The Neural Mechanisms Underlying Personality Disorders

Barbara Gawda*, Ryszarda Bernacka†, Agnieszka Gawda‡

ABSTRACT

This article reviews recent research on the neural mechanisms of personality disorders. Functional imaging studies have confirmed a neurobiological basis for personality traits. These types of studies also showed strong evidence for neurobiological foundations for personality pathology. Different types of personality disorders are discussed: borderline, antisocial, schizotypal, and avoidant disorders in terms of their neural correlates. A neuropsychological basis is shown as forming a stable foundation for impaired behavior, affectivity, and relevant cognitive function in subjects with personality disorders. This results in difficulties in the treatment of personality disorders. The presented neuropsychological findings suggest that personality disorders are best understood and treated when neurobiological and psychological findings are considered, just as Gabbard (2005) stated, without dichotomies between the 'mind and brain.'

Key Words: personality disorders, neural correlates, borderline personality disorder, antisocial personality, schizotypal personality disorder

DOI Number: 10.14704/nq.2016.14.2.948 **NeuroQuantology 2016; 2: 348-356**

Introduction

Personality disorders are one of the most prevalent human disorders (Fowler *et al.*, 2007). They are defined as a stable disposition to behave in a maladapted way. Their main characteristics are sustained maladaptive patterns of behavior and maladapted function in at least two from four areas: cognitive, affective, interpersonal, and control of impulse (ICD-10, 1992). Studies on prevalence of personality disorders report that they are widespread in both clinical and non-clinical populations. For example, it was shown that in psychiatric populations, personality disorders are linked to a wide range of prevalence and are frequently associated with drug, alcohol, and eating disorders (Chiesa *et al.*, 2002; Zimmerman *et al.*, 2005). Borderline personality is most frequently seen in psychiatric settings, and Cluster C personality disorders are commonly concurrent with other mental disorders, such as substance abuse, anxiety, and affective disorders (Kessler *et al.*, 1993; Mulder, 2002). Zimmerman, Rothschild and Chelminski (2005) established that about 30 % of psychiatric outpatients were diagnosed with at least one personality disorder. In their replication of the National Comorbidity survey within a clinical population, Lenzenweger and associates (2007) found schizoid, schizotypal, and avoidant personality disorders to be the most prevalent. Differences in findings on the prevalence of personality disorders depend on the techniques used in assessment, the type of population examined (i.e., large vs. small, clinical vs. non-

Corresponding author: Barbara Gawda, Ph.D.
Address: Department of Psychology, Maria Curie–Sklodowska University, Plac Litewski 5, 20-080 Lublin, Poland.
Phone: + 0048 604129084
Fax: 00485376062
e-mail: bgawda@wp.pl
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
Received: 12 February 2016; **Revised:** 10 March 2016;
Accepted: 20 March 2016
***e*ISSN** 1303-5150

clinical), social and/or cross-cultural aspects (i.e., differences in personality disorder rates between countries), and/or even ways of classifying personality disorders. Data on the prevalence of personality disorders in a community report a prevalence of personality disorders ranging from 10 - 15 %; about 14.79% of adult Americans had at least one personality disorder (Fowler *et al*., 2007). Prevalence is estimated in Great Britain to be 4.4 %, in Colombia is 7.9%, in Mexico 6.1 %, and South Africa 6.5% (Moran *et al*., 2001; Grant *et al*., 2004; Coid *et al*., 2006). A study from 1993 reports that the most prevalent personality disorders were dependent disorder estimated to be between 2-4%, while schizotypal, antisocial, and histrionic were around 2-3 % (Kessler *et al*., 1993). In a student population the most prevalent were histrionic and narcissistic disorders (Lenzenweger *et al*., 1997). The most prevalent personality disorders in a sampled Norwegian community were paranoid, histrionic, and obsessive-compulsive (Torgersen *et al*., 2001). In the USA, the most prevalent appears to be obsessive-compulsive personality disorder, according to Grant *et al*., 2004.

A review of recent literature on personality disorders suggests that their classification has been highly criticized. Personality disorders are inter-correlated and data do not support that they neatly fit into the three separated clusters as DSM-IV or DSM-V describes (Tyrer *et al*., 2010). Rather, research suggests that personality disorders partly overlap and the three main personality disorders clusters overlap as well. This results in difficulty in differential diagnosis, impacting not only assessment, but also treatment of the given disorder. For example, Tyrer *et al*. (2010) stated that existing classifications of personality disorders are unhelpful. This is an important remark because as there are no distinct patterns attributed to different types of personality disorders, thus it is difficult to establish the distinct neural correlates for every disorder. Subsequently, as of this date, many personality disorders have not yet been described in terms of neural correlates. With respect to this, we present the main current findings on neural correlates of four types of personality disorders: namely, borderline, antisocial, avoidant, and schizotypal.

Borderline Personality Disorder and its Neural Mechanisms

The main characteristics of every personality disorder are emotional impairments which may manifest in different ways, but, nonetheless, are entrenched in neural organization. For example, emotional instability is a core pattern observed in borderline personality disorder. Other features of this disorder are suicidality, outbursts of intense anger, stormy relationships, and identity disturbances (Koenigsberg *et al*., 2009). All these patterns are related to heightened attention or sensitivity to social-emotional cues in interpersonal scenarios, a tendency toward self-referential emotional processing, and dysregulated emotional processing mechanisms (*ibid*.). Borderline patients have great difficulty shifting from the psychic equivalence mode to the pretend mode, and they often hold on to their perception as an absolute fact (Gabbard, 2005). However, mental processing studies indicate that borderline personality disorder patients are accurate in attributing mental states to complex social stimuli (Mitchell *et al*., 2014). All these patterns are regulated by structural and functional mechanisms of the brain. The main effects highlighted in the literature are the failure of hemispheric integration, hyper-reactivity of the hypothalamic-pituitary-adrenal axis (Rinne *et al*., 2002), and hyper-reactivity of the autonomic nervous system in borderline patients (Heim *et al*., 2000). Furthermore, structural dissimilarities of the brain in people with borderline personality disorder are highlighted such as smaller amygdala, hippocampus, anterior cingulate, and orbitofrontal cortex volumes (Driessen *et al*., 2000; Schmahl *et al*., 2003; Hazlett *et al*., 2005).

Investigations with fMRI on emotional tasks documented greater bilateral activation of the amygdala, the medial, and inferolateral prefrontal cortex when viewing negative pictures in subjects with borderline personality (Herpertz *et al*., 2001). Processing of negative emotions in borderline personality disorder patients was shown as impaired, along with greater activation within the insula and posterior cingulate cortex, and lowered activation in a network of regions that extended from the amygdala to the subgenual anterior cingulate and dorsolateral prefrontal cortex (Ruocco *et al*., 2013). It was concluded that processing of negative emotions in borderline patients might be regulated by an abnormal reciprocal relationship between limbic structures and anterior brain regions (*ibid*.).

Greater activation in the fusiform gyrus when viewing negative pictures (faces) was also observed, which is explained as heightened visual sensitivity, or hyperawareness of facial negative expression (Koenigsberg *et al*., 2009). Similarly, processing of facial expressions appears to be altered in borderline personality disorder, and higher activation of the amygdala was recorded in people with borderline personality disorder when viewing facial expressions portraying various emotions (Donegan *et al*., 2003). Furthermore, affective facial expression processing elicits hyperactivation in the amygdala, altered activation in the anterior cingulate, inferior frontal gyrus, and the superior temporal sulcus in borderline personality subjects (Mitchell *et al*., 2014). It results in turn in heightened sensitivity to emotional cues in interpersonal scenarios, self-referential emotional processing, and dysregulated emotional processing; whereas hyperreactive physiological states in borderline patients is linked to the greater response of hypothalamic-pituitary-adrenal axis (Heim and Nemeroff, 2002).

Prolonged amygdala response and a functional disconnection between ventral and dorsal mPFC (medial prefrontal cortex) were found and thought to be a basis for the neural mechanisms of emotional dysregulation seen in borderline personality disorder patients (Kamphausen *et al*., 2013). Among the frontal cortical areas in borderline personality disorder, the anterior cingulate shows impaired *in vivo* serotonin synthesis capacity, serotonergic modulation of metabolic activity, and greater deactivation in response to interpersonal cues (Minzenberg *et al*., 2008). This is, in turn, related to the impaired control of emotions, which is characteristic of the disorder. Borderline patients also show greater activation in the superior temporal gyrus, precuneus, posterior cingulate area, and smaller activation in the dorsolateral prefrontal region, insula, and caudate nucleus. These brain regions' activation suggests that borderline personality disorder patients rely more on automatically responding networks, and that they are over-involved in emotional situations (Koenigsberg *et al*., 2009). The origin of these behavioral patterns may be related to early affective experiences of people with this disorder and research has suggested that symptoms of borderline personality disorder are linked to early trauma and abuse, and that early trauma can affect the developing brain (Gabbard, 2005).

Antisocial Personality Disorder and its Brain Correlates

Antisocial personality disorder is well examined in terms of neurobiological bases, however, there are still some inconsistent findings. Affective functioning of psychopaths and individuals with antisocial personality is mainly characterized by ruthlessness, narcissism, hostility, manipulation, and sensation-seeking (Pauthus and Williams, 2002; Hiatt and Newman, 2007; Lykken, 2007). Data indicate such individuals have more extensively developed representations of hostility, anger, hate, contempt, or violence than love or happiness, in addition to undeveloped schemas of sensitivity, empathy, and mutuality (Blair *et al*., 1997; Grann, 1998; Beck, 2004).

Dysfunctional affective functioning in individuals with antisocial personality disorder appears to be linked to abnormal neural processing. Studies on brain structure and on functional activity in people with antisocial personality disorder demonstrated significant abnormalities, especially in the prefrontal cortex (i.e., orbitofrontal, dorsolateral frontal, anterior cingulate) (Yang and Raine, 2009). Research on the structure of the prefrontal cortex (PFC) demonstrated a lower volume of grey matter (GM) across the entire PFC region in psychopathic offenders. Interestingly, the "successful" psychopaths and non-psychopaths did not differ in the volume of the GM (Yang *et al*., 2005). A reduced volume of GM in the lateral and ventral PFC was found in "unsuccessful" psychopaths (Yang *et al*., 2005). Another study showed reduced cortical thickness in psychopathic adult males (Yang *et al*., 2009). De Oliveira-Souza *et al*. (2008) found reduced GM volume in the vmPFC (ventromedial prefrontal cortex) and orbitofrontal cortex. These findings are accompanied by others that found reduction of GM volume in the right dorsal ACC (anterior cingulate cortex) and bilateral reduction of the dorsolateral PFC (Müller *et al*., 2003). Many other studies have confirmed that psychopathy is associated with a GM reduction in the PFC, especially in the vmPFC and ACC (Boccardi *et al*., 2011; Ermer *et al*., 2012; Ly *et al*., 2012). Furthermore, there are multiple studies reporting that subcortical regions are shown to be abnormal in antisocial personality

disorder/psychopathy, such as the hippocampus (Bocardi *et al*., 2010), insula (de Oliveira-Souza *et al*., 2008; Ly *et al*., 2012), and striatum (Buckholtz *et al*., 2010; Glenn *et al*., 2010). Psychopathy is also associated with structural abnormalities of the amygdala, with diagnosed psychopaths showing abnormal amygdala size and activity (Dolan and Fullam, 2005; Blair, 2007; Glenn *et al*., 2009; Yang *et al*., 2009; Harenski *et al*., 2010; Ly *et al*., 2012).

Functional connectivity also appears to be impaired in individuals with antisocial personality disorder, especially between PFC and subcortical regions. Studies show the reduced integrity of the uncinate fasciculus (examination of white mater structure), which is a major tract connecting the PFC with subcortical structures, such as the amygdala (Craig *et al*., 2009; Motzkin *et al*., 2011), thus confirming the dysfunction of the PFC in psychopaths. There are many studies which report abnormalities in PFC functioning, especially in regions of the vmPFC and ACC, during emotional processing and emotional regulation in psychopaths (e.g. Gordon *et al*., 2004; Dolan and Fullam, 2005; Sommer *et al*., 2010). Not only is the reduced functional connectivity between the vmPFC and amygdala in psychopaths reported (Blair, 2007; Motzkin *et al*., 2011), but also between the ACC and insula (Ly *et al*., 2012). Insula is important for emotional processing because it is included in the circuits supporting emotional awareness (Critchley *et al*., 2004).

In addition to the above structural and functional abnormalities in psychopaths, some data shows there are more impaired brain areas and connections in antisocial personality disorder. Some data present abnormalities in the superior temporal and anterior temporal cortex in psychopaths (Raine *et al*., 2000; Müller *et al*., 2008). Other data show that motor cortex excitability (MNS) is related to psychopathic personality traits, especially to the Coldheartedness Scale (Lilienfeld and Andrews, 1996). Individuals with the highest level of cold heartedness displayed the greatest reduction in the amplitude of the mirror neuron system (Fecteau *et al*., 2008). These results seem to support the thesis that psychopathic individuals only partially possess an ability to understand the affective or sensory state of another person.

All aforementioned brain regions and neural circuits are related to important affective and cognitive functions. Their importance for social and affective functioning depends mainly on the functional links between the ACC and PFC, and between subregions of the PFC which interact and interconnect with dense reciprocal connections (Ongur and Price, 2000). The ventromedial PFC may underlie aspects of self-processing, such as self-reflection and rumination, which is related to impaired regulation of emotions such as guilt and embarrassment in antisocial personality disorder (Mitchell *et al*., 2005; Beer *et al*., 2006; Blair, 2007; Glenn *et al.,* 2009; Qin and Northoff, 2011). The anterior cingulated cortex (ACC) is regarded as the main area related to cognitive and affective mechanisms of motivation such as punishment, reward, pain, empathy, emotional awareness, and cognitive control (Lane *et al*., 1998; Etkin *et al*., 2011; Shackman *et al*., 2011). All dysfunctions in neural mechanisms in psychopaths/antisocial individuals are the bases for impairments in recognizing, differentiating, and analyzing affective information. Individuals with antisocial personality disorder/psychopathy do not display cognitive impairments, but dysfunctional affectivity instead, especially of complex feelings. In turn this results in the difficulties in insight into affective states which can manifest as an inability to take a victim perspective (Hiatt and Newmann, 2007).

Avoidant Personality Disorder and its Neural Correlates

The main characteristic of avoidant personality disorder is hypersensitivity to negative evaluation, excessive fear of rejection, and avoidance in social relationships (Koenigsberg *et al*., 2014). Little is known about the neural mechanisms underlying these affective patterns in avoidant personality. However, some findings can be referred to the avoidant personality. Decreased insula-dorsal anterior cingulate functional connectivity was shown in social anxiety disorder, but not in avoidant personality disorder (Klumpp *et al*., 2012). Decreased connectivity between insula and ACC was confirmed when viewing negative pictures (Koenigsberg *et al*., 2014). In avoidant individuals there was no increased activation in the thalamus, parahippocampal gyrus, ventrolateral prefrontal cortex, dorsal anterior cingulate, and no increase in insula connectivity to the rostral anterior cingulate, posterior cingulate, medial,

and dorsolateral prefrontal cortex, which were concluded as a distinct mechanism behind borderline personality disorder accounting for emotional dysregulation (*ibid*.). Compared to healthy controls, these neural characteristics may be associated with weaker habituation to negative cues, and/or a tendency toward longer rumination of negative emotions in people with avoidant personality disorder. Subsequently, this may be what leads avoidant individuals to display excessive fear, anxiety, and hypersensitivity to negative evaluation.

Schizotypal Personality Disorder's Neural Correlates

Schizotypal personality disorder is defined as a heterogeneous group with interpersonal, perceptual, and disorganized symptoms (Cadenhead *et al*., 2002). Schizotypal personality disorder comprises three factors: 'cognitive-perceptual' (odd beliefs, perceptual disturbances, idea of reference, suspiciousness), 'interpersonal' (lack of close friendships, social anxiety, restricted affect), and 'disorganized/oddness' (odd speech/thought, odd behavior, and restricted affect) (Hummelen *et al*., 2012).

Structural and functional abnormalities of the brain in people with schizotypal personality disorder were demonstrated to be related to the aforementioned cognitive, behavioral, and emotional patterns. Functional activity was found to be impaired in those with schizotypal personality disorder, affecting working memory, among other systems. The attenuated working memory-associated activations were observed such as those of the left ventral prefrontal cortex, superior frontal gyrus, intraparietal cortex, and posterior inferior gyrus (Rosell *et al*., 2014). In addition, decreased activation of the left postcentral cingulate gyrus was found, and deactivation of the superior temporal gyrus, insula, and middle frontal gyrus were attenuated in people with schizotypal personality disorder (Vu *et al*., 2013). Prospective memory also appears to be impaired in those with schizotypal personality disorder. Studies have shown that individuals with this disorder show lowered activation in prefrontal cortex, which is associated with prospective memory (Wang *et al*., 2014).

Working memory and context processing have received particular focus in studies with schizotypal personality disorder, and the impairments of these functions are thought to be associated with abnormalities in the frontal cortex and its connections (Rosell *et al*., 2014). Current models of working memory for the schizotypal personality disorder involve a hypodopaminergic state within the fronto-cortical regions (*ibid*.). However, data on frontal lobe volume in schizotypal personality disorder are inconsistent. Some parts of the prefrontal areas are increased in size/volume, whereas others are reduced. For example, it has been shown that the size of Brodmann area 10 was increased in schizotypal personality disorder (Takahashi *et al*., 2011), while volume of Brodmann area 31 was reduced (Hazlett *et al*., 2008). Smaller ventrolateral prefrontal cortex size in schizotypal personality was also observed (Goldstein *et al*., 2011). Furthermore, structural abnormalities of the cingulate gyrus were also documented in people with schizotypal personality disorder (Rosell *et al*., 2014). Volumes of the right and left caudate nuclei were smaller in subjects with schizotypal personality disorder than in controls (Levitt *et al*., 2002). Moreover, an inverse correlation was found between volumes of caudate nucleus and working memory in schizotypal disorder, which is interpreted as cognitive psychopathology associated with structural deficits (*ibid*.). The right and left caudate nuclei volumes were found to be smaller in females with schizotypal personality disorder than in controls, and smaller caudate nuclei were associated with impaired cognitive performance (Koo *et al*., 2006). Increased putamen volumes in the ventral and dorsal parts were also shown in people with schizotypal disorder (Chemerinski *et al*., 2013). Furthermore, a reduction in temporal lobe volumes were found in schizotypal personality, especially of the left superior temporal gyrus, middle temporal gyri, fusiform, but not inferior temporal gyrus (Takahashi *et al*., 2010; Takahashi *et al*., 2011). This may result in the impairment of auditory and language-related processes such as poorer logical memory in schizotypal personality disorder, odd speech, and cognitive-perceptual symptoms (Rosell *et al*., 2014).

Resistance to Treatment due to Neurobiological Mechanisms

Personality dimensions and personality disorders are said to be stable across time and dependent on neurobiological factors (Gardini *et al*., 2009). Personality traits represent tendencies to manifest particular patters of emotion, cognition, motivation, and behavior, and these tendencies are thought to arise from regularities in the functioning of the relevant brain systems (De Young *et al*., 2010). Personality traits are associated not only with activation of brain regions, but also with the variation of the structure of brain. For example, Conscientiousness and Openness have been linked to variation in lateral prefrontal cortex (De Young *et al*., 2010; De Young, 2010). The structural variations in volume of brain regions were found as associated with the Big Five factors. Personality factors reflect structural variance in specific brain areas (*ibid*.). At the neural level, Extraversion is determined by cortical arousal system modulated by reticulothalamic-cortical pathways, AC and dlPFC form part of a general cognitive arousal system (Duncan and Owen, 2000). Increased cingulate activity in extraverts was documented (Haier *et al*., 1987), a negative relationship between Extraversion in Wernicke's and Broca's areas was found, and interpreted as increased self-talk in introverts (Kumari *et al*., 2004). Several subcortical areas, most notably amygdala, caudate, and the putamen in extraverted people, correlated with an increased activation response to positive stimuli (Canli *et al*., 2001). Another example, mindfulness, is associated with more efficient PFC inhibition of amygdala responses during affect labeling (Creswell *et al*. 2007). Mindfulness correlated negatively with depression, trait anxiety, neuroticism, and psychological distress (*ibid*.). Dispositional mindfulness involves activation in the medial prefrontal cortex, ventrolateral prefrontal cortex, and ventromedial prefrontal cortex (Creswell *et al*., 2007). All these associations between personality traits and neural correlates are explained in terms of specific neuro-morphological characteristics resulting from repetitive behaviors and environmental exposures in the course of one's life (Gardini *et al*., 2009). Similar to personality dimensions, associations of personality disorders with neural mechanisms would be the result of repeated behaviors, genetic factors, and environmental exposures. Psychological experience and behaviors have a profound effect on biological nature by changing brain function and its structure. All the above-mentioned findings confirm this, and show how challenging the treatment of personality disorders can be. Every change in behavior, emotionality, or impaired cognition in individuals with personality disorders implies inherent neurobiological change. Those changes can be achieved through long-term treatment including psychotherapy, like cognitive-behavioral therapy, which is thought to be particularly beneficial. The APA recommends a combination of psychotherapy and medication as the optimal approach to treat personality disorders (Tyrer and Bateman, 2004). Positive effects of psychotherapy on the brain is well established (Gabbard, 2005). Medication may also be of value, and antidepressants, mood stabilizers, and/or antipsychotics may facilitate psychotherapy of certain personality disorders such as borderline personality disorder (Tyrer and Bateman, 2004; Paris, 2011). However, it should also be noted that medication may also have negative effects on the brain structure/physiology in patients with personality disorders and may result in acute and/or chronic side effects or dependency (Herpertz *et al*., 2007).

Conclusion

All described findings on neural mechanisms underlying personality disorders show that personality disorders are deeply rooted in neural mechanisms. Because of this, patients with personality disorders are uncompromising in their behavior, emotion, and cognition. This presents a challenge for their treatment as they are resistant to change, though long-term treatment can have positive effects. It is a two-sided process in that biology determines psychology, and psychology can drive biological change. Such biological change can only be achieved with longer-term treatment. Hence, the current neurobiological findings suggest that personality disorders are best understood and treated without dichotomies between the "brain and mind" (Gabbard, 2005, p. 654).

References

Beck AT, Freeman A and Davis DD. The cognitive therapy of personality disorders. New York: Guilford, 2004.

Beer JS, John OP, Scabini D and Knight RT. Orbitofrontal cortex and social behavior: integrating self-monitoring and emotion-cognition interactions. J Cogn Neurosci 2006; 18: 871-879.

Blair RJ, Jones L, Clark F and Smith M. The psychopathic individual: a lack of responsiveness to distress cues? Psychoph 1997; 34, 192-198.

Blair RJ. The amygdala and ventromedial prefrontal cortex in morality and psychopathy. Trends Cogn Sci 2007; 11: 387-392.

Boccardi M, Frisoni GB, Hare RD, Cavedo E, Najt P, Pievani M, et al. Cortex and amygdala morphology in psychopathy. Psychiatry Res 2011; 193: 85-92.

Boccardi M, Ganzola R, Rossi R, Sabattoli F, Laakso MP, Repo-Tiihonen E, et al. Abnormal hippocampal shape in offenders with psychopathy. Hum Brain Mapp 2010; 31: 438-447.

Buckholtz JW, Treadway MT, Cowan RL, Woodward ND, Benning SD, Li R, et al. Mesolimbic dopamine reward system hypersensivity in individuals with psychopathic traits. Nat Neurosci 2010; 13: 419-421.

Cadenhead CS, Light GA, Geyer MA, McDowell JE and Braff DL. Neurobiological measures of schizotypal personality disorder: defining an inhibitory endophenotype? Am J Psychiatry 2002; 159: 869-871.

Canli T, Zhao Z, Desmond JE, Kang E, Gross J and Gabrieli JD. An fMRI study of personality influences on brain reactivity to emotional stimuli. Behav Neurosci 2001; 115(1): 33-42.

Chemerinski E, Byne W, Kolaitis JC, Glanton CF and Canfield EL. Newmark RE, et al. Larger putamen size in antipsychotic-naïve individuals with schizotypal personality disorder. Schizophr Res 2013; 143: 158-164.

Chiesa M, Fonagy P, Holmes J, Drahorad C and Harrison-Hall A. Health service use costs by personality disorders following specialist and non-specialist treatment: a comparative study. J Person Dis 2002; (1692): 160-173.

Coid J, Yang M, Tyrer P, Roberts A and Ulrich S. Prevalence and correlates of personality disorder among adults aged 16 to 74 in Great Britain. Br J Psychiatry 2006; 188: 423-431.

Craig MC, Catani M, Deeley Q, Latham R, Daly E, Kanaan R, et al. Altered connections on the road to psychopathy. Mol Psychiatry 2009; 14: 946-953.

Creswell JD, Way BM, Eisenberg NI and Lieberman MD. Neural correlates of dispositional mindfulness during affective labelling. Psych Med 2007; 69: 560-565.

Critchley HD, Wiens S, Rotshtein P, Ohman A and Dolan RJ. Neural system supporting interoceptive awareness. Nat Neurosci 2004; 7: 189-195.

De Oliveira-Souza R, Hare RD, Bramati IE, Garrido GJ, Azevedo IE, Tovar-Moll F, et al. Psychopathy as a disorder of the moral brain: fronto-temporo-limbic grey matter reductions demonstrated by voxel-based morphometry. Neuroimage 2008; 40: 1202-1213.

De Young CG, Hirsh JB, Shane MS, Papademetris X, Rajeevan N and Gray JR. Testing predictions from personality neuroscience: Brain structure and Big Five. Psychol Sci 2010; 21(6): 820-828.

De Young CG. Mapping personality traits onto brain systems: BIS, BAS, FFFS and beyond. Eur J Pers 2010; 24: 404-422.

Dolan M and Fullam R. Memory for emotional events in violent offenders with antisocial personality disorder. Pers and Individual Differences 2005; 38: 1657-1669.

Donegan NH and Sanislow CA, Blumberg HP, Fulbright RK, Lacadie C, Skudlarski P, et al. Amygdala hyperactivity in borderline personality disorder: implications for emotional dysregulation. Biol Psychiatry 2003; 54: 1284-1293.

Driessen M, Hermann J and Stahl K. Magnetic resonance imaging volumes of the hippocampus and the amygdala in women with borderline personality disorder and early traumatization. Arch Gen Psychiatry 2000; 57: 1115-1122.

Duncan J and Owen A. Common regions of the human frontal lobe recruited by different cognitive demands. Trends Neurosci 2000; 23: 475-483.

Ermer E, Cope LM, Nyalakanti PK, Calhoun VD and Kiehl KA. Aberrant paralimbic gray matter in criminal psychopathy. J Abnorm Psychol 2012; 121: 649-658.

Etkin A, Egner T and Kalisch R. Emotional processing in anterior cingulated and medial prefrontal cortex. Trends Cogn Sci 2011; 15: 85-93.

Fecteau S, Pascual-Leone A and Theoret H. Psychopathy and the mirror neuron system: preliminary funding from a non-psychiatric sample. Psychiatry Res 2008; 160: 137-144.

Fowler KA, O'Donohue WT and Lilenfeld SO. Personality disorders in perspectives. In: O'Donohue WT, Fowler KA, Lilenfeld SO, editors. Personality Disorders. Toward the DSM-V, Los Angeles: Sage; 2007, p.1-20.

Gabbard GO. Mind, brain and Personality Disorders. Am J Psychiatry 2005; 162: 648-655.

Gardini S, Cloninger CR and Venneri A. Individual differences in personality traits reflect structural variance in specific brain regions. Brain Res Bul 2009; 79: 265-270.

Glenn AL, Raine A and Schug RA. The neural correlates of moral decision-making in psychopathy. Mol Psychiatry 2009; 14: 5-6.

Glenn AL, Raine A, Yaralian PS and Yang Y. Increased volume of the striatum in psychopathic individuals. Biol Psychiatry 2010; 67: 52-58.

Goldstein KE, Hazlett EA, Savage KR, Berlin HA, Hamilton HK, Zelmanova Y, et al. Dorso- and vetrolateral prefrontal volume and spatial working memory in schizotypal personality disorder. Behav Brain Res 2011; 218: 335-340.

Gordon HL, Baird AA and End A. Functional differences among those high and low on a trait measure of psychopathy. Biol Psychiatry 2004; 56: 516-521.

Grann M. Personality Disorder and Violent Criminality. A Follow-Up Study with Special reference to Psychopathy and Risk Assessment. Stockholm: RiproPrint, 1998.

Grant BF, Hasin DS, Stinson FS, Dawson DA, Chou SP, Ruan WJ, et al. Prevalence, correlates, and disability of personality disorders in the United States: results from the national epidemiologic survey on alcohol and related conditions. J Clin Psychiatry 2004; 65(7): 948-958.

Haier RJ, Sokolski K, Katz M and Buchsbaum MS. The study of personality with positron emission tomography. In: Personality Dimensions and Arousal (Strelau J, Eysenck HJ, eds.) pp 251- 267. New York: Plenum, 1987.

Harenski CL, Harenski KA, Shane MS and Kiehl KA. Aberrant neural processing of moral violations in criminal psychopaths. J Abnorm Psychol 2010; 119: 863-874.

Hazlett EA, Buchsbaum MS, Haznedar MM, Newmark R, Goldstein KE, Zelmanova Y, et al. Cortical grey and white matter volume in unmedicated schizotypal and schizophrenia patients. Schizophr Res 2008; 101: 11-123.

Hazlett EA, News AS, Newmark R, Haznedar MM, Lo JN, Speiser LJ, et al. Reduced anterior and posterior cingulate gray matter in Borderline Personality Disorder, Biol Psychiatry 2005; 58(8): 614-623.

Heim C and Nemeroff CB. Neurobiology of early life stress: clinical studies. Semin Clin Neuropsychiatry 2002; 7: 147-159.

Heim C, Newport DJ, Heit S, Graham YP, Wilcox M, Bonsall R, et al. Pituitary, adrenal, and autonomic response to stress in women after sexual and physical abuse in childhood. JAMA 2000; 284: 592-597.

Herpertz SC, Dietrich TM, Wenning B, Krings T., Erberich SG, Willmes K, et al. Evidence of abnormal amygdala functioning in borderline personality disorder: a functional MRI study. Biol Psychiatry 2001; 50: 292-298.

Herpertz SC, Zanarini M, Schulz CS, Siever L, Lieb K and Möller HJ. World Federation of Societies of Biological Psychiatry (WFSBP) Guildelines for Biological Treatment of Personality Disorders. World J Biol Psychiatry 2007; 8(4): 212-244.

Hiatt KD and Newman JP. Understanding psychopathy: The cognitive side. In Handbook of Psychopathy, Patrick JC (ed.), New York, London: The Guilford Press, 2007; pp. 334-352

Hummelen B, Pedersen G and Karterud S. Some suggestions for the DSM-V schizotypal personality disorder construct. Compr Psychiatry 2012; 53: 341-349.

ICD-10, International Statistical Classification of Diseases and Related Health Problem. Geneva: WHO. 1992.

Kamphausen S, Schröder P, Maier S, Bader K, Feige B, Kaller CP, et al. Medial prefrontal dysfunction and prolonged amygdala response during instructed fear processing in borderline personality disorder. World J Biol Psychiatry 2013; 14(4): 307-318.

Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S et al. Lifetime and 12-month prevalence of DSM-II-R psychiatric disorders in the United States: Results from National Comorbidity survey. Arch Gen Psychiatry 1993; 51: 8-19.

Klumpp H, Angstadt M and Phan KL. Insula reactivity and connectivity to anterior cingulate cortex when processing threat in general social anxiety disorder. Biol Psychol 2012; 89(1): 273-276.

Koenigsberg HW, Denny BT, Fan J, Liu X, Guerreri S, Mayson SJ, et al. The neural correlates of anomalous habituation to negative emotional pictures in borderline and avoidant personality disorder patients. Am J Psychiatry 2014; 171(1): 82-90.

Koenigsberg HW, Siever LJ, Lee H, Pizzarello S, New AS, Goodman M, et al. Neural correlates of emotion processing in Borderline Personality Disorder. Psychiatry Res 2009; 172(3): 192-199.

Koo MS, Levitt JJ, McCarley RW, Seidman LJ, Dickey CC, Niznikiewicz MA, et al. Reduction of caudate nucleus volumes in neuroleptic-naïve female subjects with schizotypal personality disorder. Biol Psychiatry 2006; 60: 40-48.

Kumari V, Ffytchee DH, Williams SCR and Gray JA. Personality predicts brain responses to cognitive demands. J Neurosci 2004; 24(47): 10636-10641.

Lane RD, Reiman EM, Axelrod B, Yun LS, Holmes A and Schwartz GE. Neural correlates of levels of emotional awareness. Evidence of an interaction between emotion and attention in the anterior cingulated cortex. J of Cogn Neur 1998; 10: 525-535.

Lenzenweger MF, Lane MC, Loranger AW and Kessler RC. DSM-IV personality disorders in the National Comorbidity Survey replication. Biol Psychiatry 2007; 62: 553-564.

Lenzenweger MF, Loranger AW, Korfine I and Neff C. Detecting personality disorders in a nonclinical population. Application of a 2-stage procedure for case identification. Arch Gen Psychiatry 1997; 54: 345-351.

Levitt JJ, McCarley RW, Dickey CC, Voglmaier MM, Niznikiewicz MA, Seidman LJ, et al. MRI study of caudate nucleus volume and its cognitive correlates in neuroleptic-naïve patients with schizotypal personality disorder. Am J Psychiatry 2002; 159(7): 1190-1197.

Lilienfeld SO and Andrews BP. Development and preliminary validation of a self-report measure of psychopathic personality traits in noncriminal populations. J Pers Assess 1996; 66: 488-524.

Ly M, Motzkin JC, Philippi C, Kirk GR, Newman JP, Kiehl KA, et al. Cortical thinning in psychopathy. Am J Psychiatry 2012; 169: 743-149.

Lykken DT. Psychopathic personality: the scope of the problem. In Handbook of Psychopathy, Patrick CJ (ed.), New York, London: The Guilford Press, 2007; pp. 3-13.

Mimzenberg MJ, Fan J, New AS, Tang CY and Siever LJ. Frontolimbic structural changes in borderline personality. J Psychiatry Res 2008; 42(9): 727-733.

Mitchell AE, Dickens GL and Picchioni MM. Facial emotion processing in borderline personality disorder: a systematic review and meta-analysis. Neuropsychol Rev 2014; 24(2): 166-184.

Mitchell JP, Banaji MR and Macrae CN. The link between social cognition and self-referential thought in the medial prefrontal cortex. J Cogn Neurosci 2005; 17: 1306-1315.

Moran P, Rendu A, Jenkins R, Tylee A and Mann A. The impact of personality disorder in UK primary care: a 1-year follow- up of attenders. Psychol Med 2001; 31 (8): 1447-1454.

Motzkin JC, Newman JP, Kiehl KA and Koenings M. Reduced prefrontal connectivity in psychopathy. J Neurosci 2011; 31: 17348-17357.

Mulder RT. Personality pathology and treatment outcome in major depression: a review. Am J Psychiatry 2002; 159 (3): 359-371.

Müller JL, Ganßbauer S, Sommer M, Döhnel K, Weber T, Schmidt-Wilcke T, et al. Grey matter changes in right superior temporal gyrus in criminal psychopaths. Evidence voxelbased morphometry. Psychiatry Res 2008; 163: 313-222.

Müller JL, Sommer M, Wagner V, Lange K, Taschler K, Röder CH, et al. Abnormalities in Emotion Processing within Cortical and Subcortical Regions in Criminal Psychopaths: Evidence from a Functional Magnetic Resonance Imaging Study Using Pictures with Emotional Content. Biological Psychiatry 2003; 54: 152-162.

Ongur D and Price JL. The organization of networks within the orbital and medial prefrontal cortex of rats, monkeys and humans. Cereb Cortex 2000; 10: 206-219.

Paris J. Pharmacological treatement for personality disorders. Int Rev Psychiatry 2011; 23(3): 303-309.

Pauthus DL and Williams KM. The Dark Triad of personality: Narcissism, Machiavellianism and Psychopathy. J of Res in Personality 2002; 36 (6): 556- 563.

Qin P and Northoff G. How is our self-related to midline regions and the default-mode network? Neuroimage 2011; 57: 1221-1233.

Raine A, Lencz T, Bihrle S, LaCasse L and Colletti P. Reduced prefrontal gray matter volume and reduced autonomic

activity in antisocial personality disorder. Arch Gen Psychiatry 2000; 57: 119-127.

Rinne T, de Kloet ER, Wouters L, Goekoop JG, de Rijk RH and van den Brink W. Hyperresponsiveness of hypothalamic-pituitary-adrenal axis to combined dexamethasone/corticotropin-releasing hormone challenge in female borderline personality disorder subjects with a history of sustained childhood abuse. Biol Psychiatry 2002; 52: 1102-1112.

Rosell DR, Futterman SE, McMasterA and Siever LJ. Schizotypal personality disorder: a current review. Curr Psychiatry Rep 2014; 16(7): 452. doi:10.1007/s1120-014-0452-1.

Ruocco AC, Amirthavasagam S, Choi-Kain LW and McMain SF. Neural correlates of negative emotionality in borderline personality disorder: an activation-likelihood-estimation meta-analysis. Biol Psychiatry 2013; 73(2): 153-160.

Schmahl CG, Vermetten E, Elzniga BM and Bremmer DJ. Magnetic resonance imaging of hippocampal and amygdala volume in women with childhood abuse and borderline personality disorder. Psychiatry Res 2003; 122: 193-198.

Shackman AJ, Salomons TV, Slagter HA, Fox AS, Winter JJ and Davidson RJ. The integration of negative affect, pain and cognitive control in the cingulated cortex. Nat Rev Neurosci 2011; 12: 154-167.

Sommer M, Sodian B, Döhnel K, Schwerdtner J, Meinhardt J and Hajak G. In psychopathic patients emotion attribution modulates activity in outcome-related brain areas. Psychiatry Res 2010; 182: 88-95.

Takahashi T, Suzuki M, Zhou SY, Tanino R, Nakamura K, Kawasaki Z, et al. A follow-up MRI study of the superior temporal subregions in schizotypal disorder and first-episode schizophrenia. Schizophr Res 2010; 119: 65-74.

Takahashi T, Zhou SY, Nakamura K, Tanino R, Furuichi A, Kido M, et al. A follow-up MRI study of the fusiform gyrus and middle and inferior temporal gyri in schizophrenia spectrum. Prog Neuropsychopharmacol Biol Psychiatry 2011; 35: 1957-1964.

Torgersen S, Kringlen E and Cramer V. The prevalence of personality disorders in a community sample. Arch Gen Psychiatry 2001; 58(6): 590-596.

Tyrer P and Bateman AW. Drug treatment for personality disorders. Adv Psychiatric Treatment 2004; 10: 389-398.

Tyrer P, Mulder R, Crawford M, Newton-Howes G, Simonsen E, Ndetei D, et al. Personality disorder: A new global perspective. World Psychiatry 2010; 9: 56-60.

Vu MAT, Thermenos HW, Terry DP, Wolfe DJ, Voglmaier MM, Niznikiewicz MA, et al. Working memory in schizotypal personality disorder: fMRI activation and deactivation differences. Schizophr Res 2013; 151: 113-123.

Wang Y, Yang T, Li S, Chao Y, Wang Y, Jia H, et al. Neural correlates of prospective memory in individuals with schizotypal personality features. Neuropsychology 2014; 28(3): 373-381.

Yang Y and Raine A. Prefrontal structural and functional brain imaging findings in antisocial, violent and psychopathic individuals. Psychiatry Res 2009; 174(2): 81-88.

Yang Y, Raine A, Colletti P, Toga AW and Narr KL. Abnormal temporal and prefrontal cortical gray matter thinning in psychopaths. Mol Psychiatry 2009; 14: 561-562.

Yang Y, Raine A, Lencz T, Bihrle S, LaCasse L and Colletti P. Volume reduction in prefrontal gray matter in unsuccessful criminal psychopaths. Biol Psychiatry 2005; 57: 1103-1108.

Zimmerman M, Rothschild L and Chelminski I. The prevalence of DSM-IV personality disorders in psychiatric outpatients. Am J Psychiatry 2005; 162: 1911-1918.