Degree project

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The Evil Inside: A Systematic Review of Structural Differences in Psychopathy

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Abstract

The purpose of this systematic review was to characterize further the structural differences in the prefrontal cortex, limbic and paralimbic regions and amygdala alone in psychopaths. Psychopathy is a multifaceted personality disorder characterized by interpersonal and affective traits like lack of empathy, guilt or remorse, shallow affect, and carelessness, as well as behavioral traits such as impulsivity, and poor behavioral control. In recent years, the interest in the neuroanatomical differences in psychopaths has grown. This review aims to understand the prefrontal cortex, limbic and paralimbic areas, and how these regions differ between psychopathic patients and healthy controls. By systematically screening articles that used magnetic resonance imaging (MRI) and voxel based morphometry (VBM) the studies in this review examined people with psychopathic traits. To assess for psychopathy, the most used assessment tool, the Psychopathy Checklist-Revised (PCL-R) was used. Results show that the higher the PCL-R scores of the offenders, the less gray matter volume was found in the superior parts of the prefrontal cortex, limbic and paralimbic areas. Additionally, amygdala deficits in individuals with psychopathy were found. This systematic review may benefit in the way that if we increase our understanding of psychopathy and pave the way for the creation of effective psychopathic treatments it could prevent future acts of violence. The link between a structural brain anomaly and psychopathy may have a profound clinical, legal, and scientific impact. A psychopathy diagnosis may serve as a precursor to severe societal violence.

Keywords: psychopathy, PCL-R, structural neuroimaging, prefrontal cortex

Introduction

Individuals displaying aggressive, violent, impulsive, and antisocial behavior have been studied for many centuries. The concept of psychopathy can be traced back to the end of the 18th century, and the condition was then known as 'madness without delirium' (Cleckley, 1941). In the following 200 years, parallel with the development of several assessment tools and imaging techniques, the concept of psychopathy evolved. Psychopathy, now categorized as a personality disorder, is most commonly clinically assessed by using the Psychopathy Checklist-Revised (PCL-R; Hare, 2003).

Psychopathy is believed to affect 1% of the general population but upward 25% of the prison population (Kiehl, 2006). Due to the interpersonal and affective characteristics along with the violation of social norms and impulsivity, psychopathy is an important predictor of recidivism, especially violent recidivism (Hemphill et al., 1998). Recidivism is the act of repeating wrongdoing after experiencing negative consequences from the previous behavior, such as inmates who are rearrested for a similar offense. High PCL-R scores on an antisocial subscale which includes juvenile delinquency and criminal versatility may be an indicator of recidivism. Additionally, according to Reidy et al. (2015), people with psychopathic traits are at least five times more likely to recidivate violently than non-psychopathic offenders. Sohn et al. (2020) claim that perhaps the most broad review of psychopathy's role in predicting recidivism risk to date has concluded that behavioral features of psychopathy are more significantly and consistently associated with both future violent and general recidivism than interpersonal and affective features.

Furthermore, research has demonstrated structural and functional brain abnormalities associated with psychopathy and psychopathic traits, implicating structures such as the prefrontal cortex (PFC) (Blair, 2012; Contreras-Rodríguez et al., 2015; Ermer et al., 2012; Yang et al., 2009a, 2010), amygdala (Boccardi et al., 2011; Contreras-Rodríguez et al., 2015; Yang et al., 2009b, 2010), medial frontal cortex, hippocampus (Contreras-Rodríguez et al., 2015; Ermer et al., 2012), orbitofrontal cortex (OFC) (Boccardi et al., 2011; de Oliveira-Souza et al., 2008; Ermer et al., 2012; Tiihonen et al., 2008; Yang et al., 2009a, 2009b), and insula (Contreras-Rodríguez et al., 2015; de Oliveira-Souza et al., 2008; Ly et al., 2012). By identifying structural and functional alterations in the brains of individuals displaying deviant behavior compared to healthy controls, neuroscience has contributed to advancements in several other fields. And understanding the difference between psychopathic subgroups has provided an important baseline for further research into the depths of the darkest corners of the human mind.

The Psychopathy Checklist-Revised

The need for a validated clinical instrument for assessing psychopathy is evident from both an economic and legal perspective. Despite from the high prevalence of psychopathic individuals in prison populations and the high rate of recidivism, psychopaths commit more violent crimes compared to non-psychopathic controls, thus making them a burden to the criminal justice system as well as to their proximity (Glenn & Raine, 2009).

The most frequently used and validated instrument for assessing psychopathy is the PCL-R (Hare, 1991, 2003), which is composed of personality traits including callousness, shallow affect, manipulativeness, lack of remorse and guilt, emotional impairments, and impulsive antisocial behavior (e.g., Baskin-Sommers et al., 2016; Korponay et al., 2017; Yang et al., 2010). The PCL-R scale consists of 20 items, each item is scored on a three-point scale (0 = does not apply; 1 = applies somewhat or 2 = definitely applies). The score, ranging from 0 to 40, provides information on the dimension and severity of psychopathy displayed by the interviewed individual, cut-off score for a diagnosis of psychopathy being 30. The dimension of psychopathy is further divided into two separate factors (Factor 1: affective-interpersonal; Factor 2: impulsive-antisocial) (Hare, 1991). The affective-interpersonal dimension contains characteristics such as superficial charm, pathological lying, lack of remorse or guilt, grandiose sense of self-worth, and failure to accept responsibility for one's own actions. The second dimension of psychopathic personality traits includes poor behavioral control, irresponsibility, impulsiveness, and lack of realistic, long-term goals. These two factors and their respective items have been further subdivided into a four facet model (Hare, 2003), dividing Factor 1 into interpersonal problems (facet 1), affective traits (facet 2), and Factor 2 into lifestyle (facet 3) and an antisocial sub-scale (facet 4) (see Appendix A). It is worth noting that most studies examining prefrontal gray matter and Factor 1 scores discover a negative relationship, whereas most studies examining prefrontal gray matter and Factor 2 scores discover a positive relationship (Korponay et al., 2017). According to Korponay et al. (2017), these findings suggest that despite being highly correlated in terms of PCL-R score, Factor 1 and Factor 2 traits are separate at the neural level.

Other measurement tools, several of which derive from PCL-R, are being used in clinical and forensic settings, and for assessing the prevalence of psychopathic traits among the general and adolescent population. Examples of such assessment tools are presented in an article published by Reidy et al. (2015) on psychopathy and its implications for public health and the necessity of violence prevention. The Psychopathy Checklist: Screening Version (PCL:SV; Hart et al., 1995) is a 12-item symptom-construct rating scale intended for adults, the Psychopathy Checklist: Youth Version (PCL-YV; Forth et al., 2003) is used when

assessing adolescents in ages 12-17. These two checklists, although relevant tools are beyond the scope of this review which will focus on adults measured with PCL-R.

In the next section, the relevant neuroanatomical regions of interest that have been linked to psychopathy will be covered.

Structural Differences in Prefrontal, Limbic, and Paralimbic Regions

The PFC, the evolutionary youngest region of the brain, is frequently divided into six main regions, ventrolateral, dorsolateral, ventromedial, dorsomedial, frontopolar, and OFC. This large brain region, which makes up approximately a third of the cortex, is involved in a wide range of emotional, cognitive, social, and motivational processes (Ray & Zald, 2012). Psychopathy is believed to have a neurobiological origin (Poeppl et al., 2019). Although PFC damage does not usually result in full-blown psychopathic behavior, it may trigger pseudopsychopathic personality and behavioral changes (Ling & Raine, 2018). One name, which now holds a legendary status in the field of cognitive neuroscience, is Phineas Gage. In the mid 1800s, Gage suffered a major head trauma caused by a large metal rod piercing the PFC, resulting in major personality and behavioral changes, many of which can be observed in psychopathic individuals (Damasio et al., 1994).

The OFC, one of the main prefrontal regions, is involved in several higher functions such as reasoning, language, and consciousness. Due to its close proximity to the limbic system, in particular, the amygdala, the OFC is also involved in processing emotions. Other essential regions involved in social cognition and emotional processing are the anterior cingulate cortex and the insular cortex (Toates, 2011). Individuals with damage in the anterior cingulate cortex and the OFC often exhibit psychopathic traits from both PCL-R Factor 1 and Factor 2, such as impulsivity, lack of empathy, and reactive aggression (Ermer et al., 2012).

The amygdala is a complex structure that is involved in many normal behavioral functions as well as psychiatric conditions. Not long ago, it was a remote region of the brain that drew little scientific attention, today it is one of the most extensively researched brain areas (LeDoux, 2007). Structural and/or functional changes in the amygdala have been linked to a wide range of psychiatric disorders (e.g., anxiety disorders, post-traumatic stress disorder, phobias, depression, and schizophrenia) (LeDoux, 2007). Furthermore, the amygdala complex, according to Bell et al. (2022), is a key structure for understanding the neurobiology of violence because of its role in the regulation of fear and aggression through the rapid detection of threats and activation of fight-or-flight responses.

Overall, the limbic system is distinguished by direct involvement in processes designed to ensure the survival of the individual and species. It is considered the center of emotional and behavioral expression. Considering that the limbic system includes not only cortical structures but also subcortical areas (Roxo et al., 2011) it suggests that the limbic

structures are capable of integrating both internal and external sensations. According to Kiehl (2006), the relevant functional neuroanatomy implicated in psychopathy is the paralimbic system. Yet again, we can refer to the famous case of Phineas Gage in the 1880s to infer that the recent suggestions that limbic and paralimbic systems and their functional neuroanatomy in psychopathy are not new.

Aims

The aim of this systematic review is to answer the broader question "Is there structural neuroanatomical differences between psychopaths and healthy individuals, and if so, can this be used (1) to better understand psychopathy as a disorder; (2) as a diagnostic tool to help identify and treat the disorder; or (3) to develop interventions for repeat offenders (recidivism) and reduce crime rates?". To answer this, we will limit our review to Robert Hare's PCL-R scale since it is the most widely used and validated instrument for assessing psychopathy in adults. This scale is made up of two factors that are further subdivided into four facets (see Appendix A).

While the psychological risk factors have received considerable attention, the biological basis of psychopathy remains unclear (Craig et al., 2009). With this review, we can also add that there seem to be few structural neuroimaging studies to date that use validated and standard approaches in their methodology and design to allow for reliable comparisons. Despite the importance of examining both structural and functional differences between psychopaths and healthy individuals, this systematic review aims to examine if there are structural neuroanatomical differences between psychopaths and healthy individuals. More specifically, we will look at structural differences in the PFC, limbic and paralimbic regions, and amygdala alone and will limit our search to studies that use voxel-based morphometry (VBM) and magnetic resonance imaging (MRI) as neuroimaging methods. By more closely identifying and understanding the structural differences of psychopathy, more specific and effective treatments can be developed. Additionally, a better understanding of the disorder, as well as better treatment alternatives, may promote a reduction in crime and recidivism.

The OFC has been theorized to be particularly important in the development of psychopathy (Ling & Raine, 2018). The OFC, a subregion of the PFC and one of the regions examined in this review, is involved in information processing in the context of planning and decision-making. The medial region of the OFC is particularly crucial in tasks involving emotion-driven decision-making and regulation. Additionally, patients who have suffered damage to the OFC and anterior cingulate cortex frequently display psychopathic traits from Factor 2 (lifestyle and antisocial) of the PCL-R scale, such as impulsivity, reactive aggression, and a lack of empathy (Ermer et al., 2012). Therefore, damage to the OFC and other brain structures may predispose to psychopathic behavior by interfering with decision-making processes that enable socially appropriate behavior (Ling & Raine, 2018).

Damage to the amygdala, which is a part of the limbic system, is linked to psychopathic traits like shallow affect and lack of empathy (Factor 1 traits), but there are also signs of Factor 2 traits, such as impulsivity, poor behavioral control, and aggression (Ermer et al., 2012). This limbic structure is considered the center for a range of affective processes such as empathy and fear conditioning, as well as emotion and affect recognition (Ling & Raine, 2018). Additional knowledge on this may help predict recidivism or future danger in society. In addition, the identification of such structural neuroanatomical changes may be useful for forensic psychiatry and criminal justice system organizations in the development of intervention and treatment programs. During an 11-year follow-up period, Sohn et al. (2020) evaluated the PCL-R's utility in predicting violent versus nonviolent recidivism. Sohn et al. (2020) discovered that facet 2 (affective) rather than facet 4 (antisocial) prospectively predicted violent recidivism compared to nonviolent recidivism, which should be considered in future studies to reduce recidivism. Serin (1996) conducted a study with 81 offenders over a period of up to 67 months. Serin (1996) discovered that Factor 1 was associated with violent recidivism, whereas Factor 2 was associated with general recidivism. Furthermore, the overall recidivism rate for psychopaths was 85%. In light of such findings, our aim is to investigate whether structural changes to certain regions of the brain can lead to better being able to identify and diagnose psychopathy, but also guide certain treatments. For example, if an MRI scan shows a decrease in PFC gray matter volume, which is correlated with aggressive behavior, it might suggest to the doctors that this patient needs to undergo a psychopathic evaluation, such as being tested with the PCL-R. However, we could also look at it from a different perspective. If inmates normally take the PCL-R because doctors or prison wardens suspect a psychopathic diagnosis, an MRI scan revealing a decreased volume of the amygdala linked to Factor 2 traits, such as impulsivity, poor behavioral control, and aggression of the PCL-R scale, for example, can lead to more informed diagnosis and guided treatments of psychopathy. Decreased PFC volume is correlated with both Factor 1 and Factor 2. Revealing this could lead to treating more facets of the PCL-R scale such as lack of empathy, failure to accept actions, and pathological lying. An accurate diagnosis could in turn aid in the patient's rehabilitation, stop any further aggressive behavior, and lower the crime rate. The diagnosis might then result in a better understanding of the prison arrangement. Having an understanding of how to divide the inmates in the most safe way, may lead to fewer assaults among criminals. According to Yang et al. (2010), psychopaths who have been convicted of crimes may be more prone to risky and impulsive behaviors because their prefrontal regions have less gray matter volume, which makes it harder for them to recognize cues that indicate arrests.

Methods

Search Strategy

This literature search was done on the 3rd and 6th of March, 2023, utilizing four databases: Web of Science, MEDLINE EBSCO, PubMed, and Scopus. The literature search was conducted by using Boolean operators and a combination of certain keywords, such as psychopathy, psychopathic trait, magnetic resonance imaging, and neuroimaging (along with the respective abbreviations and alternatives). The complete search terms and combination were as follows: (psychopath OR psychopaths OR psychopathic OR psychopathy OR "psychopathic trait*") AND ("MRI" OR "magnetic resonance imaging" OR "structural magnetic resonance imaging" OR "structural imaging" OR "structural MRI") NOT ("fMRI" OR "functional magnetic resonance").

The search generated a total of 782 articles (Web of Science: n=131; MEDLINE EBSCO: n=164; PubMed: n=232; Scopus: n=255). The result was exported from the databases to Excel version 16.70. The Excel software was used to detect duplicates (n=404), which were then manually removed. Leaving 378 articles to be screened. Records excluded (n=335) included reviews, letters, proceedings papers, meeting abstracts, no year included or published earlier than the year 2000, articles not fully written in English, and articles that were not eligible for the PICO model used in this review leaving 43 articles to be screened. Two of these were not accessible to retrieve, leaving 41 for further scrutiny. After reading the remaining articles to their full extent, the authors removed an additional 35 articles due to them not meeting the inclusion criteria, thus leaving 6 articles to be included in this systematic review (see Figure 1).

Inclusion and Exclusion Criteria

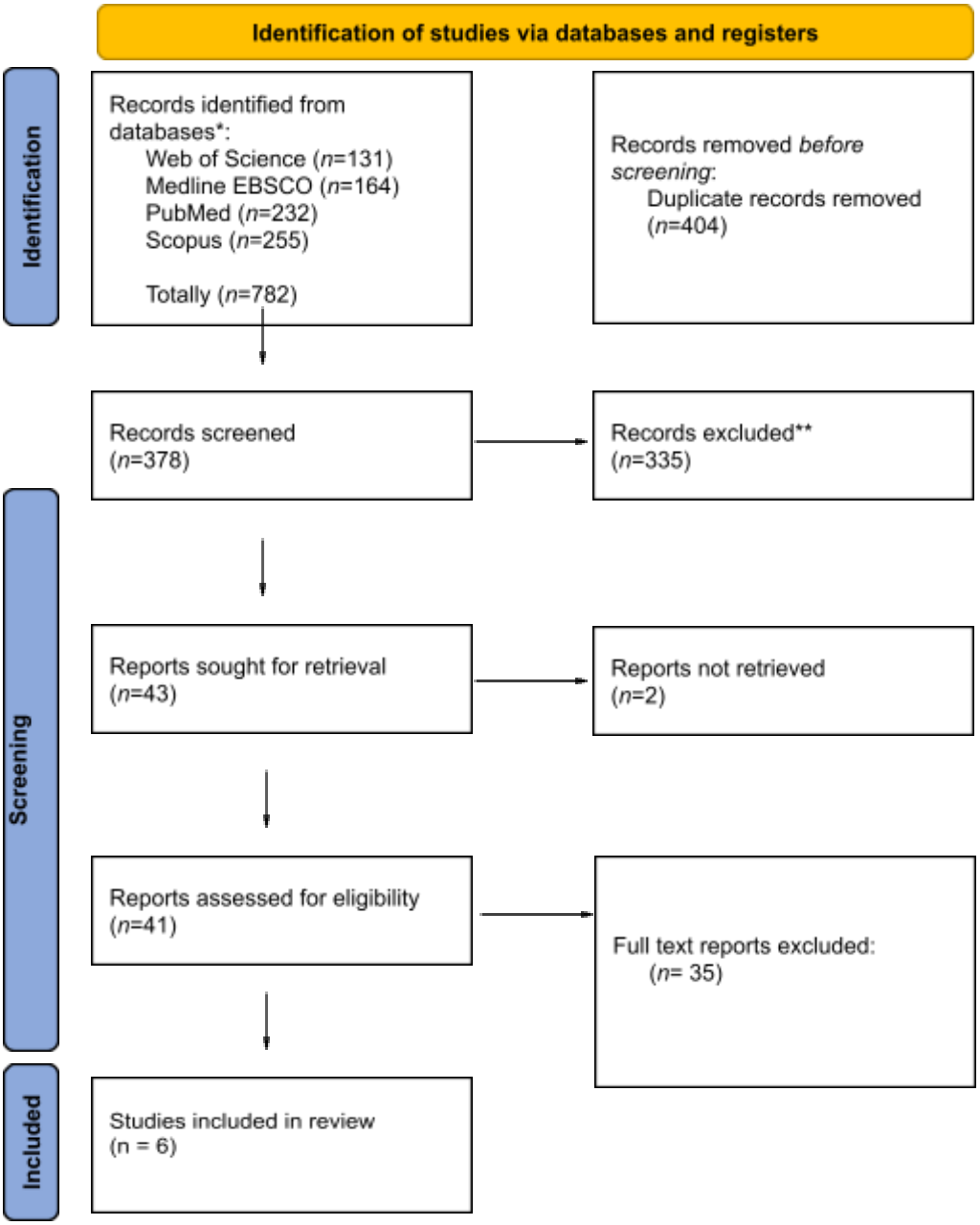
With the aid of MRI and VBM, this systematic review will examine the volumetric structural differences in the PFC , limbic and paralimbic system, and amygdala of adult psychopaths compared to healthy subjects and the Montreal Neurological Institute (MNI 152) template, a standard coordinate system used in neuroimaging. The MNI template consists of 152 healthy brains and makes it easier to analyze and compare neuroimaging data. Therefore, only articles that used MRI or VBM to search for structural differences in the PFC, limbic and paralimbic system, and amygdala in adult psychopaths compared to healthy individuals were eligible for inclusion. As such, people under the age of 18, such as adolescents and children, were excluded. Furthermore, the participant samples that were included had to be diagnosed with psychopathy using the PCL-R scale (with the cut-off score being 30 in a 0-40 scale). The chosen time frame is 2000 until the present, and only articles in English, published in reputable journals are included.

Data Extraction

The following data will be extracted from the included articles: information on the test used to assess psychopathy and which neuroimaging technique was used in the study, the brain regions studied, and the outcome measures for volumetric structural differences in the selected brain regions, information about the participants (number of participants, age, and gender) (see Table 1.).

Figure 1

A flow diagram of the literature search and study selection process



Note: Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ

2021;372:n71. doi: 10.113

Results

Research from studies using different neuroimaging techniques (e.g., structural [MRI], [VBM], diffusion tensor imaging, and functional magnetic resonance imaging) has implicated brain regions associated with emotional and behavioral deficits displayed in psychopathic individuals. Evidence shows that activity in the PFC, limbic and paralimbic systems, and the amygdala alone differs in people with psychopathy compared to healthy individuals. Decreased gray matter volume has been found in the PFC, limbic, and paralimbic areas, and significant bilateral reduction in the amygdala compared to controls. One article screened in this review however, showed larger prefrontal subregions in psychopaths.

Ermer et al. (2012) hypothesized that psychopathy appears to have structurally reduced brain regions in the paralimbic cortex and limbic areas. Ermer and colleagues found psychopathy to be negatively associated with gray matter volume in the OFC and the posterior cingulate cortex (PCC). These areas play important roles in emotional processing, moral judgment (PCC; Kiehl et al., 2001), decision-making, and planning (OFC; Rolls, 2004). Furthermore, decreased gray matter volume and gray matter concentration were observed in both limbic and paralimbic areas, including the amygdala, hippocampal and parahippocampal regions, anterior superior temporal gyrus, and inferior temporal cortex. The anterior cingulate cortex and insula, two paralimbic regions, showed no signs of reduced gray matter volume, according to Ermer et al. (2012). Although there have been conflicting reports on structural variations in the anterior cingulate cortex in psychopathy, earlier research has discovered variations in the insula. This study used 296 male participants in their study which is a significantly larger sample size than most of the studies on structural differences in psychopathy. A large sample size indicates that the researchers put in the effort, and time and have equipment and the capital for a larger study. It will also give a broader significance to the result.

Yang et al. (2005) investigate the hypothesis that psychopathy is associated with a decrease in prefrontal gray volume, but that this abnormality is only found in unsuccessful psychopaths. The difference between successful and unsuccessful in this case is either succeeding in some aspects of life (and not being convicted for potentially committed crimes) or not succeeding in life (and being convicted for committed crimes) (Yang et al., 2010, 2005). Yang and colleagues found significantly reduced PFC gray matter volume in unsuccessful psychopaths compared with their successful counterparts and controls. The PFC is involved in emotional expression and modulation, decision-making, and executive functioning, deficit in the PFC may offer an explanation for some of the observed differences between successful and unsuccessful psychopaths. An interesting issue was not answered in this article for further studies to look into. The issue question is whether prefrontal structural

impairments only cause poor decision-making, which leads to capture of the unsuccessful psychopaths, or whether they also predispose to multiple psychopathic traits. Yang et al. (2005) have doubts that prefrontal structural deficits cause psychopathic behavior in and of themselves. Instead, a more complicated disruption to neural circuitry related to the PFC is more likely to predispose to psychopathic behavioral traits. However, this is something that future research ought to investigate.

Yang et al. (2010) sought to uncover noticeable and subtle morphological changes in the PFC and amygdala of successful and unsuccessful psychopaths. When compared to controls, unsuccessful psychopaths had significantly lower gray matter volume and cortical thickness in the amygdala and OFC. Unsuccessful psychopaths had a 20% volume reduction in the right amygdala and a 26% volume reduction in the left amygdala compared with controls. Successful psychopaths showed a 9.3% volume reduction in the left amygdala and a 12.7% volume reduction in the right amygdala compared to controls. Additionally, across the entire hemisphere, unsuccessful psychopaths showed a significant reduction in cortical gray matter thickness compared to controls. Specifically, there was significant cortical thinning in the right medial frontal cortex and OFC in unsuccessful psychopaths. Successful psychopaths on the other hand showed no significant cortical thinning across the hemispheres compared to controls. Yang et al. (2010) suggest that this study is the first to show that unsuccessful psychopaths have greater prefrontal and amygdala structural deficits, which may cause them to have poor behavioral control and impaired decision-making, indicating that impairment of these structures may be another contributing factor resulting in behavior leading to criminal convictions. The sample size in this study, like many others, was relatively small. The authors point out that the successful psychopath group, in particular, was moderate, which is something to consider in future studies. Furthermore, the difference in PCL-R facet 1 and facet 4 scores between the two psychopathy groups may have contributed to the lack of significant findings in several analyses in this study. The authors also highlight that the findings could be influenced by differences in psychopathy levels between the two psychopathy groups.

Korponay et al. (2017) investigated PFC volume in psychopathy using multimodal neuroimaging, which means that Korpany and colleagues used different neuroimaging techniques. In this systematic review, we will only present the structural findings of the study since the other result is beyond the scope of this review. Korponay and colleagues discovered increased prefrontal subregion volumes, in contrast to the other articles in this review which found a decrease. The strongest correlations were found between Factor 2 scores and the volume of right medial OFC and left dorsolateral PFC. There were no significant relationships between PFC focal volumes and Factor 1 scores or PCL-R Total scores. The findings of Korponay et al. (2017) are consistent with previous research that has found positive

relationships between Factor 2 scores (impulsive/antisocial psychopathy traits) and various PFC subregions (Contreras-Rodríguez et al., 2015; Ermer et al., 2013). According to Korponay et al. (2017), the majority of studies examining prefrontal gray matter and Factor 1 scores discover a negative relationship, whereas the majority of studies examining prefrontal gray matter and Factor 2 scores discover a positive relationship. This finding suggests that assessments of prefrontal gray matter structure in a given sample of psychopathic individuals are impacted by the relative severity of Factor 1 (interpersonal and affective psychopathic traits) and Factor 2 traits in that sample (Korponay et al., 2017). Korponay and colleagues specifically looked at PFC subregion volume by using multimodal neuroimaging, whereas the other five articles looked at gray matter volume. This could explain why their results differed from the other five articles screened in this review. Although the data of Korponay et al. (2017) do not directly address this level of analysis, one possibility according to the authors for why positive and not negative results are shown is that the identified positive associations between Factor 2 scores and PFC subregion volumes indicate deficient synaptic and neuronal pruning in the region of interest of the study, showing either dysfunctional and/or ineffective processing. As with many similar studies, Korponay et al. (2017) acknowledge the link between psychopathy and substance abuse which both seem to decrease gray matter volume. To account for this aspect of the study population, Korponay and colleagues included a continuous substance use severity variable in their regression models.

Yang et al. (2009b) hypothesized structural amygdala deficits in psychopaths, suggesting that structural amygdala abnormalities contribute to emotional and behavioral symptoms of psychopathy. In their study, they implemented a cross-sectional design using structural magnetic resonance imaging. Twenty-seven psychopaths examined with the PCL-R scale were included in the study. Yang and colleagues discovered that individuals with psychopathy had significantly lower bilateral amygdala volume than healthy controls who matched on age, ethnicity, and sex. When compared with controls, the left amygdala showed a 17.4% reduction and the right amygdala showed an 18.93% reduction in volume. After adjusting for socioeconomic status and substance and alcohol dependence, these results remained significant. Yang et al. (2009b) also sought to determine whether amygdala reduction was connected to a specific aspect of psychopathy. According to their findings, the affective and interpersonal facets of the PCL-R scale such as lack of remorse, guilt and empathy from the affective factor and superficial charm, glibness and pathological lying from the interpersonal factor, have the strongest correlations. The authors speculate, structural defects of the amygdala may predispose psychopathy individuals to have emotional and social dysfunction. Alcohol and drug dependence were taken into account in this study, which is important because they may reduce brain volume. Even though the participants were matched in age, gender, and ethnicity, their study only used 27 psychopaths and 32 normal

controls, making it a relatively small group to study. A larger sample size would be preferable for the study's replication.

The purpose of the study of Hofhansel et al. (2020), was to investigate the relationship between various aspects of aggressive and psychopathic behavior and brain morphology. Hofhansel et al. (2020) discovered that psychopathic behavior was negatively correlated to prefrontal gray matter volume. That is, with increasing scores on the PCL-R scale, they found a greater reduction in gray matter volume in the PFC, specifically the superior frontal gyrus. Hofhansel and colleagues sought to determine whether their results correlated to any facets of the PCL-R scale. Not only was gray matter volume in the PFC found to be negatively correlated with psychopathy (PCL-R sum score), this finding was primarily attributed to the PCL-R's second factor which is impulsive-antisocial behavior. No other PCL-R sub-scales could be significantly linked to specific brain structures looked at in this study, and these results demonstrate that the reduction in gray matter volume in the PFC was mainly driven by the antisocial behavior factor of the PFC-R scale. Only 27 psychopaths and 27 controls were recruited in this study. Despite the small sample size, they discovered decreased gray matter volume in the PFC, as larger studies also have shown. According to the authors, when compared to controls, psychopaths had a higher prevalence of substance use disorders, fewer educational years, and significantly lower verbal IQ. Despite efforts to match the control group for IQ, education, and substance use disorders, Hofhansel and colleagues were unable to find a non-psychopathic control group that met these criteria. As a result, potential influences of intelligence and substance use on the brain structure cannot be completely ruled out, as both factors may be associated with gray matter volume reductions.

All these studies found similar results, except Korponay et al. (2017) who instead of finding decreased gray matter volume, found increased prefrontal subregion volumes. All of the chosen articles are in one way conceptual replications of each other using different random sampling and neuroimaging techniques to find structural differences in the brains of psychopaths. This is essential since it counteracts the sample bias. Dr. Yaling Yang is the lead author in three of the six studies, which might be seen as a bias. The same could be said about Dr. Yang's colleagues who appear in multiple of the chosen studies. In research, replication is essential. It might have been better to choose six completely different lead authors with completely different researchers all of them who have different personal agendas, which could have changed the outcome of the results. Another way of thinking is that Dr. Yang is a professional in this topic and articles including her are highly preferable. How this influenced the outcome is hard to predict, all of the articles are replicated. Dr. Kent Kiehl is a well-known neuroscientist and he is traveling around in his famous camper which is equipped with a Siemens 1.5T Avanto Mobile MRI System. This machine is used in two of the

articles chosen, which is a relatively low sample, but one should keep in mind that utilizing different tools would counteract possible errors as calibration and other issues of the machine which would lead to a misleading finding.

Table 1

A summary of studies investigating structural differences in psychopaths

Lead Author & Publication Year	Sample	Gender	Age (Mean±SD)	Brain Imaging Technique/ Psychopathy Assessment	Brain Regions Looked at	Main Findings
Hofhansel et al. (2020)	Criminal offenders (n= 27) Controls (n=27)	All male	18-55	VBM /PCL-R	Prefrontal gray matter volume, right superior frontal, left inferior parietal regions, right middle, and superior temporal gyrus	The first main finding of this study was an inverse correlation between global psychopathy and gray matter volume. The higher the PCL-R sum scores of the offenders were, the less gray matter volume was found in the superior parts of the prefrontal cortex
Korponay et al. (2017)	All (n= 124) Non-psychopathic (n= 35) Intermediate (n= 48) Psychopathic (n= 41)	All male	All: 31.6 ± 7.1 Non-psychopathic 31.3 ± 7.9 Intermediate 31.8 ± 6.7 Psychopathic 31.5 ± 7.7	MRI + RSFC + / PCL-R	PFC, mOFC and dlPFC	PCL-R Total scores and Factor 2 scores were exclusively linked to larger prefrontal cortex subregion volumes. The most robust relationships were observed between Factor 2 scores and the volume of right mOFC

Lead Author & Publication Year	Sample	Gender	Age (Mean±SD)	Brain Imaging Technique/ Psychopathy Assessment	Brain Regions Looked at	Main Findings
						and left dlPFC (middle and superior frontal gyri).
Ermer et al. (2012)	Adult male inmates (n=296)	All male	All: 33.9 years ± 9.50	MRI + VBM / PCL-R	ACC, PCC, parahippocampal gyrus, amygdala, hippocampus, temporal pole, OFC, and insula	Psychopathy was associated with decreased gray matter volume and gray matter concentration in several paralimbic and limbic areas, including bilateral parahippocampal, amygdala, and hippocampal regions, bilateral temporal pole, bilateral inferior temporal cortex, and right and left regions of the OFC. Psychopathy was also associated with decreased GMV in the PCC.
Yang et al. (2010)	Unsuccessful psychopaths UP (n=16)	Male (n=45) Female (n=8)	Unsuccessful psychopaths 32.62 ± 6.94 Successful psychopaths	MRI / PCL-R	PFC, OFC, and Amygdala	Significant reduced gray matter volume and cortical thickness/ surface shape in the middle frontal,

Lead Author & Publication Year	Sample	Gender	Age (Mean±SD)	Brain Imaging Technique/ Psychopathy Assessment	Brain Regions Looked at	Main Findings
	Successful psychopaths SP (n=10) Controls (n=27)	UP Male (n=15) Female (n=1) SP Male (n=9) Female (n=1) Controls Male (n=21) Female (n=6)	30.20 ± 6.39 Controls 30.11 ± 7.33			orbitofrontal cortex and the amygdala were found in unsuccessful psychopaths but not successful psychopaths, compared with controls.
Yang et al. (2009b)	Psychopaths (n=27) Controls (n=32)	Male (n= 31) Female (n= 8) Psychopath M= 25 F= 2 Control M= 26 F= 6	Psychopathy 32.22 ± 6.57 Controls 30.84 ± 7.14	MRI / PCL-R	Amygdala	Structural amygdala deficits in individuals with psychopathy
Yang et al. (2005)	Successful psychopaths SP (n= 13)	All male	Successful psychopaths 29.62 ± 6.13	MRI / PCL-R	PFC	Individual differences in psychopathy correlate with volume of prefrontal gray

Lead Author & Publication Year	Sample	Gender	Age (Mean±SD)	Brain Imaging Technique/ Psychopathy Assessment	Brain Regions Looked at	Main Findings
	Unsuccessful psychopaths UP (n=16) Control (n=23)		Unsuccessful psychopaths 33.81 ± 6.62 Controls 28.35 ± 6.63			matter, with high total PCL-R scores associated with low prefrontal gray volume. Second, the relationship between psychopathy and prefrontal gray volume is nonspecific in that it was found for all psychopathy factors. Third, unsuccessful psychopaths, but not successful psychopaths, had a 22.3% reduction in prefrontal gray matter volumes compared with control subjects

Note: VBM = Voxel-based morphometry; PCL-R = The Hare Psychopathy Checklist-Revised; sMRI= structural Magnetic Resonance Imaging; RSFC = Resting-state functional brain connectivity; PFC = Prefrontal cortex: mOFC = medial Orbitofrontal cortex; dlPFC = dorsolateral Prefrontal cortex; ACC = Anterior Cingulate Cortex; PCC = Posterior Cingulate Cortex

Discussion

Six articles were included in the qualitative analysis. The included studies use similar, but not the same approach to investigate the structural differences in the brain of psychopaths. Four of the articles (Ermer et al., 2012; Korponay et al., 2017; Yang et al., 2010, 2005) used human subjects for control, whereas the latter two additionally split these subjects into successful and unsuccessful psychopaths based on their history of criminal convictions to compare the result. Yang et al. (2009b) and Hofhansel et al., (2020) in contrast, used the MNI template. All the articles used the PCL-R scale to measure psychopathy. Hofhansel et al. (2020) used VBM in their study, Ermer et al. (2012) used both VBM and MRI while Korponay et al. (2017) used multimodal neuroimaging data containing structural and functional MRI, as well as VBM. Yang et al. (2010), Yang et al. (2009b), and Yang et al. (2005) used only MRI. Despite this, all studies found significant structural differences in the prefrontal areas, amygdala, and regions of the limbic and paralimbic systems of adult psychopaths compared to healthy controls.

The current understanding of psychopaths has provided an important baseline for research into the depths of the human mind's darkest corners. Still, some questions remain. It is unclear whether prefrontal structural defects only result in faulty decision-making, which captures criminal adult psychopaths, or whether they also predispose to a variety of psychopathic traits. Studies suggest that structural defects in the PFC are unlikely to be the direct cause of psychopathic traits (Yang et al., 2005). The likelihood that someone will exhibit psychopathic behavior increases with the complexity of the neuronal circuitry in the area. Results from the screened articles in this review also revealed a negative correlation between psychopathy and the quantity of gray matter in the PFC and its subregions, the OFC and the PCC (Ermer et al., 2012; Hofhansel et al., 2020; Yang et al., 2010, 2009b, 2005). These regions are crucial for emotional expression, modulation, processing, moral judgment, planning, and decision-making. Deficits such as decreased gray matter volume in these regions may be seen as why psychopaths have an issue with for example emotional expression and the other characteristics explained above. This can be viewed as a contribution for future studies to replicate and establish a baseline of PFC deficits and psychopathic traits. The findings of Korponay et al. (2017) showed positive relationships between Factor 2 scores (impulsive/antisocial psychopathy traits) and various PFC subregions instead of negative. According to the authors, one possibility for why positive rather than negative results are shown is that the identified positive associations between Factor 2 scores and PFC subregion volumes indicate deficient synaptic and neuronal pruning in the study's region of interest, indicating either dysfunctional and/or ineffective processing. These findings can also be seen as a contribution to future studies. Most of the articles

screened in this review found negative correlations however Korponay and colleagues found positive, this is crucial in science since replication of studies can for example find different outcomes. Different results could contribute to the expanding of the topic of research. Future studies on the topic will be interesting to follow since two opposite results have been found. The authors hope to one day read about more substantial findings about the specific topic.

In the authors opinion society would benefit by recognizing and understanding psychopathy better to answer questions about how crucial the structural variations found are for treatment. A better understanding of the disorder and improved treatment options may also encourage a decrease in crime and recidivism, which would also be beneficial in a societal view since studies show that people with psychopathic traits are at least five times more likely to recidivate violently.

Limitations

In the majority of studies evidence shows that psychopaths have decreased gray matter volume, but psychopathy is not the only factor decreasing gray matter. Limitations in this systematic review include the effect of alcohol and drug abuse on people displaying psychopathic behavior. Substance use is frequently comorbid with psychopathy (Smith & Newman, 1990). According to volumetric analysis, the gray matter volume also negatively correlates with lifetime alcohol consumption. Another VBM study revealed a significant negative correlation between the gray matter volumes of the bilateral middle frontal gyri and lifetime alcohol intake (Taki et al., 2006). The authors of this review had to take both lifetime alcohol and drug intake and various diagnostic tests regarding it to show how much the intake of alcohol and drugs differs between psychopaths and healthy controls. Ermer et al. (2012) further discuss that substance use has been related to gray matter volume, which could make a difference in structural imaging studies. In their study the total PCL-R score significantly correlated with substance dependence, leading them to include substance abuse as a covariate in their analyses to ensure they were assessing psychopathy and nothing else.

Another crucial aspect is the fact that gray matter volume also decreases with age. In the case of Ermer et al. (2012), the writers used age as a covariate in their analyses as well. Age was related to Factor 1 scores in the PCL-R score but not Factor 2 (Ermer et al., 2012). This systematic review chose not to include children or adolescents and an age range of 18-55 with most of the participants being in their thirties (see Figure 1).

When searching for qualitative articles for this review, the authors had to take into consideration the similarities between antisocial personality disorder and psychopathy since antisocial personality disorder diagnosis is similar to psychopathy. The debate of whether the two are the same is disputed. According to the DSM-V, psychopathy is another term for

antisocial personality disorder and many similarities exist between the two diagnoses, including a lack of remorse, deception, impulsivity, and juvenile delinquency (American Psychiatric Association, 2013). Furthermore, they show very different prevalence rates, with approximately between 50%-80% of inmates diagnosed with antisocial personality disorder and only 15% diagnosed with psychopathy, supporting the idea that the antisocial personality disorder criteria are broader (Ogloff, 2006).

Society and Ethics

Psychopathy is a disorder of high public concern because it predicts violence and offense recidivism (Poeppl, 2019). According to economic analyses, the societal cost of all criminal behavior in the United States is a staggering $1.705 trillion per year. Psychopaths are known to commit a disproportionate amount of violent crime, accounting for up to 25% of prison populations (Ermer et al., 2012). Psychopathy is thought to affect 1% of the general population, 15-25% of male and female prison populations, and 10% to 15% of substance abuse populations (Kiehl, 2006). The discovery of a link between psychopathy and a specific brain abnormality could have significant clinical, legal, and scientific effects (Motzkin et al., 2011). Psychopathy diagnosis could be an early warning sign of severe violence in society. According to Reidy et al. (2015), psychopathy is one of the strongest dispositional predictors of aggression and violence. Violence attributed to psychopathy accounts for a significant societal burden on the public and criminal justice systems. Increasing public health attention to the individual-level factor of psychopathy may improve our ability to reduce violence at the community and societal levels (Reidy et al., 2015). For the development of successful treatments for psychopathic traits that may avoid future violence, a greater awareness of the elements that put youth at risk for psychopathic violence is required (Reidy et al., 2015).

Psychopaths are typically seen as people who make unethical decisions. It is important though, not to treat them unethically. The amended ethical guidelines and code of conduct of the American Psychological Association provide general standards to which examiners should adhere when conducting any type of psychological evaluation, as well as general guidelines to which examiners should aspire when engaged in such work (Patrick, 2018). When measuring psychopathic scores, and having the interview during PCL-R assessment, it brings up personal questions and private answers which are crucial to keep anonymous and for research matters only.

Returning to structural differences, how ethical is it to base or predict a psychopathy diagnosis solely on structural neuroimaging without taking into account functional or psychosocial factors? If that alone labels you as a psychopath, it may have consequences in that person's social life. It is a useful technique for assisting with diagnosis; however, because diagnosing a psychopath is such a sensitive subject, other tools should be used.

Little is known about how successful psychopaths deal with the ethical quandaries that come with being labeled as a psychopath (Stevens et al., 2012). They have not engaged in any criminal behavior that has resulted in incarceration, but they still bear the label of a psychopath, which can be problematic.

Although neuroscientific evidence is increasingly being used in court, the extent to which neuroscience should play a role in the legal system has been debated (Ling & Raine, 2018). Having critical evidence in the form of neuroimaging that demonstrates psychopathy traits could influence the verdict. With that being said, no one should be using neuroscientific evidence as an excuse for criminal behavior.

Conclusion

According to the studies reviewed, the amygdala, prefrontal, limbic, and paralimbic regions play a crucial role in psychopathy, as structural differences and decreased gray matter volume are shown in these areas. The study of Korponay et al. (2017) however found larger subregions of PFC, but strong correlations between PCL-R scores and regions of interest in this review similar to the other five articles. Several subregions were implicated such as the OFC and PCC which are areas that play important roles in emotional processing, moral judgment, decision-making, and planning. Articles in this review also sought to determine whether regions of interest were connected to a specific facet or factor of the PCL-R scale. The amygdala, which is a part of the limbic structure has, according to the findings, the strongest correlation to the affective and interpersonal factors of the PCL-R scale. As widely implicated, gray matter volume was found to be negatively correlated with psychopathy. This finding was primarily attributed to the PCL-R's second factor, impulsive-antisocial behavior in one study. Patients with damage in the anterior cingulate cortex and OFC often exhibit psychopathic traits from both Factor 1 and Factor 2 of the PCL-R test, such as impulsivity, lack of empathy, and reactive aggression. In conclusion, it seems like psychopathy is not linked to one single brain region but an interplay of several regions. To conclude from the articles mentioned, an area for future studies is the PFC since it takes up one-third of the cortex, the subregions are evidently crucial for psychopathy and is an important region for our personality. That being said, other regions should not be overlooked in future research on psychopathy simply because of this. Research on this topic is a growing field of interest. It is reasonable to conclude that the differences seen in these regions in psychopaths compared to healthy controls result in cognitive control deficits. Abnormal brain activity may not only be a symptom of psychopathy but also be closely linked to the psychopathology of the disorder.

This systematic review aimed to find structural differences in the PFC, limbic and paralimbic regions which all of the articles reviewed indicate. It is still undetermined exactly how structure and function interact, and abnormalities in gray matter volume are by no

means the only ways that the brain's activity can be affected. It is logical to assume that the functional abnormalities seen in psychopathy are also influenced by the ways in which neurons are arranged and communicate with one another (Ermer et al., 2012). However, this review offers a starting point that may help future research on where to look initially for more connected functional abnormalities in adult psychopaths. All of the articles showed a negative correlation between gray matter volume in these regions except Korponay et al. (2017) who found a positive correlation between prefrontal subregion volume and psychopathy. Interestingly, most studies examining prefrontal gray matter and Factor 1 scores discover a negative relationship, whereas most studies examining prefrontal gray matter and Factor 2 scores discover a positive relationship. These findings suggest that (1) Factor 1 and Factor 2 traits are dissociable at the neural level despite being highly correlated in terms of PCL-R score; (2) the severity of Factor 1 and Factor 2 traits may influence measures of prefrontal gray matter structure in a given sample of psychopathic individuals (Korponay et al., 2017).

The authors wanted to see if there are structural neuroanatomical differences between psychopaths and healthy individuals, and if so, can this be used (1) to better understand psychopathy as a disorder; (2) as a diagnostic tool to help identify and treat the disorder; or (3) to develop interventions for repeat offenders (recidivism) and reduce crime rates? Articles in this review show evidence that (1) several of the regions of interest studied in this paper is linked with psychopathy; (2) high PCL-R score are negatively correlated with gray matter volume in prefrontal regions and reduced amygdala volume in structural neuroimaging studies; (3) evidence of structural deficiencies in prefrontal regions which may make unsuccessful psychopaths less aware to environmental cues signaling danger and capture, making them more likely to be convicted of crimes. In contrast to nonviolent recidivism, the study by Sohn et al. (2020) found that facet 2 (affective) and not facet 4 (antisocial) prospectively predicted violent recidivism, which is something to take into consideration in the future studies for lower recidivism. Additionally, evidence is presented that psychopaths who have been convicted of crimes may be more likely to engage in risky and impulsive behaviors since they have decreased gray matter volume in their prefrontal regions, which makes it more difficult for them to recognize cues that indicate arrests. These findings could be studied further for the benefit of capturing psychopathic adult criminals and reducing recidivism, which was one of the purposes of this review.

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Appendix A

PCL-R Items Classified According to Factors and Facets (Hare, 2003)

Factor 1	Factor 2
Facet 1: Interpersonal	Facet 3: Lifestyle
1. Glibness/superficial charm 2. Grandiose sense of self-worth 4. Pathological lying 5. Conning/manipulative	3. Need of stimulation/proneness to boredom 9. Parasitic lifestyle 13. Lack of realistic, long-term goals 14. Impulsivity 15. Irresponsibility
Facet 2: Affective	Facet 4: Antisocial
6. Lack of remorse or guilt 7. Emotionally shallow 8. Callous / lack of empathy 16. Failure to accept responsibility for own actions	10. Poor behavioural control 12. Early behavioural problems 18. Juvenile delinquency 19. Revocation of conditional release 20. Criminal versatility
Items that did not saturate any factor	
11. Promiscuous sexual behaviour 17. Many short-term marital relationships	