Degree project

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The Functional Role of the Prefrontal Cortex in Antisocial Personality Disorder

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Abstract

Patients with antisocial personality disorder (ASPD) are deceptive, apathetic, and impulsive. Their social behavior is often inappropriate, and they fail to follow social norms, leading to frequent criminal behavior. Understanding the neural correlates of ASPD could alleviate issues for the patients, such as unstable living conditions, as well as financial costs for the justice system and society. Due to previous research and theoretical implications of the prefrontal cortex (PFC) and its role in emotion-regulation and decision-making, it is likely that ASPD patients would show differences in the PFC relative to healthy individuals. Therefore, emphasis is placed on this region. By systematically reviewing articles which used fMRI to examine ASPD patients, this paper aims to understand if the brain activity in the PFC or functional connectivity within these regions differs between ASPD patients and healthy controls. Decreased activity was found in the anterior cingulate cortex (ACC) and dorsolateral PFC (dlPFC) in ASPD patients compared to healthy controls. Further, decreased functional connectivity was found in the frontoparietal control network, default mode network, and attentional network. Other prefrontal regions implicated include the medial frontal cortex, orbitofrontal cortex, and medial prefrontal cortex. Most of these regions are important for cognitive control, enabling integration of information regarding, e.g., errors and conflict. Abnormal processing of such information can lead to the impulsive or inappropriate actions often seen in ASPD patients. The PFC seems to play an important functional role in ASPD, mainly the regions responsible for cognitive control, such as the ACC and dlPFC.

Keywords: antisocial personality disorder, prefrontal cortex, functional magnetic resonance imaging

The Functional Role of the Prefrontal Cortex in Antisocial Personality Disorder

Antisocial Personality Disorder

Antisocial personality disorder (ASPD) is defined by impulsivity, lack of remorse, proneness to lying, and a disregard for others. People with the disorder may struggle, for example, to maintain a job, be financially responsible, or commit to monogamous relationships. According to the Diagnostic and Statistical Manual of Mental Disorders V (DSM-V), to be diagnosed with ASPD the individual must be 18 years old but also should have shown signs of derelict behavior since childhood or adolescence (American Psychiatric Association, 2013). The disorder can develop due to both genetic and environmental factors, and the symptoms generally subside in older age, usually around 40 years old (American Psychiatric Association, 2013; Glenn et al., 2013). One point in a criterion for ASPD is a "failure to conform to social norms with respect to lawful behaviors, as indicated by repeatedly performing acts that are grounds for arrest" (American Psychiatric Association, 2013, p. 659). While the prevalence rates of ASPD are low in the general population (0.2-3.3%), more than 70% of those individuals diagnosed have been, or are currently incarcerated (American Psychiatric Association, 2013). The disorder contributes to criminal behavior and recidivism – posing a serious societal problem.

According to Visdómine-Lozano (2022), it is notoriously difficult to treat, and currently no treatment methods exist specifically for ASPD. Traditionally, cognitive behavioral therapy (CBT) has been used, but the response to treatment has not been significant (Glenn et al., 2013). In a review of several different psychological interventions, including CBT and contingency management, Gibbon et al. (2020) found that existing methods do not provide a significant change in antisocial behavior. The authors conclude that more studies on ASPD are required in order to develop more efficient treatment methods (Gibbon et al., 2020).

Antisocial Personality Disorder Compared to Psychopathy

Antisocial personality disorder was added to the DSM-II first in 1968. Then in the DSM-III, published in 1980, the criteria were updated to have greater diagnostic reliability (Paap et al., 2020). To this day there is debate regarding the heterogeneity of ASPD, claiming that the criteria are too general, leading to an excessive number of diagnosed cases.

The ASPD diagnosis resembles psychopathy. Whether or not the two are the same is a heated topic. In the DSM-V it is stated that psychopathy is another term for ASPD (American Psychiatric Association, 2013). The two diagnoses bear many similarities such as lack of remorse, deceitfulness, impulsivity, and juvenile delinquency (American Psychiatric

Association, 2013; Brazil & Forth, 2016). However, the criteria for ASPD are mainly concerned with behavior, while the test commonly used for psychopathy, i.e., Hare Psychopathy Checklist Revised (PCL-R), is more concerned with personality (Ogloff, 2006), including criteria such as glibness and egocentricity (Brazil & Forth, 2016). Further criteria for psychopathy are being prone to boredom, struggling to accept responsibility, and lacking empathy. The different focuses of the tests (PCL-R and the Structural Clinical Interview for DSM) render them incomparable, leaving the question of diagnosis unanswered. Additionally, they provide very different prevalence rates, with about 70% of inmates being diagnosed with ASPD, while only 15% are diagnosed with psychopathy, supporting the notion that the ASPD criteria are broader (Ogloff, 2006).

Neural Correlates. Some attempts to identify the neural correlates of ASPD and psychopathy have previously been made, mainly by use of magnetic resonance imaging (MRI) or functional magnetic resonance imaging (fMRI). Some areas that have been found to show either structural or functional differences include the amygdala, angular gyrus, prefrontal cortex (PFC), and the posterior cingulate (Glenn et al., 2012). Pera-Guardiola et al. (2016) used Voxel-based Morphometry (VBM) during a morphed emotional face expression recognition task to determine structural correlates of emotion recognition in psychopaths, assessed with PCL-R. They found that greater gray matter volume in the PFC, anterior insula, cingulate cortex, and the cerebellum correlated with better emotional face recognition in psychopaths. Birbaumer et al. (2005) used fMRI to examine brain activation in ten psychopaths, as defined by the PCL-R, during a fear conditioning task. Reduced activation was found in the amygdala, PFC, and insula for psychopaths compared to healthy controls.

However, many studies have not specifically differentiated between ASPD and psychopathy. If they would prove to be separate diagnoses, much previous research would be rendered inconclusive. Concurrently, in a study using structural MRI and VBM analyses to assess gray matter volumes, Gregory et al. (2012) differentiated between ASPD and psychopathy. This was done by using both the Structural Clinical Interview for DSM-IV to diagnose ASPD, and the PCL-R to determine psychopathy. Sixty-six participants were split into three groups, (i) ASPD and comorbid psychopathy (ASPD+P), (ii) ASPD without a comorbidity of psychopathy (ASPD-P), and (iii) healthy controls without either diagnosis. Results showed that the gray matter volume was significantly reduced in the PFC of the ASPD+P group compared to ASPD-P and controls. No significant difference was found for ASPD-P compared to controls. This lends support for classifying them as separate diagnoses (Gregory et al., 2012).

The Prefrontal Cortex and Antisocial Personality Disorder

One area of the brain that seems to be consistently identified in the array of studies is the prefrontal cortex (PFC). The PFC is located in the frontal lobe and consists of the frontal pole, lateral prefrontal cortex, medial frontal cortex (including anterior cingulate cortex (ACC)), and the ventromedial cortex (including orbitofrontal cortex (OFC)). The PFC is responsible for important executive functions, such as decision-making, planning, and emotion-regulation (Gazzaniga et al., 2019). These are functions which individuals with ASPD generally have difficulty with, providing a theoretical background for the involvement of the PFC (American Psychiatric Association, 2013). In a meta-analysis of studies using at least one structural or functional brain imaging method to study the prefrontal cortex in antisocial individuals, Yang and Raine (2009) found both structural and functional reductions in the PFC in antisocial participants compared to controls.

Further, some brain networks include connections with prefrontal regions. For example, the frontoparietal control network (FPN), which is responsible for coordinating behavior based on incoming information, includes connections with the lateral PFC (Marek & Dosenbach, 2018), and the default mode network (DMN), which is active in the brain during rest and is suggested to be involved in self-referential processing, includes connections with the ventral and dorsal medial PFC (Gazzaniga et al., 2019; Sormaz et al., 2018). While these networks are responsible for very different functions in the brain, if the PFC is affected in ASPD patients, it is likely that the connectivity of these networks would also be affected.

What is the functional role of the PFC in ASPD, as assessed with the DSM criteria? Due to previous research, along with theoretical implications of the PFC and its role in emotion-regulation and decision-making, it is likely that individuals with ASPD would show differences in the PFC relative to a healthy individual. Therefore, emphasis is placed on this region. By systematically reviewing articles which use fMRI to examine the brain of participants with ASPD, this systematic review aims to understand if the brain activity in the PFC or functional connectivity within the region differs between ASPD patients and healthy controls.

By more closely identifying and understanding the neural correlates of ASPD, more specific and affective treatments can be developed. With today's knowledge of neuroplasticity and both behavioral and cognitive treatment methods, knowing more specifically which brain areas are involved in the disorder could generate treatment programs specifically for ASPD. Moreover, further knowledge about the disorder, along with better treatment alternatives could lead to less crime and lower recidivism. Benefits would be seen for the individuals, as consequences of ASPD often result in unstable living conditions and few, if any meaningful relationships in life, as well as frequent incarceration. Benefits may also be seen for society, such as safer communities and lowered economic costs for the criminal justice system. It is

important to understand the neural correlates of ASPD, not only to help the afflicted individual, but also to help society.

Method

Search Strategy

A literature search was completed in three databases: MEDLINE EBSCO, Scopus, and Web of Science. For the search string, a combination of antisocial personality disorder, prefrontal cortex, and functional magnetic resonance imaging (along with the respective abbreviations as alternatives) were used: ("antisocial personality disorder" OR ASPD) AND ("Prefrontal Cortex" OR PFC) AND ("functional magnetic resonance imaging" OR fMRI). This search generated a total of n=148 articles (MEDLINE EBSCO: n=40, Scopus: n=81, Web of Science: n=27). The results of the search were exported to the online review-tool Rayyan. This tool was used to detect duplicates between the databases, n=89 duplicates were detected and deleted manually, leaving n=100 articles to be screened. Thereafter, the abstracts and titles were reviewed to ensure suitability based on the exclusion/inclusion criteria. At this step n=83 articles were excluded and n=17 articles were included. After the initial exclusion based on title and abstract, a second exclusion was completed based on the full-text articles, where n=13 articles were excluded. Each of these exclusions were made due to the following reasons: the participant group did not have ASPD (n=2); the participant group had ASPD with a comorbidity of schizophrenia (n=2) or borderline personality disorder (n=3); ASPD diagnosis was not made based on DSM criteria (n=3); the study focused on psychopathy rather than ASPD (n=1); the study looked at neurochemical markers rather than neural activity/functional connectivity (n=1); a pharmaceutical intervention was used (n=1). Finally, n=4 articles remained and were included in the qualitative synthesis; see Figure 1.

Inclusion & Exclusion Criteria

This systematic review will be looking both at neural activity in the PFC and functional connectivity in networks which include prefrontal regions, measured using fMRI, in patients with antisocial personality disorder (ASPD).

To be eligible for inclusion, studies must regard people diagnosed with ASPD, in accordance with the DSM-V or IV criteria. Previous reviews on the ASPD brain have mainly used structural brain imaging methods. In order to further the scientific progress, this systematic review focuses instead on the most common functional method used in ASPD studies: fMRI. Therefore, only studies using fMRI will be included. As the focus in this systematic review lies on the role of the PFC, this part of the brain must be investigated in the

included studies. Only published and pre-print (i.e., e-published, but not yet printed) articles written in English or Swedish will be used. The time period used will be 1980 until present, as this was the year the DSM-III was published with the updated ASPD criteria based on research to ensure greater diagnostic reliability (Paap et al., 2020).

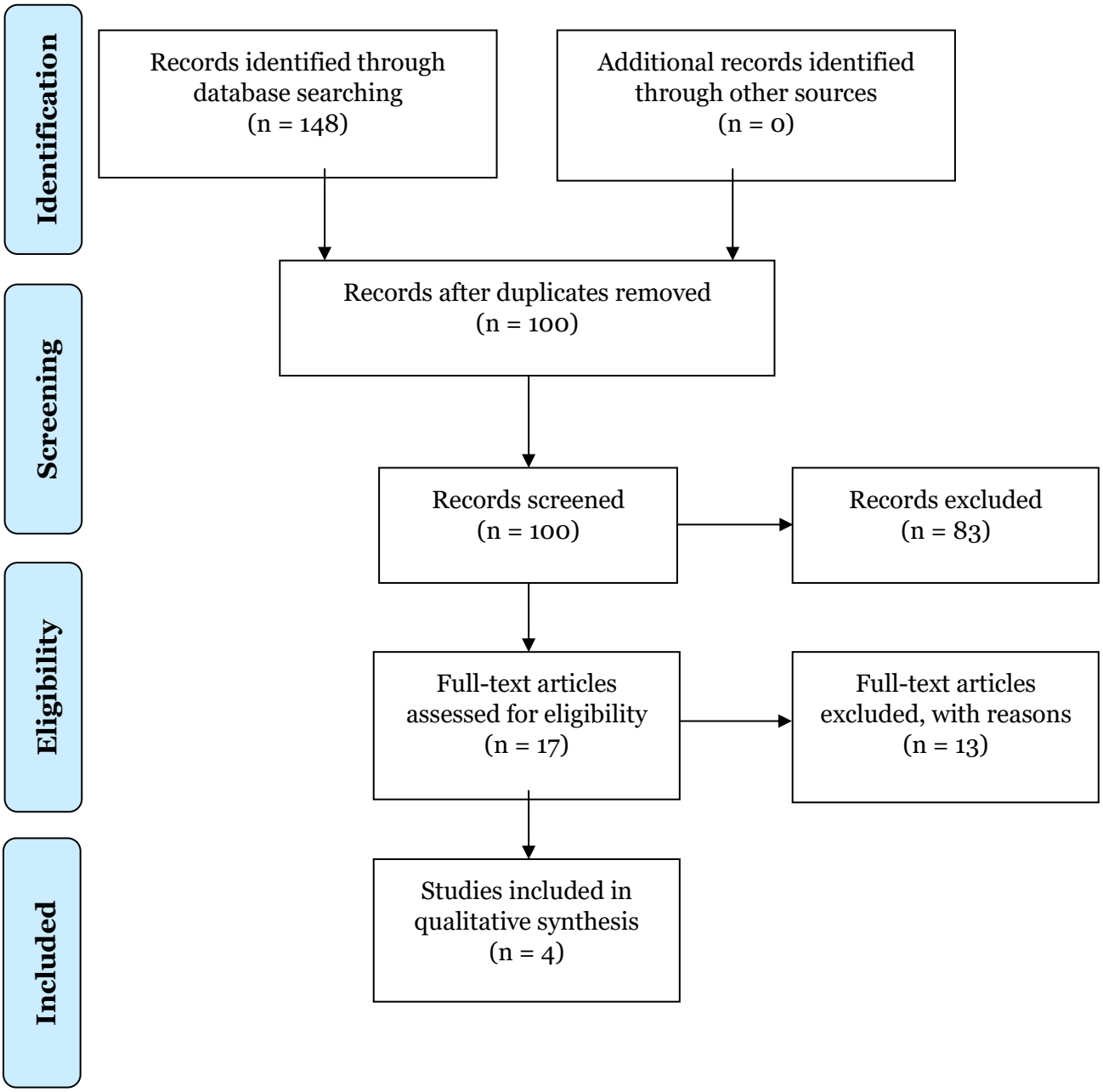
Exclusion criteria include youths (<18 years of age), as only adults can be diagnosed with ASPD, and ASPD with a comorbidity such as schizophrenia, borderline personality disorder, or substance abuse, as these factors could affect the neural activity separately from ASPD. This systematic review will treat ASPD and psychopathy as separate diagnoses, and therefore articles regarding psychopathy instead of ASPD will be excluded. Additionally, no pharmaceutical intervention should be used in the study design. Also, studies using assessment methods based on criteria other than those in DSM-V or IV will be excluded.

Data Extraction

The following data will be extracted from the included articles: data regarding the participants (number of participants, gender, and age), information about what test was used to assess ASPD, the method the researchers used to measure the functional connectivity and/or brain activity, what regions of the brain were investigated, and the outcome measures regarding the functional connectivity and/or brain activity in the prefrontal cortex.

Figure 1

A flow diagram of the literature search and study selection process (Moher et al., 2009)



Note: Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., Altman, D., Antes, G., Atkins, D., Barbour, V., Barrowman, N., Berlin, J. A., Clark, J., Clarke, M., Cook, D., D'Amico, R., Deeks, J. J., Devereaux, P. J., Dickersin, K., Egger, M., Ernst, E., … Tugwell, P. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. In *PLoS Medicine* (Vol. 6, Issue 7). https://doi.org/10.1371/journal.pmed.1000097

Results

Four articles were included in the qualitative analysis. All studies used fMRI to investigate the whole brain of ASPD patients, but with slightly different approaches. Two of the studies (Jiang et al., 2013; Schiffer et al., 2014) investigated neural activity, while the other two (Jiang et al., 2017; Tang et al., 2013) studied the functional connectivity of brain networks. All studies used only male, adult participants; see Table 1 for details. Between 20 and 35 participants were included in each group, across all studies. Jiang et al. (2013) investigated only ASPD patients, while the others compared ASPD patients with healthy controls (Jiang et al., 2017; Schiffer et al., 2014; Tang et al., 2013). Jiang et al. (2013) were, however, able to compare their results to similar research done in healthy participants. To assess ASPD, Jiang et al. (2013), Tang et al. (2013), and Jiang et al. (2017) used both Personality Diagnostic Questionaire-4+ (PDQ-4+) and Personality Disorder Interview (PDI-IV). Schiffer et al. (2014), however, used the Structured Clinical Interviews for DSM-IV (SCID) axis I and II for the ASPD assessment instead. All these assessment methods are based on DSM-IV criteria.

Despite the diverging methods of investigation (neural activity and functional connectivity) the results of the studies bore a certain similarity: all found significant activation in prefrontal regions in ASPD patients compared to healthy individuals, with two areas seeming to be of most relevance: the dorsolateral PFC (dlPFC) and the anterior cingulate cortex (ACC).

Neural Activity

Two of the articles (Jiang et al., 2013; Schiffer et al., 2014) included in the qualitative analysis investigated neural activity of ASPD patients. The studies used different tasks to investigate separate aspects of neural activity: deception and cognitive control. Nonetheless, they found somewhat similar results. Jiang et al. (2013) conducted an fMRI study on deception in offenders with ASPD in order to identify the functional neural correlates of the disorder. All participants (n=32) were diagnosed with ASPD by use of PDQ-4+ and PDI-IV. Based on their capacity for deception, which was tested in accordance with the deceitfulness criterion in the PDI-IV for ASPD, participants were sorted into three groups: (i) non-liars (n=11), (ii) mild liars (n=10), and (iii) severe liars (n=11). The picture choice task was used as the experimental procedure. First, the participants selected three pictures out of ten. One picture was later presented in the scanner and the participants were asked if this was one that they had previously selected. They were instructed to answer in one of three ways: “true” condition (honest answer); “inverse” condition (converse answer); “lie” condition (devise a deceptive stratagem to support the dishonest answer). Jiang et al. (2013) found significant activation during deception in the “bilateral dorsolateral prefrontal cortex (DLPFC)

extending into the middle frontal gyrus (MFG), the left inferior parietal lobule (IPL) including the supramarginal gyrus (SMG), and the bilateral anterior cingulate gyrus (ACC)/medial superior frontal gyrus" (Jiang et al., 2013, p. 94). Additionally, Jiang et al. (2013) used BOLD contrast in the "lie" versus "true" conditions to determine the effect of capacity for deception. As the capacity for deception increased, activity decreased in the right medial frontal gyrus, left and right MFG, and the left IPL. The areas implicated in deception in ASPD patients are almost identical to the brain regions correlated with deception in healthy people seen in other studies (Christ et al., 2009; Lee et al., 2005), implying that there is no difference in the location of activation in ASPD patients as compared to healthy individuals (Jiang et al., 2013).

Schiffer et al. (2014) used the Stroop color-naming task in an fMRI study to determine the neural correlates of cognitive control in ASPD. Participants were divided into two groups: ASPD patients (n=21) and healthy controls (n=23). To assess ASPD, SCID axis I and II were used. In the scanner, participants were presented with color words, such as 'RED' or 'GREEN'. The words were presented in two trials, either congruent (the color of the text matches the color word) or incongruent (the color of the text is different than the color word). Overall, the two groups performed similarly, especially in regard to error interference and behavioral adjustments, i.e., both groups made approximately the same number of errors and modified their responses in a similar manner. Results showed that the ASPD patients had reduced error-related activity (i.e., activity when the participant made an erroneous response in any trial, minus activity when a correct response was made during congruent trials) in the dorsal ACC and the dlPFC, as well as in the left putamen, left thalamus, and right postcentral gyrus. Additionally, the ASPD group showed less conflict-related activity (i.e., activity during incongruent trials minus activity during congruent trials) in the dorsal ACC and left superior temporal cortex, but greater activity in the left amygdala compared to healthy controls (Schiffer et al., 2014).

Functional Connectivity

Two of the articles (Jiang et al., 2013; Schiffer et al., 2014) included in the qualitative analysis investigated functional connectivity in ASPD patients compared to healthy controls. Both studies used resting-state fMRI and investigated the whole brain. However, they found somewhat different results. Jiang et al. (2017) conducted a resting-state fMRI study on ASPD patients (n=32) versus healthy controls (n=35). To assess ASPD, PDQ-4+ and PDI-IV were used. The researchers completed a small-world analysis, functional connectivity analysis, and a modularity analysis on the data (Jiang et al., 2017). Modules are individual brain sub-networks, and modularity facilitates quicker adjustments of behavior based on incoming information of the surroundings (Gallen & D'Esposito, 2019). The modularity analysis found

four functionally oriented modules in the healthy controls: posterior (I), central (II), frontal-subcortical (III), and frontoparietal (IV). However, in the ASPD patients, only three modules were detected. While I and II were the same as in the control group, the ASPD group's modules III and IV were combined as one, including the medial frontal cortex, frontal regions, inferior parietal and temporal regions, as well as subcortical structures, and part of the orbitofrontal cortex (OFC). Additionally, both the modularity within the modules, as well as the inter-module connectivity between the modules were decreased in the ASPD group. The small-world analysis measures the efficiency of a network's information transfer and showed that the ASPD patients had decreased local and global network efficiency but increased characteristic path length compared to the healthy controls. Jiang et al. (2017) suggest that the decreased efficiency could mean that ASPD patients have poorer parallel information transmission within a network compared to healthy controls. To analyze the connectivity Jiang et al. (2017) used network-based statistics (NBS), which can be used to identify connections and networks (Zalesky et al., 2010). This showed decreased connectivity mainly in the frontoparietal control network in the ASPD patients. Jiang et al. (2017) speculate that these connectivity differences could also be the reason for the decreased efficiency seen in the small-world analysis.

Tang et al. (2013) employed resting-state fMRI to better understand the neural mechanisms of ASPD, and eventually develop a method of identifying the disorder. Two groups were compared: ASPD patients (n=32) and healthy controls (n=35). The PDQ-4+ and PDI-IV were used for ASPD assessment. They looked at seven different networks: default mode, attention, visual recognition, auditory, sensory-motor, subcortical, and cerebellar. Results showed that the ASPD patients had significantly altered functional connections. Mainly, decreases in connectivity were found between the default mode network (DMN), and the attention network, and some between these networks and the cerebellar network. In the DMN the rectus gyrus, precuneus, middle temporal gyrus, posterior cingulate cortex, and the superior frontal gyrus were the regions correlated with uncoupled connections. In the attention network, the uncoupled connections were mainly correlated with the superior and inferior parietal cortices, the inferior frontal gyrus, and the middle frontal gyrus (Tang et al., 2013). While the ventral and dorsal medial PFC are involved in the DMN (Gazzaniga et al., 2019), no significant uncoupled connections were found to be correlated with prefrontal regions (Tang et al., 2013).

Table 1

A summary of neuroimaging studies investigating the neural correlates of antisocial personality disorder

Lead Author & Publication Year	Sample	Gender	Age (Mean± SD)	ASPD Assessment	Brain Imaging Technique/ Outcome Measure	Brain Regions Looked at	Main Findings
Jiang et al. (2013)	ASPD (n=32) Non-liars (n=11) Mild liars (n=10) Severe liars (n=11)	All male	Non-liars: 19.36 ± 0.51 Mild liars: 21.80 ± 2.96 Severe liars: 19.45 ± 0.93	PDQ-4+ & PDI-IV	fMRI – neural activity	Whole brain	Significant activation in the dlPFC and ACC during deceptive behavior in ASPD patients.
Schiffer et al. (2014)	ASPD (n=21) Healthy controls (n=23)	All male	ASPD: 35.2+-8.2 Controls: 34.1+-8.9	SCID I & SCID II	fMRI – neural activity	Whole brain	Decreased activity in the ACC and dlPFC in ASPD patients compared to controls.
Jiang et al. (2017)	ASPD (n=32) Healthy controls (n=35)	All male	ASPD: 20.5 ± 1.37 Controls: 21.67 ± 2.54	PDQ-4+ & PDI-IV	fMRI – functional connectivity	Whole brain	Decreased connectivity in the frontoparietal control network in ASPD patients compared to controls.

Tang et al. (2013)	ASPD (n=32) Healthy controls (n=35)	All male	ASPD: 20.5 ± 1.37 Controls: 21.67 ± 2.54	PDQ-4+ & PDI-IV	fMRI – functional connectivity	Whole brain	Decreased connectivity in the default mode network and attention network in ASPD patients compared to controls.

Note: ASPD = Antisocial Personality Disorder; PDQ-4 = Personality Diagnostic Questionaire-4+; PDI-IV = Personality Disorder Interview; SCID = Structured Clinical Interviews for DSM-IV; dlPFC = dorsolateral Prefrontal cortex; ACC = Anterior Cingulate Cortex

Discussion

By examining articles which used fMRI to examine the brain of participants with ASPD, this systematic review aimed to understand if the brain activity in the PFC or functional connectivity within prefrontal regions differs between ASPD patients and healthy controls. ASPD is a disorder signified by impulsivity, deception, and criminal behavior. It poses serious issues for both the patients suffering from it, as well as for society. Understanding the neural correlates of ASPD could assist in the development of treatments.

The included studies had very different approaches to the investigation of ASPD. Two looked at the functional connectivity (Jiang et al., 2017; Tang et al., 2013), while the other two looked at separate aspects of neural activity: deception and cognitive control (Jiang et al., 2013; Schiffer et al., 2014). Despite this, the prefrontal areas were consistently found to show significant differences in ASPD patients compared to healthy controls across all studies. Two areas of the prefrontal cortex were identified in most of the studies and, therefore, seem to play a larger role in ASPD: the anterior cingulate cortex (ACC) and the dorsolateral prefrontal cortex (dlPFC).

Anterior Cingulate Cortex

The anterior cingulate cortex (ACC) is located in front of the corpus callosum and is responsible for aspects of cognitive control such as attention, response monitoring, and error detection in healthy humans. According to the error detection hypothesis, when an error occurs, the activity in the ACC generally increases. Additionally, the response conflict hypothesis suggests that the ACC plays a role in action generation as a reaction to conflict. When presented with an error or conflict, activity in the ACC increases, which can then further modulate activity in other brain regions in order to generate the appropriate reaction in line with information about the error or conflict (Gazzaniga et al., 2019). The study by Schiffer et al. (2014) showed that the ASPD group had decreased error- and conflict-related activity in the ACC, despite performing similarly as the healthy controls in the Stroop task overall.

The ACC also plays an important role in executive attention, the ability to regulate responses in accordance with, e.g., conflict or error information, (Raz, 2004). While Tang et al. (2013) did not find any significant uncoupled connections in prefrontal areas, the researchers did find decreased connectivity within the attention network, and between this network and the default mode network (DMN). This disruption in the attention network could possibly affect executive attention. However, more research is needed to draw a proper conclusion.

In the study by Jiang et al. (2013), the ACC was found to be activated in ASPD patients during deceptive behavior. Deception has been suggested to require some aspects of cognitive control, such as inhibitory control and task switching (Christ et al., 2009). As deception is a defining factor in the ASPD diagnosis (American Psychiatric Association, 2013), and cognitive control seems to be an important function for deception, it is reasonable that the results seen in the studies by Schiffer et al. (2014), Tang et al. (2013), and Jiang et al. (2013) are all related to deficient cognitive control in ASPD. This may suggest that ASPD patients have difficulties using conflict or error information to alter their behavior and actions appropriately to the situation, which could lead to the antisocial, deviant, and impulsive behavior seen in ASPD patients.

Further, the ACC is involved in empathy (Gazzaniga et al., 2019). A decrease in ACC activity compared to healthy controls could, in part, explain the lack of empathy that is a hallmark for ASPD.

Dorsolateral Prefrontal Cortex

When exposed to conflict, activity in the ACC increases to initiate action in regulatory regions. One such regulatory region is the dorsolateral prefrontal cortex (dlPFC). While the ACC modulates and maintains control, the dlPFC supports initiation of actions and adjusts control according to incoming information. The lateral PFC is important for goal-oriented behavior and working memory, as it sustains goal-related information that helps regulate and control a person's actions. Goal-oriented behavior is a main aspect of cognitive control (Gazzaniga et al., 2019; Marek & Dosenbach, 2018). As actions that are not goal-oriented are often impulsive, and impulsivity is a key trait in ASPD, it is likely that such goal-oriented behavior is impaired in ASPD patients. Both Schiffer et al. (2014) and Jiang et al. (2013) found decreases in the dlPFC in ASPD patients in their studies on cognitive control and deception respectively. Further, the lateral PFC is also involved in executive attention, which may explain part of the decrease in connectivity found by Tang et al. (2013). The close relation between the ACC and the dlPFC in cognitive control, taken along with impulsivity in ASPD, may give reason for these findings.

Additionally, Jiang et al. (2017) found decreased connectivity within the frontoparietal control network (FPN) in ASPD patients compared to healthy controls. As one of the main regions in this network is the lateral PFC, FPN has also been suggested to play a role in cognitive control (Marek & Dosenbach, 2018). Jiang et al. (2017) also found abnormalities in the modularity within and between the frontoparietal and frontal-subcortical modules, which mainly include frontal regions required for cognitive control. As modularity generates faster adjustments of actions based on incoming information of the surroundings, modularity has been implicated in cognitive control as well (Gallen &

D'Esposito, 2019). Decreased connectivity and modularity in frontoparietal regions, along with abnormal activity in the dlPFC, all point to deficits of cognitive control in ASPD patients, possibly explaining the impulsive, risk-taking behaviors often seen in these individuals.

Other Regions of Interest

While the ACC and the dlPFC were the main regions implicated across the reviewed studies, Jiang et al. (2017) and Tang et al. (2013) found some additional prefrontal regions that showed significant differences in ASPD compared to healthy controls, namely the medial frontal cortex (MFC), orbitofrontal cortex (OFC) and the medial prefrontal cortex (mPFC).

Jiang et al. (2017) found decreased modularity in both the OFC and MFC. The OFC is suggested to play a part in social cognition, by evaluating social information and generating an appropriate response. Studies on patients with OFC lesions have shown that, despite knowing of social norms, OFC lesions can cause the patient to make inappropriate social actions (Gazzaniga et al., 2019). Inappropriate social behavior and failure to follow social norms are key characteristics of ASPD (American Psychiatric Association, 2013). Both the MFC and the OFC are involved in cognitive control as well. The OFC is involved in decision-making by providing a representation of value. The MFC detects errors and evaluates conflict, which can then be processed by the ACC and dlPFC. Also, the MFC is important for the attentional network as it coordinates activity (Gazzaniga et al., 2019), which could explain the decreased connectivity within the attentional network found by Tang et al. (2013).

Tang et al. (2013) also found decreased connectivity in the default mode network (DMN), which includes the ventral and dorsal mPFC. Functions of the mPFC include making social decisions and perception of others. Much like with OFC lesions, patients with mPFC lesions make inappropriate social decisions, which is common in ASPD patients. Regarding the perception of others, the mPFC is important for interpreting the mental states of other humans and animals (Gazzaniga et al., 2019). ASPD patients are known for being apathetic and lacking empathy (American Psychiatric Association, 2013). This could be linked to difficulties with attributing internal states to people. However, Tang et al. (2013) did not find any uncoupled connections with the mPFC. This region may anyway be affected by the disruption found in the DMN, but more research is needed to determine if this is accurate.

Limitations

This systematic review suffers from certain limitations. First, all participants were male. While the majority of ASPD patients are male, there are females with ASPD as well. There is a possibility that the neural correlates are different in men and women, and these differences will not be represented in this systematic review. Second, three of the four studies

included in this systematic review recruited participants from the same reformatory establishment. As they also used the same test to assess ASPD, it is likely that some, or all, of the participants were the same across the three studies, possibly providing a small population size. Last, while the PFC seems to play a significant role in ASPD, other brain regions are also affected in the disorder. It should be acknowledged that this systematic review was limited to the PFC, and other brain areas will, therefore, not be evaluated. This was, however, an intentional decision in order to enable a more thorough analysis of the PFC.

Society and Ethics

Understanding the neural correlates of ASPD bears both societal and ethical implications for ASPD patients, as well as society. Mainly, development of therapeutic methods focused on increasing cognitive control could help alleviate symptoms for many ASPD patients. Symptom alleviation could have a large impact on the patients, as antisocial behavior often leads to instability in maintaining a job, home, and meaningful relationships. Decreases in antisocial behavior may also lower crime rates, as many ASPD patients partake in criminal activity. This would, in turn, lower costs for the justice system and society as a whole.

Conclusion

From the studies reviewed it can be concluded that the prefrontal cortex plays an important functional role in ASPD, as patients show significant differences in both neural activity and functional connectivity. Several prefrontal regions were implicated, but the main regions of importance were the ACC and the dlPFC. These regions are mainly important for cognitive control and executive attention, which enables the integration of information in order to generate appropriate actions. ASPD patients are impulsive, apathetic, and prone to lying. These traits are often classified as inappropriate actions. From this, it is reasonable to assume that the differences seen in prefrontal regions in ASPD patients compared to healthy controls are due to deficits of cognitive control.

However, it seems ASPD cannot be identified by deficiencies in one single brain region, but rather the interplay of several regions. From the studies reviewed here, some areas can be recommended for future research, including the middle frontal gyrus and parietal regions. Although the PFC is an important piece of the puzzling disorder that ASPD is, one must also investigate other brain regions to see the whole picture.

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