggested that abnormal gray matter and white matter volumes may be related to online gaming abuse. These abnormal brain areas included the right orbitofrontal cortex, insular cortex, and right supplementary motor cortex. Furthermore, white matter volume was decreased in the right genus of the corpus callosum, frontal cortex, and right external capsule, whereas gray matter volume increases were correlated with the right orbitofrontal cortex, insular cortex, and right external capsule in Internet gaming abusers (Weng et al. 2013). A recent functional magnetic resonance imaging (fMRI) study of Internet addiction to the online game World of Warcraft provided supporting evidence implicating similar brain regions, suggesting that some common neural substrates may mediate online game craving behaviors in Internet addiction (Ko et al. 2009). The common neural substrates of the brain comprise the right orbitofrontal cortex and bilateral anterior cingulate cortex. Moreover, the right nucleus accumbens, medial frontal cortex, dorsolateral prefrontal cortex, and right caudate nucleus may also be involved in craving behavior in Internet addiction (Ko et al. 2009). Thus, reward-related brain areas

may mediate the specific form of Internet addiction, such as the online game Word of Warcraft; however, another study with the online game, Counter Strike, has not implicated neural reward mechanisms in this category of Internet gaming addiction (Montag et al. 2012). This raises questions as to whether neural reward pathways are selectively implicated in internet (gaming) addiction dependent on game-specific characteristics (e.g., role-player, point of view, the accumulation of "point", story narrative etc.).

With regard to craving behavior and cue-induced Internet addiction, a brain mapping study of Internet video game play showed that the anterior cingulate cortex and orbitofrontal cortex were significantly activated when subjects encountered Internet video game cues (Han et al. 2010). Another study found greater brain activity in a cue/picture exposure condition, including in the dorsolateral prefrontal cortex, bilateral temporal lobe, cerebellum, right inferior parietal lobe, right cuneus, right hippocampus, parahippocampus, parahippocampal gyrus, and left caudate nucleus (Sun et al. 2012). These results suggest that these brain areas may be involved in cue-induced Internet addiction or craving behavior.

A recent study that used resting-state fMRI brain mapping found that Internet gaming addicts exhibited higher brain activity in the brainstem, inferior parietal lobule, left posterior cerebellum, and left middle frontal gyrus. Additionally, regional homogeneity measures of the temporal, occipital, and parietal lobes were significantly decreased in Internet gaming abusers. The authors suggest that these brain areas may be involved in sensory and motor coordination or visual and auditory function, but the data did not suggest the involvement of these areas in reward and hedonic effects (Dong et al. 2012b). Another study indicated that Internet gaming abusers had significantly greater increases in regional homogeneity in the cerebellum, brainstem, right cingulate gyrus, bilateral parahippocampus, right frontal lobe, left superior frontal gyrus, left precuneus, right postcentral gyrus, right middle occipital gyrus, right inferior temporal gyrus, left superior temporal gyrus, and middle temporal gyrus. The results suggested that the neural networks among the cerebellum, limbic cortex, brainstem, and frontal cortex might be correlated with the rewarding and hedonic effects of Internet addiction (Liu et al. 2010).

In summary, the results of human Internet addiction studies are more complex than the findings from animal drug addiction research. The mesolimbic and mesocortical dopamine systems may comprise the framework for Internet addiction. Unfortunately, the dopamine hypothesis, which was developed using evidence from animal studies, is not fully consistent with Internet addiction findings related to the neural circuitry of the brain. This suggests a need for the development of a novel hypothesis of Internet addiction in the future.

7.5 Internet Addiction: Pathogenesis and Interventions

A growing body of evidence has shown that Internet addiction can induce depression or that the pathogenesis of Internet addiction is induced by uncontrolled Internet use; moreover, Internet abusers often show numerous psychopathological

symptoms and behaviors related to Internet addiction (Karim and Chaudhri 2012; Carli et al. 2013). For example, Internet abusers can exhibit uncontrollable use of the Internet, distressing feelings, and time-consuming habits that result in social and occupational difficulties (Shapira et al. 2000). Some Internet abusers suffer from depression and guilty feelings. They may also exhibit an increase in the probability of aggressive behavior when exposed to long-term use of the Internet (Treuer et al. 2001). Therefore, many Internet abusers state that they encounter relational, academic, familial, and occupational impairments (Young 2007).

Internet addition was not defined as a mental disorder by the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV), but the current version, the DSM-5, includes Internet gaming addiction (American Psychiatric Association 2013). Internet addiction was first proposed as a psychological or psychopathological disorder by Ivan Goldberg in 1995 (Eppright et al. 1999; Garrison and Long 1995). He adapted the psychopathological symptoms of pathological gambling to describe the compulsive symptoms of Internet addiction, such as pathological Internet use and uncontrolled Internet use that results in physical, social, psychological, and occupational dysfunction (Young 1998). Moreover, the characteristics of Internet addiction may be associated with symptoms of substance dependence that involve mood alterations, tolerance, abstinence, and withdrawal symptoms (Griffiths 1995). Internet addiction is also correlated with some psychopathological behaviors, such as depression, anxiety, hostility, psychoticism, interpersonal sensitivity, attention-deficit/hyperactivity disorder, obsessive-compulsive disorder, novelty seeking, and social anxiety disorder (Carli et al. 2013; Cho et al. 2013). However, all of these psychopathological behaviors are not required simultaneously to define an Internet abuser. Rather, some number of characteristics may present in one Internet addict, while additional and/or different characteristics may typify another Internet addict. Similar to many psychological disorders, e.g. substance addiction and depression, the presentation of symptoms can be heterogenous across patients. The symptoms and psychopathological behaviors associated with Internet addiction are very diverse. Thus, therapeutic interventions for Internet addiction may be complicated.

Recently, some studies have examined the relationship between Internet addiction and psychopathology. For example, Cho et al. (2013) found that withdrawal and anxiety/depression symptoms during childhood could predict the occurrence of Internet addiction. These authors suggested that clinicians should consider withdrawal and anxiety/depression behaviors during childhood to protect humans with an increased vulnerability for Internet addiction (Cho et al. 2013). The psychopathological compulsive behavior associated with Internet addiction is similar to that in alcohol use, resulting from implicit cognition to the exclusion of explicit cognition to control substance abuse (Yen et al. 2011). Xiuqin et al. (2010) investigated pathological symptoms, personality, and parental rearing styles in adolescents with Internet addiction, suggesting that Internet abusers might have higher obsessive-compulsive behavior, interpersonal sensitivity, depression, anxiety, hostility, and paranoid ideation. Additionally, the personality traits of Internet abusers trend toward a lower magnitude of extraversion and a higher degree of psychoticism, while parental rearing styles often lean toward being over-intrusive, punitive, and

lacking in responses during parent-child interactions (Xiuqin et al. 2010). A recent study of Internet addiction suggested that obsessive-compulsive symptoms develop before Internet abusers become addicted to the Internet. Depression, anxiety, hostility, interpersonal sensitivity, and psychoticism are present after Internet addiction develops (Dong et al. 2011). Our recent study further showed that Internet addiction is associated with depressive states but not depressive traits (Huang et al. 2013). This suggests that the psychopathological depression associated with Internet addiction is not related to a depressive personality trait. Instead, psychopathological depressive symptoms are a temporary depressive state. Therefore, interventions for psychopathological depression should target temporary depressive states rather than permanent depressive traits. Interestingly, the notion that depressive state is more important than personality trait as a vulnerability factors for depression has been challenged by recent findings (Mehroof and Griffiths 2010; Tsai et al. 2009). This requires further scrutiny in future studies.

In conclusion, some crucial points are the following. Obsessive-compulsive symptoms disorder, depression, anxiety, hostility, and interpersonal sensitivity may be common psychopathological symptoms of Internet addiction. Obsessive-compulsive behavior can also effectively predict the occurrence of Internet addiction. Moreover, obsessive-compulsive behavior is a critical precursor for Internet addiction. Depression, anxiety, hostility, and interpersonal sensitivity are psychopathological symptoms of Internet addiction; thus, these symptoms and behaviors are the sequelae that appear after Internet addiction develops. Dissociations between depressive states and depressive traits with regard to psychopathological depressive behavior are important considerations for interventions. Finally, the occurrence of Internet addiction may involve many factors in addition to psychopathological symptoms, including personality traits and parental rearing styles.

7.6 Conclusions

Interventions for Internet addiction should include pharmacological and non-pharmacological approaches. The pathogenesis of Internet addiction involves complicated and multiple psychopathological and behavioral symptoms. The role of the autonomic nervous system and the neural circuitry involved in the multiple psychopathological symptoms of Internet addiction require elucidation to enable development of novel and effective interventions. The development of new drugs that focus on the sympathetic-parasympathetic divisions of the peripheral autonomic nervous system is also a crucial line of research. With regard to interventions associated with the peripheral autonomic nervous system, the antagonism of sympathetic nervous system activity may be a key way to prevent against Internet addiction. Thus, research in this basic area requires replication and verification in the future studies.

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