The Barroom Blitz: Competing Neural Underliers of Impulsive Aggressive Phenotype Have Different Implications in Antisocial Personality Disorder

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Imagine a meeting of three characters in McLush's Pub. Steve--a generally well-functioning, popular guy with a bit of a manipulative streak--is out at the pub having fun with friends. He is celebrating his recent pay raise, which he "earned" by blackmailing his supervisor, who Steve discovered having an affair with an intern. Nick, who has a more colorful (documented) legal history than Steve, is spending more money than he can afford drinking himself into a stupor over the possibility of being evicted after a dispute with his landlord nearly led to a fistfight, as well as the restraining order his ex-girlfriend recently filed against him. Nick is really not a bad guy under most circumstances, he just has a very short fuse. He is trying to forget how ashamed he is of himself. Andrea is sitting in the corner of the bar feeling anxious about her workload and is trying to relax with some wine, but she's considering leaving because the bar is very loud due to Steve and his party. Unfortunately, Steve and Nick both spot Andrea at the same time.

Steve would like to get Andrea's phone number, and he sees that Nick is also flirting with her. Steve says something snarky to make Nick look foolish. Nick did not need help with this because he is already heavily intoxicated. Andrea is annoyed and tries to communicate that she is not interested. Nick becomes incensed at the injustice of it all. He is reminded of his ex-girlfriend and his landlord. Nick is angry at everything. He decides to take it out on Steve, who "started it." Steve normally has much better self-control, but he has already had a few drinks. He thinks he will look pretty cool if he "subdues" this potentially dangerous jerk in front of a crowd. He continues goading Nick because he wants a chance to show off. The fighting between the two intensifies and becomes physically

aggressive after Nick predictably snaps and starts the fight. Steve employs unnecessarily zealous restraints to make it look as if he is merely "subduing" Nick while deliberately trying to break Nick's arms. Andrea becomes progressively more irritated by their behavior. Even as they move farther away, she can't bring herself to get up and leave because she keeps stewing about how loud, boorish, and annoying they are. Feeling overwhelmed by her pre-existing anxiety, combined with her rage at Steve and Nick and the overall noise level in the bar, Andrea snaps. Almost before she knows what she is doing, Andrea is across the bar, picking up a stool and smashing it directly over the two men fighting on the ground, injuring both while screaming at them to shut up in florid language.

Based on the information given about each character's thoughts and emotions, it is easy to tell that different subjective experiences motivate Steve, Nick, and Andrea's aggression, but this may not be as obvious if the same story is told describing only their actions. Unluckily, this hypothetical second version of the story is often the only one that psychiatric and criminal justice professionals hear.

Introduction

The diagnostic criteria for antisocial personality disorder (ASPD) described in the *Diagnostic and Statistical Manual of Mental Disorders (DSM-V)* focus on criminal history, confrontational behavior, impulsivity, social and occupational unreliability, manipulative behavior, lack of remorse, and failure to take responsibility for the seriousness of one's offenses (APA, 2013). Therefore, although violence and impulsiveness are not necessary for all forms of criminal or aggressive behavior, impulsive/ aggressive phenotype is a salient feature associated with ASPD. Unfortunately, concentrating primarily on behavioral data casts a very wide diagnostic net, enabling the criteria to describe various individuals with little in common aside from a history of rule-breaking (Hare, Hart, & Harpur, 1991). This is illustrated by the fact that ASPD is frequently co-diagnosed with externalizing disorders such as borderline personality disorder (BPD) and intermittent explosive disorder (IED; Lenzenweger, Lane,

Loranger, & Kessler, 2007) or with psychopathy, all of which manifest with impulsive/aggressive behaviors like substance abuse, risk-taking, aggression, and criminal history but are also characterized by specific affective and attentional symptoms that can differ significantly. Due to the poor discriminant validity of ASPD diagnostic criteria, individuals in these three clinical populations are easily conflated with one another, although the underlying reasons for their behavior may be quite different (Hare et al., 1991). By reviewing literature on psychopathy, BPD, and IED, the current paper aims to highlight the different motivations for aggression in these three populations by describing the distinct neural traits of each. Discussion of these differences will clarify processes that lead to distinct subjective experiences contributing to impulsive/aggressive behavior.

Psychopathy: Fearlessness, Reward Sensitivity, and Proactive Aggression

Disorder Overview

Psychopathy is not a diagnosis included in the *DSM-V*, but it is a well-defined construct recognized by academics in the field of psychology. As a diagnostic term, ASPD has been used interchangeably with psychopathy by both laymen and clinicians (Hare, 1996). However, only 50% of the diagnostic criteria for psychopathy overlap meaningfully with those for ASPD, and measures of psychopathic traits suggest that psychopathy is less prevalent than ASPD.

The Psychopathy Checklist (PCL-R) is the preferred tool for assessing psychopathic traits due to evidence of high reliability and validity. The maximum score is 40, with scores above 25 or 30 reflecting clinical severity. Two factors are assessed by the individual's self-report or other sources. Factor 2 overlaps considerably with the behavior-focused ASPD criteria, measuring criminal history and recidivism, parasitic lifestyle, impulsiveness, brief relationships, substance abuse, lack of long-term goals, and irresponsibility. Factor 1, however, reflects personality traits, empathic capacity, and interpersonal behaviors by assessing superficial charm, grandiosity, need for stimulation, pathological

lying, manipulation, lack of empathy or remorse, and limited affect. Research suggests that, while total PCL-R scores strongly correlate with ASPD symptom scores, much of the relationship is attributable to items measuring Factor 2, while items measuring Factor 1 traits contribute least (Hare et al., 1991). Constructs on other assessments that are particularly effective at distinguishing psychopaths from non-psychopaths include "fearless dominance," "arrogant and deceitful interpersonal style," and "deficient affective experience" (Patrick, Venables, & Drislane, 2013).

Comorbidity statistics bolster the claim that psychopathy as a clinical construct is distinct from ASPD. While as many as 50-80% of inmates meet ASPD criteria, only 15-25% of most prison samples have clinically severe PCL-R scores. Studies considering incarcerated and community samples estimate that while 81% of psychopaths meet ASPD criteria, only 38% of ASPD-sufferers meet the PCL-R cutoff score. Overall prevalence rates of ASPD (3-5% of the general population) are also higher than those of psychopathy (roughly 1% of the population; Ogloff, 2006). The small overlap of clinical PCL-R score with ASPD diagnosis suggests that psychopaths may have unique reasons for participating in criminal/aggressive behaviors, that they may commit fewer crimes than expected, or that they are simply less likely to be caught. These possibilities are consistent with the neural profile associated with psychopaths, as compared to other ASPD-qualifying individuals.

Neural Profile

Converging evidence from a large number of studies suggests that psychopathy is characterized by primarily right-lateralized grey matter volume reductions, hypoactivity, and poor structural and functional connectivity amongst structures mediating limbic (emotion) function, impulse control, error-monitoring and healthy levels of anxiety in uncertain situations, and social cognition including emotional perspective-taking (Kiehl et al., 2001). It is therefore unsurprising that psychopaths display reduced anxiety, occasional lapses in impulse control, and blunted feelings of remorse (Hare, 1996).

While structures like the anterior cingulate--which aids impulse control--and the insula--which contributes to emotional sensations of introspection, shame, and uncertainty--clearly show disturbances in psychopaths, dysfunction in the amygdala and its disrupted connections with prefrontal regions receive the most focus from researchers. Amygdala dysfunction correlates strongly with both Factors 1 and 2 and offers a parsimonious explanation for most of the symptom complex (Blair 2007, 2008).

In healthy individuals, the amygdala mediates rapid attention to emotional stimuli, particularly threat. Lesions abolish the ability to quickly attend to threats, demonstrating that this structure is crucial for appropriate fear responses (Vuilleumier, 2005). The natural result is that a psychopath's ability to notice and respond to threat is very limited, leading to fearless, overconfident, uninhibited, and emotionally insensitive behavior. Psychopaths are slower and poorer at recognizing emotional stimuli. For example, they present with average accuracy but much slower reaction time than controls when identifying scrambled emotion words, implying impaired use of emotional cues to identify words (Lorenz & Newman, 2002). Their emotional responses to negative stimuli are blunted, as suggested by psychopaths making low moral transgression severity ratings when asked to react to images depicting injustice (Harenski, Harenski, Shane, & Kiehl, 2010), and they present with poor recognition of facial expressions (Dadds et al., 2006). Psychopaths are also more willing to make risky decisions under conditions of uncertainty, such as in gambling or Go/No-Go tasks (Bechara, Tranel, Damasio, & Damasio, 1996). This is likely due to impairment of their natural fear and anxiety responses, as suggested by blunted physiological responses to emotional stimuli, uncertainty, or anticipation of an aversive stimulus. Psychopaths have been distinguished from non-psychopathic ASPD-qualifying individuals by demonstrating blunted startle-potentiated blink, electrodermal (sweat) response, and P300 wave (reflects attention to novelty) in response to sudden auditory probes, negative images, and

impulse-control tasks (Drislane, Vaidyanathan, & Patrick, 2013; Patrick, Bradley, & Lang, 1993; Verona, Sprague, & Sadeh, 2012).

Interestingly, humans and animals with full amygdala lesions do not demonstrate these behaviors, suggesting specific, rather than general, amygdala dysfunction in psychopaths. In fact, grey matter reductions are most prominent in the basolateral amygdala (BLA) of psychopaths, with central amygdala (CeA) structure often appearing unaltered (Yang et al., 2009). Human neuroimaging studies and animal lesion studies have demonstrated that BLA activity is associated with directing attention and processing comparative values of stimuli, while CeA activity is associated with understanding valence of stimuli and with reward-seeking behavior. Studies of contingency and reversal learning indicate that BLA damage or lesion impairs the ability to learn from experience to avoid threats, but spares normal acute approach/avoid responses. Conversely, CeA damage spares the ability to learn from changing experiences but blunts approach responses. Therefore, the combination of hypoactive BLA and normally-functioning CeA may predispose to a pattern of behavior marked by oversensitivity to positive stimuli and disinterest in negative stimuli, regardless of the comparative importance of each, and aggressive pursuit of reward even when threatened with punishment, regardless of prior punishments (Moul, Killcross, & Dadds, 2012). This pattern of amygdala damage clarifies psychopaths' tendency to ignore threats to themselves and others when pursuing a goal, as well as their low anxiety levels, fearlessness, excessive optimism and overestimation of abilities, and recidivism.

The orbitofrontal cortex (OFC) mediates impulse control, and the ventromedial prefrontal cortex (vmPFC) associates emotional stimuli with previous scenarios and outcomes. Together and via connections with other limbic structures, they mediate social and emotional decision-making. Neuroimaging results have revealed grey matter reductions and hypoactivity in these areas in psychopaths (de Oliveira-Souza et al., 2008; Yang & Raine, 2009), corresponding to evidence of

impoverished decision-making in behavioral tasks (Bechara et al., 1996) and leading researchers to believe that executive function deficits are a defining characteristic of psychopathy. However, more recent research has implied that prefrontal disturbances do not correlate as strongly with Factors 1 and 2 as do other neural markers, such as amygdala hypofunction (Yang et al., 2009), and they are more common in incarcerated psychopaths, even if incarcerated and non-incarcerated pairs have similar PCL-R scores (Yang et al., 2005). Furthermore, findings of grey matter loss or hypoactivity in the vmPFC, OFC, dorsolateral prefrontal cortex (dlPFC), or anterior cingulate sometimes occur in the context of ASPD, without distinguishing between those who do and do not meet psychopathy criteria (Verona & Patrick, 2015). Psychopaths have in some cases shown improved medial PFC activity when explicitly asked to perspective-take and have demonstrated excessive activation in the dlPFC during emotional processing or empathizing tasks. This may relate to the fact that the dorsal and lateral PFC have fewer limbic connections and are associated with overall cognitive processing power and flexibility, planning and fact-based decision-making, deception, and problem-solving. Thus, psychopaths may be forced to rely on highly logic-based reasoning in situations that typically require emotional reasoning (Meffert, Gazzola, den Boer, Bartels, & Keysers, 2013). Finally, PFC impairments are common in "acquired" or "secondary" psychopathy, which results from damage to the frontal or temporal lobes, such as by traumatic brain injury or frontotemporal dementia. It is worth noting that those with "acquired" psychopathy display comparable impulse control and moral decision-making deficits to primary psychopaths but overall less callous behavior (Kiehl et al., 2001). These facts suggest that PFC disturbance is less related to psychopathy than amygdala hypofunction.

Although prefrontal dysfunction on its own may not be critical to symptom development, impoverished interaction between limbic and prefrontal structures clearly plays a role. Poor coordination of activity amongst areas like the amygdala, anterior cingulate, insula, and medial PFC,

during task-performance as well as at rest, has been correlated strongly to Factors 1 and 2 (Motzkin, Newman, Kiehl, & Koenigs, 2011; Pujol et al., 2012) and has predicted poor performance by psychopaths in various social interaction and moral judgment tasks (Li, Mai, & Liu, 2014). This is unsurprising, considering that coordination within this network enables certain complex cognitive abilities, including learning to approach rewards and avoid threats according to context and in response to experiences, recognizing and responding appropriately to the emotions of others, moral decision-making, emotional perspective-taking and empathizing. Poor physical connections amongst these structures appear related to stunted development of a major white matter tract, the uncinate fasciculus. Reduced volume and stability of the uncinate has been observed in the right hemispheres of incarcerated psychopaths and community members with psychopathic traits. These disturbances correlate strongly with both factors, but most strongly with Factor 1. Intriguingly, the uncinate appears sensitive to developmental stressors--common in primary psychopathy--and traumatic brain injury--common in acquired psychopathy (Wolf et al., 2015).

Based upon these findings, field expert R.J. Blair (2007, 2008) and others have suggested that, although it may not seem this way to victims, most of a psychopath's behaviors do not stem from malicious intent. Hypoactivity of structures mediating limbic and impulse control functions would not predispose to chronic irritability, reactive aggression, or vindictiveness--in fact, it would do the opposite. Instead, psychopaths' thoughtless actions are an epiphenomenon of disinhibition caused by impaired attention to threats and other emotional stimuli and subsequent reduced fear and emotional responses. This prevents them from acknowledging risks to themselves or the physical and emotional well-being of others and may prompt excessive optimism or grandiose belief in one's ability to succeed. Failure to learn connections between emotional stimuli and appropriate social responses makes the viewpoints of others difficult to understand on an affective level and genuine remorse

unachievable. Use of non-limbic-mediated decision-making abilities may enable them to function reasonably well and conceal their deficits in daily life, but it reinforces a logic-driven, utilitarian mindset that values personal benefits over communal ones. Failure to respond to or learn from fear, juxtaposed with normal reward-seeking responses, results in impulsivity in the presence of potential rewards and maintained fearlessness even after repeated punishments, prompting recidivism. Although the public associates psychopathy with violent crime, the low emotional reactivity of the average psychopath may lend itself just as well to non-violent unethical behaviors.

Relationship Between Neural and Behavioral Features in Research

This neural profile aligns itself quite well with research suggesting that Factor 1 of the PCL-R and the "fearless dominance" construct are critical to differentiating psychopathy from ASPD. It also coheres with the characteristics of psychopaths highlighted by prominent early researchers such as Cleckley (1951) and Hare (1996), including low physiological response to threat or risk, suicidal threats that are rarely carried out, and low levels of affective distress. Criminal activities and incarceration trends displayed by both inmates and community members with psychopathic traits also make sense in light of this information. The capacity for superior non-limbic-mediated executive function may explain the disparity between ASPD-qualifying inmates and psychopathic inmates by enabling some psychopaths to plan and conceal their discretions more carefully. For example, in self-report research on community members with moderate PCL-R scores, a large number of participants admitted to criminal behavior, but less than 40% reported an arrest record (DeMatteo, Heilbrun, & Marczyk, 2005). Another trademark psychopathic quality, "criminal versatility," was recognized by Cleckley, who wrote, "The typical psychopath, as I have seen him, usually does not commit murder or other offenses that promptly lead to major prison sentences." Both Cleckley and Hare have described symptomatic individuals who function successfully in the community and are nonviolent, instead

presenting with serial lying; fraud, theft, or embezzlement; blackmail; corrupt politics; professional malpractice; callousness while engaging in traditionally care-based professions like teaching or nursing; and various interpersonal betrayals. Current studies have established that while PCL-R score predicts recidivism, it does not necessarily predict violence (Shepherd, Campbell, & Ogloff, 2016).

Conversely, this neural profile makes associations made between psychopathy and certain other disorders appear particularly dubious. Although Factor 1 correlates negatively with anxiety and internalizing problems (Verona & Patrick, 2015), some literature, which generalizes all "antisocial" behaviors to reflect psychopathy, has described a subtype of "anxious psychopaths" (Schmitt & Newman, 1999). This potentially occurred due to the conflation of psychopathy with ASPD in the context of comorbidity data associating ASPD with anxiety, mood disorders, and suicidality (Werner, Few, & Bulcholz, 2015). It is not unlikely that many diagnosed with ASPD are anxious; however, it should become immediately apparent that those individuals are not psychopathic.

This information collectively suggests that only a minority of ASPD-sufferers are likely to show clinically-relevant features of psychopathy. The majority of ASPD-qualifying individuals may have more in common with populations that consistently display signs of impulse control deficits and anxiety disorders, and that are predisposed to less planned, more emotional and potentially violent criminal behavior--qualities that are observed in the BPD and IED populations.

Borderline Personality Disorder: High Emotionality, Threat Sensitivity, Poor Impulse Control

Disorder Overview

The National Comorbidity Survey Replication and other research has reported moderately high correlations (r=0.64) and percentages reflecting ASPD/BPD comorbidity, with roughly 25-45% of BPD inmates meeting ASPD criteria (Black et al., 2007; Lenzenweger et al., 2007). However, the diagnostic criteria for BPD, unlike ASPD, focus on impulsive behaviors that are not necessarily

criminal or aggressive. Furthermore, many such non-violent impulsive behaviors--such as self-harm or suicide attempts, frantic efforts to avoid abandonment, frequent interpersonal disputes, substance abuse, or reckless spending or sexual activity--appear to be driven by emotional lability, depression, and irritability. Because ASPD is often associated with psychopathy, the link between disorders may seem unusual. However, additional data suggests that the diagnostic overlap is influenced by gendered expressions of BPD symptoms. For instance, Zanarini et al. (1998) reported that only 16% of female inmates, but 48% of male inmates diagnosed with BPD also met ASPD criteria, and men are 3 to 5 times more likely than women to be diagnosed with ASPD. Public misperception of psychopaths as hostile misanthropes may stem from the fact that the ASPD criteria capture many BPD-sufferers, whose hyperemotional natures can predispose them to reactive aggression at times.

Neural Profile

In sharp contrast with psychopaths, individuals with BPD demonstrate predominantly right-lateralized grey matter increases (Minzenberg, Fan, New, Tang, & Siever, 2008) but left-lateralized decreases in the amygdala (O'Neill & Frodl, 2012) and amygdala hyper-response to emotional stimuli and facial expressions. This reaction is more profound in response to aversive than positive stimuli, and BPD patients often interpret neutral expressions as threatening, suggesting the processing of ambiguity as negativity (Herpertz, 2009). Amygdala hyper-reactivity is accompanied increased activity of structures enabling visual functions--including the fusiform gyrus, which mediates facial recognition--in these subjects, suggesting that the amygdala influences the visual perceptual system to create high attentional bias to emotional stimuli (Koenigsberg et al., 2009). While executive function deficits do not appear universally in psychopaths, BPD patients regularly display impulse control and emotion suppression-related executive function deficits, which are unrelated to intelligence. Neuroimaging studies have revealed grey matter reductions in prefrontal impulse control areas, such as

the left orbitofrontal cortex (OFC) and right anterior cingulate (Minzenberg et al., 2008), as well as reduced activity in the ventromedial PFC (vmPFC), OFC, anterior cingulate, dorsolateral PFC (dlPFC), and premotor cortex at baseline and under conditions of negative emotion (O'Neill & Frodl, 2012).

As in psychopaths, structural and functional connections between the amygdala and PFC are disturbed in BPD, although the implications are different, due to the combination of a hyperactive amygdala and underactive medial PFC rather than hypoactive amygdala and less impaired PFC. Reduced stability of inferior frontal white matter tracts connecting to limbic structures has been observed in BPD and associated with a higher degree of impulsivity, aggression, and suicidality (Grant et al., 2007). New et al. (2007) observed reduced functional connectivity between the amygdala and OFC in BPD participants, compared to controls, both at baseline and during pharmacological challenge. In multiple studies, the extent of the medial PFC hypoactivation in combination with amygdala hyperactivation during an impulse control task, emotion-suppression task, or viewing images of emotional (especially angry) human faces--understood as a failure of the prefrontal regions to regulate emotional response--correlated with self-reported impulsivity and aggression (Silbersweig et al., 2007). While BPD patients display less activity than controls in medial PFC and less functional connectivity with limbic structures under conditions of negative emotion, BPD patients appear to recruit more right-sided dlPFC than medial PFC activity in conjunction with amygdala activity when attempting to suppress emotion. Decreases in medial PFC activity and increases in right dlPFC activity in response to negative emotion were associated with the degree of difficulty suppressing emotion and the severity of BPD symptoms (New et al., 2007). Intriguingly, while numerous studies have observed hypo-response in the medial PFC, others have reported hyperactivity in the vmPFC, OFC, and anterior cingulate when describing characteristics of the self and others, and under conditions of emotional challenge or provocation, such as the Point Subtraction Aggression Paradigm, lab-simulated social

exclusion, viewing emotional faces, and remembering negative life events (Ruocco et al., 2010). Mixed findings may hint at heterogenous participant samples.

Neuroimaging findings implying intensified processing of emotional information and altered attention are supported by electrophysiological findings. Late positive potential (LPP) waves--which are related to the P300 wave and indicate the active (usually emotional) processing of stimuli--are exaggerated in BPD patients, compared to controls, in response to negative stimuli during an emotion suppression task (Marissen, Meuleman, & Franken, 2010). Also consistent with neuroimaging results, the exaggerated LPP wave suggests hyperactivity in the visual perceptual system (Sabatinelli, Lang, Keil, & Bradley, 2007). P3a, a wave associated with novelty detection and attention switching, is also elevated in the right, but not left, PFC of BPD patients during an auditory change-detection task, and is more elevated in BPD patients than in controls. In BPD patients, the P3a wave also does not habituate over time, a finding reflecting poorer inhibitory control and disrupted attentional orienting. Because right-lateralized structures bear more overall responsibility for mediating emotional responses than left, the right-lateralization of the disturbance implies poor regulation of emotional responses (Meares, Schore, & Melkonian, 2011). Although emotional processing may be altered during initial exposure to a negative stimulus, such as an image, memory, or social event, BPD patients show comparable EEG activity to that of controls when asked to "reappraise" their reactions (Marissen et al., 2010).

Clearly the inverse of the typical psychopath, this is a high emotional-responder with poor impulse control, as indicated by high limbic system response to emotional stimuli and potential threats, and impaired or abnormal prefrontal performance during attempts to inhibit emotional responses. The attentional patterns of BPD patients, as indicated by EEG and neuroimaging studies, depict individuals whose attention is easily captured by emotional cues, making them sensitive to changes in the social environment. Their pattern of general amygdala hyperactivation unaccompanied by indicators of

exaggerated reward seeking, greater attentional processing of negative than positive stimuli, and interpretation of neutral stimuli as threatening, suggests that, while impulsive, they may not be excessively reward-driven and may have averse reactions to uncertainty or ambiguity. While this may predispose to mood swings in general, it may also encourage irritability or quickness to anger. This may make reactive aggression due to perceived threat more likely than instrumental aggression driven by goal-pursuit, leaving BPD-sufferers potentially prone to aggressive "crimes of passion" under certain circumstances. Still, it is ironic that BPD patients are sometimes described as "psychopathic" due primarily to their capacity for violent behavior, because these individuals are far more likely to feel genuinely remorseful for criminal acts. This is suggested by their relatively normal cognitive reappraisal abilities and their high limbic activation and attentional biases toward emotional cues from others, which, when not mediating aggressive responses, may be associated with enhanced empathy. This capacity for intense hostility followed by genuine remorse and exaggerated emotional experience may lead to low self-esteem, unlike psychopaths' grandiosity.

Relationship Between Neural and Behavioral Features in Research

This neural pattern coheres very well with behavioral patterns exhibited by BPD patients. While prone to angry outbursts that may or may not involve violence, and comprising about 35% of inmates, they are also prone to auto-aggression and self-defeating behaviors, such as suicide attempts and non-suicidal self-injury, which tend to be triggered by social threats such as abandonment, insults, or betrayals. Furthermore, individuals with BPD tend to suffer from low self-esteem, often related to retrospective views of their own outbursts. Unlike psychopaths, BPD patients tend to respond with elevated startle and other physiological responses to stressors (Hazlett et al., 2007), indicating increased fear of potential punishment. They make more errors of commission and display shorter reaction time than controls on the "No-Go" trials of Go/No-Go tests, implying poor impulse control

that is not driven primarily by reward-sensitivity (Rentrop et al., 2007). BPD patients also exhibit slower performance related to emotional interference during a Stroop Task (Wingenfeld et al., 2009) and often suffer from comorbid mood or anxiety disorders (Zanarini et al., 1998).

The fact that Factor 2 of the PCL-R has been shown to correlate not only with criminal activity but also with anxiety, mood disorders, and suicidality may partly explain the confusion of the BPD and psychopathy communities within the context of ASPD. The close relationship of BPD to ASPD may help to explain the confusing association of ASPD with anxiety, mood disorders, and suicide attempts, and prefrontal grey matter loss or executive function deficits, which leads some to mistakenly associate such traits with psychopathy. Furthermore, recall the aforementioned studies showing blunted P300 waves and limbic activity in psychopathic inmates who were reacting to emotional stimuli. In the context of BPD research findings, it makes more sense that the same studies found that members of non-psychopathic but ASPD-qualifying comparison groups displayed increased P300 during "No-Go" requirements, more interference of emotional stimuli during impulse control tasks, and higher moral transgression severity ratings associated with increased limbic activity (Harenski et al., 2010).

Intermittent Explosive Disorder: High Emotionality, Poor Attentional Switching

Disorder Overview

Reasonably high percentages reflecting comorbidity of ASPD with IED have been documented in the National Comorbidity Survey Replication, with 34.2% of ASPD-sufferers meeting IED criteria (Lenzenweger et al., 2007). However, as is the case with ASPD-sufferers with comorbid BPD, this does not appear to imply an overlap with psychopathy. In a study of self-report data from personality assessments of psychiatric and control participants, Coccaro, Lee, and McCloskey (2014) found that only a modest proportion of IED-qualifying participants displayed features of psychopathy, and that measures of trait aggression and anger, rather than psychopathic traits, correlated most strongly with

IED assessment scores. Measures of psychopathic traits also failed to discriminate between IED participants and healthy controls. The percentages depicting BPD/IED comorbidity (38%) are also higher than those depicting IED/ASPD comorbidity, suggesting that these two populations may have more common traits. Indeed, IED is a controversial diagnosis, as some believe the syndrome is merely an epiphenomenon of BPD. However, while over 25% of those with primary ASPD or BPD diagnosis meet criteria for IED, much smaller percentages of those with primary IED diagnosis meet the criteria for ASPD (4.5%) and BPD (12.3%). These numbers imply that while many ASPD and BPD patients share symptoms with IED- sufferers, IED likely has its own distinctive characteristics and is not completely subsumed by BPD or ASPD (Kessler et al., 2006).

Little research on IED has been completed, but the limited body of findings suggests that IED patients have more in common with BPD patients than with psychopaths. Findings suggest hyperactive amygdala response to negative stimuli, including angry facial expressions (McCloskey et al., 2016); interpretation of neutral facial expressions as threatening (Best, Williams, & Coccaro, 2002); reduced grey matter volume in the orbitofrontal (OFC) and ventromedial prefrontal cortex (vmPFC), anterior cingulate, amygdala, and insula (Coccaro, Fitzgerald, Lee, McCloskey, & Phan, 2016); reduced amygdala and medial OFC coupling; reduced OFC activity while viewing negative social stimuli (Coccaro, McCloskey, Fitzgerald, & Phan, 2007); and reduced white matter tract connectivity between limbic and frontal lobe structures (Lee et al., 2016). However, due to the large number of studies in which participants have a primary or comorbid diagnosis of BPD, IED may be overly-confounded with BPD in a manner similar to how ASPD is closely, but mistakenly, associated with psychopathy. This is further indicated by aforementioned patterns in prevalence data. IED patients do consistently self-report a greater degree of impulsivity and aggression. Compared to other psychiatric patients, in laboratory tasks, IED patients show more impulsivity and aggression, are more likely to attribute

negative intentions to others' behavior, and show profound interference of anger-related words when completing emotional Stroop Tasks (Coccaro, Noblett & McCloskey 2009). Still, these findings cannot definitively distinguish IED patients from BPD/ASPD patients, as IED-sufferers could merely be a group of personality-disordered patients with especially severe symptoms. However, researchers have begun to observe and replicate findings distinguishing IED based on prefrontal function.

Neural Profile

Field expert Michael McCloskey and others have, in fact, observed IED participants demonstrating PFC hyperactivation, rather than hypoactivation, and increased functional connectivity between the OFC and amygdala at baseline and under stress. In some studies, McCloskey and colleagues observed hyperactive amygdala activity, but also no significant differences between medial OFC responses in IED-sufferers and controls, and greater positive coupling between OFC and amygdala than what was observed in controls or personality-disordered patients, during exercises involving provocation or elicitation of negative emotion (McCloskey et al., 2016). McCloskey (2013) and colleagues also observed greater dorsolateral prefrontal cortex (dlPFC) activation when viewing negative images in IED subjects compared to controls, and Moeller et al. (2014) similarly observed greater dlPFC error-related activity in IED patients than in controls, which corresponded to the self-reported anger levels of IED participants. Note that BPD, in contrast, has not been associated with elevated dlPFC activity, per se, but with above-average functional connectivity of dlPFC with amygdala when medial OFC coupling is more appropriate (New et al., 2007).

At least one study that employed EEG assessments of IED patients reported excessive beta band (fast wave) activity and reduced theta and alpha (slower wave) activity in frontal and frontotemporal areas at baseline and in response to both calm and emotional musical stimuli, which the authors speculate reflects higher responsiveness to sensory stimuli in general (Koelsch, Sammler, Jentschke, &

Siebel, 2008). This could potentially be an important discriminating characteristic, and may also explain the occasional, perplexing reports of medial PFC hyper-response in the BPD literature, if in fact that finding resulted from a heterogenous sample. Another EEG study observed no aberrant amygdala activation in these patients at baseline (Koelsch, 2008). Considering this, and the fact that other observations of amygdala hyperactivity in IED have been made in response to a task and not at baseline, it is possible that in IED, agitation is purely in reaction to transient stimuli and not chronic.

Providing an additional distinguishing factor, IED-sufferers, unlike BPD-sufferers, demonstrate a blunted prefrontal P3a response to sensory stimuli (Koelsch, 2008), indicating poor attentional switching. One might expect excessive attention switching comparable to what is observed in BPD. However, it is possible that, while a state of easy distraction and automatic orienting toward negative emotional stimuli may lead to agitation and possibly aggression in BPD patients, a state of hyperfocus may do the same for IED-sufferers. This is not intentional hyperfocus, which would more likely be indicated by a blunted P3b wave (a marker of manual, rather than automatic, attentional switching), but hyperfocus induced by failure of other stimuli in the environment to distract from an aversive stimulus. Perhaps, once focused on a stressor, IED individuals have difficulty allowing their attention to be naturally captured by competing stimuli, allowing some focus to remain on the stressor or predisposing to rumination, which is also associated with prefrontal hyperfunction (Yoshimura et al., 2014).

Although IED's distinguishing features have been obscured by research conducted on comorbid BPD and ASPD patients, the available information suggests that IED may be characterized by the combination of amygdala hyper-responsiveness to stressors, excessive prefrontal feedback to amygdala during these situations, and difficulty switching attention. What emerges is the profile of a person who may not be chronically irritable but is hypersensitive to aversive stimuli when they appear because they are unable to distract themselves. This state of hyperfocus, unlike that of a psychopath pursuing a

goal, takes on a different tone in the presence of strong amygdala activation, generating a sense of anxiety or irritability that stands in stark contrast to the indifference that would be experienced by the average psychopath. This may result in uninterrupted, escalating emotion that results in an outburst.

Relationship Between Neural and Behavioral Features in Research

Indeed, this profile corresponds well to the *DSM-V* criteria for IED and subjective reports describing a pattern of a few intense, interspersed outbursts (e.g. 3 intense outbursts in a 12 month period) that can be separated by periods of normal socio-emotional functioning and impulse control, during which much more subdued expressions of aggression may occur (e.g. heated verbal disputes). This stands in contrast to the more frequent irritability and outbursts observed in BPD (APA, 2013). Also speculative but thought-provoking are comparisons between the experience of IED outbursts and clinically-defined panic attacks or compulsive urges. One study of self-report data describing subjective experiences of IED-sufferers during outbursts found frequent reports of not only feelings of rage, but also of intense anxiety and panic, hot flashes, trembling, and heart palpitations that were experienced as a "prodrome" minutes before the outburst. The outbursts were followed initially be feelings of relief, which was transient and rapidly replaced by remorse and embarrassment (Kulper, Kleiman, McCloskey, Berman, & Coccaro, 2015). It is worth noting that IED shows high comorbidity with anxiety and mood disorders, and many anxiety and mood disorders have also been associated with excessive medial PFC and anterior cingulate activity (Kessler et al., 2006). BPD and some ASPD patients are prone to anxiety as well, but these panic attack-like phenomena are not a guaranteed aspect of either symptom complex, whereas virtually all IED-qualifying patients experience them.

Limited Treatment Opportunities as a Result of Misinterpretations

As many citations in this review have already served to indicate, one result of conflating individuals with different neural presentations based on IAP alone is the use of heterogenous research

populations that do not generate useful or generalizable results (Hare et al., 1991). One negative outcome of non-generalizable research is difficulty determining ideal treatments across individuals with the same diagnosis, or even limiting treatment opportunities for some patients. This has serious consequences for the ASPD population, which is more than likely to cover a very heterogenous group.

There is evidence that ASPD-sufferers who do not meet psychopathy criteria, such as those who meet criteria for BPD and IED, can benefit from specific behavioral and pharmacological treatments (McCloskey, 2013). Unfortunately, because of the ill-supported association of ASPD with psychopathy, if an individual who presents with qualities of BPD or IED is given a primary or secondary diagnosis of ASPD, he/she may not be referred for appropriate treatment due to the belief that psychopaths are a completely treatment-refractory population. This is technically supported by a large body of evidence linking high PCL-R scores to high recidivism rates and poor outcomes in various rehabilitation programs (Ogloff, 2006). In spite of the obvious need for intervention, however, few targeted treatments for ASPD-sufferers have been developed, few that have been developed have achieved success, and few appear to be in development, in part due to clinicians remaining pessimistic about the treatability of this population. Literature on the subject includes statements such as, "The only effective treatment for ASPD appears to be the passage of time. Those individuals who do not get killed or kill themselves and survive into their 40s tend to mellow" (Hatchett, 2015). Such stigma is harmful both to individuals diagnosed with ASPD who present with features akin to BPD or IED, as there are treatments that have been proven effective for these populations, and to those with psychopathic traits, as stigma quashes creativity and innovation amongst medical professionals, thus hindering potential treatment development.

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