CHANGE DOESN'T COME EASY:

dynamics of adaptive
behavior in psychopathy

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dynamics of adaptive behavior in psychopathy

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Introduction

1. Introduction

The term 'psychopath' is often used to describe individuals showing behavior regarded as highly disruptive to society. However, this term is often used inappropriately as the exact formulation of what truly constitutes psychopathy is still lacking. The existence of personality structures that resemble the psychiatric condition nowadays referred to as clinical psychopathy can be found in writings that date back several centuries [1]. For instance, in the early 1800s Prichard [2] described a condition characterized by deeply disturbed affective functioning and a reduced capability of conforming to social norms and rules. At that time, individuals suffering from this condition were considered to lack the will power to control themselves and to follow social norms and were therefore considered to be 'morally insane'. Now, almost two centuries later, the idea that emotional disturbances and lack of morality play key roles in psychopathy is still prominently present [3], although the exact definition of the clinical construct is still a matter of debate.

Still, in the past 20 years researchers and clinicians have relied heavily on the definition of psychopathy as a personality disorder that is typified by disturbed affect and interpersonal style combined with antisocial behavioral tendencies [4]. This has been fuelled by the development of the Psychopathy Checklist [5] and its successor the Psychopathy Checklist-Revised [6], which have solidified this conceptualization of psychopathy in the field of forensic mental health and also in the legal system.

2. Psychopathy according to the PCL-R

The PCL-R consists of 20 items that are scored based on information from clinical history records combined with a semi-structured interview. Each item represents a certain behavioral tendency that is scored as either completely absent (0), moderately present (1) or prominently present (2). This yields a dimensional total score ranging between 0 and 40, but the total score has also been used to indicate the presence psychopathy when a predefined cut-off score is exceeded. A cut-off score of 30 is usually maintained in North America, meaning that individuals scoring equal to or higher than 30 can be considered psychopathic. In European countries a cut-off score ≥26 is often used [7] in clinical and legal practice. Cooke and colleagues [7] have argued that cultural differences between Europe and the North America are also reflected by differences in the clinical expression of psychopathy. The cut has been extended to research on psychopathy in Europe [8,9].

Factor analyses have shown that the PCL-R measures two correlated factors. Factor 1 consists of items that capture behaviors related to interpersonal and affective functioning (e.g. glibness, lack of empathy, manipulativeness) and Factor 2 describes

aspects related to a deviant lifestyle and antisocial behavior (e.g., parasitic lifestyle, juvenile delinquency) [10,11]. Interestingly, while Hare and colleagues argue that both factors are key components of psychopathy, others have argued that antisociality is of secondary importance to the definition of psychopathy [12].

Hare and his co-workers have worked on further refinement of the original two-factor model. The resulting body of work has shown that each factor can be subdivided in two facets, which lead to the emergence of the four-factor model of psychopathy [6]. More specifically, the original Factor 1 can be subdivided into a facet that captures interpersonal traits and a second facet that measures distortions in affective functioning. The original Factor 2 can be decomposed into a facet capturing lifestyle and impulsivity and a facet representing antisocial behavioral tendencies. Nowadays, Factor 1 is often labeled 'Interpersonal/Affective' and Factor 2 'Impulsive/Antisocial' to include both the two superordinate factors and the presence of the 4 facets.

2.1 Other conceptualizations of psychopathy
Despite the fact that Hare's definition of psychopathy has been very influential in the modern view on psychopathy, others have argued that this conceptualization places too much focus on maladaptive aspects of psychopathy [13]. In his seminal work, Cleckley [14] described what seem to be different expressions of a similar core deficit in individuals with psychopathy. He described callous and unemotional individuals with a tendency of being disinhibited and engaging in antisocial and destructive behaviors, but also that some of these individuals appeared to be well skilled in understanding social conventions and using them to their advantage. Based on these observations Cleckley formulated sixteen criteria for diagnosing psychopathy, which were later grouped into three categories: (1) criteria related to positive psychological functioning and adequate social adjustment in general, (2) a set of items related to disinhibited and antisocial tendencies, sexual promiscuity, reduced learning from experience and lack of foresight, and (3) criteria reflecting disturbed affective and interpersonal functioning [15].

Some researchers have argued that the conceptualization used by Hare only captures the maladaptive aspects of psychopathy and cannot account for the indicators of positive adjustment [13]. Also, it has been proposed that psychopathy should be measured dimensionally rather than categorically and that psychopathic tendencies can also be measured among the general population rather than only in offender samples [13,16,17]. These ideas have led to the development of alternative frameworks that seek to explain psychopathy from a broader perspective and not only as a clinical condition present in offender samples. Next, I will briefly discuss two prominent frameworks based on such conceptualizations of psychopathy.

Based on some of Cleckley's ideas, Lilienfeld and Andrews [16] have proposed that psychopathy can be described in terms of individual variations on eight common personality traits such as anxiety, fear and impulsivity, and individuals are considered increasingly psychopathic as the these traits become more prominent. In order to measure the traits they used student samples to develop the Psychopathy Personality Inventory (PPI), a self-report questionnaire that indexes scores on eight general personality traits. Psychometric research has shown that the traits cluster into two independent higher-order factors initially termed Fearless Dominance (PPI-I) and Antisocial Impulsivity (PPI-II) [18]. The PPI-I is believed to reflect social-affective functioning and the PPI-II captures behaviors related to externalizing proneness. Thus, to a certain extent these higher-order factors show parallels with factors 1 and 2 of the PCL-R, respectively. One key difference with the PCL-R is that this definition of psychopathy is not bounded by the presence of specific criminal tendencies, making it suitable to assess psychopathy-related tendencies in non-criminal samples [19]. However, it has been pointed out that extreme scores on psychopathic traits in samples of healthy individuals who generally do not pose a threat to society (i.e. non-clinical psychopathy) cannot be equated with the severe pathological expression of psychopathy seen in offenders scoring high on the PCL-R (i.e. clinical psychopathy) [20]. In addition, studies in offender samples have shown that the PPI has poor psychometric properties in offender populations and that the two factor structure found in healthy community samples is not viable in offender samples [21,22], also supporting the claim that this self-report measure might not be suitable for assessing clinical psychopathy. It should be mentioned that despite the concerns regarding the usefulness of self-report measures to assess psychopathy, Neumann and colleagues have succeeded in developing an instrument known as the Self-Report Psychopathy Scale (SRP) that seems capable of measuring psychopathic tendencies reliably in offender and healthy samples and in both males and females [23].

More recently, Patrick and colleagues [24] have developed the Triarchic model of psychopathy. The core of this model is that psychopathy can be conceptualized dimensionally based on three components that resemble those proposed by Cleckley. This framework tries to account for the different manifestations of psychopathy in terms of individual variations on these three core dimensions and their interactions. The components are disinhibition, meanness and boldness, and the idea is that each can be indexed individually by measuring unique behavioral and neurobiological markers reflective of an underlying genetic predisposition (called endophenotypes). Disinhibition is held to reflect a general inclination towards problems with impulse control and negative affectivity and is related to pathological behaviors such as addiction, reactive aggression, and criminality. Meanness captures maladaptive phenotypic expressions related to reduced affective responsivity such as lack of empathy, sensation seeking, and a tendency to be confrontational and to seek personal gratification at the expense of others. The predominance of these two facets in an individual is assumed to be influenced by the presence of a difficult

temperament (e.g., high irritability, proneness to experience excessive frustration and anger). Boldness describes phenotypic markers indicative of characteristics such as low-stress reactivity and neuroticism, calmness, social efficacy and social dominance. Importantly, both meanness and boldness are believed to be phenotypic expressions of an underlying biological predisposition towards experiencing low fear, but the expression of this predisposition as either meanness or boldness may depend (in part) on the interactions with environmental factors such as parenting style. According to the Triarchic conceptualization of psychopathy the combination of meanness and disinhibition can result in the characteristics often seen in offenders with psychopathy, while the combination of boldness and disinhibition can be observed in individuals with reduced fear reactivity but positive psychological functioning and adequate social adjustment.

In addition, this model postulates that antisocial individuals without psychopathy are characterized by high disinhibition and relatively low meanness and boldness. This highlights that although psychopathy and general antisociality show overlap at the behavioral level they should not be equated. This notion has been subject to considerable debate in psychiatry partly because the 4th edition of the Diagnostics and statistical manual of mental disorders (DSM-IV) [25] does not include psychopathy as a separate disorder but as part of antisocial personality disorder (ASPD). The importance of distinguishing psychopathy from generic antisociality is also bolstered by studies showing that while 50 to 80% of offenders can be diagnosed with ASPD, only 20% of these individuals score above threshold on the PCL-R [26]. Also, more recent approaches employing electrophysiology have shown that psychopathy and generic antisociality differ at the neurocognitive level despite showing similar behavior [27].

2.2 Interim summary
In summary, the PCL-R has been very influential in establishing the currently dominant conception of psychopathy. Although this instrument was initially developed as a dimensional measure of psychopathy, it is often used to dichotomize this dimension for the classification of behavior into psychopathic or non-psychopathic. This feature has made the PCL-R of great value in both clinical and legal settings. Note, however, that other conceptualizations exist in which psychopathy is defined as the presence of extreme variations in common personality traits/facets among the general population rather than being a forensic condition [16,24]. The existence of multiple definitions of psychopathy clearly points out that there is no consensus about the nature, cause and exact personality characteristics of this disorder. This has led to heated discussions and arguments among researchers and clinicians over the years [28,29], which in turn have fuelled a large amount of research by groups of scientists with competing clarifications as well as further polarization of the groups. Another factor contributing to the lack of consensus is that while some argue in favor of a conceptu-

alization of psychopathy from a predominantly personality-based perspective, others have defined psychopathy and distinguished it from general antisociality based on a cognitive and/or neurobiological point of view. There are also various competing neurocognitive accounts of psychopathy. In the next section I will provide an overview of the most influential neurocognitive models of psychopathy.

3. Neurocognitive models of psychopathy

The technological advances of the last three decades have been pivotal in increasing our understanding of the basic cognitive and neurobiological mechanisms driving animal and human behavior. Findings from studies on cognition in the general population have also facilitated research aimed at understanding abnormal cognition in various personality disorders, including psychopathy. In this section, I will discuss some influential contemporary models that seek to explain psychopathy as a disorder characterized by cognitive and/or neurobiological dysfunctions rather than one predominantly based on personality factors. It is important to note that the term 'cognitive' is used here to refer to both affective and non-affective processes that take place in the brain. First, I will discuss the low-fear accounts [30,31], followed by the Response Modulation hypothesis [32] and finally the Integrated Emotion Systems model [33].

3.1 The low-fear accounts of psychopathy
David Lykken [30] argued that a deficiency in processing and responding to anxiety- and fear-evoking events lies at the core of psychopathy. This idea led to the development of fear-centered accounts of psychopathy, which have received a considerable amount of empirical support throughout the years, and offer an explanation for various psycho-physiological and cognitive impairments seen in psychopathy. The psychophysiological abnormalities include reductions in galvanic skin response in anticipation to threat [34] and impaired fear-potentiated startle [31]. Also, healthy individuals are held to experience fear in the light of impending aversive outcomes and associate this fear to the actions that induced it, resulting in avoidance of these actions. This form of associative learning is known as fear-conditioning [35]. As individuals with psychopathy show reduced fear responsivity, they should demonstrate impairments in associating fear with the actions inducing it. This would ultimately result in weaker associations and thus the endurance of undesirable behaviors. Indeed, a study conducted by Birbaumer and colleagues [36] found impaired fear-conditioning in offenders with psychopathy, while another study from the same lab found evidence for a more general impairment in aversive affective conditioning [37].

Fear is also believed to play a key role in the acquisition of social behavior through a process known as social fear learning, a process that occurs according to the same

associative learning principles as classical fear-conditioning [38]. Impairments in social fear learning are believed to hamper the socialization process, leading to disturbed empathic processing and moral development [39]. From the perspective of the low-fear accounts it can be predicted that reduced fear reactivity should have a detrimental effect on social fear learning and the moralization process. While this explanation for the antisocial behavior seen in psychopathy is very appealing, it leans heavily on the assumption that fear is a unitary system, an assumption that has been challenged by neuroscientific evidence [40]. In addition, Blair et al. [40] have also argued that the low-fear hypotheses also suffer from other weaknesses such as underspecificity and disconcordance with the literature on moral development. These problems have led to other explanatory frameworks that are more consistent with neuroscientific theories in general and empirical findings in psychopathy research in specific. However, the position that disturbances in affective reactivity lye at the core of psychopathy has repeatedly been challenged by an alternative, attention-based account of psychopathy known as the Response Modulation hypothesis [32,41]. This framework will be discussed in the following section.

3.2 The Response Modulation hypothesis

The Response Modulation (RM) hypothesis is one of the oldest frameworks among contemporary neurocognitive accounts of psychopathy, finding its roots in cognitive research performed in the 1980s by Newman and his co-workers. This theory has been subjected to revisions and refinements throughout the years [32,41–43], but the core of the RM hypothesis remains that psychopathy is characterized by an inability to automatically regulate goal-directed behavior because of a deficiency in modulating attention to accommodate meaningful information that is of secondary importance to on-going behavior [44]. That is, psychopathic individuals are believed to have deficits in shifting their focus of attention away from information that is of primary importance for their current goals (e.g., win money) and therefore neglect information that is unattended or that provides secondary/peripheral information (e.g. cues signaling that they will lose money, others' negative emotional reactions) when there is a certain amount of uncertainty involved. By defining psychopathy as a disorder of attention rather than one of affect, this account differs fundamentally from other emotion-based theories of psychopathy.

Throughout the years, Newman and his colleagues have collected an extensive amount of data and have gathered a lot of evidence supporting their position that various impairments seen in psychopathy are driven by a problem with (re)allocation of attention. For instance, they have shown that the reduced fear-reactivity typically associated with psychopathy is moderated by limited attentional capacity rather than amygdala-mediated impairments in affective processing [45]. The RM hypothesis has also been held to account for various other types of behavioral impairments seen in

psychopathy, such as passive avoidance learning [46], response reversal [47] and incorporation of secondary contextual information in speech [44].

Most of the evidence in favor of the RM hypothesis has been acquired using behavioral paradigms, thus precluding direct assessment of the underlying neurocognitive mechanisms. However, in their more recent work, Newman and colleagues have been employing neuroscientific methodologies to further specify the possible neurocognitive correlates of their theory [32,45]. This has led to the development of the latest refinement of the RM model, which postulates that the abnormal selective attention seen in psychopathy is due to an early attention bottleneck [32]. More specifically, it is argued that a bottleneck in early selective attention results in an overfocus on relevant information because information that is secondary of nature is filtered out in a very early stage of processing. As a consequence, psychopathic individuals are less aware of the presence of contextual information relevant for guiding goal-directed behavior, resulting in the endurance of less appropriate/sub-optimal behavior. Still, the RM hypothesis has been criticized for not being compatible with modern neurobiological accounts of attention and for not providing a specification for the neurocognitive mechanisms driving the shift of attention [48]. Next, I will turn to a model that was developed based on neurobiology that claims to offer a better account of psychopathy than the low fear accounts and the RM hypothesis.

3.3 The Integrated Emotion Systems model

The IES model is currently the leading neurobiological theory of psychopathy, as it has a strong neuroscientific basis and can account for a large amount of behavioral and neuroscientific findings. Before discussing how the IES model links brain systems to psychopathic behavior, I will first provide a general description of main brain regions and the overlapping networks incorporated in the model.

One of the central tenets of the IES model is that a large portion of the behavioral disturbances seen in psychopathy is primarily driven by deficient functioning of the amygdala and specific prefrontal brain areas, from which especially the interaction between the amygdala and orbitofrontal cortex (OFC) has received a great deal of attention [33]. The orbitofrontal cortex is located in the front of the brain above the upper extremities of the eye sockets (see Figure 1A) and is believed to play a central role in functions such as reward processing, decision-making, associative learning [49], and social cognition [50,51]. It is strongly connected to the amygdala, an almond-shaped structure located in the deeper region of the medial temporal lobe well known for its importance for affective functioning (see Figure 1B). These amygdala shares much of the functions of the OFC, but is also involved in autonomic processes such as threat detection [52] and the modulation of fear- and anxiety-potentiated startle [53], and the modulation of general stimulus saliency [54].
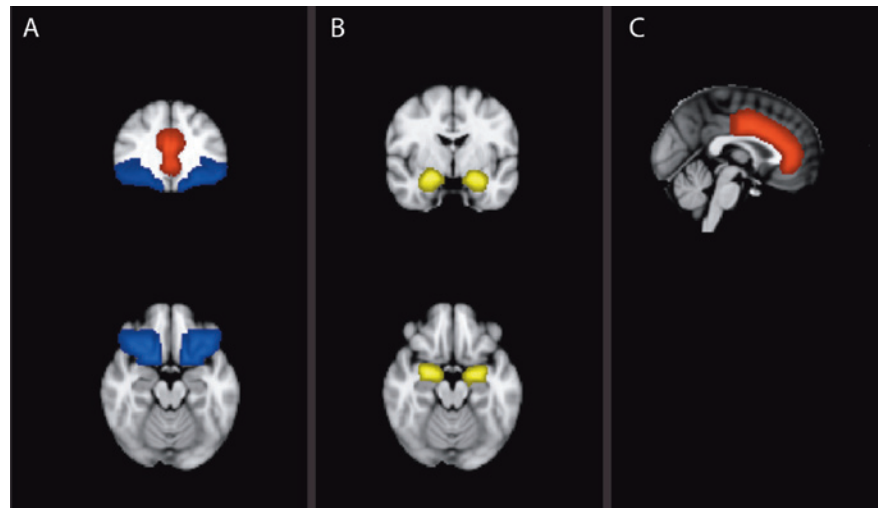
Figure 1 Location of the orbitofrontal cortex (blue), amygdala (yellow) and the anterior cingulate cortex (red).

One question that arises is how a relatively small structure like the amygdala can be implicated in so many different autonomic and cognitive functions. Part of the answer lies in a growing body of empirical evidence pointing out that the amygdala is a modular structure rather than a unitary one. The amygdala consists of 13 anatomically interconnected nuclei [55], which have been parcellated into 3 subregions based on their connectivity patterns [56] or have been subdivided in 2 groups known as the central nuclei (CeN) and the basolaretal nuclei (BLA) based on differences in evolutionary development [57].

The latter subdivision played a key role in the development the IES model and three interacting neural networks centered on the amygdala have been incorporated in this model; (1) a forebrain system that is believed to provide sensory input to the amygdala through reciprocal connections, (2) a network anchored in the CeN that projects downwards to various structures located in the brain stem and (3) a system with reciprocal connections between the BLA and various frontocortical regions that is held to modulate goal-directed behavior [40]. These systems, as well as their mutual interactions, are proposed to drive various cognitive deficiencies characteristic of psychopathy. More specifically, the IES model postulates that psychopathic behavior is driven by impairments in representing affective information, thus leading to disturbances in specific associative learning processes in the amygdala that are modulated by OFC [33]. The premise is that psychopathic individuals are less capable of linking negative outcomes (e.g., loss of money) and the corresponding negative

affective states (feeling sad about losing money) to the event that led to the negative outcome. One prediction that follows is that individuals with psychopathy should show impairments when they have to adapt their behavior to move away from undesirable outcomes. Indeed, psychopathic offenders have been found to show impairments in avoiding stimuli that lead to punishment [46] and also in adapting their behavior when previously rewarded stimuli start leading to punishment [47,58,59].

3.4 Interim summary

The IES model and the RM hypothesis have generated competing neurocognitive explanations for the core dysfunctions in psychopathy. On one hand, the IES model builds on previous models positing that the core feature of psychopathy lies in abnormal affective processing and impairments in specific amygdala-centered associative learning processes. In contrast, the RM hypothesis postulates that psychopathy is not typified by affective dysfunctions but by abnormalities in early selective attention processes which in turn lead to behavioral impairments.

4. Adaptive behavior

In spite of the fundamental differences between these neurocognitive models, one important commonality is that they were all developed with the goal to explain various impairments in changing goal-directed behavior (i.e., adaptive behavior) seen in psychopathy. Understanding the origins and the modulatory mechanisms of maladaptive behavior might also be of great clinical value. Ultimately, one of the goals of therapeutic interventions is to teach patients to modulate pathological behavior and to facilitate the learning of novel behaviors that are more functional and beneficial. In line with this, most studies on adaptive behavior in psychopathy have defined and measured changes of behavior in terms of learning. In the 1980s Newman and co-workers studied adaptive behavior in psychopathy using passive avoidance learning paradigms [41,46,47,60]. During passive avoidance learning participants are required to learn that responding to certain events will be rewarded and that they have to avoid responding to other events that are unrewarded or punished. Others have focused on response reversal more recently [61], which entails changing previously learned behavior when responding to an event that previously led to positive outcomes starts leading to negative outcomes. From these examples it becomes evident that appropriate adaptation of behavior requires the constant monitoring and evaluation of our actions and their outcomes (i.e. action monitoring). This demands sensitivity to information indicating that our actions did not lead to the expected results, and errors might be some of the most salient and powerful indicators of suboptimal performance.

The neurocognitive underpinnings of action monitoring have received a large amount of attention in the general literature since the discovery of event-related potentials (ERPs) considered to be its electrophysiological correlates. In the early 1990s two separate groups of researchers discovered an ERP with a negative deflection occurring after the detection of an error, which was labeled the error negativity (Ne) [62] or the error-related negativity (ERN) [63]. The ERN is generated in the anterior cingulate cortex (see Figure 1C) [64]. It is the first observable component related to error processing and typically peaks as early as 50-100 msec after an erroneous response has been given [65]. The ERN is followed by a second ERP component known as the error positivity (Pe) [66], a slowly evolving wave with a positive polarity that peaks in a later time window (between 200-400 msec) after the response has been given. Together, these ERPs and their derivates (for instance, the feedback-related negativity) have proven to be reliable electrophysiological indicators of how well we process the outcomes of our actions.

Despite indications that action monitoring might be compromised in psychopathy this subject has received no attention in empirical research until recently. Therefore, investigating action monitoring might yield valuable novel information regarding possible impairments in the brain mechanisms involved. Another factor that has often been overlooked is that changes in behavior and learning are often triggered by the requirements of the current environment [43]. In order to adapt behavior appropriately we need to use and combine the various sources and types of information present in the context in which adaptation should take place. In clinical forensic settings, learning and adapting are highly dependent on information provided by the (social) context in which they occur. Context plays a key role in guiding the acquisition of desirable tendencies and cognition, such as prosocial behavior, control over aggressive urges and a proper sense of morality. Therefore, it seems crucial to gain more knowledge on the possible role of context in explaining maladaptive behavior in psychopathy.

5. Outline of this thesis

This thesis is divided into two sections. The first part encompasses a series of experiments in which various aspects of error-related processing were investigated using electrophysiology in psychopathic offenders. The first chapter of this section (**chapter 2**) describes an experiment in which the electrophysiological correlates of monitoring of own actions were investigated in psychopathy. In **chapter 3**, I will present a study in which the role of error processing was investigated during trial and error learning. **Chapter 4** consists of an experiment that builds on the results described in chapter 2 and extends them to the social domain. In this study, action

monitoring was investigated in a social context and ERPs related to monitoring of own and another person's actions were assessed.

Part two consists of three chapters. The first two describe studies that were designed and conducted based on the electrophysiological results presented in section one. These studies were conducted with the aim to translate some of the electrophysiological findings to different learning impairments in psychopathy. **Chapter 5** is devoted to the impact of learning context on response reversal. A study will be presented that tested the hypothesis that the response reversal deficit previously found in psychopathy is dependent on the learning context in which response reversal occurs. The impairments were expected to follow the distinction between intact automatic and hampered controlled adaptation that are discussed in chapter 2. **Chapter 6** describes a study in healthy individuals in which the amount of information that was used to learn from various sources and the succeeding changes in behavior were quantified using formal computational modeling. Importantly, a second aim of this experiment was to isolate common personality traits related to psychopathy that showed a relationship with the active use of information to learn. **Chapter 7** is devoted to the debate around the definition of psychopathy and generic antisociality and builds on one of the findings discussed in chapter 6. I will show an experiment in which we succeeded in dissociating psychopathy from generic antisociality based on differences in ERP patterns, thus providing evidence for a fundamental difference between psychopathy and generic antisociality on a neurocognitive level. The final chapter of this thesis (**chapter 8**) will provide a summary of the findings reported in each chapter, integrate some key results and discuss them in the light of current theories, hypothesize about a theoretical expansion of current models, and lastly speculate about possible explanations for the findings presented in this thesis and on the significance for treatment.

1

PART I

2

Early and late components of error monitoring in violent offenders with psychopathy

Abstract

One of the most recognizable features of psychopathy is the reduced ability to successfully learn and adapt overt behavior. This might be due to deficient processing of error information indicating the need to adapt controlled behavior. Event related potentials (ERPs) and behavioral components of error-monitoring processes were investigated in 16 individuals with psychopathy and in 18 healthy subjects. A letter version of the Eriksen flanker task was used in two conditions. The first condition ("Normal" condition) required participants to press one of two buttons depending on the identity of the target stimulus. The second condition ("Signaling" condition) required them to signal each time they had committed an error by making a second press on a signaling button. Early stages of error monitoring were investigated by using the error-related negativity (ERN/Ne) and post-error slowing as indexes. Later stages were explored by examining the error positivity (Pe) and signaling rates. Both groups showed similar ERN amplitudes and amounts of post-error slowing. The psychopathic group exhibited both reduced Pe amplitudes and diminished error-signaling rates compared to the control group. Individuals with psychopathy show intact early error processing and automatic behavioral adaptation, but have deficits in later stages of error processing and controlled behavioral adaptation. This is an indication that individuals with psychopathy are unable to effectively use error information to change their behavior adequately.

1. Introduction

One of the most recognizable characteristics of psychopathy is the reduced ability to successfully learn and adapt overt behavior in order to comply with social rules and norms. The deficient behavioral adaptation exhibited by psychopathic individuals has been investigated using different kinds of learning paradigms. These studies consistently point out that psychopathic individuals fail to adapt their behavior to meet the rules provided by external sources [46,61,67]. Newman and colleagues [67] indicated that individuals with psychopathy are deficient in avoiding monetary loss in situations in which they have to avoid punishment and earn monetary rewards. More recent research conducted by Budhani et al. [61] demonstrated that individuals scoring high on psychopathy showed impaired behavioral adaptation on a probabilistic reversal learning task. In this task, participants were expected to implicitly learn stimulus-reinforcement associations based on trial-by-trial feedback on performance. At some point, the contingencies were reversed without the participants knowing this, and they had to adapt their behavior in order to continue to receive positive feedback. Psychopathic individuals failed to make this reversal, providing further evidence for their inability to effectively adjust their behavior to meet the demands of the environment. Furthermore, these studies suggest that individuals with psychopathy are less sensitive to negative feedback following erroneous responses, consequently showing impairments in reinforcement-guided decision-making.

Rushworth et al. [51] have proposed a functional neuroanatomical model of reinforcement-based decision making. In their model, decision-making is guided by the involvement of the anterior cingulate cortex (ACC) and orbitofrontal cortex (OFC). These areas are anatomically interconnected to other areas involved in encoding reward and reinforcement information, such as the ventral striatum and the amygdala [68,69]. The amygdala has been found to be responsive to both aversive and reinforcing stimuli [70]. Functionally, the OFC and the ACC are responsible for different aspects of reinforcement-guided decision making. The OFC shows greater involvement in the processing of information regarding stimuli, such as the formation of stimulus-reinforcement associations and representations of reward expectations. The ACC on the other hand, is thought to use reinforcement information to adapt behavior [51].

The possibility that psychopaths are unable to adequately use error feedback to adapt their future behavior and the anatomical relationship between the ACC and the OFC suggest that there may also be deficiencies in one or more facets of error monitoring, which include the involvement of the ACC according to the reinforcement-learning theory proposed by Holroyd and Coles [71]. This theory states that an error signal is conveyed by the dopamine system from the basal ganglia to the ACC, resulting in the generation of an electro-cortical waveform with a negative deflection. This waveform has been termed the error negativity (Ne) or error-related negativity

(ERN) and is succeeded by a second component known as the error positivity (Pe) [63,72]. The ERN is generated after error commission and negative feedback [71] and peaks between 0-100 milliseconds (msec) after an erroneous response has been given [66]. Source localization studies have localized the source of the ERN in the ACC [64,73], which is in accordance with functional Magnetic Resonance Imaging (fMRI) studies demonstrating ACC involvement in error monitoring (for an overview see [74]). The Pe is a slow wave with maximum amplitude peaking between 200-400 msec after response onset [66] and can be regarded as a reflection of a later stage in error processing. Previous studies have shown that the ERN is a reflection of early stages in error processing that is not dependent on error awareness, while the Pe has been linked to later stages involving conscious error recognition [66,75-77].

Further evidence for the dichotomy between early and late components of error monitoring on the behavioral level has been provided by Debener et al. [78]. They found that the amplitude of the ERN predicts the magnitude with which participants adapted their behavior by slowing down on the trial following an error. Slowing down after an error is a type of behavioral adjustment known as post-error slowing, first reported by Rabbitt [79], and has been interpreted as an involuntary and cautionary response strategy. To explore the impact of remedial actions, Ullsperger and von Cramon [80] investigated the differences between immediately correcting an error and signaling an error. The results showed that error correction is a fast, often involuntary, process that does not necessarily have to be preceded by conscious detection (see also [79]). In contrast, signaling errors is an intentional, much slower, and complex process based on conscious error recognition. Recognizing and signaling an error implies that at least some degree of error awareness is involved in the process. A study conducted by O'Connell and colleagues [77] demonstrated that the Pe was only present when participants were aware that they had committed an error, which was measured by pressing an "awareness button" to signal error commission. Thus, the ERN has been associated with early unconscious processing of errors and the automatic adaptive processes of post-error slowing, while the Pe is believed to be related to conscious behavioral adaptations such as error signaling.

Research on error monitoring in psychopathic individuals has recently begun to emerge. In one study, Munro and colleagues [81] compared ERN amplitudes of psychopathic individuals on both neutral and emotional stimuli. In this study, participants with psychopathy did not show abnormal ERN amplitudes on neutral stimuli when compared to healthy control subjects. However, the size of the ERN was significantly smaller in psychopathic offenders when the stimuli carried negative emotional valence.

Considering the findings on error monitoring together with the behavioral mal-adaptation that psychopathic individuals exhibit, we hypothesized that psychopathic individuals may show normal early processing in emotionally neutral conditions, but

are unable to effectively use error signals to guide their behavior. If this is the case, we expect that this inability should be reflected in a diminished Pe and lower error-signaling rates.

2. Methods and materials

2.1 Subjects

The psychopathic group was recruited from the in-patient population of the Pompe-stichting Forensic Psychiatric Institute Nijmegen, The Netherlands. The Pompestichting is a "TBS-clinic" located in Nijmegen. TBS is a disposal to be treated, on behalf of the state, for people who committed serious criminal offenses in connection with having a mental disorder. TBS is not a punishment, but an entrustment act for mentally disordered offenders (diminished responsibility). These court orders are an alternative to either long-term imprisonment or confinement in psychiatric hospital, with the goal to strike a balance between security, treatment, and protection.

Patients were selected based on available information about clinical status and prior history. Educational level was coded according to the Dutch educational system into three levels (level 1 = primary education; level 2 = secondary education; level 3 = higher education). The patient group consisted of 16 male patients (mean age = 39 years, SD = 9.5, mean education = 2.3), who were violent offenders diagnosed with psychopathy, as assessed with the Hare Psychopathy Checklist-Revised (PCL-R) [6]. In this study, participants with a PCL-R score ≥ 26 were considered psychopaths and thus suitable for the first group. The psychopathic group had a mean PCL-R score of 32 (SD = 3.6).

The control group consisted of 18 healthy male volunteers (mean age = 37, SD = 6.4, mean education = 2.9). They were recruited by use of advertisements among the staff of the Forensic Institute who were not directly involved in patient care and known to have no criminal records and an absent history of psychiatric disorders. They were matched with the patients on age, and educational level. Compliance to the exclusion criteria was determined for both groups using the Dutch version of Mini International Neuropsychiatric Interview (MINI) [82] and the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II) [83]. Exclusion criteria included all major Axis-I and Axis-II disorders (except antisocial personality disorder in the patient group), somatic disorders, pre-test use of medication and chronic use of intoxicating substances. All assessments were conducted by trained psychologists based on interviews with the participants and on available information from each patient's clinical files.

The protocol was approved by the local medical ethics committee. All participants received written information about the experiment and gave written informed consent. All participants received financial reward for their participation.

2.2 Task and procedure

All subjects participated in two sessions, a screening session and a test session, during which experimental recordings were made. During the screening session, a number of self-report questionnaires[1] were completed and compliance to the exclusion criteria was determined.

Behavioral and electroencephalography (EEG) data were collected during the execution of a simple computer task. A modified version of the Eriksen Flanker task [87] was used for the purposes of this study. In this task, participants responded with a button press of either their left or right index finger to the central letter (H or S) of a letter string. Four different letter strings were presented randomly with equal probabilities. The letter strings were either congruent (HHHHH or SSSSS) or incongruent (SSHSS or HHSHH) and appeared in black on a white background on a 100-Hz monitor at a distance of approximately 75 cm from the participant. Participants responded with a response button device with four buttons placed in a row. The left and right outer buttons were used to respond to the central letter of the target string.

The experiment consisted of two conditions. In both conditions, participants were instructed to focus on a fixation spot and to press the button corresponding to the letter presented in the centre of the array as fast as possible. When an error was made in the first ("Normal") condition, no additional responses were required. However, when an error was made in the second ("Signaling") condition, participants were additionally asked to signal the error by pressing the button located on the inside of the target button (i.e., the button on the right of the left button or the button on the left of the right button).

A practice block of 40 trials preceded each experimental condition. The experimental phase was divided into four blocks of 100 trials. A fixation point was displayed in the centre on the screen for 750 msec. After this, the 'flanking' letters, that is, the surrounding letters without the central target letter was presented for 80 msec followed by the entire letter string for another 30 msec. After presentation of the stimulus, a blank screen was presented for 1000 msec during which the participants had to respond. After an inter-trial interval of 300 msec, the next trial was presented. The entire experimental session lasted about 1.5 hours including preparation and breaks.

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1   To identify possible covariates, anger, anxiety and impulsivity were also measured using Dutch versions of the State-Trait Anxiety Inventory (STAI; [84]), the State-Trait Anger Expression Inventory (STAXI; [85]), and the Behavioral Inhibition System and Behavioral Activation System scales (BIS/BAS scales; [86]). However, inclusion of these lists as covariates did not show any significant group differences (all p's > 0.093), nor any significant within-subject effects (all ps >0.220).

2.3 Apparatus and recordings

Scalp potentials were collected using active electrodes (ActiCap, Brain Products, Munich, Germany) arranged according to an extended version of the 10-20 system at F7, F3, Fz, F4, F8, FC5, FC1, FCz, FC2, FC6, T7, C3, Cz, C4, T8, CP5, CP1, CP2, CP6, P7, P3, Pz, P4, P8, O1, Oz, and O2. All electrodes were referenced to the left ear during recording and were re-referenced to the average of the earlobes during analysis. Electrooculography (EOG) recordings were also obtained; vertical eye movements were recorded by placing electrodes above and below the left eye, and another set located at the outer canthi recorded horizontal eye movements. The recorded signals were digitized with a sampling rate of 500 Hz using the QuickAmp amplifier (Brain Products) and filtered offline using a 0.02-20 Hz band-pass filter.

Reaction times faster than 150 msec (1.9%) and slower than 1000 msec (0.2%) were removed from the behavioral and EEG data for both groups. Brain activity was recorded continuously during the whole experiment. EOG artifacts were removed using independent component analysis (ICA) [88]. EEG signals for incongruent trials were time-locked to response onset and were averaged separately for each participant to event-related potentials (ERPs) for correct and incorrect responses relative to a 200 msec pre-response baseline.

Difference waves were computed on individual averages by subtracting the correct ERP waveforms from the incorrect ERPs [89]. The ERN was defined on this difference wave as the most negative peak between the 0-150 msec period following response onset. These analyses were conducted at FCz and Cz, where ERN amplitudes were at a maximum. The Pe is a waveform known to evolve relatively slow and to be susceptible to jittering. For these reasons, it was defined as the average of the rectified amplitude between 250-400 msec following response onset in the difference wave. Analyses of the Pe activity were conducted at Cz, where Pe activity was maximal.

Values for the ERN were analyzed using a 2x2x2 repeated measures General Linear Model (GLM) with Electrode site (FCz, Cz) and Condition (normal, signaling) as within-subject variables and Group (psychopaths, controls) as between-subject factor. The Pe was examined using a Univariate GLM with mean activity at Cz as dependent variable and Group as between-subjects variable. The analyses of Pe values were only conducted for the Normal condition to avoid ERP distortion of motor activity related to the second button press in the Signaling condition [90].

Behavioral data were analyzed by entering individual averages of reaction times (RTs) and error rates into different repeated measures GLMs with Condition (normal, signaling), Correctness (correct, incorrect), Congruency (congruent, incongruent), and Post-correctness (post-correct, post-error) as possible within-subject factors and Group as between-subject factor. Post-error slowing analyses were limited to the Normal condition, because of the different instructions and additional signaling

responses in the Signaling condition. Error signaling rate was examined using a one-sided independent samples t-test with Group as independent variable.

3. Results

3.1 Behavioral analyses

The RT analyses revealed a main effect for Group, with patients responding slower (347 msec) than controls [325 msec; $F_{(1, 32)}$ = 6.21, p = 0.018]. There was a marginal trend for Condition indicating slightly slower RTs in the signaling condition [$F_{(1, 32)}$ = 3.91, p = 0.057]. Incorrect responses (293 msec) were faster than correct responses [379 msec; $F_{(1, 32)}$ = 831, p < 0.001]. A significant interaction with Group indicated that this effect was larger for psychopathic individuals (93 msec) compared to controls [79 msec; $F_{(1, 32)}$ = 5.89, p = 0.021].

As expected, a main effect for Congruency was present [$F_{(1, 32)}$ = 616, p < 0.001]. Participants responded faster to congruent stimuli (338 msec) than to incongruent ones (430 msec). The interaction between Group and Congruency was not significant [$F_{(1, 32)}$ = 1.45, p = 0.238]. Also, the interaction between Congruency and Condition was significant [$F_{(1, 32)}$ = 18.7, p < 0.001], indicating that the congruency effect was larger in the Signaling condition (99 msec) than in the Normal condition (85 msec). The three-way interaction did not reach significance [$F_{(1, 32)}$ = 0.843, p = 0.366].

With regard to error rates (see Table 1), only a main effect for Congruency was present [$F_{(1, 32)}$ = 276, p < 0.001], indicating that participants made more errors on incongruent trials (9.7 %) than on congruent ones (1.2 %). The interaction between Congruency and Group was not significant [$F_{(1, 32)}$ = 3.11, p = 0.087]. There was a marginal trend for the main effect of Group, indicating that controls made slightly more errors (6.0 %) than psychopathic subjects (4.9 %) [$F_{(1, 32)}$ = 4.04, p = 0.053] and no significant differences were found between the two conditions [$F_{(1, 32)}$ = 0.106, p = 0.75].

Table 1 Mean percentages of error rates for congruent and incongruent trials for each condition and mean percentages of signaling rate measured in the Signaling condition. Standard deviations are displayed in parentheses.

| Group | Errors | | | | Signaling |
| | Condition 1 | | Condition 2 | | |
	Congruent	Incongruent	Congruent	Incongruent	
Control group	1.4 (1.0)	10 (3.4)	1.3 (0.9)	11 (3.3)	97 (3.4)
Psychopathic group	1.3 (1.2)	9.1 (3.9)	1.0 (0.9)	8.2 (2.6)	87 (19)

RTs for post-error trials (351 msec) were significantly slower than for post-correct trials (336 msec) in the Normal condition [$F_{(1, 32)}$ = 9.99, p = 0.003]. However, the performance of the groups did not differ on post-correct and post-incorrect trials, as the interaction between Group and Post-correctness failed to reach significance [$F_{(1, 32)}$ = 0.11, p = 0.75].
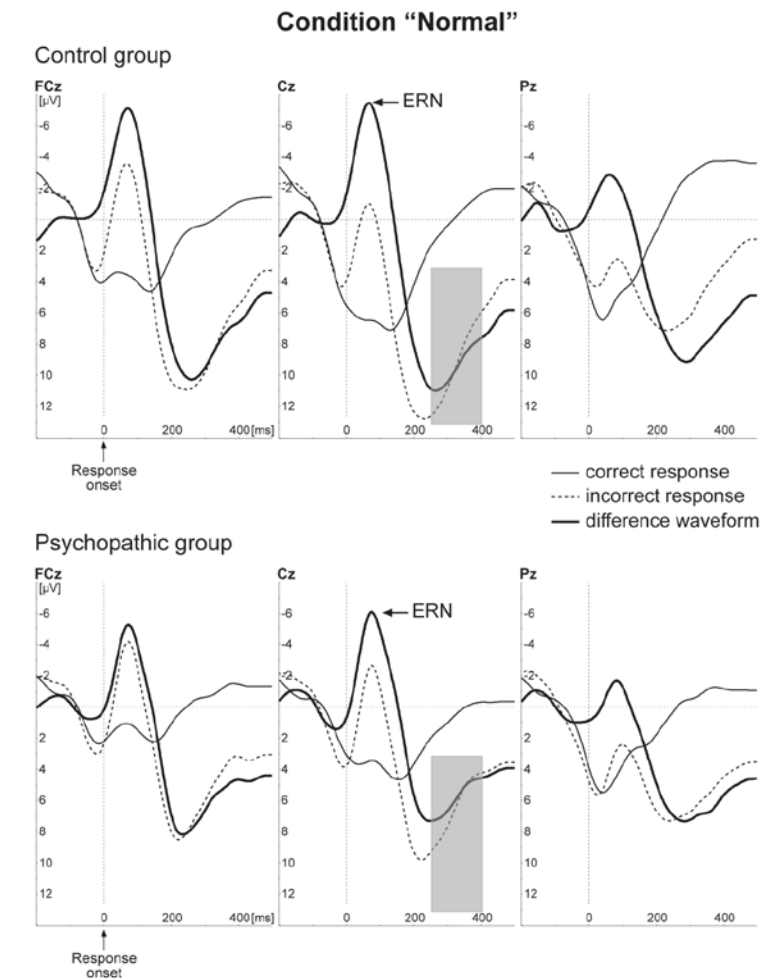

Figure 1 Grand average response-locked waveforms in the Normal condition for correct and incorrect responses, and the average difference waveform for the control and the psychopathic group. Electrodes FCz, Cz, and Pz are depicted.

Figure 2 Grand average response-locked waveforms in the Signaling condition for correct and incorrect responses, and the average difference waveform for the control and the psychopathic group. Electrodes FCz, Cz, and Pz are depicted.
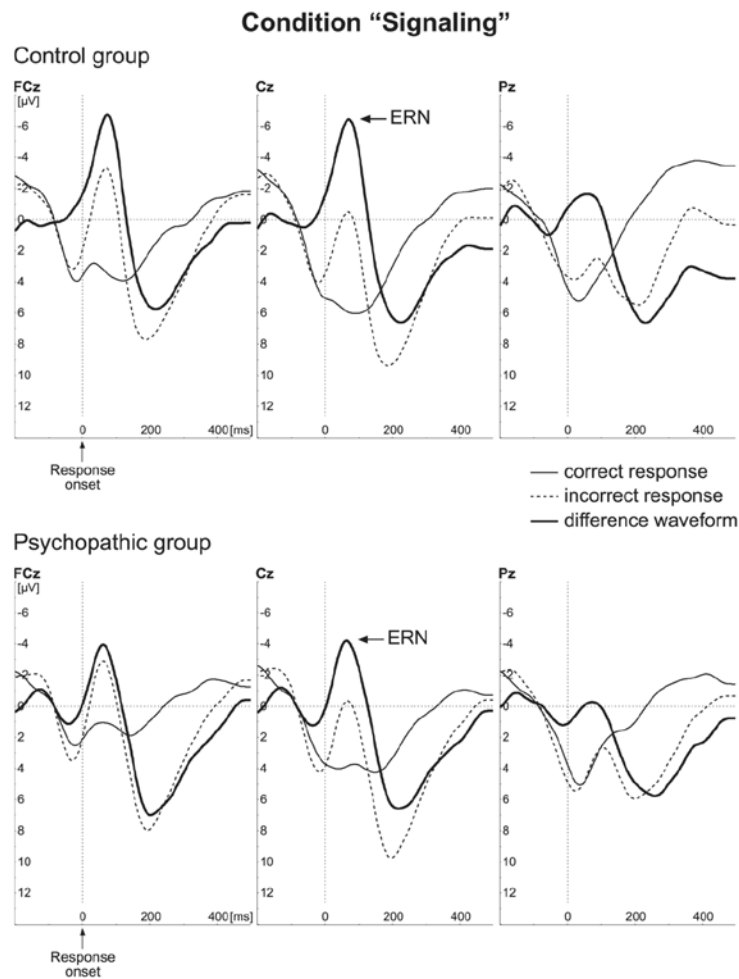
3.2 ERP analyses

The difference waves and the average waveforms for correct and incorrect trials for both groups are depicted in Figures 1 and 2 for each condition. With regard to ERN amplitudes, the main effect for Group was not significant, demonstrating that ERN amplitudes did not differ between controls (-8.41 µV) and psychopathic subjects

[-6.32 µV; $F_{(1, 32)}$ = 2.12, p = 0.16]. There was a marginal effect of electrode site with a slightly larger ERN on electrode Cz [-7.47 µV; $F_{(1, 32)}$ = 0.33, p = 0.57] (see Figure 3). Both groups showed comparable latencies with the ERN peaking around 73 msec on average [$F_{(1, 32)}$ = 0.10, p = 0.31][2]. Analyses of Pe activity revealed a significant main effect for Group at Cz [$F_{(1, 32)}$ = 4.22, p = 0.048], indicating larger Pe activity for the control group (10.5 µV) compared to the psychopathic group (7.4 µV) (see Figure 3).

3.3 Signaling-rate analyses

Analyses of signaling rate showed that patients signaled less errors (87%) compared to the control group [97%; $t_{(16)}$ = -1.98, p = 0.033].
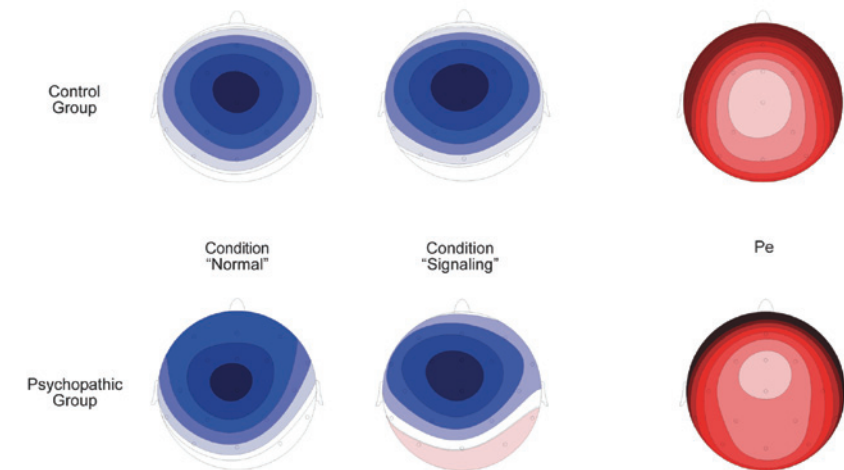
Figure 3 Scalp topographies of the ERNs at 70 msec for each group at Cz in the Normal condition, in the Signaling condition, and the mean Pe activity of each group in the Normal condition (250 – 400 msec). Dark colored shades indicate negative polarities and lighter shades depict positive polarities.

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2   The same analyses were also conducted using peak to peak differences of the ERN on incorrect response waveforms obtained by subtracting the most positive peak within -120 - 80 msec time window from the most negative peak within 0 – 150 msec relative to the response.

4. Discussion

Our results indicate that psychopathic individuals show unimpaired early processing of error information, while showing deficits in the later stages implicated in controlled behavioral adaptation. The behavioral results indicated that the psychopathic group had error rates comparable to the control group, though displaying longer overall reaction times. This finding has previously also been reported by Munro et al. [81]. Also, the increased RT differences between correct and incorrect responses for the psychopathic group might be interpreted as reflecting a more impulsive response style, with erroneous responses given relatively too fast [91]. This interpretation is also in line with the general clinical image of psychopathy. However, recent findings from Munro et al. [92] did not provide evidence for a more impulsive response style in individuals with psychopathy. So, although the currently found RT patterns suggest a more impulsive response style, it is still rather unclear whether increased impulsivity of individuals with psychopathy is always reflected in these speeded choice-reaction tasks.

Psychopathic subjects did not show differences in ERN amplitudes compared to healthy controls. This provides further evidence demonstrating that individuals with high levels of psychopathy show normal early error-detection processes when presented with affectively neutral stimuli. The same pattern was found for post-error slowing, with both groups showing a comparable amount of slowing after error commission. As such, current outcomes are in line with recent findings by Munro et al. [81], demonstrating similar ERNs in psychopathic individuals and healthy individuals on a letter version of the flanker task highly comparable to the task currently used. They also found that the behavioral performance of the psychopathic group on trials following correct and error trials resembles that of healthy subjects. Hence, the current study and the study by Munro et al. [81] both show that individuals with psychopathy and healthy controls share commonalities in early unconscious error detection processes.

Interestingly, in a previous study by Dikman and Allen [93] reduced ERN amplitudes were reported in response to punishment in low socialized individuals compared to high-socialized subjects. However, while Dikman and Allen [93] used low socialization in healthy subjects as an analogue for psychopathy, our experimental sample consisted of incarcerated patients actually diagnosed with psychopathy. Also, our task did not include reward/punishment manipulations. These large differences in sample characterization and task make a direct comparison between the two studies rather difficult and may explain the divergent outcomes regarding ERN amplitudes.

Contrary to the ERN outcomes, but in line with our expectations, the current results show decreased Pe amplitudes for individuals with psychopathy compared to healthy controls. Munro et al. [81] did not demonstrate differences in Pe amplitudes

between psychopathic subjects and healthy controls, but they did report a marginal trend that suggests decreased Pe sizes in the psychopathic group. However, it is possible that their Pe analysis did not reach significance due to the relatively small sample size of nine subjects meeting the criteria for psychopathy. So, psychopathic subjects showed a smaller Pe compared to healthy controls, with a reduction of approximately 30%. These findings demonstrate that individuals with psychopathy show deficits in a later stage involved in conscious error processing.

Finally, the behavioral findings of intact post-error slowing on the one hand, and diminished error signaling on the other, corroborate the ERP findings. Apparently, automatic behavioral adaptations resulting from early error-detection processes are unaffected, while more controlled adaptive behavior related to later stages of error processing seems to be diminished. The signaling rate of the healthy controls (97%) is comparable to a previous study (95% in Ullsperger and von Cramon [80]), but the individuals with psychopathy were only capable of signaling 87% of their errors.

An alternative explanation for the functional significance of the Pe has been discussed by Overbeek et al. [94]. The affective-processing hypothesis states that the Pe is involved in affective processes in such a way that the Pe could be a manifestation of emotional appraisal following an error. Emotional bluntness is considered to be a core feature of psychopathy [4]. Research has shown that psychopathic individuals show reduced eye blink reflexes in response to stimuli with negative emotional valence [95]. An fMRI study conducted by Muller et al. [96] demonstrated that psychopathic individuals exhibit reduced activation in the anterior cingulate, among other areas, in response to negative slides. Reports of abnormal affective processing in highly psychopathic subjects concord with the reduced Pe we found in our study, suggesting that psychopathic offenders have deviant emotional appraisal following errors.

However, Munro and colleagues [81] mention that their analyses indicate that the processing of affective information might not have a specific influence on the Pe. Note that our results also converge with outcomes of studies of error awareness in healthy individuals [66,75–77], providing further support for the dissociation between early unconscious components of error processing and later components leading to controlled adaptation of behavior.

Additionally, our results provide evidence for our suggestion that ACC functioning is compromised in psychopathy. Source localization studies of the Pe indicate that this component is generated within the ACC [77,97]. The reduced Pe activity shown by our psychopathic subjects supports the idea that the ACC is involved in the anatomical networks that are considered to be deficient in psychopathy and might play a role in the abnormal learning behavior associated with this disorder.

We would like to note that we do not believe that possible ERN differences are precluded by relatively small sample sizes. On the contrary, our group sizes are comparable or even larger than previous between group studies on error monitoring

that did show ERN differences [91,98]. Moreover, in the previous study by Munro et al. [81] similar results were obtained using the same neutral letter version of the flanker task.

5. Conclusion

In summary, these results indicate that early error processing and automatic adaptive behavior are intact in highly psychopathic individuals, as reflected in normal ERN amplitudes and normal post-error slowing. More importantly, individuals with psychopathy display impairments in later stages of error processing and controlled adaptive behavior, as reflected in decreased Pe amplitudes and lower signaling rates. These findings may help us develop a better understanding of the relationship between the abnormal behavioral characteristics of psychopathy and broader concepts encountered in everyday life, such as learning and adapting their behavior to the ever-changing demands of their environment.

2

3

Neural correlates of error-related learning deficits in individuals with psychopathy

Abstract

Psychopathy is associated with a performance deficit in a variety of stimulus-response and stimulus-reinforcement learning paradigms. We test the hypothesis that failures in error monitoring underlie these learning deficits. We measured electrophysiological correlates of error monitoring (error-related negativity or ERN) during a probabilistic learning task in individuals with psychopathy (n=13) and healthy matched control subjects (n=18). The task consisted of three graded learning conditions in which the amount of learning was manipulated by varying the degree to which the response was predictive of the value of the feedback (50%, 80%, 100%). Behaviorally, we found impaired learning and diminished accuracy in the group of individuals with psychopathy. Amplitudes of the response ERN were reduced. No differences in the feedback ERN were found. The results are interpreted in terms of a deficit in initial rule learning and subsequent generalization of these rules to new stimuli. Negative feedback is adequately processed at a neural level, but this information is not used to improve behavior on subsequent trials. As learning is degraded, the process of error detection at the moment of the actual response is diminished. Therefore, the current study demonstrates that disturbed error monitoring processes play a central role in the often-reported learning deficits in individuals with psychopathy.

1. Introduction

Individuals with psychopathy show little concern about the consequences of their actions for others and themselves. They often show poor planning skills and fail to avoid behaviors that have been punished previously [4]. The latter is reflected in, for example, the amount and types of incidents occurring in clinical settings [99] and in their poor response to treatment and the high relapse rates of criminal behavior [100].

In line with these observations, psychopathic individuals show performance deficits in different stimulus-response and stimulus-reinforcement learning situations. Cleckley [14] found individuals with psychopathy to have a reduced capacity to learn from experience. Other studies have demonstrated abnormally low levels of aversive learning [37], instrumental learning [101], and avoidance learning [46,102]. The latter is the process by which one learns that omitting a certain response will result in the termination or prevention of an aversive stimulus. Additionally, impairments in decision making to rewarding and punishing stimuli have been found [103]. Furthermore, studies of post-error slowing - the phenomenon of slower response times (RTs) following erroneous trials - have shown that individuals with psychopathy fail to utilize feedback to alter future responses [104]. Finally, recent behavioral data from a probabilistic response reversal task indicated that individuals with psychopathy showed learning deficits in the reversal phase only, in which the earlier learned reinforcement contingencies were suddenly reversed [61].

These findings are mainly in line with the Integrated Emotion Systems interpretation of psychopathy (IES) [33,40], which assumes orbitofrontal and amygdala abnormalities in psychopathy. The model predicts individuals with psychopathy to show deficits in both stimulus-reinforcement learning involving the amygdala, and in reversal learning served by orbitofrontal areas and basal ganglia [105,106]. Importantly, the model would not predict deficits in stimulus-response learning, a process that crucially relies on posterior medial frontal cortex (pMFC) including pre-SMA and anterior cingulate [73].

In our view, the above suggests that psychopathic individuals have difficulties in using negative feedback or error information to adapt their behavior. Recently, Holroyd and Coles [71] have proposed the reinforcement-learning (RL) theory of performance monitoring. The RL theory assumes that whenever outcomes are worse than expected, an error signal is conveyed from the basal ganglia to the anterior cingulate cortex (ACC). Upon arrival of this error signal in the ACC, the error-related negativity (ERN), an ERP component measurable at the scalp, is generated [64,71,73,89]. The ERN not only occurs when participants make errors, but also when they receive feedback indicating that they gave an incorrect response (for an overview on ERN and performance monitoring, see [107]).

The onset of the ERN coincides with response initiation (rERN)[108], or occurs 200 msec after the delivery of error feedback (fERN) [109]. The former reflects internal error

signals, the latter external error signals. Studies have demonstrated that the ERN is generated at the first moment in time when the error can be detected [71,110]). Thus, fERNs are elicited when the negative feedback itself was not or only partly predicted by earlier events. This is for example the case when subjects are still learning the correct stimulus–response mapping by trial and error. However, as the system gradually learns the stimulus-response mapping, subjects will eventually be able to detect errors at the moment of response onset. At an electrophysiological level, this is reflected in the fERN 'propagating back in time' and 'becoming' a rERN. Consequently, while learning takes place, rERN amplitudes increase [71].

Although several studies have investigated learning in individuals with psychopathic traits at a behavioral level, learning deficits in individuals diagnosed with psychopathy have never been studied in relation to the underlying electrophysiological markers of performance or error monitoring. Until now, most studies either focused on individuals with behavioral patterns related to psychopathy [93,111] or investigated aspects of error monitoring unrelated to learning [81,112]. An investigation of reward and avoidance learning in low socialized individuals (a concept related to psychopathy [113]) has shown diminished rERN amplitudes only in the punishment condition [93]. Another study demonstrated reduced rERN amplitudes in healthy individuals scoring high on externalizing psychopathology, a factor comparable to the behavioral deficit cluster in individuals with psychopathy [111]. Only two studies investigated the rERN directly in individuals diagnosed with psychopathy. Munro et al. [81] used a neutral and an emotional choice-reaction task and found reduced rERNs in the emotional task only. Brazil et al. [112] reported no differences in rERN amplitude between healthy controls and individuals with psychopathy on a neutral task, but did demonstrate problems in the conscious evaluation and signaling of errors. Taken together these studies point towards learning deficits associated with a failure to detect and use internal and external error signals.

The present study was designed to examine the relation between error monitoring and reinforcement learning in individuals diagnosed with psychopathy, by investigating the rERN and fERN, and the relationship between the two while learning progresses. To investigate this, a probabilistic learning task was used in which participants learned stimulus-response mappings based on feedback about their performance (trial and error learning, see e.g. [71,110]). A crucial aspect of the task is that the imperative stimulus presented on each trial, differed in the degree to which the response was predictive of the value of the feedback (50%, 80%, 100%).

Compared with healthy controls, we expected individuals with psychopathy to display learning difficulties, reflected behaviorally by reduced accuracy and electrophysiologically by smaller amplitudes of rERN, fERN and a slower propagation in time of the fERN to become a rERN.

2. Methods and materials

2.1 Participants

Thirteen male violent offenders between 18 and 55 years of age (Mean age = 37, SD = 9.5) diagnosed with a psychopathy score of ≥ 26 according to the PCL-R [6] were selected from the in-patient population of a forensic psychiatric institute in The Netherlands (Mean PCL-R score = 31, SD = 3.4). Educational level was coded according to the Dutch educational system (1 = primary education, 2 = secondary education, 3 = higher education; mean education patients = 2.8, mean education controls = 2.3). Eighteen healthy male controls matched for age (Mean age = 37, SD = 6.5), educational level and without criminal records or a history of psychiatric disorders were recruited by advertisement. Participants in both groups were checked for drug use and for medical/neurological history. Exclusion criteria included the use of alcohol more than 3 units/day during in the week preceding the experimental measure and use of alcohol within 24 hours of the measurement. Use of cannabis or other illicit drugs within the week before measurement, use of psychotropic medication other than oxazepam during the 5 days before measurement, use of oxazepam within 12 hours before measurement, and smoking within 3 hours before measurement. The somatic exclusion criteria were a history of trauma capitis, visual and auditive disorders, neurological disorders, first degree relative with any relevant neurological disorders. Psychiatric exclusion criteria: were the presence of a depressive Disorder, bipolar disorder, schizophrenia, schizoaffective disorder, schizophreniform disorder, delusional and other psychotic disorders, schizoid or schizotypical personality disorder, current alcohol and substance intoxication, first degree relatives with schizophrenia or schizophreniform disorder. The study was approved by the local Medical Ethics Committee and carried out in accordance with the Declaration of Helsinki.

2.2 Task and Procedure

Participants received written information about the experiment and signed an informed consent before being screened for psychiatric exclusion criteria by trained psychologists using the SCID-II [83] and the MINI [82]. Participants performed the experimental task and received a financial reimbursement. Additionally, all subjects received the bonus money earned during the experiment.

Participants performed a probabilistic learning task requiring a two-choice-decision to an imperative visual stimulus [71] (see Figure 1). Following each response, a feedback stimulus representing reward information was presented informing participants whether their response was correct (green dollar signs: +2 cents), incorrect (red dollar signs: -2 cents) or too late (a cherry; - 4 cents).

The amount of learning possible was manipulated in three different conditions (50%, 80%, and 100%) by varying the degree to which the response was predictive of

the value of the feedback. For stimuli in the 50% control condition, the value of the feedback was uncorrelated with the selected response, making it impossible to learn stimulus-response mappings. In the 100% and 80% learning conditions, participants could learn the stimulus-response mappings to varying degrees.

In each experimental block, a new set of six different stimuli (for task and stimulus details see [110,114]) - i.e. two for each condition - was presented. The two stimuli from the 100% condition congruently mapped to either the left or the right response button throughout the entire block. For two stimuli, feedback was delivered randomly (50% condition). Of the two remaining stimuli, one required a left button press in 80% ('80% valid'), but a right button press in 20% of the trials ('80% invalid'), and vice versa for the other stimuli.

Participants started with a bonus of € 2.50 and were informed about the status of this bonus at the end of each block. The aim was to infer the financially most beneficial strategy by trial and error. First, participants completed a practice block of 100 trials followed by four experimental blocks of 300 trials each. The six stimuli in each block were presented randomly 50 times each. Figure 1 depicts details about trial duration, which are identical to previous studies using the same paradigm [71,110,114].

2.3 Electrophysiological recording

A QuickAmp amplifier with an ActiCap system (Brain Products, Munich, Germany) holding 32 active electrodes was used for data acquisition. EEG was recorded at a sampling rate of 500 Hz and referenced to the left ear, but was re-referenced offline to the average of both ears. Signals were filtered offline using a band-pass filter of .019-20 Hz.

2.4 Data analysis

Trials with RTs below 150 msec or above 700 msec were excluded from the analyses (6.06%, SD = 5.44%). For the ERP analyses, single-trial epochs were extracted relative to the presentation of the feedback stimulus for the fERNs and relative to the response for the rERN. Single trial EEG signals were corrected for EOG artifacts [115] and averaged for each subject and condition separately using a 200 msec pre-response/feedback baseline.

In line with previous studies using the current paradigm [71,110,114], difference waves were created by subtracting the individual averages for correct responses/feedback from the individual averages for incorrect responses/feedback. The rERN amplitude was defined as the most negative peak of the response-locked difference waves at electrode Cz in a window of 0-200 msec [116]. For the fERN a window of 200-400 msec on the feedback-locked difference waves was chosen [117].

Analyses were conducted using repeated measures General Linear Models (GLMs) with Group (psychopathy, controls) as a between subject factor, and the
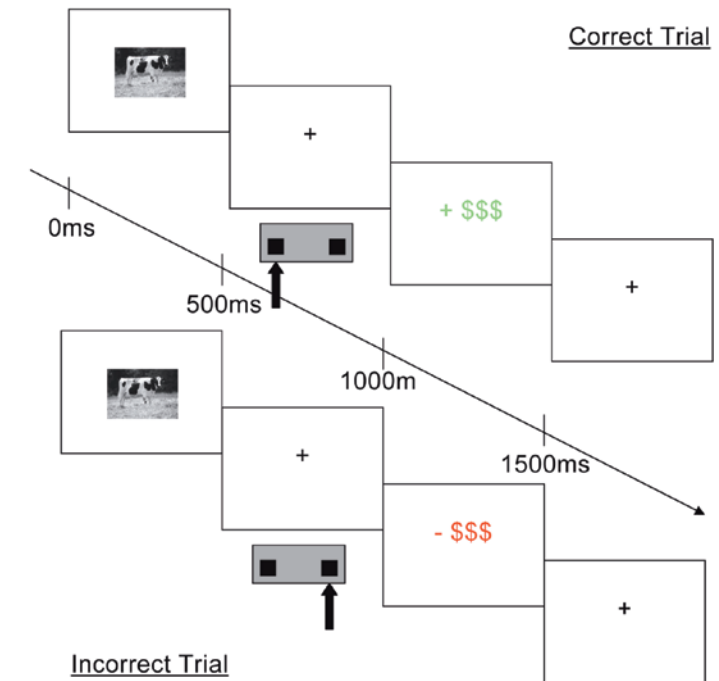

Figure 1 Trial details for a correct and incorrect trial: each trial started with the presentation of the imperative stimulus for 500 msec, a blank screen with fixation-cross (500 msec), the presentation of a feedback stimulus (500 msec), and a blank screen with a fixation-cross (500 msec). For each imperative stimulus one of two buttons had to be pressed with the index finger (right or left). A response deadline (1000 msec) was handled to ensure that participants made enough errors in the 100% easy learning condition.

following as possible within subject factors: Block Half (first, second), Block (1, 2, 3, 4), and Condition. Depending on the independent variable entered into the GLM, the number of levels for the factor Condition varied. First, to test the validity of our design, all four levels (100%, 80% valid, 80% invalid, and 50%) were entered. Second, to investigate learning processes in more detail the two learning conditions (100% and 80%) were analyzed by means of a repeated measures GLM with Group as a between subject factor and Block Half (first, second) and Condition as within-subject factors. Because any response-locked error-related activity in the 50% condition is known to result from random fluctuations in the EEG signal [71,110,114] and learning cannot

occur, we excluded this condition from the analyses. Note that for the rERN analyses the factor Condition includes the 80% condition but that no distinction is made between valid and invalid trials, as the actual validity of a trial in the 80% condition is unknown to the subject until the moment of feedback.

3. Results

3.1 Behavioral results

Confirming the validity of our design, an overall analysis of Condition (100%, 80% valid, 80% invalid and 50%) revealed that accuracy was highest in the 100% conditions, followed by the 80% valid condition and lowest in the 80% invalid condition [$F(3, 27)$ = 86,0, $p < 0.001$]. Accuracy in the 50% condition was around chance level (see Figure 2).

An analysis of the two learning conditions (100% and 80% valid) including Block Half revealed no overall group differences between psychopathic individuals and controls in accuracy [$F(1, 29)$ = 1.65, p = 0.209]. However, the significant interaction between Condition and Group showed that, compared to controls, psychopathic subjects were less accurate in the 100% condition, but not in the 80% valid condition [$F(1, 29)$ = 6.90, p = 0.014]. Planned comparisons by means of an independent t-test confirmed this (two-tailed t-test 100%: $t(29)$ = 2.00, p = 0.055; 80% valid: $t(29)$ = 0.449, p = 0.657). Accuracy was higher in the second block half than in the first [$F(1, 29)$ = 23.8, $p < 0.001$] and this was the same for both groups [$F(1, 29)$ = 0.03, p = 0.87]. The interaction between Condition and Block Half revealed that the increase in accuracy with block half was more pronounced for the 100% condition (6.9%) than for the 80% valid condition [2.6%; $F(1, 29)$= 14.9, p = 0.001]. Most importantly, the three-way interaction between Condition, Block Half and Group showed a clear trend towards significance [$F(1, 29)$ = 4.05, p = 0.054]. Psychopathic individuals show less increase in accuracy between block halves for the 100% condition compared to controls, but a steeper increase between block halves in the 80% valid condition (see Table 1, Figure 2). These effects were confirmed by planned independent t-tests (two-tailed t-test 100% BH1: $t(29)$ = 1.74, p = 0.093; 100% BH2: $t(29)$ = 2.05, p = 0.049; 80% valid BH1: $t(29)$ = 0.804, p = 0.428; $t(29)$ = 0.136, p = 0.892).

To examine acquisition and generalization of learning rules in the two learning conditions (100% and 80% valid), we investigated accuracy per block. Accuracy increased with each block [$F(3, 27)$ = 37.2, $p < 0.001$; all contrasts: p< 0.05] without an interaction between Block and Group [$F(3, 27)$ = 1.78, p = 0.175]. Planned comparisons showed that individuals with psychopathy had lower accuracy in the first block but not in the fourth [$F(1, 29)$ = 5.07, p = 0.03, see Figure 3].
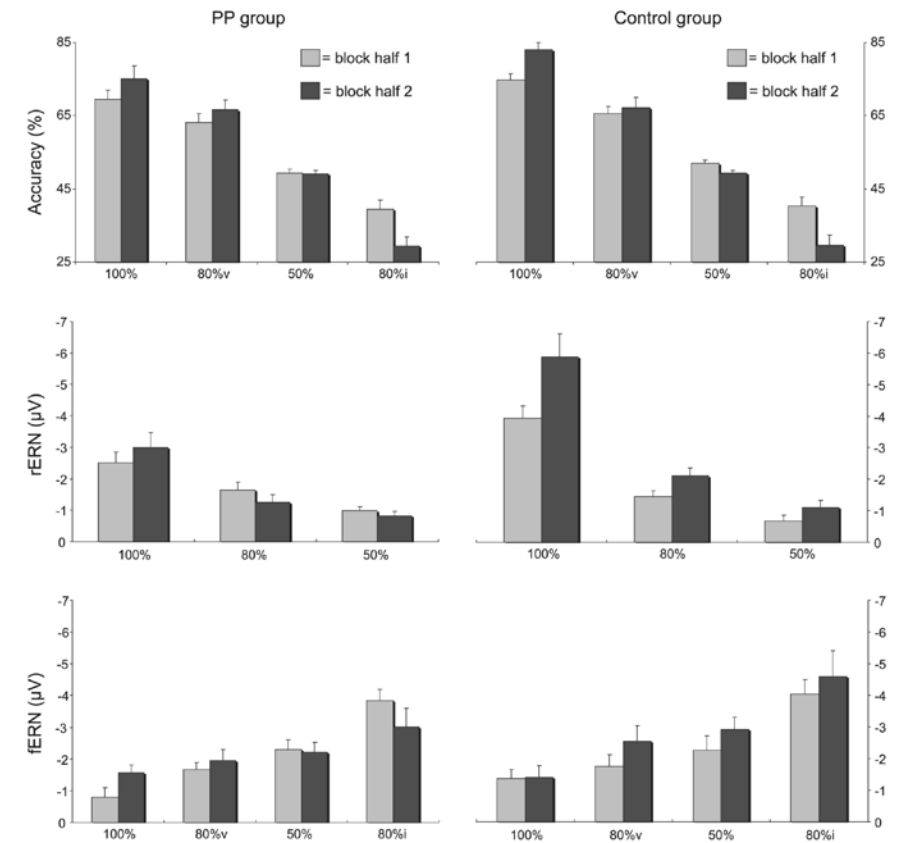
Figure 2 Behavioral accuracy for individuals with psychopathy and controls for each condition and the two block halves. Error bars indicate standard errors. Mean amplitudes for the rERN and fERN, for each of the two groups, each condition and the two block halves. Error bars indicate standard errors.

3.2 ERP findings

3.2.1 Feedback ERN (fERN)

In line with previous studies [71,110,114], comparison of fERN amplitudes between conditions revealed that amplitudes were largest in the 80% invalid condition, in which negative feedback was most unexpected, followed by the 50% condition, the 80% valid condition, and finally the 100% condition [$F(3, 27)$ = 7.97, p = 0.001, all contrast $p < 0.05$, see Figures 2 and 4]. For the fERN in the learning condition (80% valid, 80% invalid and 100%) we did not find any differences in fERN amplitudes between groups or block half nor an interaction between the two (all ps > .10; see Figures 2 and 4).

Table 1 Mean percentage correct responses (and standard deviations) for each group, condition and both block halves separately and across block halves (total).

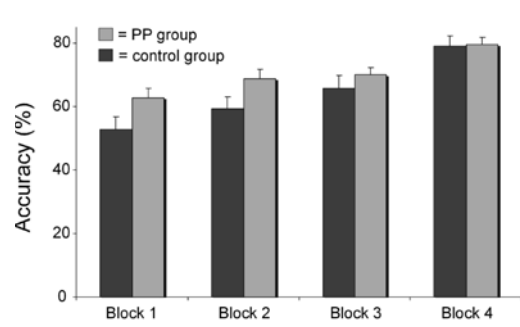| Condition	Psychopathy group (N=13)			Control group (N=18)		
	Block Half 1	Block Half 2	Total	Block Half 1	Block Half 2	Total
100%	69 (9)	75 (13)	72(11)	74 (7)	82 (8)	79 (8)
80% valid	63 (8)	66 (9)	65(9)	65 (7)	67 (11)	66(9)
50%	49 (3)	49 (2)	49(3)	52 (3)	49 (2)	51(2)
80% invalid	39 (9)	29 (9)	34(8)	40 (10)	29 (12)	35(10)

Figure 3 Average amount of correct responses (%) in the two learning conditions (100% and 80% valid) for control and psychopathic individuals (PP), separately for each block. Error bars indicate standard errors.

3.2.2 Response ERN (rERN)

Comparison of rERN amplitudes revealed a main effect of Condition ($F(2, 28) = 42.9$, $p < 0.001$, all contrast $p \leq 0.003$). Amplitudes were largest in the 100% condition, followed by the 80% condition and virtually absent in the 50% condition (see Figures 2 and 5).

For the rERN in the learning conditions (80% and 100%) we found a main effect for Group [$F(1, 29) = 7.94$, $p = 0.009$] and a main effect for Block Half [$F(1, 29) = 8.50$, $p = 0.007$; see Figures 2 and 5]. The interaction between Condition and Block Half revealed that amplitudes in the 100% condition were larger in block half 2 than in block half 1, but such a difference was present to a lesser extent or absent in the 80% condition [$F(1, 29) = 9.03$, $p = 0.005$]. This was confirmed by means of a paired t-test (two-tailed rERN100BH1 − rERN100BH2: $t(30) = 3.383$, $p = 0.002$; rERN80BH1 − rERN80BH2: $t(30) = 1.2$, $p = 0.240$).
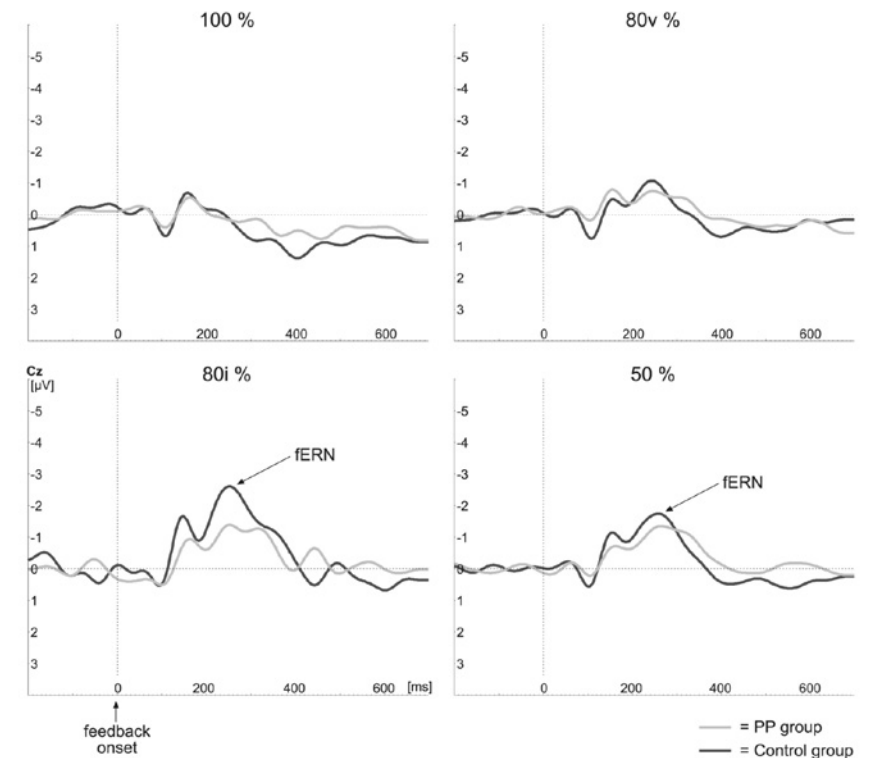
Figure 4 Grand average fERN difference waves (incorrect feedback minus correct feedback) for the control group (solid line) and the group with psychopathy (dashed line) for electrode site Cz and all four conditions (100%, 80% valid, 50% and 80% invalid). Feedback was given at 0 msec; the fERN is indicated by the arrow.

The significant interaction between Group and Condition showed that while amplitudes in the 80% condition did not differ between groups, subjects with psychopathy displayed smaller amplitudes in the 100% condition [$F(1, 29) = 11.4$, $p = 0.002$]. Most importantly, the interaction between Group and Block Half was significant [$F(1, 29) = 7.29$, $p = 0.011$], indicating that subjects with psychopathy showed a smaller difference in amplitudes between block half 1 and 2 compared with control subjects. Finally, the three-way interaction between Group, Condition and Block Half was not significant [$F(1, 29) = 0.285$, $p = 0.598$].

Figure 5 Grand average ERP difference waves (incorrect responses minus correct responses) of the 100%, 80%, and the 50% condition for the control group (solid line) and the group of psychopaths (dashed line) at electrode Cz. Responses were given at 0 msec.

4. Discussion

The present study revealed that individuals with psychopathy showed lower accuracy in a reinforcement-learning paradigm. Furthermore, diminished response ERN but normal feedback ERN amplitudes were found in psychopathic individuals.
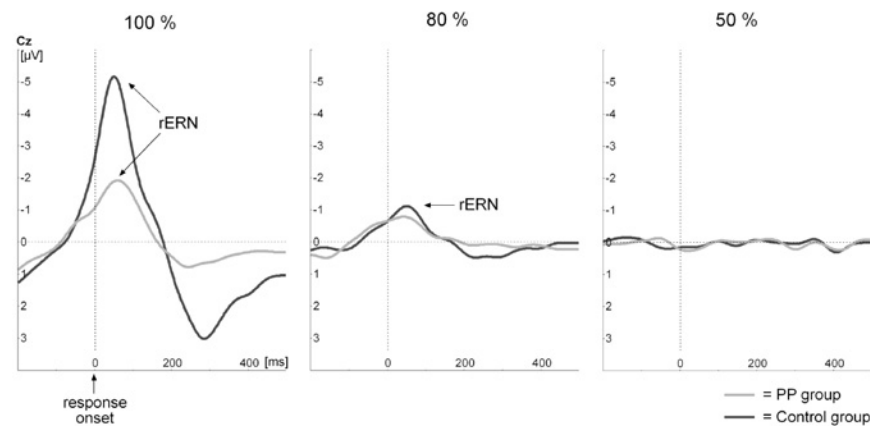
The current study investigated the relation between error monitoring and learning in individuals with psychopathy and healthy controls. At an electrophysiological level, psychopathic individuals showed similar responses as controls to negative external feedback, reflected in the fERN. However, individuals with psychopathy did display problems in using this signal to optimize performance, which was reflected in both the behavioral and the electrophysiological data. Behaviorally, participants with psychopathy showed reduced accuracy in the 100% learning condition, but not in the 80% learning condition. Additionally, the psychopathy group had a lesser increase in accuracy between block halves in the 100% learning condition and the accuracy-rate analyses over blocks demonstrated that individuals with psychopathy had specific problems in the initial learning phase in the first block, but not in the later blocks. Importantly, diminished learning was also associated with the compromised propagation of the fERN to become a rERN. This was mainly reflected in a diminished increase in rERN amplitudes while learning progressed.

4.1 Behavioral findings

To master the present task, one has to learn the principle rules, and apply these to new pictures in subsequent blocks. Therefore, accuracy is expected to be low in the initial learning phase (the first block), but to increase rapidly during the generalization process (later blocks). While this pattern was found in both groups, individuals with psychopathy showed diminished accuracy during the first block, suggesting a deficit in initial rule learning. Similar accuracy levels in the last block suggest that psychopathic individuals do reach the same performance level as healthy controls but need more time to do so.

Interestingly, differences in accuracy were only found in the easiest learning condition and not for the more difficult 80% condition. One explanation for this finding is based on the so-called low fear hypothesis of psychopathy [118]. The low-fear hypothesis assumes that psychopathic individuals are insensitive to punishment due to a low level of fear. Furthermore, some studies suggest that punishment based learning is more impaired in psychopathy than reward based learning [102]. If we assume that subjects with psychopathy are impaired in learning based on (negative) feedback, subjects with psychopathy will use substantially less trials to learn from than control subjects in the 100% condition. This then leads to a higher amount of uncertainty, which in turn leads to less accurate responding. In the 80% condition on the other hand, accuracy does not purely depend on the amount of feedback information used. In this condition accuracy increases if one reacts as if this was a 100% condition, ignoring the 20% invalid unpredictable trials. Performance thus depends on how many valid trials are processed as useful information and how much of the invalid information is ignored. It thus does not depend on the total amount of feedback information used, but on the proportion of valid versus invalid feedback that is used to learn the rule. This is not affected in psychopathy, which explains why they show the same levels of accuracy in this condition.

Impaired learning under conditions of reward and punishment in psychopathic individuals has been shown before. For example, psychopathic individuals showed impairments in passive avoidance learning [46,102] and on a differential reward/punishment task [103]. Contrary to the present results, Budhani and colleagues [61] found no acquisition problems in psychopathic individuals during the initial learning phase of a probabilistic response-reversal task. However, some important differences between the response-reversal task by Budhani et al. [61] and the present task exist that may explain the different outcomes. First of all, the current task involved more complex learning material because we included three different reinforcement contingencies, whereas Budhani et al. [61] included only two. Furthermore, the total stimulus-response associations to be learned in our study were 24. In the response reversal task of Budhani et al. [61] only six stimuli had to be associated with a response. Additionally, their task had no RT restriction, while the present study employed a

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deadline of 1000 msec. It seems plausible that these differences in complexity largely account for the divergent findings of the two studies. Moreover, the differences crucially demonstrate that possible impairments in psychopathy may only become evident in more complex situations and might be missed in less demanding tasks.

4.2 Electrophysiological findings

According to the RL-theory [71], the fERN elicited by negative feedback is used to update and learn the earliest predictor of punishment. The error signal is carried to posterior medial frontal cortex (pMFC) where it is used as a reinforcement-learning signal, guiding the adaptation of behavior. While individuals with psychopathy show intact processing of external negative feedback at an electrophysiological level, they do not seem to optimally use the error signal to form an internal template of the rules (stimulus-response mappings) at hand. In order for a rERN to occur, detection of a mismatch between expected and real outcome has to take place [119]. Prerequisite for this is an internal template of the rules to which the current behavior can be compared. As no internal template is formed a comparison between real and expected outcome cannot be made and hence learning - reflected in adaptive behavior - is compromised. The reduced rERN amplitude thus reflects higher uncertainty due to diminished learning at an electrophysiological level [120]. It has been demonstrated that performance of individuals with psychopathy in certain learning paradigms is modulated by reward but not by punishment [102]. Additionally, it has been shown that low socialized individuals (a trait closely related to psychopathy) show diminished rERNs under conditions of punishment but not reward [93]. With regard to the current task, individuals with psychopathy might have learned based on reward cues, but not on punishment cues, which leads to diminished learning performance due to the fact that only part of the trials (the rewarded but not punished) are used to adapt behavior. An earlier investigation of the rERN in individuals diagnosed with psychopathy outside a learning context [92] reported no indications for diminished amplitudes. Even though Brazil et al. [112] replicated this finding at an electrophysiological level, their behavioral data demonstrated problems in error signaling in individuals with psychopathy. This suggests that rERN amplitudes are only decreased in psychopathy when related to explicit behavioral adaptations or learning processes but not in the context of simple error detection in a neutral task.

4.3 Integration

Interestingly, the currently found learning deficits in individuals with psychopathy would not have been predicted by the IES hypothesis of psychopathy [40]. The IES interpretation proposes that an underlying amygdala deficit leads to impairments in stimulus-reinforcement associations but not in stimulus-response associations in individuals with psychopathy. However, while the amygdala plays a central role in the first process, other brain structures are involved in the latter process. Functional Magnetic Resonance Imaging (fMRI) and ERP studies using similar paradigms as the current one have demonstrated a crucial role for pMFC (including the ACC and preSMA; [121,122]) and the basal ganglia [71,123] in learning from errors. Currently, the IES interpretation of psychopathy does not include these processes and brain areas and hence does not allow for any specific predictions to be made. Therefore, we argue that for a better understanding of the learning deficits in psychopathy, neurocognitive models should additionally focus on the areas involved in the processing of internal and external error messages and the subsequent adaptation of behavior.

5. Conclusion

In sum, our results indicate that learning from negative feedback is compromised in psychopathy. These results are supported by both behavioral and electrophysiological data. Deviancies in error processing may play a crucial role in the learning deficiencies associated with psychopathy. The IES interpretation of psychopathy predicts deficits in certain forms of learning, but does not relate these deficits to the processing of errors. Furthermore, while the model includes aspects of stimulus-response learning and stimulus-reinforcement learning, aspects of internal and external error processing relevant to trial and error learning are not included. This differentiation between learning processes also fits with a more recent model of decision making proposed by Rushworth and colleagues [51], in which the OFC, ACC and the amygdala are part of a neural network involved in learning, action monitoring and social behavior. Our data suggests that extending the IES model to include error monitoring and areas involved in error monitoring, as well as more diverse forms of learning, may lead to a broader understanding of the relationship between learning and psychopathy.

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4

Neurophysiological correlates of the detection of own and others' errors in individuals with psychopathy

Abstract

Psychopathy is a severe personality disorder often leading to violent and disruptive antisocial behavior. Efficient and proper social behavior crucially relies on monitoring of own as well as others' actions, but the link between antisocial behavior in psychopathy and action monitoring in a social context has never been investigated. Event-related potentials (ERPs) were used to disentangle monitoring of one's own and others' correct and incorrect actions in psychopathic subjects (N=18) and matched healthy controls (N=18). The error-related negativity (ERN) was investigated following own and others' responses in a social flanker task. While both groups showed similar ERPs in response to own actions, amplitudes after the observation of others' action-outcome were greatly reduced in psychopathy. More specifically, the latter was not unique to observed errors as the psychopathic group also showed reduced brain potentials after the observation of correct responses. In contrast, earlier processing of observed actions in the motor system, as indicated by the lateralized readiness potential (LRP), was unimpaired. Monitoring of own behavior is not affected in psychopathy, while processing of the outcome of others' actions is disturbed. Specifically, although psychopathic individuals do not have a problem with initial processing of the actions of others, they have problems with deeper analyses of the consequences of the observed action, possibility related to the reward-value of the action. These results suggest that aspects of action monitoring in psychopathy are disturbed in social contexts and possibly play a central role in the acquisition of abnormal social behavior.

1. Introduction

Psychopathy is a personality disorder characterized by distortions in emotional processing and antisocial behavior [4]. Psychopathic individuals are known to show an almost total lack of empathy, guilt or remorse combined with antisocial behavior fuelled by impulsivity, poor planning skills and frequently criminal intents. In clinical practice, psychopathy is often labeled as highly resistant to treatment. The antisocial lifestyle of psychopathic offenders clearly indicates that they have experienced severe problems in acquiring social norms and rules [3]. One way of acquiring social norms and rules and appropriate behavior is by observing others. More specifically, we learn by monitoring other individuals' performance and imitating behavior leading to desired outcomes, while avoiding other's behavior ending in undesired outcomes [124]. This implies that we need to be susceptible to errors committed by others in order to learn appropriately.

Research on performance monitoring has predominantly focused on processing of one's own errors. The detection of error commission by oneself is associated with the generation of the error-related negativity (rERN)[63,72,121], an event-related brain potential (ERP) in posterior medial frontal cortex (pMFC) [74]. This component has been linked to the processing of the reward-value of the action and subsequent behavioral adjustments [71,78]. Previous results on monitoring of own actions in psychopathy are mixed, although there appears to be dissociation between studies using students with psychopathic traits [93,111] and actual psychopathic offenders [81,112]. While the former studies reported reduced ERNs in tasks consisting of affectively neutral stimuli, these deficiencies were not demonstrated in diagnosed psychopathy.

More recently, investigations on ERPs during action monitoring in social contexts have been initiated, focusing on two aspects of processing others' actions. First, components related to initial processing of the action. Studies on motor resonance have shown that the observation of movements activates brain systems in the motor cortices similar to those activated by the self-generation of the same actions [125–127]. Motor activation can be measured with the lateralized readiness potential (LRP), a marker for automatic motor preparation, visible prior to the execution of a movement over the contralateral hemisphere. During observation, the development of the LRP seems to be susceptible to the correctness of the observed response. LRPs for both correct and incorrect responses start to develop in the same direction before the onset of the observed response ('anticipation') and continue to increase in amplitude after the observation of a correct response, but will decrease if the observed response was incorrect [128]. Thus, motor resonance during action observation extends further than only making copies of observed movements by showing differential activation susceptible to response correctness, a function that might play an important role in observational learning [129].

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The second component identified during observation of others' actions is a later ERN-like component, which is generated when participants observe other individuals commit errors, the so-called 'observed ERN' (oERN)[109,128,130]. The source of the oERN has been localized in the same medial frontal areas as the traditional ERN, suggesting that both waveforms are a reflection of the same underlying mechanism [128]. This was confirmed by fMRI data showing that both the detection of own and others' errors activate the same networks [131,132].

The aim of the present study is to investigate error monitoring during the observation of actions in psychopathy. We hypothesized that deeper processing of others' erroneous outcomes is compromised in psychopathy, made evident by reduced oERN amplitudes in the psychopathic group. In contrast and in line with earlier research, we expected normal ERNs to own errors, reflecting unaffected monitoring of own actions [112]. Additionally, we investigated the onset and course of the LRP as a marker for differential involuntary motor activation during the commission and observation of correct and erroneous responses.

2. Methods and Materials

2.1 Subjects
The psychopathic group was recruited from the in- and out-patient population of the Pompestichting Forensic Psychiatric Institute in the Netherlands, a treatment facility for mentally disordered offenders. Stay in the clinic is designed to resemble everyday life outside of detention, requiring patients to follow treatment, schooling, work, practice sports, etc.

Patients were selected based on available information about clinical status and prior history. An estimation of each participant's IQ level was obtained with the Dutch version of the National Adult Reading Test (NLV)[133](see Table 1). The patient group consisted of 18 male violent offenders diagnosed with psychopathy, as assessed with the PCL-R [6]. According to European standards, patients scoring above the cut-off score (PCL ≥ 26) were considered suitable for inclusion in the psychopathic group (see also [112,134]).

The control group consisted of 18 healthy male volunteers without criminal records and no history of psychiatric disorders recruited by use of advertisements. They were matched with the patients on age and IQ. The Dutch version of MINI Psychiatric Interview [82] and the SCID-II [83] were used in both groups in order to determine compliance to the inclusion criteria. Exclusion criteria included all major Axis-I and Axis-II disorders, somatic disorders, any form of (self-)reported or documented head trauma, chronic use of intoxicating substances, use of psychotropic medication up to

Table 1 Demographics of the control and the psychopathic group. Means are reported with SDs between brackets.

	Control group (*n*=18)	Psychopathic group (*n*=18)
Age	36 (8)	39 (8)
IQ	101 (6)	98 (9)
PCL-R	-	31 (3)

No significant group differences.

5 days before the test session, pre-test use of alcohol or tobacco, and for the patient group, a positive result on any of the unannounced randomly administered urinal drug tests. All assessments were conducted by trained psychologists based on interviews with the participants and on available information from each patient's clinical files.

The protocol was approved by the local medical ethics committee. All participants received written information about the experiment, gave written informed consent and received a financial reward.

2.2 Task and procedure
All clinical assessments were conducted during a screening session. In a second session, behavioral and electroencephalography data were collected during the execution of a modified version of the arrowhead Eriksen flanker task [87,128]. Participants were seated across the table facing the experimenter. A LED device was situated at the center of the table with a custom-made joystick device in front of it at a distance of approximately 25 cm on both the right and the left side of the LED device. The LED device had two display sides, one facing the participant, the other toward the actor at a viewing distance of approximately 75 cm. Stimuli consisted of arrowheads pointing to the left or to the right in four arrays (<<<<<, >>>>>, << ><<, >>< >>) occurring randomly with equal probabilities.

The experiment was divided in two conditions. In the first condition (Perform condition), participants were instructed to respond as quickly and accurately as possible by using their thumb to push the lever on the joystick in the same direction indicated by the arrowhead in the center of the array displayed.

In the second condition (Observe condition), participants received instructions to observe the actor (experimenter) while he performed the same flanker task and to count and report the amount of errors committed by the actor after each block. The counting provided an accuracy measure for the engagement of the observer in the task. Only the center arrowhead was displayed to the observers, making sure that error detection was not compromised by the presence of flankers. Observers were

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able to see both the LED device and the actor's responses without moving their eyes and were instructed to stay focused on the fixation point and to identify responses without making eye movements [128]. All subjects participated in the Perform condition first, establishing their understanding of the task before participating in the Observe condition [128,131,132].

The experimental conditions started with a practice block of 40 trials. Each condition consisted of 6 blocks of 100 trials. A trial started with the presentation of a fixation point presented at the center of the LED device for 200 msec, followed by a stimulus-free interval of 200 msec. In succession, one of the four stimulus arrays was displayed for 300 msec followed by a response window of 900 msec. An error-check was added to the task in order to make sure participants committed enough errors. After 15 consecutive correct trials an array of hash marks (#####) was presented, indicating that the performer had to increase his response speed. In the observe condition, subjects were instructed to write down the amount of errors they had observed at the end of each block.

2.3 Data acquisition
Scalp potentials were collected using 27 active electrodes (ActiCap, Brain Products, Munich, Germany) arranged according to an extended version of the 10-20 system. All electrodes were referenced to the left ear during recording and were re-referenced to the linked earlobes during analysis. Electrooculography recordings were also collected for vertical and horizontal eye movements by placing electrodes above and below the left eye and at the outer canthi. The recorded signals were digitized with a sampling rate of 500 Hz using a QuickAmp amplifier (Brain Products, Munich, Germany) and filtered offline using a 0.02-20 Hz band-pass filter for analyses of all ERPs. No filtering was applied during acquisition.

Reaction times (RTs) below 150 msec (1.6%) and slower than 3 standard deviations from the mean (558 msec; 0.8%) were removed from the data for both groups. Ocular artifacts were removed using Independent Component Analysis [88].

2.4 ERN
A matching procedure was used to diminish the impact of stimulus-related activity on the ERN and the LRP [119,128]. Through this procedure, each incorrect trial was randomly matched to a corresponding correct trial based on RT (±4 msec), for each participant in both conditions.

EEG signals for correct and incorrect trials in both conditions were time-locked to response onset (700 msec epoch) and were averaged separately for each participant for correct and incorrect responses relative to a 200 msec pre-response baseline. The rERN was defined as the most negative peak between the 50-150 msec period following response onset. For the oERN, the most negative peak between 150-350

msec time-locked to the response of the actor was determined. These analyses were conducted at FCz and Cz, where ERN amplitudes were at a maximum.

2.5 LRP
LRPs were calculated using signals recorded from C3 and C4 electrodes. The average asymmetry, defined as the difference between C3 and C4, was derived by averaging the asymmetries associated with trials where the left movements were correct and those where right movements were correct according to the following equation [135]:

$$LRP = [\text{left hand}(C4-C3) + \text{right hand}(C3-C4)]/2$$

Negative values of the LRP indicate relative activation of the correct response and positive values indicate relative activation of the incorrect response. As for the ERN, this analysis was performed on trials matched for RTs.

Peak LRP amplitudes were determined in a window around the response (-150-50 for the Perform condition; 50-400 msec for the Observed condition). To determine when the LRPs first significantly differed between correct and incorrect responses, the difference between correct and incorrect trial waveforms was assessed by a stepwise series of one-tailed serial t-tests (step size of 2 msec; cf. [136]). For each test, data were averaged from a time window of 40 msec. The latency of the significant difference between the two waveforms was defined as the first point at which 10 consecutive t-tests shows a significant difference at $p < 0.05$. This procedure was applied in a time window around the response (-350-300 msec for the Perform condition; 50-470 msec for the Observe condition).

2.6 Additional analyses
Stimulus-locked P3 amplitudes were computed on unmatched correct incongruent trials in the Observe condition to check for abnormal stimulus processing and attention. The P3 was defined as the most positive peak between 400-800 msec at Cz, where this component was maximal.

Also, correlations between the oERN, the PCL-R scores and its subscales were investigated for the psychopathic group.

2.7 General Linear Models
Behavioral data were analyzed by entering individual averages of RTs and error rates from the Perform condition into different repeated measures GLMs with Correctness (correct, incorrect), Congruency (congruent, incongruent), and Post-correctness (post-correct, post-error) as possible within-subject (WS) variables and Group (patients, controls) as between-subject (BS) factor. For the Observe condition, accuracy rates were determined by calculating the ratio between the amount of errors reported by the participants and the actual amount of errors committed by the actor. Also, the amount of errors committed by the actor in the Observe condition

and the percentage of observed errors reported by the subjects were entered in the Univariate GLMs with Group as a BS-factor.

The rERN was analyzed for the Perform condition and the oERN was examined for the Observe condition using separate 2×2×2 repeated measures GLMs with Electrode site (FCz, Cz) and Correctness as WS-factors and Group as BS-factor. The LRP amplitudes and latencies were analyzed separately by entering Condition (perform, observe), Correctness and Group as possible factors. For the additional P3 analyses, Group was entered as BS-factor in a Univariate GLM.

3. Results

3.1 Behavioral analyses

RT analyses yielded significant results for Correctness [$F_{(1,34)}$ = 274, p < 0.001], with incorrect responses being faster than correct ones (Table 2). There was no main effect for Group [$F_{(1, 34)}$ < 1, p = 0.402] and no significant interaction of Group × Correctness [$F_{(1, 34)}$ < 1,p = 0.973].

A main effect was found for Congruency [$F_{(1,34)}$ = 112, p < 0.001], indicating that subjects were faster on congruent trials compared to incongruent ones. There was no main effect for Group [$F_{(1, 34)}$ < 1, p = 0.420], but a significant Group × Congruency interaction showed that the congruency effect was larger for the psychopathic group (24 msec) compared to the control group [16 msec; $F_{(1, 34)}$ = 4.78, p = 0.036].

There was also a main effect for Post-correctness [$F_{(1, 34)}$ = 4.98, p =0.032]. Participants responded slower on post-error trials compared to post-correct trials. The groups did not differ on this measure [$F_{(1,34)}$ < 1, p = 0.522] and the interaction also failed to reach significance [$F_{(1,34)}$ = 1.91, p = 0.176].

For error rates, a main effect for Congruency was found [$F_{(1,34)}$ = 66.7, p < 0.001], indicating that more errors were committed on incongruent trials compared to congruent trials (Table 3). The Congruency × Group interaction did not reach significance [$F_{(1,34)}$ = 1.74, p = 0.197] nor did the main effect for Group [$F_{(1,34)}$ < 1, p = 0.852]. Analyses of the amount of errors committed by the actor in the Observe condition revealed that both groups had the opportunity to observe a comparable amount of errors [119 vs. 118; $F_{(1,34)}$ < 1, p = 0.907] and that the groups did not differ significantly on the percentage of observed errors reported [89.4% vs. 93.5%; $F_{(1,34)}$ < 1, p = 0.373].

3.2 ERP analyses

A main effect for Correctness was found for the rERN [$F_{(1,34)}$ = 65.5, p <0.001, Figure 1]. Neither the main effect for Group was significant [$F_{(1,34)}$ < 1, p = 0.593], nor the interaction [$F_{(1,34)}$ < 1, p = 0.788]. The main effect for Electrode was significant

Table 2 Mean RTs (ms) for the control and the psychopathic group (SD between brackets).

Measure	Trial Type	Control group (n=18)	Psychopathic group (n=18)	Overall mean
Correctness	Correct	345 (41)	355 (35)	351 (38)
	Incorrect	295 (26)	304 (35)	300 (31)
Congruency	Congruent	327 (37)	333 (33)	330 (35)
	Incongruent	343 (42)	357 (40)	350 (41)
Post-correct-ness	Post-error	350 (44)	356 (36)	353 (40)
	Post-correct	343 (42)	354 (36)	349 (39)

No significant group differences.

Table 3 Mean percentage error rates in the Perform condition for the control and the psychopathic group (SD between brackets).

Measure	Control group (n=18)	Psychopathic group (n=18)	Overall mean
Congruent	7.8 (5.5)	6.1 (6.0)	6.9 (5.7)
Incongruent	15.0 (5.1)	16.1 (5.0)	15.6 (5.0)

No significant group differences.

[$F_{(1,34)}$ = 39.8, p < 0.001], with larger negativity at FCz (0.2 µV) compared to Cz (1.7 µV). The groups showed comparable latencies for the rERN at FCz [64 msec; $F_{(1,34)}$ = 4.25, p = 0.519].

Results for the oERN (Figures 2 and 3) revealed a main effect for Correctness [$F_{(1,34)}$ = 4.84, p = 0.035] but not for Electrode [$F_{(1,34)}$ = 1.21, p = 0.277]. The maximum oERN amplitudes was at Cz (-1.38 µV). Although there was a main effect for Group [$F_{(1,34)}$ = 6.60, p = 0.015], the Group × Correctness interaction failed to reach significance [$F_{(1,34)}$ < 1, p = 0.936].[3] The latency of the oERN did not differ between the control and the psychopathic group [227 msec; $F_{(1,34)}$ < 1, p = 0.548].

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3   An alternative analysis suggested by one of the reviewers also included Condition as a WS-factor. As expected, a main effect for Condition was found [$F_{(1,34)}$ = 23.1, p < 0.001] and an interaction for Group × Condition [$F_{(1,34)}$ = 4.68, p = 0.038]. Further examination revealed reduced overall amplitudes in the Observe condition for the psychopathic group [$F_{(1,34)}$ = 6.60, p = 0.015]. Importantly, the 3-way interaction of Group × Condition × Correctness was not significant [$F_{(1,34)}$ < 1, p = 0.782], thus confirming the findings obtained in our initial analyses.

Figure 1 Grand average response-locked waveforms for correct and incorrect responses in the Perform condition for the control (n=18) and the psychopathic (n=18) group. Abbreviations; rERN, response error-related negativity.
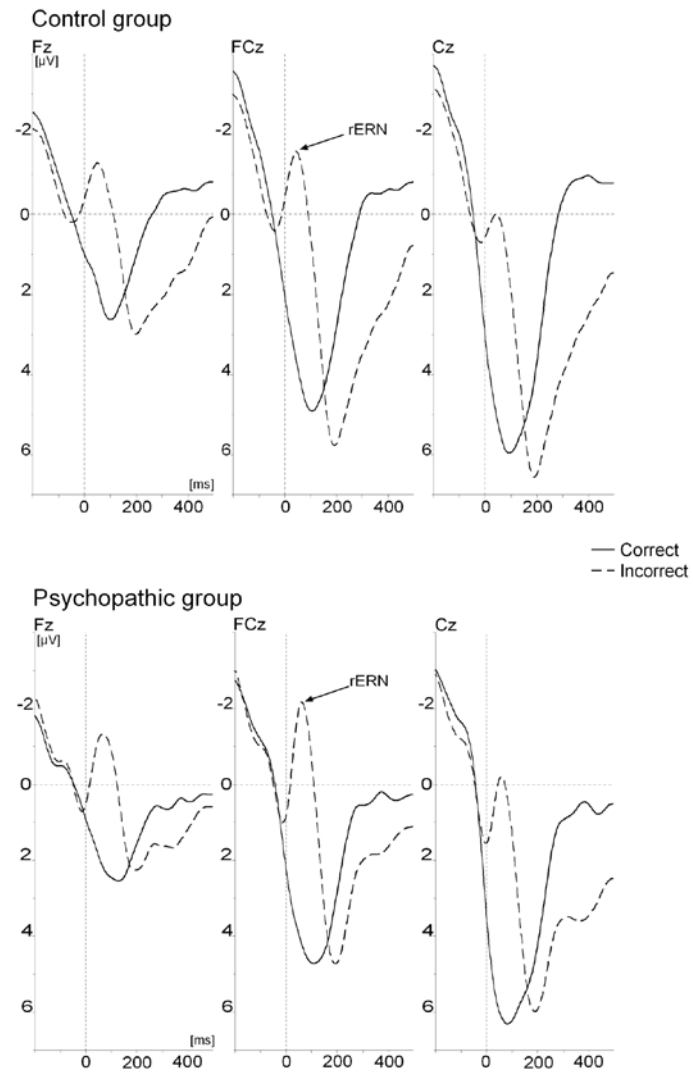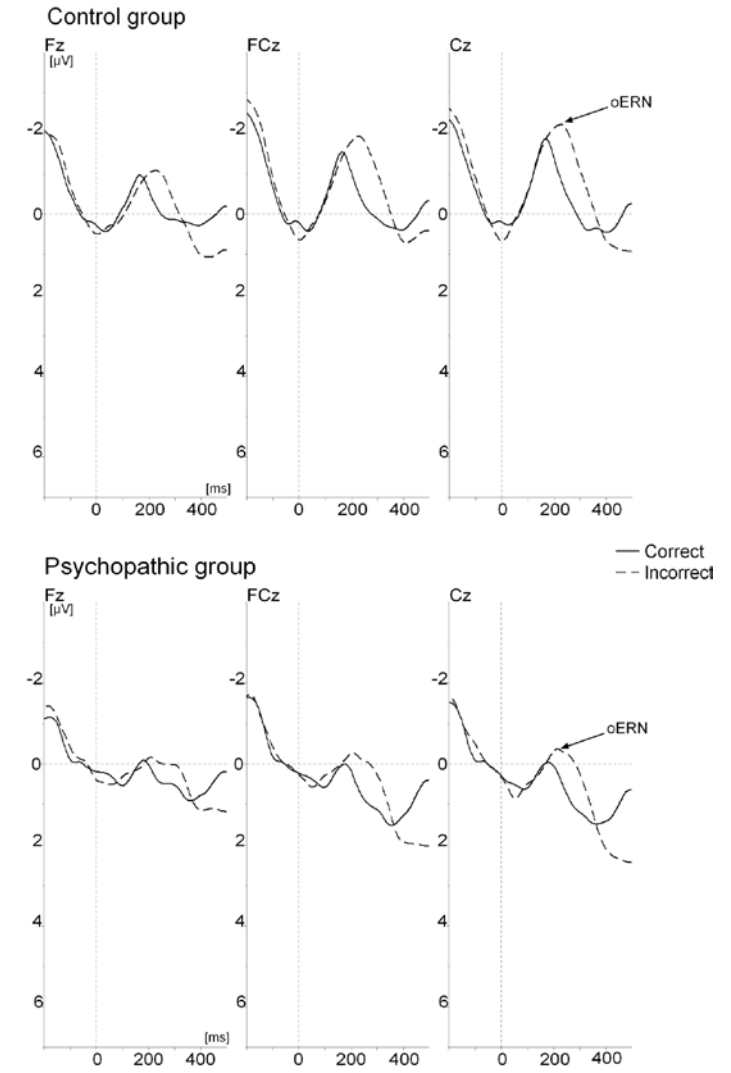

Figure 2 Grand average response-locked waveforms for correct and incorrect responses in the Observe condition for the control (n=18) and the psychopathic (n=18) group. Abbreviations; oERN, observed error-related negativity.
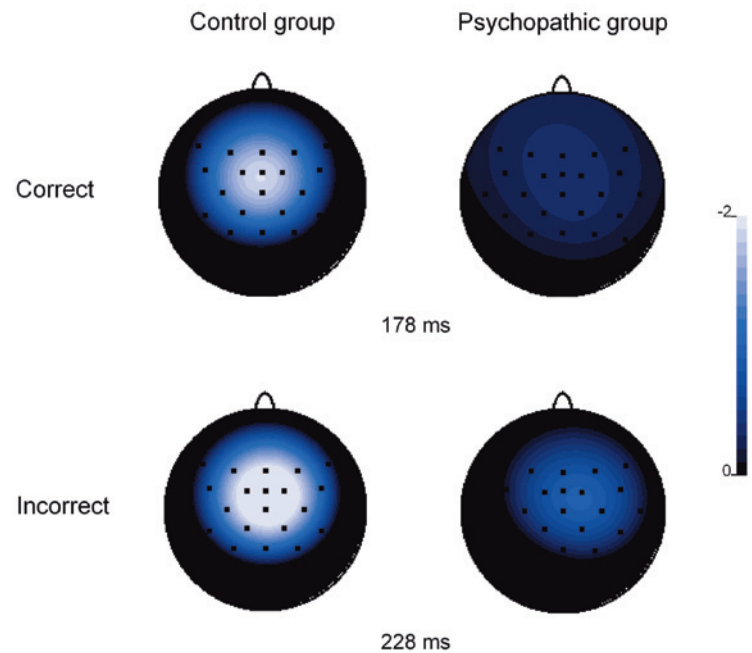
Figure 3 Scalp topographies of the peak amplitudes of the correct and incorrect waveforms for each group (n=18) in the Observe condition. Light colored shades indicate negative polarities and darker shades depict more positive polarities.

3.3 LRP
Figure 4 depicts the LRPs from both groups in the Perform condition. As expected, LRPs just peaked before the response showing opposite sign amplitudes for correct and incorrect responses [126,136]. An ANOVA on peak LRP amplitudes showed that the difference between correct (8.5 µV) and incorrect (-7.1 µV) waveforms was significant [$F(1,34) = 181$, $p < 0.001$], but did not differ between groups (main effect of Group [$F(1,34) = 2.06$, $p = 0.16$]; Group × Correctness interaction [$F(1,34) < 1$, $p = 0.403$]).

LRPs from both groups in the Observe condition peaked at or just after the response of the actor was recorded by the response device (Figure 5). As in the Perform condition, there was a significant difference between correct (3.2 µV) and incorrect (-1.9 µV) LRP peak amplitudes, as shown by a main effect of Correctness [$F(1,34) = 71.9$, $p < 0.001$]. Again, these effects were similar for both groups (main effect of Group [$F(1,34) = 1.04$, $p = 0.314$], Group × Correctness interaction [$F(1,34) < 1$, $p = 0.381$]).
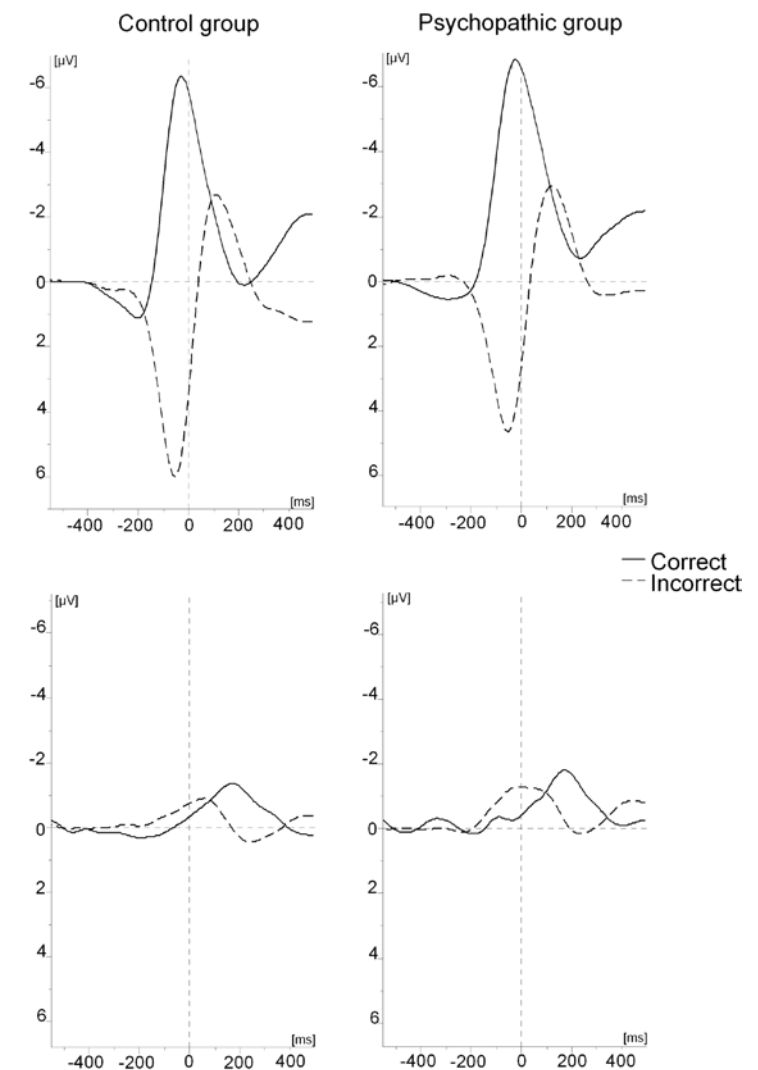
Figure 4 Grand average response-locked LRPs for correct and incorrect responses in the Perform condition (top row) and the Observe condition (bottom row) for the control (n=18) and the psychopathic (n=18) group.

Correct and incorrect LRPs differed significantly from one another at -152 ms (relative to the response) in the controls and at -120 msec in the patients in the Perform condition. During observation, correct and incorrect LRPs first differed

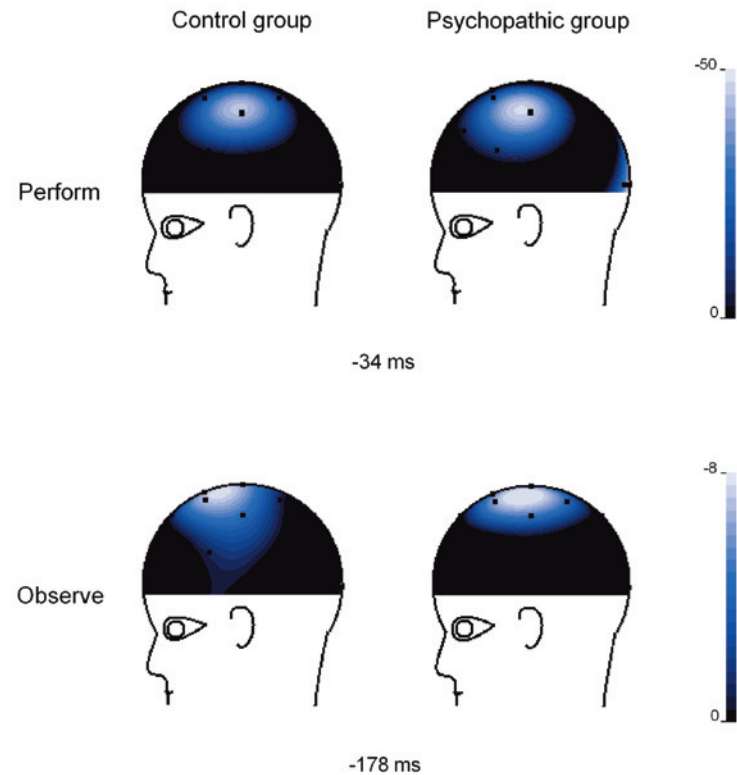**Figure 5** Current source density maps of the peak amplitudes of the correct and incorrect LRPs in the Perform condition (top row) and the Observe condition (bottom row) for the control (n=18) and the psychopathic (n=18) group. Light colored shades indicate negative polarities and darker shades depict more positive polarities.

significantly from one another 182 ms and 174 msec after the response was registered in controls and patients respectively. A WS ANOVA on the LRP peak latencies with factors Condition, Correctness and Group showed main effects of Condition [F(1,34) = 641, *p* < 0.001], Correctness [F(1,34) = 10.9, *p* = 0.002] and a Condition × Correctness interaction [F(1,34) = 29.8, *p* < 0.001], reflecting (a) that LRPs peaked before the response in the Perform condition, but only after the response was observed in the Observe condition and (b) that the LRP peak latency was modulated by correctness in the Observe condition only. These effects are indicative of the fact that LRPs in the Observe condition are due to the observation of the action, rather than covert task performance.

3.4 Additional analyses

The stimulus-locked P3 peak amplitudes did not differ between the two groups [F(1,34) < 1, *p* = 0.423]. No correlations were found between the PCL-R scores and oERN amplitudes at Cz, nor between the factor scores and the oERN (all *p*s > 0.35).

4. Discussion

The main goal of the present study was to dissociate monitoring of own and others' actions in psychopathic individuals. Our results show that while there were no deficits in rERN in psychopathy, monitoring the outcome of another individual's responses is compromised in this disorder, as indicated by reduced ERPs after the observation of both correct and incorrect outcomes.

While the rERN can be regarded as the result of a cognitive mechanism relying completely on internal processes, the oERN is a reflection of a mechanism additionally reliant on external processes. Monitoring the outcome of others' actions during social interaction requires the integration of information from different modalities and external sources into an own internal representation of the action. Although latter aspect of action monitoring during observation is deficient in psychopathy, both automatic motor preparation, as indexed by the observed LRP, and stimulus processing, as indexed by the P3, are unaffected. Together these results provide robust neurophysiological corroboration of previous suggestions that psychopathy is associated with disorders in the processing of social information [3,137].

Behaviorally, action execution was unimpaired in psychopathic patients. Both groups showed the expected congruency effects, comparable accuracy levels and post-error slowing. Post-error slowing is a cautionary response strategy, in which participants slow down their responses on trials following incorrect trials [79]. In contrast to previous studies [81,112], psychopathic subjects did not show slower RTs. The presence of the observer during task execution might have led to faster RTs in the psychopathic group, as predicted by the drive theory of social facilitation [138].

In line with prior reports, rERNs were of similar amplitudes in both groups, showing unimpaired monitoring of one's own actions in psychopathy [112]. Results obtained during the observation of the actions of others are more complicated. Initial automatic processing of others' actions in terms of the identity of the response (left or right joystick movement) was unimpaired in patients, as indicated by a normal pattern of oLRPs reflecting correct processing of the kinematic properties of the observed actions. The oLRPs on incorrect trials initially developed in the same direction as for correct responses, but showed deactivation after observation of the incorrect responses. The deactivation points out that participants did not commit the errors themselves covertly. Thus, automatic processing of the observed action is similar to healthy controls.

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In contrast, deeper processing of the consequences of the action, as indexed by the oERN, shows a different pattern in patients as compared to controls. Psychopathic patients showed diminished oERNs after observing errors. Surprisingly, brain potentials were also reduced after observation of correct responses. In other words, the psychopathic group showed an overall reduced neural response for the outcome of observed actions, but still differentiated between observed correct and incorrect responses. These findings suggest a broader deficiency in processing the consequence of others' actions, rather than abnormal processing of observed errors only.

The ERN has been linked to reward-based learning mechanisms [71], but monitoring of correct behavior is also crucial in order to optimize gains. Recent insights point out that an organism's learning and adaptation rate is driven by the value of the information that becomes available with the outcome of each action [139,140]. Thus, both incorrect and correct responses can be regarded as useful cues for behavioral adaptation through their informative value. The reduced neural activity after the observation of both correct and incorrect outcomes in psychopathy is a clear indicative that performance monitoring is disturbed in social contexts and we believe this might play an important role in the abnormal acquisition of social behavior. More specifically, our results suggest that psychopathic individuals are less able to process observed cues in social settings, leading to reduced availability of usable information about outcomes. Consequently, the association of the outcome of a specific observed action to the action itself could be compromised. Thus, deficient processing of this type of social cues (human action) might be the first stage where 'things go wrong' during action observation in psychopathy, probably also altering subsequent stages of behavioral adaptation and social learning.

An alternative interpretation is that psychopathic individuals would simply care less about others' actions, especially in a neutral context in which the observed actions had no direct consequences for themselves. However, we do not believe that a lack of motivation was the driving force behind our results. If the psychopathic subjects were less motivated, they would be expected to miss more errors in the observe condition and subsequently report significantly less errors compared to controls. This was not the case, as evident by comparable accuracy between the groups in the amount of observed errors reported. Additionally, the analyses of the stimulus-locked P3 amplitudes in the observe condition did not show any significant group differences, indicating that the psychopathic group paid attention and processed the stimuli equally well and that our results cannot be attributed to a more general stimulus-processing deficiency. Nonetheless, it would be interesting to address this issue more in future research by, for example, introducing an evaluation of the observed action on a trial-to-trial basis, or by introducing dependency between the observer and the actor. The first will not only enable an objective measure of accuracy in the observation condition. It will also allow for investigating whether any

observed error-related processes are reflected in the ERPs following the observation of correct actions and also the functional significance of the reduced amplitude of the negativity during observation of correct responses in patients. Dependency can be achieved by making the outcome of the response have relevant consequences for the observer, such as monetary loss or reward in a cooperative or competitive context. These manipulations would allow for more objective measures of attention and motivation in future studies.

A limitation of the present study is that it did not include any measures of learning, therefore the actual relationship between the reduced signals and using them to learn and adapt behavior through observation is not made evident by our results. There has been only one study on the electrophysiological correlates of external feedback cues and learning in psychopathy [141]. The results showed that although psychopathic participants elicited normal electrophysiological responses to external feedback, they were less able to learn by using negative feedback optimally in a computerized reinforcement learning task. Thus, in such settings, using negative signals to adapt behavior seems compromised. While the latter study was focused on processing of non-social external error cues, our findings suggest that in social settings, which are also more complex by nature, both negative and positive external cues are processed deficiently in psychopathy.

5. Conclusion

In conclusion, the current study demonstrates that psychopathic individuals show unaffected monitoring of own performance, but specifically show altered processing of other's action-outcomes. The impact of the latter is more likely to be reflected in behavior during daily social situations, which are obviously richer in nature and more complex than the task currently used. This alteration may play an important role in the acquisition of disturbed social behavior in psychopathic offenders. As previous studies have demonstrated that healthy individuals learn from both positive and negative feedback [140] and that pMFC plays a crucial role in these learning processes [142], the current study may provide support for disturbed observational learning in social contexts in psychopathic individuals. Obviously, future studies should address this question more directly to investigate how specific these disturbances are in psychopathy. Finally, the results show a potential new direction for future investigations of performance monitoring in clinical populations, particularly in psychiatric disorders characterized by severe social deficits, like autism and schizophrenia.

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PART **II**

5

Reversal deficits in psychopathy in explicit but not implicit learning conditions

Abstract

Psychopathy is a severe personality disorder that has been linked to impaired behavioral adaptation during reinforcement learning. Also, recent electrophysiological studies relate psychopathy to impairments in intentionally using information relevant for adapting behavior, while these impairments remain absent for behavior relying on automatic use of information. The aim of the present study was to investigate whether previously found impairments in response reversal in psychopathy also follow this dichotomy. Response reversal was expected to be intact when the automatic use of information was facilitated. In contrast, impaired response reversal was expected when intentional use of information was required. Offenders with psychopathy and matched healthy control individuals were included in two experiments with a probabilistic cued go/no-go reaction time task. The task implicated the learning and reversal of two predictive contingencies. In Experiment 1, participants were not informed about the inclusion of a learning component, thus making cue-dependent learning automatic/incidental. In Experiment 2, the instructions required participants to actively monitor and learn predictive relationships, giving learning a controlled/intentional nature. While there were no significant group differences in acquisition learning in either experiment, the results revealed impaired response reversal in psychopathy when controlled learning was facilitated. Interestingly, this impairment was absent when automatic learning was predominant. Response reversal deficits in psychopathy are modulated by the context provided by the instructions, according to the distinction between automatic and controlled processing in psychopathy.

1. Introduction

Our ability to learn associations between events with rewarding or punishing outcomes plays an important role in guiding our behavior [140]. Of equal importance is our capacity to successfully alter established associations in order to maximize performance when the environment requires us to change our behavior. When an event that previously led to reward (event A) currently leads to punishment and a previously punished event (event B) now yields a reward, the optimal behavior would be to reverse the initial response tendencies by starting to respond to event B instead of event A. This principle is a driving force behind a form of behavioral adaptation known as response reversal. Response reversal can be defined as a change of behavior following a reversal of the previously established relationships between events and their reinforcing value [106]. Response reversal contributes to flexibility in behavior, both under social and non-social circumstances [143]. The amygdala and orbitofrontal cortex (OFC) have been shown to play a crucial role in response reversal [143,144]. The amygdala has been linked to the establishment of stimulus-outcome associations [52], while the OFC has been implicated in behavioral adaptation based on contingency changes [144].

Patients with lesions of the OFC have been found to show intact acquisition of associative relationships during initial learning (hereafter termed 'acquisition'), but disturbed response reversal [52]. Interestingly, disturbed response reversal has also been demonstrated in individuals with psychopathy [59,61]. Psychopathy is regarded as a severe personality disorder typified by emotional abnormalities in combination with severe antisociality [4]. There is growing evidence that cognitive deficiencies observed in psychopathy include abnormalities in emotional processing [31,96], modulation of attention [45,145], aspects of action monitoring [81,112,146], and importantly, associative learning [46,59,61,102,141]. Behavioral results on associative learning in psychopathy show deficiencies in tracking stimulus-outcome contingencies and in subsequently altering behavior in the face of changes in these contingencies [59,61]. In the study by Budhani et al. [61], individuals with psychopathy showed normal acquisition, but impaired response reversal in a task in which stimulus-outcome contingencies varied according to predetermined probabilities of gaining reward/punishment (i.e. probabilistic reinforcement learning). These results are in line with the predictions made by the Integrated Emotion Systems hypothesis of psychopathy [33]. This account was developed from a neurobiological perspective and proposes that cognitive, affective and behavioral abnormalities in psychopathy are due to deficiencies in a cortical network involving the amygdala and OFC. The model predicts that individuals with psychopathy should not display impaired acquisition of initial stimulus-response associations, as acquisition is not reliant on intact OFC and amygdala functioning. However, these individuals should show deficient response reversal, during which the

integrity of OFC and amygdala functioning is crucial for modifying previously established stimulus-response relationships based on information conveyed by the outcomes [61].

However, there are also contradicting indications that learning deficiencies can also become evident during initial acquisition learning. Von Borries et al. [141] studied probabilistic reinforcement learning in psychopathy using event-related potentials (ERPs) and behavioral measures in a different paradigm. Participants were explicitly instructed to monitor and learn probabilistic associations through trial and error. This study did not include a reversal phase and revealed that individuals with psychopathy can also exhibit deficiencies during acquisition. Moreover, the electrophysiological results indicated that participants with psychopathy showed a specific deficiency in using information provided through negative feedback to learn and adapt their behavior. This is consistent with other results suggesting impairments in the intentional use of available information to adapt behavior in psychopathy. Brazil et al. [112] showed that both behavioral and electrophysiological correlates of automatic (unconscious) processing of errors are intact in psychopathy, while later stages involved in controlled (conscious) processing of errors and behavioral adaptation are compromised.

Combined, the previous findings from our lab [112,141] suggest that in psychopathy automatic adaptation of behavior is unaffected, but impairments are present when adaptation is reliant on intentional use of available information. From this perspective it can be hypothesized that response reversal is compromised in psychopathy specifically when instructions provide a context promoting controlled behavioral adaptation. This prediction is additionally supported by the observation that the OFC-lesioned patients tested by Rolls et al. [147] were aware of (and could verbalize) the fact that the contingencies had changed, but were still unable to execute response reversal. Also, in the studies by von Borries et al. [141] and Budhani et al. [61] participants were aware that the goal of the task was to learn based on reinforcement. A second prediction offered by the distinction between automatic and controlled behavioral adaptation in psychopathy is that response reversal should be intact when automatic learning is predominant. It is important to note that our use of automatic learning refers to an implicit learning mechanism that does not rely on awareness of what is being learned [148], occurring incidentally. To our knowledge, there has been no previous exploration of response reversal in circumstances promoting automatic learning.

The aim of the current study was to explore the effect of learning context (automatic/incidental vs. controlled/intentional) on response reversal in psychopathy. This was achieved by manipulating task-awareness through the instructions given in two separate experiments. In Experiment 1, the instructions facilitated automatic learning during a probabilistic cued go/nogo task [149]. Participants were instructed to react as quickly as possible whenever the go stimulus appeared. Importantly, they were not made aware that the task contained predictive relationships. Reversal

learning was expected to be intact in psychopathy relative to a healthy control group under these conditions. In the second experiment, the same task was used but the instructions were altered in order to make participants aware of the predictive relationships and the ability to learn from them, thereby facilitating intentional learning. Participants were instructed to actively monitor for predictive relationships and to respond appropriately in order to receive reward. Response reversal was expected to be compromised in psychopathy under these circumstances.

2. Methods

2.1 Participants and procedure
Participants in the group with psychopathy were recruited from the in- and outpatient population of the Pompestichting Forensic Psychiatric Institute in Nijmegen, The Netherlands. This is a treatment facility for offenders who have committed offences partly due to a DSM-IV Axis-I and/or Axis-II disorder. For inpatients, life in the clinic is designed to resemble everyday life outside of detention as much as possible, requiring patients to follow treatment, engage in educational activities, work, practice sports, socialize, etc.

Suitable candidates were initially selected based on available information about clinical status and prior history. Subsequently, the Dutch version of the MINI Psychiatric Interview [82] and the SCID-II [83] were used to screen candidates that were willing to participate. Exclusion criteria included: bipolar disorder, depressive disorder, schizo-affective disorder, schizophrenia, schizophreniform disorder, delusional and other psychotic disorders, schizotypal or schizoid personality disorder, first degree relatives with DSM-IV axis I schizophrenia or schizophreniform disorder. Also, psychopathy and/or antisocial personality disorder were excluded in the healthy control groups. All assessments were conducted by trained psychologists based on interviews with the participants and on available information from each patient's clinical files. In addition, each participant's IQ was estimated using The Dutch version of the National Adult Reading Test [133,150]. Psychopathy was scored using the Hare Psychopathy Checklist-Revised (PCL-R), an instrument yielding a psychopathy score based on file information and a semi-structured interview [6]. As is customary in Europe, the cut-off score was defined as a PCL-R score ≥ 26 [8,145]. The group with psychopathy consisted of 18 participants scoring above this threshold in Experiment 1 and of 21 participants in Experiment 2. These sample sizes are comparable to those used in related studies [59,61]. Nine individuals with psychopathy participated in both experiments, which were conducted 2.5-3 years apart. In each experiment, the group with psychopathy was matched for age and IQ with a community sample of healthy male volunteers with a similar level of intelligence and without a history of psychiatric

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disorders and criminal records (see Table 1), recruited through advertisements. As the controls did not have criminal records, no PCL-R scores were assessed in this population. Eighteen[4] healthy controls participated in Experiment 1 and 21 were included in Experiment 2 (1 participant participated in both studies). None of the participants reported being color-blind and they all had normal or corrected-to-normal vision.

The experimental protocol was approved by the local ethics committee. All participants received written information about the experiment, gave written informed consent and received a financial compensation.

Table 1 Group characteristics of the group with psychopathy and the control group for each experiment. For the general characteristics, group means are reported with their corresponding standard deviations between parentheses. The frequencies of identified comorbid disorders are reported as counts.

Characteristic	Psychopathy		Controls	
	Experiment 1 (n=18)	Experiment 2 (n=21)	Experiment 1 (n=18)	Experiment 2 (n=19)
General				
Age (years)	39 (7.9)	43 (7.0)	38 (8.4)	36 (8.8)
IQ	98 (9.1)	97 (10)	102 (6.8)	102 (5.6)
PCL-R Score	31 (3.5)	31 (3.4)[a]	-	-
Range PCL-R scores	26-38	26-38	-	-
Comorbid disorders (counts)[b]				
Borderline	0	1	0	0
Antisocial disorder	12	15	0	0
Narcissism	5	5	0	0

[a] The exact PCL-R scores of 2 participants scoring above threshold were not accessible
[b] Only current disorders identified in the populations are reported.

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4   Twenty participants were initially included in the healthy control group in Experiment 1. However, 2 participants were excluded because they indicated that they did not completely understand or follow the instructions correctly.

Table 2 Information concerning substance use in each sample, indicated as the percentage of participants in the sample that reported having used a specific substance.

Characteristic	Psychopathy		Controls	
	Experiment 1 (n=18)	Experiment 2 (n=21)	Experiment 1 (n=18)	Experiment 2 (n=19)
Self-reported drug use (%)[c]				
Alcohol use[d]	0	0	0	32*
Cannabis	44	43	17	21
Cocaine	28	33	0	5
Amphetamine	22	24	0	0

[c] Differences in percentage reported drug use were examined with two-proportion z-tests. For each group, the proportions for Experiment 1 were tested against those of Experiment 2. Significant differences are flagged.
[d] Alcohol use was defined as consumption of more than 2 glasses of alcohol a day on average.

2.2 Task and design
2.2.1 Experiment 1: Automatic learning
An adapted version of a probabilistic cued go/no-go reaction time (RT) task developed by Fillmore and Rush [149] was employed. Participants were seated in front of a 100-Hz computer screen on which events were presented against a white background. A trial started with the presentation of a fixation cross in the middle of the screen for 800 ms, followed by a blank screen for 500 msec, a cue and either a go or a no-go stimulus (see Figure 1). The cue consisted of a white rectangle (65 mm x 20 mm) with black borders presented in either a horizontal (flat cue) or a vertical orientation (tall cue) and was followed by a go or a no-go stimulus. Five different stimulus onset asynchronies (SOAs: 100, 200, 300, 400, 500 msec) were used for the presentation of the cues in order to promote allocation of attention to the cues and to prevent anticipation effects for the onset of the imperative stimuli. The latter consisted of a green (go) and a blue (no-go) rectangle (65 mm x 25 mm) displayed in the center of the screen for 1000 msec following the cue signal. The orientation of the cue indicated whether a go or a no-go stimulus was more likely to appear.

Participants were instructed to press a button on a response button device as quickly as possible when a go stimulus was presented and to suppress their response when a no-go stimulus was displayed. Positive or negative feedback was provided on all go trials but only on incorrect presses on no-go trials. More specifically, the RT relative to the onset of the go stimulus was displayed after a correct button press, which functioned as positive feedback. However, when a button press was made on

a no-go trial or when the participant did not press on a go trial the word 'INCORRECT' appeared on the screen, representing negative feedback. In order to encourage fast responding, participants were told that they would receive 5 points if the RT was equal to or below 300 msec, no points if the RT was larger than 300 msec and that they would lose 5 points if 'INCORRECT' appeared on the screen. No feedback or reward was given for not responding on no-go trials.

The task consisted of two phases, an acquisition phase and a reversal phase, each consisting of 500 trials, divided into 5 blocks of equal size. The whole experiment lasted about 50 minutes. During the acquisition phase, the go stimulus was preceded by the flat cue in 80% of the trials and by the tall cue in 20% of the trials. The no-go stimulus had a reversed cue mapping: 80% tall and 20% flat. Thus, the orientation of the white cue was linked to the likelihood of a go or a no-go stimulus being presented. Each SOA, stimulus, cue and cue-stimulus combination appeared an equal number of times during each block (for more details see [149]). Participants were informed that a cue would appear to signal that a stimulus was coming and that they did not have to react to the cues. During acquisition, participants were expected to learn the probabilistic associations between the orientation of the cues and the type of stimulus that followed without explicit information about the true function of the cues. Thus, participants were not told that there was a predictive relationship between the cues and the stimuli, priming context-facilitated automatic learning of the predictive associations. After reversal occurred, the mappings between the cues and the stimuli were reversed without informing the participants. The acquisition learning effects were expected to become evident by a decrease in RTs associated with the flat cue predictive of the occurrence of the go stimulus on 80% of the trials during acquisition, while the RTs on go trials following the less predictive tall cue should increase. After reversal, the opposite pattern was expected: RTs after the flat cue that was previously predictive of the go stimulus on 80% of the trials should increase (as this cue no longer predicted the go stimulus) and RTs after the tall cue that previously signaled the no-go stimulus on 80% of the trials should now start to decrease. A short resting period was offered between blocks and participants were not informed about predictive relationships between the cues and the stimuli after the task.

2.2.2 Experiment 2: Controlled learning context
The same experiment was repeated approximately 2.5-3 years later. However, in the second version the color scheme of the stimuli was adapted and participants received different instructions. Participants were told to react if a red rectangle (go stimulus) was presented and to withhold their response if a yellow rectangle (no-go stimulus) appeared after a cue. The key difference with Experiment 1 was that the participants were explicitly instructed that there was a predictive relationship between the cues
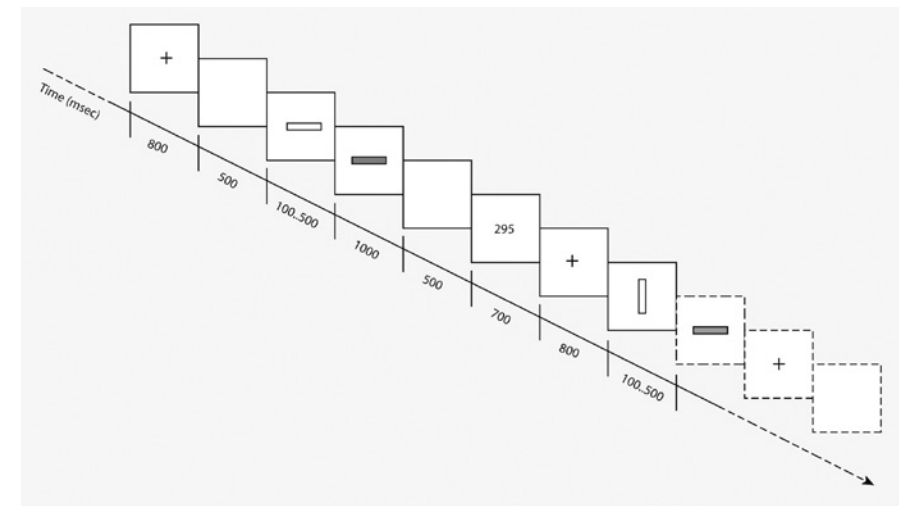

Figure 1 Depiction of the sequence of events and their timings during in the experiments.

and the rectangles. They knew in advance that each of the two cues was more often followed by either the go or the no-go stimulus, but that these predictive relationships were probabilistic. These instructions increased awareness of the cue-stimulus contingencies and also resemble those used in the studies conducted by von Borries et al. [141] and Budhani et al. [61], except that in our study participants were not explicitly informed about the fact that the predictive relationships could change during the task. This was done to prevent the task from becoming too easy, thereby reducing the risk of floor effects.

2.3 Analyses
Reaction times on correct go trials were analyzed using repeated measures General Linear Models (GLMs) for each experiment separately. Acquisition learning was expected to become evident by a cue-dependent change in RTs between the start of the task (start acquisition) and the end of acquisition learning (end acquisition), and reversal learning by a change in RTs between the end of acquisition and the end of the reversal phase (end reversal). Therefore, the GLMs included Block (start acquisition, end acquisition, end reversal) and Cue (tall, flat) as within-subjects (WS) factors and Group (psychopathy, control) as between-subjects factor. The alpha level was set at $p = 0.05$. The levels of the Block WS-factor corresponded with the average RT of the first and last 100 trials of the acquisition phase and the last 100 trials of the reversal phase, respectively. The RTs between 100 ms and 2 standard deviations (SDs) above

the mean overall RT were calculated for each subject and RTs outside this range were excluded from the analyses in order to reduce the impact of outliers [151]. Approximately 1.1% of the trials were excluded in Experiments 1 and 2, respectively. Group differences in cue-dependent learning were expected to become evident by significant Group × Block × Cue interactions [149]. This interaction would indicate that the mean RTs differ significantly between the groups as a function of the Cue factor in one or more blocks. Post-hoc analyses were conducted with Bonferroni-corrected paired-samples t-tests. Effect sizes (η2) were calculated for each of the WS- and BS- effects by dividing the corresponding sum of squares by the total sum of squares [152]. Greenhouse-Geisser corrected p-values are reported, where appropriate.

3. Results

3.1 Experiment 1: automatic learning
The left panel of Figure 2 displays the mean RTs for each of the groups, cues, and trial blocks. As can be seen, there were no large differences between groups, both showing large RT differences between cues on trial Blocks 2 and 3, but not on Block 1. Statistical analyses indeed revealed there was neither a significant main effect for Block [$F_{(2, 68)}$ = 1.40, p = 0.253, $η^2$ = 0.012], nor for Cue [$F_{(1, 34)}$ = 3.69, p = 0.063, $η^2$ = 0.023], or Group [$F_{(1, 34)}$ = 0.116, p = 0.735, $η^2$ = 0.003]. A significant Block × Cue interaction was indicative of successful learning in general [$F_{(2, 68)}$ = 34.6, p < 0.001, $η^2$ = 0.229]. This interaction reflected significantly faster responding after the more predictive cue than the less predictive cue on the final block of the acquisition and reversal phases [264 vs. 292 ms; $t_{(35)}$ = -4.89, p < 0.001] and [286 vs. 273 ms; $t_{(35)}$ = 5.03, p < 0.001], respectively, but not on the very first acquisition trial block [282 vs. 283 ms; $t_{(35)}$ = -0.436, p = 0.666]. The non-significant Block × Group [$F_{(2, 68)}$ = 0.793, p = 0.457, $η^2$ = 0.007], Cue × Group [$F_{(1, 34)}$ = 0.377, p = 0.543, $η^2$ = 0.002], and Block × Cue × Group interactions [$F_{(2, 68)}$ = 0.681, p = 0.509, $η^2$ = 0.005], indicated comparable performance between the groups.

3.2 Experiment 2: controlled learning
The right side of Figure 2 shows the groups' mean RTs for each cue and trial block. It can be seen that the major difference between groups concerns responding during the reversal phase: on Block 3, the control participants clearly displayed a difference in RTs between the two cues, whereas the psychopathic individuals did not. There was a significant effect for Cue [$F_{(1, 38)}$ = 11.1, p = 0.002, $η^2$ = 0.039], reflecting higher RTs to the tall cue. The main effect for Block [$F_{(2, 76)}$ = .565, p = 0.534, $η^2$ = 0.006] and Group [$F_{(1, 38)}$ = 3.20, p < 0.001, $η^2$ = .078] did not reach significance. A significant Block × Cue interaction was present [$F_{(2, 76)}$ = 39.2, p < 0.001, $η^2$ = 0.207], while the
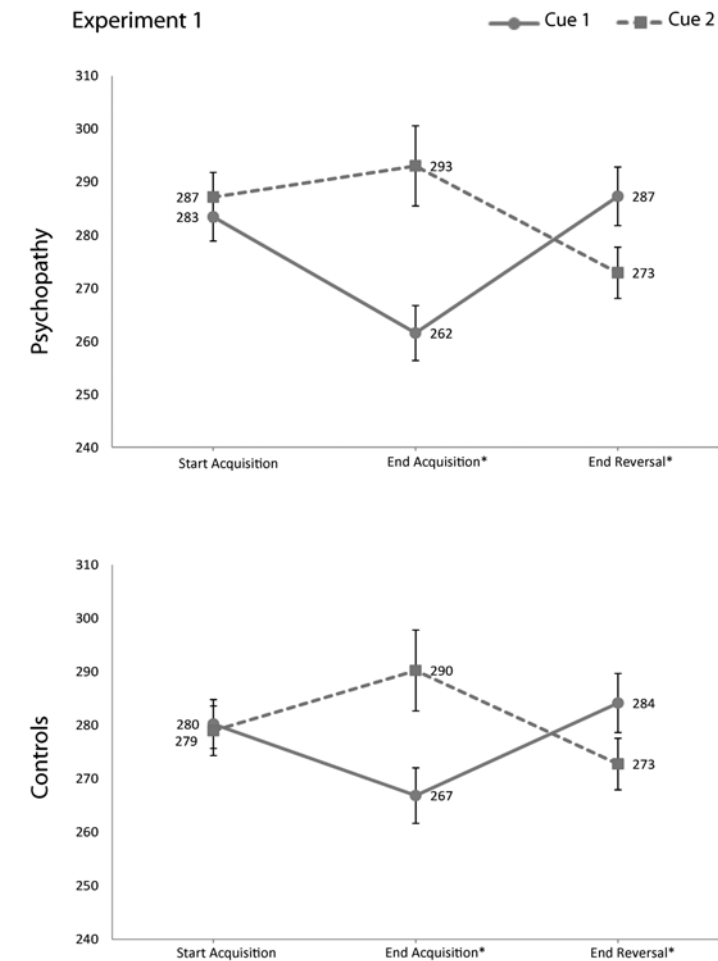

Figure 2 Performance for each group in each experiment during the start of acquisition, end of acquisition and end of reversal. Mean group reaction times are reported with the error bars indicating their corresponding standard error.
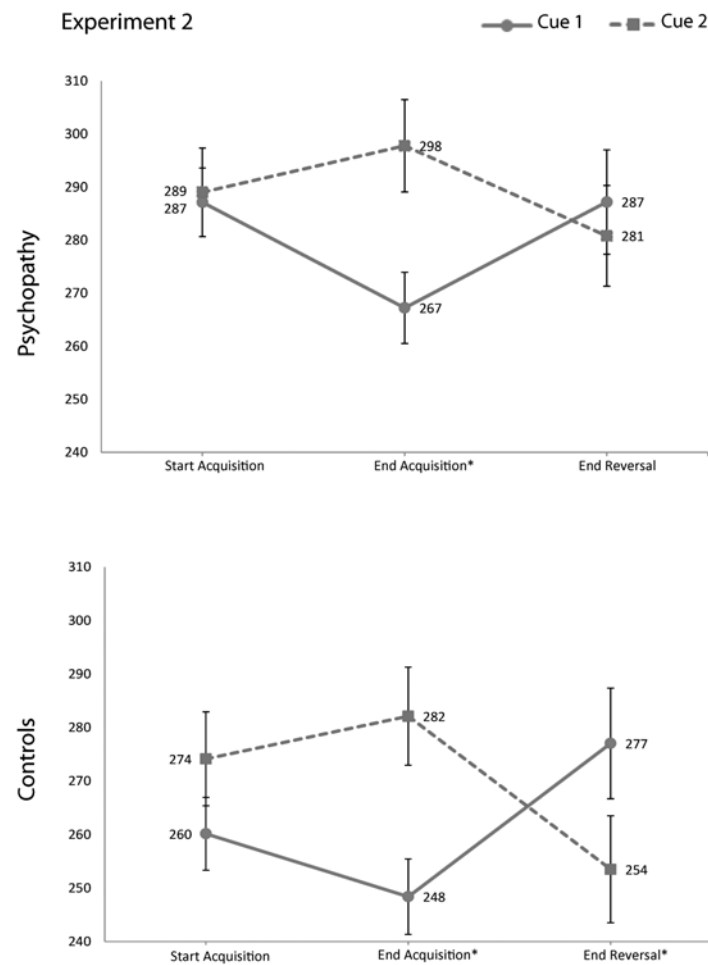
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Figure 2 Continued.

Block × Group [$F_{(2, 76)}$ = 0.124, p = 0.884, η^2 = 0.001] and Cue × Group [$F_{(1, 38)}$ = 0.015, p = 0.902, η^2 < 0.001] interactions were not significant. More importantly, the Block × Cue × Group interaction was significant [$F_{(2, 76)}$ = 3.97, p = 0.023, η^2 = 0.021]. Bonferroni-corrected paired-samples t-tests comparing RTs between the two cues in each block and for each group showed that in the psychopathic group, the difference in RT between the two types of cue was only significant at the end of the acquisition phase [$t_{(20)}$ = -4.94, p_{bonf} < 0.001]. However, in the control group, the difference between cues was significant both at the end of acquisition [$t_{(18)}$ = -5.26, p_{bonf} < 0.001] and at the end of the reversal phase [$t_{(18)}$ = 5.39, p_{bonf} < 0.001].

Accuracy data indicated that each group achieved near-perfect levels of accuracy in the experiments. The accuracy level in the group with psychopathy was 97.7% in the acquisition phase and 97.2% in the reversal phase in Experiment 1, and 99.8% and 99.5% in Experiment 2. The control group had 97.3 % and 96.9% accuracy in the acquisition and reversal phases, respectively, and 99.9% and 99.7% in Experiment 2.

5. Discussion

The aim of the present study was to investigate response reversal under automatic and controlled learning conditions in psychopathy. The findings point out that the presence of a response reversal deficit in psychopathy is modulated by the context in which learning occurs and are in line with the notion that some of the disturbances seen in psychopathy are related to a reduced capacity to intentionally use and manipulate information in order to adapt behavior. More specifically, the results show that the deficiency is not present when response reversal occurs in a context in which automatic learning is predominant (Experiment 1). Interestingly, however, abnormal response reversal was found in psychopathy when participants were instructed to actively monitor and manipulate associative relationships in order to perform successfully (Experiment 2). The data also suggest that response reversal is not completely impaired in psychopathy, but that there is slower adaption of behavior when the active use of information is required. The latter corroborates previous results showing delays in learning in psychopathy [141]. These findings have important implications for current accounts of disturbed learning in psychopathy.

The IES model cannot accommodate the results from Experiment 1. That is, when the true nature of the task is made less salient by omitting any reference to the predictive relationship between stimuli, psychopathic individuals are very well capable of performing response reversals successfully. However, the current formulation of the IES model postulates general response reversal deficits in psychopathy irrespective of learning context and level of awareness. Therefore, one would not expect abnormal response reversal to be limited to explicit learning conditions.

The distinction between automatic and controlled cognitive processing in psychopathy offers novel predictions. On a neurocognitive level, our results can be explained by considering the role of the prefrontal cortex (PFC) in adapting behavior. The PFC has been proposed to selectively bias cognitive processing to focus attention on relevant information while de-emphasizing competing information [153], in order to use the relevant information to guide goal-directed behavior [154]. Cohen et al. [154] originally classified this mechanism as a driving force behind cognitive control, a term now used to describe several types of cognitive functions. From this perspective, the impaired response reversal in Experiment 2 indicates that by making the cues more

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salient we tapped into a deficiency in properly using information provided by both cues and imperative stimuli to guide behavior in the group of participants with psychopathy, resulting in hampered response reversal. This interpretation is also consistent with previous findings pointing out that psychopathic inmates showed impaired performance under dual-task conditions when equal priority was given to both tasks [60], as well as more recent results relating psychopathy to impairments in cognitive control [155]. Moreover, considering cognitive control deficits also offers an explanation for the unaffected response reversal found in Experiment 1. Automatic processing is assumed not to rely on the integrity of the (prefrontal) brain system regulating cognitive control. During automatic learning in Experiment 1 this system was bypassed, resulting in normal performance in the group with psychopathy. Thus, the predictions offered by the dichotomy between automatic and controlled processing on a cognitive level converge with those made based on the biasing mechanism being referred to as cognitive control. However, there are also studies using other behavioral measures reporting unaffected cognitive control in psychopathy [156,157]. These studies point out that a) not all aspects of cognitive control are compromised or b) that different behavioral indexes vary in sensitivity and suitability depending on the function being assessed. For instance, Blair et al. [156] employed a series of neuropsychological tests each known to be sensitive to different executive functions in different cortical areas. Their results indicated that the group with psychopathy did not show deficiencies on behavioral measures preferentially sensitive to functions of the anterior cingulate and dorsolateral prefrontal cortex, while measures quantifying functions of the OFC did.

One limitation of the present study is that it could be argued that the use of non-psychopathic offenders would have constituted a more valid comparison group. However, previous studies from Blair and co-workers have shown that response reversal deficits are characteristic of psychopathy relative to general antisociality in both adult offender samples [59,61] and in children with high levels of psychopathic traits [158]. Accordingly, it was not our primary intention to re-establish the link between response reversal deficits and psychopathy relative to generic antisociality. Furthermore, the absence of a difference in Experiment 1 between the two groups is especially noteworthy given that the comparison involved more 'contrasting' populations (psychopathic vs. healthy individuals) than used in many other studies with similar sample sizes (psychopathic vs. non-psychopathic offenders), which, if anything, should have increased the chance of detecting group differences in this experiment. Still, it will be beneficial to replicate these results in a study that includes a group of non-psychopathic offenders. Reversal deficits have also been reported in (poly)drug users [149] and psychopathy has been linked to higher rates of (poly)drug use [159]. One could argue that the reversal deficit seen in Experiment 2 could be attributed to a history of drug use in the samples with psychopathy. However, (self-reported) rates

of drug use of the patient samples did not differ between the two experiments (Table 2) while the outcome did, implicating that drug use cannot be responsible for the difference. Finally, another argument is that the use of a different measure of response reversal (RTs vs. amount of reversal errors) compared to previous studies in adult psychopathy [59,61] reduces the comparability between studies. However, if disturbed response reversal is an essential aspect of the psychopathic syndrome it should also be present when a different method of assessing the same cognitive mechanism is employed, thus providing additional support for the robustness of this cognitive deficiency. Further studies are needed to address the exact impact of manipulating the saliency of different pieces of information using these types of paradigms.

6. Conclusion

In sum, the present study shows that deficient response reversal in psychopathy can be modulated by altering the nature of the learning context. The findings support the notion that some aspects of automatic processing of behavior are intact in psychopathy, but that disturbances arise when information processing reaches controlled stages of processing and has to be used to guide goal-directed behavior [112]. This view suggest that abnormal processing of information relevant for appropriate (re)adjustment of current behavior becomes apparent when individuals with psychopathy have to actively monitor and manipulate information. These results also highlight the importance of considering the way information is offered to offenders with psychopathy during therapeutic interventions in forensic psychiatric settings. Employing approaches relying on automatic learning mechanisms might be an effective way of modifying rigid and disruptive behavior.

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6

Psychopathy-related traits and the use of reward and social information: A computational approach

Abstract

Psychopathy is often linked to disturbed reinforcement-guided adaptation of behavior, and the same core deficit is believed to also lead to impaired learning from social information in both clinical and non-clinical populations. Recent work suggests that these disturbances might be due to a deficit in actively using information to guide changes in behavior, rather than learning itself. However, how much information is actually used to guide behavior has never been quantified. Forty non-clinical subjects were recruited based on their scores on a self-report psychopathy list, and performed a task involving simultaneous learning of reward-based and social information. A computational model was used to parameterize the extent to which subjects used each source of information in guiding their decisions. Subsequently, the psychopathy-related personality traits that were more strongly related to each parameter were isolated through a variable selection procedure, and we assessed how these covaried with model parameters. Use of reward-history information was negatively related to levels of trait anxiety and fearlessness, whereas use of social advice decreased as the perceived ability to manipulate others and trait guiltlessness increased. These results corroborate previous findings indicating that sub-optimal use of information is implicated in psychopathy. Moreover they isolate key features of psychopathy that can be related to model-based descriptions of subject behavior.

1. Introduction

In general, psychopathy is typified by reduced affective-interpersonal functioning often accompanied by an antisocial lifestyle in both its clinical and non-clinical manifestations in adults [4,27,160] and children [161]. Research from our own and other labs has shown that clinical psychopathy is related to deficiencies in associative learning of reward and punishment [46,61,141]. It has also been advocated that these deficiencies might lead to impaired associative learning using social information, resulting in antisocial behavior and a lack of morality [3,146,162]. This claim is also in line with findings in healthy individuals showing that associative learning of reward and social values follow the same mechanistic principles in the brain, albeit via separable neural substrates [163,164].

However, recent findings in clinical psychopathy challenge the current interpretation of these deficiencies as manifestations of a disturbance in the process of acquiring and manipulating information to drive behavioral adaptation during learning, rather than learning in itself [112,141,165]. For instance, we recently demonstrated that impaired response reversal in psychopathy was modulated by the need to actively monitor information relevant for performance [165]. More specifically, psychopathic offenders showed intact response reversal when they were *uninformed* that successful performance required monitoring and responding according to predictive relationships during the task. In contrast, impairments were found when psychopathic participants were instructed to actively monitor and implement these predictive relationships. These results suggest that disturbed adaptive behavior in psychopathy might not be modulated by a *learning deficiency* per se, but by a deficit in purposely *using* relevant information. A similar deficiency has been proposed to be present during social learning in psychopathy [146].

So far, there has been no direct quantification of how social and non-social information is used during associative learning, nor has there been an investigation of how the use of information in relation to personality traits is linked to psychopathy in non-clinical samples. One reason is that the mainstream experimental approaches in psychiatry do not allow the direct quantification of how much information is used [166]). However, this limitation can be overcome by incorporating computational modeling of behavior and known neurobiology in understanding psychiatric conditions [167–169]. Computational models of associative learning have proven to be increasingly helpful in explaining pathological behavior in neurological disorders like Parkinson's disease [170], but also in psychiatric disorders such as schizophrenia [171,172] and addiction [173]. In these conditions, key model parameters can be related to specific aspects of these patients' impaired behavior [170] or neurobiology [174], thus allowing the quantification of latent processes that are characteristic of these conditions (i.e. computational phenotypes) [166]. However, this model-based approach has been notably absent thus far in research

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into personality disorders with a less clear conceptual and neurocognitive background such as antisocial personality disorder and psychopathy [33,175]. Here, we adopt such an approach [168] and show that we can isolate specific psychopathy-related traits that covary with different parameters in a behavioral model.

Thus, the goals of the present study were to use computational modeling to provide the very first direct quantification of the amount of information used during associative learning and to specify the psychopathy-related personality traits linked to problems in using both social and non-social information. We reasoned that if the diminished *use* of information is a computational phenotype pertaining to psychopathy, it should also be present in the non-clinical expression of this condition and be related to traits associated with psychopathy among the general population. To achieve this we sampled a population with varying degree of psychopathic traits, based on the conceptualization of non-clinical psychopathy as being characterized by extreme scores on a conglomeration of dimensional personality traits that can be measured throughout the general population, and not only in clinical/forensic populations [16,17,24]. We then quantified the use of reward history and social advice information in an established reinforcement learning paradigm in which participants have to combine information from both sources to make optimal choices [163] and used a variable selection method to identify the psychopathy-related traits with the most explanatory power.

2. Methods and Materials

2.1 Measure of psychopathy traits

Traits were assessed with the Dutch translation of the Psychopathic Personality Inventory [16], a self-report questionnaire used to index the presence of traits related to psychopathy in non-clinical samples [19]. The PPI consists of 187 items that are scored on a 4-point Likert scale. Each item loads on one of eight subscales, each subscale representing a different personality trait. As the scores for a trait become more extreme they are considered increasingly psychopathic. The scales are Stress Immunity (displays reduced anxiety), Social Potency (is able to manipulate others), Fearlessness (lacks fear of harmful consequences), Machiavellian Egocentricity (is self-centered), Blame Externalization (blames others), Carefree Nonplanfulness (lacks forethought), Impulsive Nonconformity (is reckless and unconventional) and Cold-heartedness (is callous, guiltless).

2.2 Participant recruitment

A large pool of potential participants was created through advertisements on a university website and on a national news website with a link to a digital version of the PPI (N=485). Subsequently, total PPI scores were calculated and divided in

Table 1 Mean total PPI score and subscale scores for the experimental sample (n=40).

Variable	Mean (SD)
Age	23.9 (8.5)
Total PPI score	343 (47.6)
Stress Immunity	29.2 (5.3)
Social Potency	57.9 (13.1)
Fearlessness	42.1 (10.2)
Coldheartedness	46.7 (7.6)
Blame Externalization	32.2 (6.8)
Carefree Nonplanfulness	41.0 (6.0)
Machiavellian Egocentricity	56.3 (14.3)
Impulsive Nonconformity	34.3 (6.4)

quartiles, and participants were invited based on their scores. Participants from all quartiles were invited to participate, but the top and bottom quartiles were oversampled in order to enhance the presence of extreme scores on both sides of the distribution [176]. The experimental sample consisted of a single group of 40 individuals (36 females) willing to participate (see Table 1), from which 26 (65%) belonged to the top and bottom quartiles of the selection pool and 14 from the 2nd and the 3rd quartile.

In the present total sample (N=485), the internal consistency of the subscales was acceptable (Chronbach's alpha=.71). Also, a lack of differentiation between males (N=160, Mean=343, SD=39.9) and females (Mean=350, SD=38) was found, indicating that scores were distributed equally between genders. All participants received either course credits or a financial compensation and gave written informed consent. The study was approved by the local ethics committee of the Faculty of Social Sciences at the Radboud University in Nijmegen.

2.3 Experimental task

Each subject completed 290 trials of a decision-making task in which they had to learn about the probability of receiving reward on two options (blue and green rectangles, Figure 1)[163]. Subjects repeatedly chose between the two rectangles in order to accumulate points. The number of points available (a random number between 1 and 100) was shown in the centre of each rectangle; this number was added to the subject's score if the option was chosen and rewarded on that trial. Either blue or green could be correct on each trial, but the probability of the two colors being correct was not equal ($p_{blue}=1-p_{green}$). The chance of each color being correct could be inferred based upon the recent outcome history, but was subject to

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reversals during the course of the experiment (see below). However, the reward magnitudes available were independent of the probabilities of each color being correct; thus, as a result of the difference in reward magnitudes associated with the blue and green options, subjects would sometimes choose to pick the less likely color if it was associated with a higher reward. Subjects saw a red bar onscreen, whose length depicted their current score; they aimed to reach a silver target to win €5, or a gold target to win €7,50.

Subjects simultaneously learnt about the reliability of advice from a social partner. On each trial, subjects received advice (red box around choice in Figure 1) about which rectangle to choose from a "human partner" (the experimenter), supposedly playing with them (in reality, the advice was computer-generated). The experimenter sat on the other side of a custom-made shield that divided the room, preventing any visual contact between the participant and the experimenter. Prior to the experiment, both 'players' went through the instructions together. The partner's advice constituted what we refer to as the 'social information' or 'social advice' in the results. The partner's advice was predetermined prior to the experiment (and was, by design, uncorrelated with the reward history-based probability). A cover story was provided such that the partner might be incentivized to give either helpful or unhelpful advice in the experiment, and that this might change during the course of the experiment (for details see [163]).Irrespective of whether the advice was trustworthy or untrustworthy, the subject could exploit the advice to gain further information about which of the two options was the best choice on each trial. After the subject had responded (indicated by the grey box around the choice in Figure 1), the correct answer was revealed in the centre of the screen, and was then replaced by a fixation point before the next trial began.

In summary, subjects had *three independent* sources of information available on each trial to guide their choices – (i) the magnitude of reward available on each option; (ii) the estimated probability of green/blue yielding reward, based on past experience; (iii) the estimated fidelity of the social partner's advice, based on past experience. The true (underlying) probabilities of both (ii) and (iii) were predetermined such that they varied independently of one another, and underwent several reversals during the course of the experiment [163]. This meant that subjects had to continually monitor and learn about each source of information throughout the experiment, and also that each source of information had unique explanatory power in explaining variation in choice behavior. Our key question focused on the degree to which subjects used (ii) and (iii) to guide their choices – a feature of their behavior that can be captured formally with a computational model.
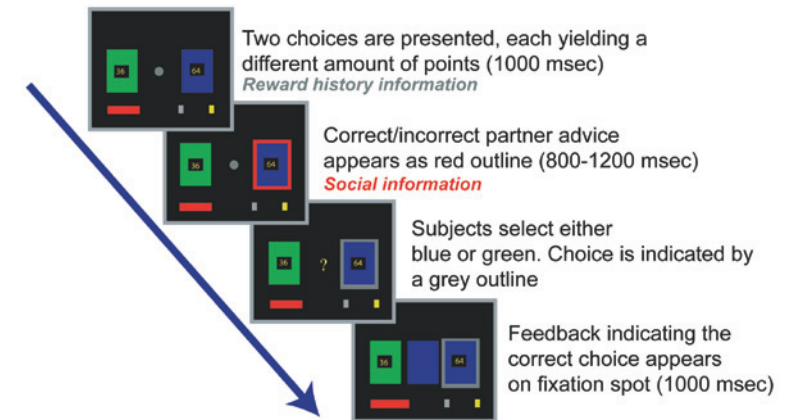

Figure 1 Sequence of events and their timings during in the experiments.

2.4 Modeling

We fit a behavioral model to estimate the *influence* of each source of information on each subject's behavior (see mathematical description below). Based on behavioral and neuroimaging results from our previous study [163],the model assumes that subjects use Bayesian reinforcement learning (RL) [177] to track both the probability of green/blue being correct and the probability of receiving truthful advice, and then use this information to guide their behavior. Bayesian RL allows for a learning rate that *varies* depending upon the current stability or volatility of the environment [177,178]. To capture the *extent* to which each subject used each source of information in guiding their choices, we fit a model that contains two parameters, $\gamma_{reward\ history}$ and γ_{social}, which have analogous functions for reward history and social information respectively; importantly, these parameters are independent of the rate at which information is *learnt* in the task (which varies through the task via the RL model, and is not fit as a free parameter). If γ is high for a given source of information, then it means that the objective probability associated with that source of information is *amplified*, i.e. pushed more towards 1 if it is greater than 0.5, and more towards 0 if it is less than 0.5 (e.g. the steepest line in Figure 2A). Conversely, if γ is low, the objective probability is pulled towards 0.5, and so has less influence (e.g. the shallowest line in Figure 2A). We estimated these parameters (and a further temperature parameter β, capturing choice stochasticity) separately for each subject (see below), in order to investigate cross-subject variability in their expression.

The magnitudes of $\gamma_{reward\ history}$ and γ_{social} then become important when we *combine* the sources of information to obtain an *overall probability of selecting green* on each

trial. This is illustrated in Figure 2B, where we show the effect of varying the two parameters on the eventual probability of the subject wanting to select green for an example trial. In this trial, there is a 0.3 probability of green being rewarded given the recent reward history. However, the confederate has advised green, and there is a 0.7 probability that the confederate will give good advice. Hence, these two sources of information would cancel one another out – but *only* if the subject uses each source of information equally (i.e. $\gamma_{reward\ history}=\gamma_{social}$). Conversely, if $\gamma_{social}>\gamma_{reward\ history}$, then the subject will favor the social information and become more likely to pick green (green area in Figure 2B), whereas if $\gamma_{reward\ history}>\gamma_{social}$, the subject will become more likely to pick blue (blue area in Figure 2B). Note that for simplicity, we have shown an example where the points on green and blue are equal; however, further interactions occur with the number of points available as these vary from trial to trial, and also as the probabilities of social and non-social information fluctuate independently of one another.
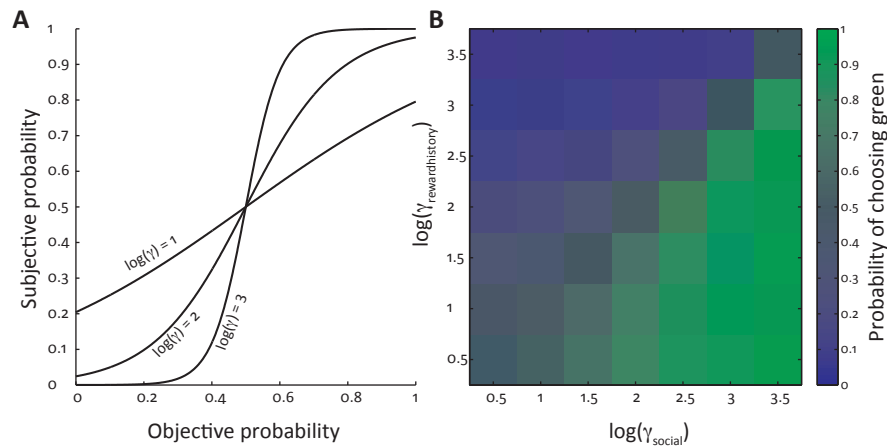

Figure 2 Left: Example transform between objective (RL model-derived) probability and subjective probability, parameterized by γ. Right: Posterior probability of choosing green for varying levels of $\gamma_{reward\ history}$ and γ_{social}, for one example trial. See 'Modeling' section in methods for details.

2.5 Mathematical model description

The model takes estimates of the probability of receiving good advice (p_i) and the probability of green being rewarded (r_i) at trial i, estimated via a Bayesian reinforcement learning optimized for adapting behavior depending upon the underlying volatility of the environment (for details see [177]). These probability estimates are converted into *subjective* probabilities using the following transforms:

$$\hat{p}_i = \frac{1}{1+e^{-\gamma_{social}(p_i-0.5)}}\hat{p}_i = \frac{1}{1+e^{-\gamma_{social}(p_i-0.5)}}\hat{p}_i = \frac{1}{1+e^{-\gamma_{social}(p_i-0.5)}} \tag{1}$$

$$\hat{r}_i = \frac{1}{1+e^{-\gamma_{reward\ history}(r_i-0.5)}} \tag{2}$$

These subjective probabilities are then converted into an overall subjective probability of green yielding reward, q:

$$\hat{q}_i = \frac{\hat{p}_i\hat{r}_i}{\hat{p}_i\hat{r}_i + (1-\hat{p}_i)(1-\hat{r}_i)} \tag{3}$$

if the partner suggests green on trial i, and

$$\hat{q}_i = \frac{\hat{p}_i(1-\hat{r}_i)}{\hat{p}_i(1-\hat{r}_i) + (1-\hat{p}_i)\hat{r}_i} \tag{4}$$

if the partner suggests blue.
The overall expected value of each option is then calculated as:

$$g_{green,i} = \hat{q}f_{green,i} \tag{5}$$

and

$$g_{blue,i} = (1 - \hat{q})f_{blue,i} \tag{6}$$

where $f_{green,i}$ and $f_{blue,i}$ are the number of points available on green and blue options respectively on trial i. Finally, the probability of choosing the green option at trial i is calculated via a softmax function [179,180]:

$$P(C_i = green) = \frac{1}{1+e^{-\beta(g_{green}-g_{blue})}} \tag{7}$$

and

$$P(C_i = blue) = 1 - P(C_i = green) \tag{8}$$

where β is an additional, third free parameter that determines the stochasticity of choice behavior.
We then used this model to estimate the log-likelihood of the observed data, at given values of the parameters $\gamma_{reward\ history}$, γ_{social}, and β:

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$$LL\left(\gamma_{social}, \gamma_{reward\ history}, \beta\right) = \sum_i \log(P(C_i = c_i | \gamma_{social}, \gamma_{reward\ history}, \beta)) \quad (9)$$

where c_i denotes the option chosen by the subject on trial i. We custom-implemented a Bayesian estimation procedure in MATLAB (MathWorks, Massachusett, U.S.A.) to obtain the best-fitting parameters γ_{social}, $\gamma_{reward\ history}$ and β.

2.6 Relating fitted model parameters to psychopathic traits

The key question addressed here is which psychopathic traits are related to the *between-subject variation* in the degree to which each optimally-tracked source of information is used to guide behavior, which is indexed in the model by the free parameters $\gamma_{reward\ history}$ and γ_{social}. To test this, we conducted two separate optimal scaled variable selections using the CATREG module in SPSS. This was done in order to establish the subscales of the PPI with the highest contributions in explaining the variance of each free parameter. Two models were created which included all subscales of the PPI and the estimates for $\gamma_{reward\ history}$ and γ_{social}, respectively. Subsequently, variable selection with *lasso* (least absolute shrinkage and selection operator; [181]) regularization was implemented to identify the 'optimal' model for each free parameter. The optimal model was taken to be the model with the lowest expected prediction error and thus the highest accuracy given the data. This approach relies on shrinking the sum of the model coefficients by adding penalty terms to the model, resulting in coefficients that represent independent contributions as well as better model accuracy [182]. This procedure yields an optimal model, which is the model with the smallest error margin. The latter was estimated with .632 bootstrapping [183] of 100 samples.

One advantage of this selection approach is that it overcomes a lot of the limitations of variable selection when using traditional stepwise regression analyses, such as the need for normality of variables [182], the related loss of power due to lack of compliance with assumptions for frequentist testing, and the need for multiple comparison corrections associated with sequential F-testing. After selection of the optimal model for each computational parameter, Pearson correlations were calculated between the scales in each model and the corresponding computational parameter in order to establish whether these covary and if the covariance differed from zero.

3. Results

First, we carried out an initial check to ascertain that participants were learning and were engaged in the task by comparing the amount of points earned at the end of the task with chance level performance. The results showed that the average amount of

points earned (Mean = 10.364, SD = 759) was significantly higher than the amount that could be earned by guessing the correct choice on each trial (Mean = 7.276, SD = 586; t(39) = -23.5, $p < 0.001$), indicating above change performance and that participants were actively engaged in the task.

3.1 Variable selection and correlations

Here, we present the results of the two variable selection procedures ran after the estimation of $\gamma_{reward\ history}$ and γ_{social}, which are displayed in Figure 3. The initial model is depicted at the far right of each panel. The systematic shrinkage of the standardized sum of coefficients forces the coefficients towards zero and for each step the resulting model is depicted to the left of the previous model. In both panels, the dashed vertical line indicates the optimal model. Note that for our purpose of solely identifying the
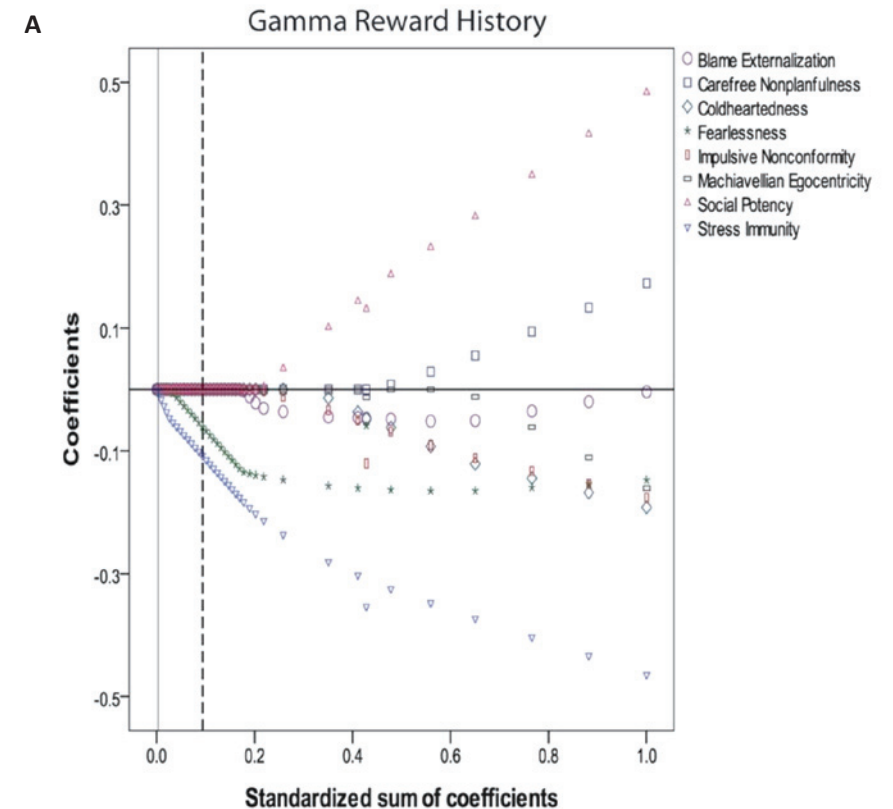

A

Figure 3 Results of the variable selection procedure for $\gamma_{reward\ history}$ (left) and γ_{social} (right).

B

Gamma Social Advice

○ Blame Externalization
□ Carefree Nonplanfulness
◇ Coldheartedness
* Fearlessness
⬚ Impulsive Nonconformity
▱ Machiavellian Egocentricity
△ Social Potency
▽ Stress Immunity

Figure 3 Continued.

A

Figure 4 Scatter plots for the correlations between the selected PPI scales and $\gamma_{reward\ history}$ (A) and γ_{social} (B).
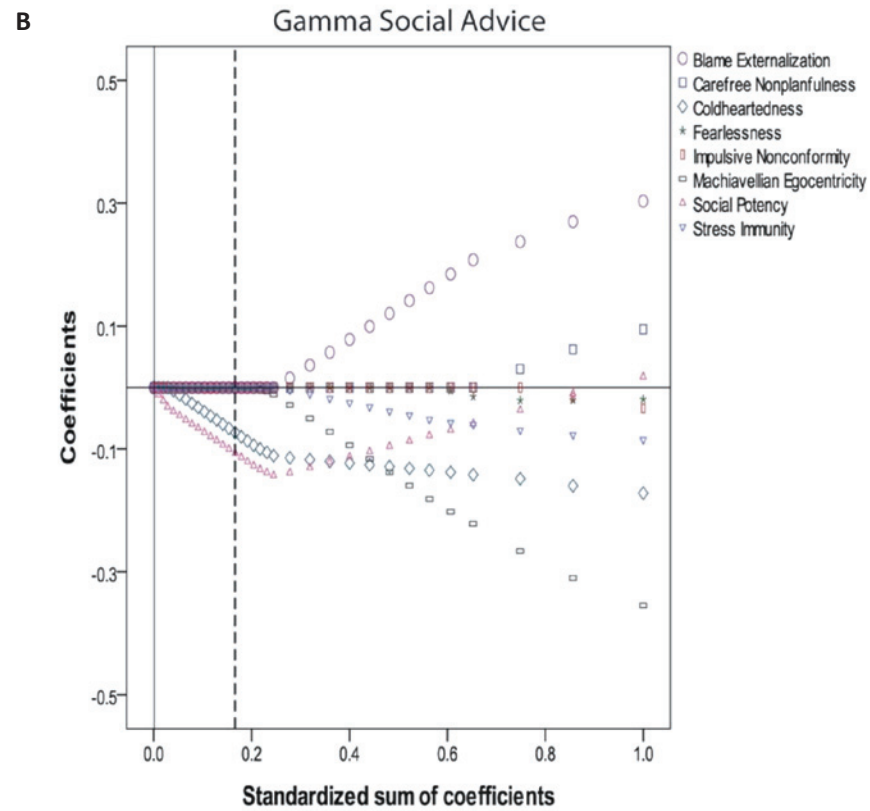
variables with the greatest contribution to the computational parameters, the magnitude and significance of the variable coefficients (indexed on the Y-axis) are of less interest and that the results do not warrant statistical significance in subsequent tests.

For $\gamma_{reward\ history,}$ Stress Immunity and Fearlessness were the traits that had the largest contributions to the variability of $\gamma_{reward\ history}$ (Figure 3A). Subsequent correlation analyses yielded significant negative correlations between $\gamma_{reward\ history}$ and Stress Immunity (r = -0.37, p = 0.018) and $\gamma_{reward\ history}$ and Fearlessness (r = -0.35, p = 0.028; Figure 4). The optimal model for γ_{social} included the variables Social Potency and Cold-heartedness (Figure 3B). The correlation analyses revealed a negative relationship between γ_{social} and Social Potency (r = -0.33, p = 0.037; Figure 4) and γ_{social} and Cold-heartedness (r = -0.32, p = 0.046).

3.2 Additional tests

To show that the two computational parameters were uncorrelated and that the traits identified were uniquely related to either of the either γ_{social} (Range = 1.57-25.2) or $\gamma_{reward\ history}$ (Range = 0.42-12.9), we additionally examined the correlations between (a) γ_{social} or $\gamma_{reward\ history}$, (b) Stress Immunity and Fearlessness with γ_{social} and (c) Social Potency and Coldheartedness with $\gamma_{reward\ history}$. As expected, the computational

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B

Figure 4 Continued.

parameters were not significantly correlated (r = 0.067, *p* = 0.68). Stress Immunity and Fearlessness were uncorrelated with γ_{social} (r's < -0.25, *p*'s > 0.13), as were Social Potency and Coldheartedness with $\gamma_{reward\ history}$ (r's < -0.13, *p*'s > 0.43). These results indicate trait specific modulation of the estimated parameters.

4. Discussion

The present study is the first to use formal computational modeling to quantify how information from different sources is used during associative learning in order to provide evidence that variations in personality traits linked to psychopathy are differentially related to diminished use of social and reward information. This was achieved by establishing which specific traits related to psychopathy covary with the ability to actively use social and reward information to guide behavior. Thus, we succeeded in quantifying latent variables that cannot be observed overtly using traditional experimental approaches [184], and were able to relate these to personality traits associated with core aspects of psychopathy.
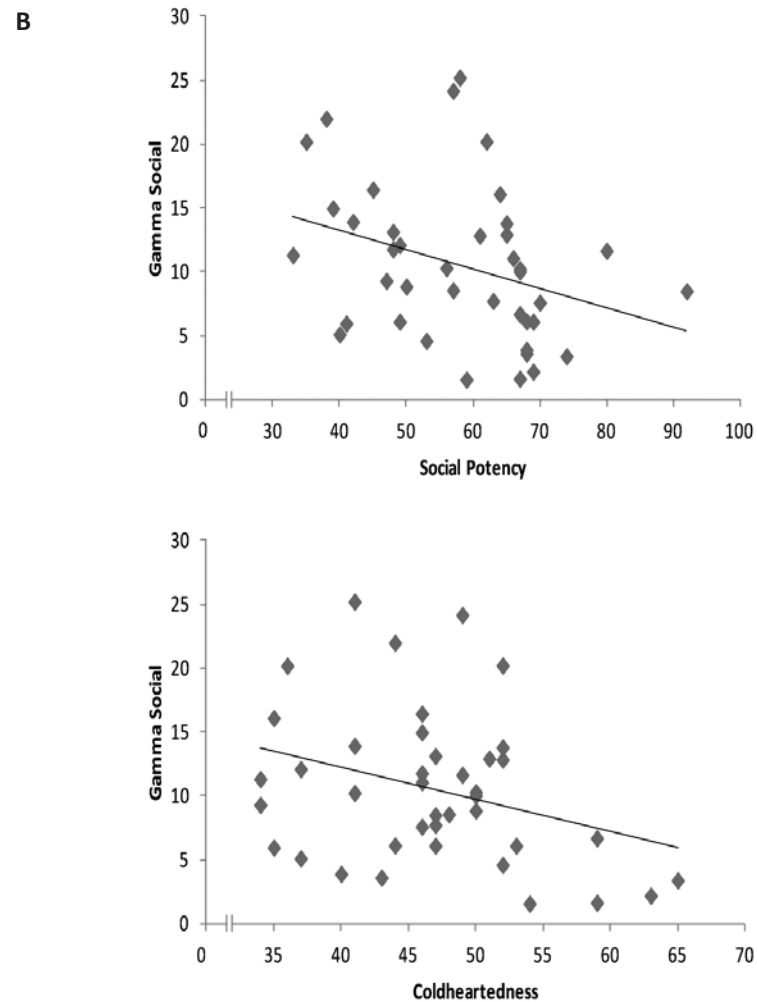
First, scores on Stress Immunity and Fearlessness were negatively correlated with the extent to which previous reward history was used to make decisions. These findings converge with substantial evidence relating both low anxiety and low fear to disturbed associative learning in clinical psychopathy [36,185]. Particularly, work by Newman and colleagues has shown that disturbed passive avoidance learning is predominantly found in psychopathic individuals with low trait anxiety relative to those with high anxiety [185,186]. Similarly, psychopathic behavior has also repeatedly been linked to reduced fear reactivity in both clinical and non-clinical samples [95,187–189] and, importantly, impaired fear-conditioning [36,37]. The central premise here is that aversion to negative outcomes induces fear/anxiety, which is in turn associated with the actions/contexts that lead to these negative affective states. A low propensity to experience these negative affective states leads to weak associations with events leading to negative outcomes and thus impaired associative learning [33]. The present findings indicate that although trait fear and anxiety play a key role in associative learning, they do so by modulating the *active implementation* of available information to guide changes in behavior. This suggests that impairments in associative learning previously found in clinical psychopathy might also be due to a deficiency in using reinforcement information appropriately, which, depending upon the experimental paradigm used, may manifest as disturbed adaptation of behavior during learning.

Second, the use of social information was found to have a negative relationship with participants' perceived ability to manipulate others and their level of guiltlessness and affective reactivity to others' distress. Both Social Potency and Coldheartedness encompass behavior relevant for social functioning. High Social Potency is commonly associated with one's belief that one is able to successfully manipulate others. We hypothesize that people who believe that they can manipulate others are more likely to believe that others will try to manipulate them, when *mentalizing* about the likely intentions of the social partner [163,190,191]. These inferences about what others may think we believe, i.e. second-order beliefs, have also been found to motivate prosocial behavior through the modulation of the amount of guilt that people anticipate they

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will experience during social decision-making [191]. Chang and colleagues [191] used a formal model to show that higher guilt aversion resulted in increased prosocial behavior. Conversely, individuals experiencing low amounts of guilt should show less prosocial behavior. High Coldheartedness encompasses callousness and guiltlessness [192], so our data indicate that individuals scoring high on this trait might experience less anticipated guilt or care less about discarding the confederate advice. In general, our results suggest that second-order belief systems might play an important role in explaining social cognition in psychopathy. Future studies should focus on mapping the exact role of second-order beliefs in explaining various aspects of psychopathic behavior at both clinical and non-clinical levels.

Interestingly, exploratory factor analyses of the PPI have revealed the presence of two superordinate factors in community samples [18,21], which have traditionally been termed Fearless Dominance (PPI-I) and Antisocial Impulsivity (PPI-II), respectively. The subscale Coldheartedness is the only scale not to load on either of these superordinate factors. The PPI-I includes the scales Social Potency, Stress Immunity and Fearlessness, which together with Coldheartedness, are believed to represent core personality features that are specific to psychopathic personality [160,192]. The factor PPI-II represents a set of traits related to antisociality in general. Importantly, none of the traits from the PPI-II were substantially related to the computational parameters in the present study, while our effects are (selectively) associated with the traits included in the PPI-I. This indicates that the deficient use of reward and social information might be specific to traits related to psychopathy rather than general antisociality and that deficient use of information could be a potential phenotype for clinical and non-clinical psychopathy.

One potential caveat is that we used learning rates produced by our model in this experiment. However, we do not consider this a limitation as previous studies have shown that healthy individuals combine different sources of information in an optimal fashion to learn, and that this is reproduced reliably by our computational model [163,177]. This should also to be the case in the present sample of healthy functioning individuals. Given this, the current study was designed to explicitly test the hypothesis that variations in traits related to psychopathy can be linked to deficiencies in using information. In the same vein, individuals with heightened psychopathic tendencies who generally show normal behavior, and therefore do not pose a threat to society, may differ fundamentally from convicted offenders diagnosed with clinical psychopathy [20]. It is possible that behavioral and neurocognitive manifestations of psychopathy are present in both clinical and non-clinical populations, but that these populations differ in the extent to which these tendencies are pathological and have a detrimental impact on own daily functioning and society. Future studies in clinical psychopathy should try to confirm the predictions that (a) it is the use of information, rather than learning per se, that is compromised in this disorder and that (b) altered

use of specific sources of information are selectively linked to behavior that is specific to clinical psychopathy, i.e. Factor 1 of the Psychopathy Checklist-Revised [4]. This can be achieved by using similar paradigms to estimate the amount of information used during reinforcement learning while controlling for the amount of *actual learning* that occurs. Finally, our sample consisted predominantly of female participants and it could be argued that the findings might not extent to the male population. However, previous studies in clinical psychopathy suggesting deficient use of information included only male participants [112,141,165] and the fact that the current results converge with those obtained in male-only samples supports the notion that the deficiency is typical of psychopathy and is not gender-specific.

5. Conclusion

In conclusion, the present study is the first to directly assess the relationship between psychopathic variation in personality traits and the amount of information that is used during associative learning of social and reward information. The findings show that the use of both types of information to guide behavior decreases as the presence of personality traits that are unique to psychopathic behavior increases. More specifically, lower trait anxiety and fearlessness are associated with reduced use of one's reinforcement history and an increased perceived ability to manipulate others and guiltlessness are related to diminished use of social advice. Additionally, the findings also provide an extension to the non-clinical population by showing that the newly-discovered latent variables are linked to core traits that are important for the construct of psychopathy. The results also highlight the advantages of employing formal models to discover computational phenotypes in clinical populations [166] as well as their usefulness in gaining more insight into the exact personality traits related to the cognitive deficiencies observed in many personality disorders. The present findings might also have implications for treatment aimed at altering behavior, as this relies on the patient's ability to incorporate and use information from past experience and information provided by therapists.

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Differentiating psychopathy from general antisociality using the P3 as a psychophysiological correlate of attentional allocation

1. Introduction

Severe antisocial behavior can be observed across a wide span of disorders, including conduct disorder and antisocial personality disorder. Within the spectrum of antisocial disorders there is a group of individuals classified with psychopathy, which has traditionally been typified by disturbances in affective functioning combined with severe antisociality. In the past two decades, disturbed functioning in these two domains has been assessed with the Psychopathy Checklist-Revised (PCL-R)[6], which has been the golden standard for the assessment of clinical psychopathy. The PCL-R measures behavior reflecting interpersonal-affective functioning and antisociality and yields a total score indicating the presence of psychopathy. Studies assessing the cognitive counterparts of these behavioral indexes have linked psychopathy to impaired processing of affective information [193], and to disturbances in other non-affective cognitive domains such as learning [141] and attention [41]. In contrast, non-psychopathic antisocial behavior has been linked to a broader range of problems in executive processing relative to psychopathy [194,195]. The latter points out that while the concepts of psychopathy and generic antisociality show overlap on the behavioral level, they seem to differ in the cognitive processes that are affected and the extent to which these are deficient.

Attention is one of the cognitive processes that have been investigated extensively in comparative studies between psychopathy and non-psychopathy. There are numerous behavioral results indicating abnormalities in attentional processes that seem to be unique to PCL-R diagnosed psychopathy compared to non-psychopathic antisociality [44]. In contrast, relatively few studies have examined the electrophysio-logical correlates of attention in psychopathy [32,196,197,198,199,200]. A recent study using event-related potentials (ERPs) found that the abnormal allocation of attention in psychopathy seems to be due to disturbances at an early stage of selective attention, reflected by an increased positive ERP around 140 ms after stimulus presentation (P140)[32]. These ERP results were interpreted as additional support for the Response Modulation (RM) theory, which predicts that psychopathy is related to a tendency to over-allocate attention to goal-relevant information and to ignore potentially relevant secondary information. Apart from these early effects, selective attention is also involved in later stages of processing [201].

Previous ERP studies on attention in psychopathy have mainly focused on this later aspect of attention by looking at components belonging to the P3-family [92,196,197,198(p300),199,200]. The term P3-family refers to a conglomeration of ERP components with a positive deflection occurring in a separate, much later time-window than the P140. The components belonging to the P3-family have been implicated in various functions such as attentional processing [202], inhibition [203] and error processing [94]. Two P3 potentials have been shown to be modulated by attentional allocation and task

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demands [204]. These components can be assessed using the oddball paradigm, in which infrequent target stimuli are presented in a string of frequent nontarget stimuli. Voluntary detection of the infrequent target stimuli elicits a P3 with a parietal distribution, also known as the P3b [205]. A variant of this task, the three-stimulus oddball paradigm, also includes the occurrence of highly salient task-irrelevant novel stimuli. In this version, participants respond to infrequent target stimuli but withhold their response to both infrequent novel and frequent standard stimuli. Task-irrelevant novel stimuli are known to elicit a P3 with a frontocentral distribution termed the P3a (or the novelty P3)[206]. The P3a reflects an involuntary automatic orienting of focused attention to novel stimuli and this mechanism is governed by anterior cingulate cortex (ACC)[207].

The results of the aforementioned studies on the P3 potentials in individuals with PCL-R diagnosed psychopathy have been inconclusive. Jutai et al. [196] investigated the P3b under single-task and dual-task conditions and did not find differences in amplitudes. In contrast, Raine and Venables [197] employed a continuous performance task and reported enhanced P3b amplitudes in subjects scoring high on psychopathy. Later studies by Kiehl et al. [198,199] found the P3b to be reduced in psychopathic samples compared to non-psychopathic incarcerated offenders, as did Gao et al. [200] in a community sample of unsuccessful (caught) psychopaths. In sum, the P3b has been found to be reduced, normal and enhanced in samples scoring high on psychopathy. Until now, only two studies specifically investigated the frontal P3 to novel oddballs in psychopathy [199,200]. Kiehl et al.[199] reported the P3a to be reduced, but only in one of the two psychopathic samples tested and no differences were found in the other sample. Gao et al. [200] reported no differences in P3a amplitudes between controls, successful (uncaught) and unsuccessful psychopaths. Furthermore, a study on another frontal P3 component known as the NoGo P3 found reduced amplitudes in psychopathy [208], while a more recent investigation found the NoGo P3 to be unaffected in psychopathy [92]. Thus, the results on frontal components are also contradicting. One general explanation for these mixed results might be that the different tasks used tap into slightly different cognitive processes and these discrepancies are in turn reflected by differences in ERPs (for more details see [209]). In short, more research on the relationship between the P3s and PCL-R diagnosed psychopathy is needed in order to increase our understanding of these inconclusive results.

In sharp contrast to psychopathy, P3 findings in various *non*-psychopathic samples related to antisocial behavior have shown much more convergence. In general, both the P3a and the P3b tend to be reduced in these populations, which include disorders such as substance abuse disorder [210,211], conduct disorder [212,213], and populations at risk of developing these types of disorders [214,215]. A recent meta-analysis found a negative relationship between antisocial behavior in general and the P3 [194]. It was suggested that the reduced P3 in antisocial reflects faulty utilization of neural

resources, resulting in hampered processing of relevant information. However, it was pointed out that this deficiency might be less prominent in psychopathy. These results highlight the need to establish how well each of these two groups can recruit neural resources in order to process information that is relevant to the task at hand. As processing of information is continuous and dynamic, one approach is to regard the P3 components as electrophysiological manifestations of neural recruitment during this process. More specifically, the automatic orienting of focused attention reflected by the P3a facilitates the allocation of attentional resources to successive memory storage operations in the hippocampal formation. The output is then passed on to the parietal cortex. This latter, controlled attentional process in parietal regions is reflected by the P3b [207]. This interactive mechanism between frontocentral and parietal areas is indicative that monitoring events is a continuous process. Although the distributions are frontocentral for the P3a and parietal for the P3b, an electrophysiological response to targets can also be observed in frontocentral areas, albeit smaller in amplitude relative to novels. The opposite pattern can be observed in parietal areas. More specifically, the P3 to novels is larger than the electrophysiological response to targets in frontocentral areas, while the P3 to targets is larger than the response to novels in parietal areas. To our knowledge, this dynamic switch in electrophysiological pattern resulting from the interplay between frontocentral and parietal areas has not been explicitly assessed before in either healthy or patient samples. Examining whether the switch in pattern is present in the ERPs to targets and novels in frontocentral in relation to parietal regions could yield valuable information about the quality of neuronal recruitment and the extent to which the cognitive processing driving these potentials are functionally affected. Thus, the current approach offers a more sensitive electrophysiological measure for examining and comparing the quality of cognitive processing in psychopathic and non-psychopathic clinical samples.

The main goal of the present study was to assess cognitive processing of rare novel and target events in psychopathy relative to a non-psychopathic sample of institutionalized offenders and a group of matched healthy control individuals. Based on the converging findings in non-psychopathic samples, a diminished P3a to novel stimuli was expected in non-psychopathic offenders compared to both psychopathic and healthy individuals. In contrast, due to the lack of group differences in the majority of the samples in which a frontocentral P3 was assessed in clinical psychopathy [92,199,200], combined with reports on intact automatic processing in ACC [112], the P3a was expected to be intact in psychopathic subjects relative to the non-psychopathic participants (thus similar to healthy controls). Second, reductions were found in three out of five reports on the P3b in psychopathy and in a large amount of studies in non-psychopathic samples of antisocials, and we subsequently predicted reduced P3b amplitudes in both non-psychopathic and psychopathic offenders

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relative to healthy controls. Finally, the quality of processing and attentional allocation during the continuous monitoring of infrequent stimuli was also investigated in the offender groups by examining the switch in the pattern of the ERPs to targets and novels in frontocentral and parietal areas.

2. Methods

2.1 Participants and procedure

Two offender groups were recruited from the population of the Pompestichting Forensic Psychiatric Institute Nijmegen, The Netherlands. The Pompestichting is a clinic for individuals who have committed serious criminal offences in connection with having a DSM-IV axis-I and/or axis–II disorder. Placement in such clinics falls under a measure known as 'Ter Beschikking Stelling' (TBS). TBS is a treatment measure on behalf of the state and is not a punishment, but an entrustment act for offenders with mental disorders. The TBS measure is ordered by the court and offers an alternative to confinement in psychiatric hospital or long-term imprisonment, with the aim of balancing treatment, security and protection.

The offenders were selected based on prior history and information about their clinical status. Twenty offenders diagnosed with psychopathy and twenty-three non-psychopathic offenders were included in this study. Psychopathy was assessed with the PCL-R, which consists of twenty items representing different behavioral charac-teristics that are scored as being absent (0), moderately present (1) or clearly present (2) based on file information and a semi-structured interview [6]. The PCL-R was administered by trained psychologists upon admittance to the Dutch forensic mental health system. Therefore, available PCL-R scores were retrieved from participants' files. In Europe, a cut-off score of 26 is usually maintained for the PCL-R [8,112]), thus offenders with a PCL-R score ≥ 26 were included in the psychopathic group and those with a score < 26 in the non-psychopathic patient group (Table 1).

Sixteen healthy control participants were recruited through advertisements. The control group consisted of volunteers without criminal records and a history of psychiatric disorders. Because none of our healthy controls had criminal records, which are essential for reliably assessing PCL-R scores, the PCL-R scores were not assessed in the healthy control group. All participants were males and the groups were matched for age and educational level. Educational level was categorized into three subdivisions based on the Dutch educational system (level 1 = primary education, level 2 = secondary education, level 3 = higher education) [112].

All subjects participated in two sessions; a screening session and a test session. During the screening session, compliance to the inclusion criteria was determined *for*

Table 1 Group characteristics for the psychopathic, non-psychopathic and the control group.

Characteristic	Psychopathy (n=20)	Non-psychopathy (n=23)	Healthy controls (n=16)
Age	40 (10)	37 (8.8)	37 (6.7)
Educational Level	2.5 (0.6)	2.6 (0.6)	2.9 (0.4)
PCL-R Score	30 (4.2)*	15.7 (4.8)	

Group means are reported with their standard deviation between brackets. Significant Group differences are flagged.

all three groups using the Dutch version of MINI Psychiatric Interview [82] and the SCID-II [83]. In addition, information from criminal records was used for the offender groups. Participants were excluded if one or more of the following disorders were present: depressive disorder, bipolar disorder, schizophrenia, schizoaffective disorder, schizophreniform disorder, delusional and other psychotic disorders, schizoid or schizotypical personality disorder, attention deficit hyperactivity disorder, antisocial personality disorder and/or psychopathy were excluded only in healthy volunteers, and first degree relatives with DSM-IV axis I schizophrenia or schizophreniform disorder. Other exclusion criteria were the use of intoxicating substances or psychotropic medication within the week preceding the experimental session, and a positive result on any of the unannounced urinal drug tests that were randomly administered. All assessments were conducted by trained psychologists. If the criteria were met, an appointment was made with the participants for the test session in which behavioral and EEG data were acquired.

2.2 Ethics statement

All participants received written information about the experiment, a financial compensation, and gave written informed consent. Potential participants were allowed a period of at least two weeks to consider and discuss their participation before signing the following consent form: *By signing this form I confirm that I voluntarily give consent to participate in this study. I have received and read a copy of the information for participants. I am informed about the study and have had enough time to think about my participation. My questions have been answered satisfactorily. I am aware that I can withdraw my consent at any time without giving any reason and without any adverse consequences on my further treatment.* For each participant, the experimenter signed the following section: *I confirm that this participant has been given explanations concerning the nature, purpose and possible risks of this research, and has voluntarily agreed to participate in the study. The participant confirmed his voluntary consent by signing above.*

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For each potential participant from the offender population, the full capacity to consent was established by consulting the head therapist in charge of the participant's treatment and care. Potential participants lacking the capacity to consent themselves (i.e. having a low level of competence) as indicated by the presence of mental retardation or any psychiatric condition associated with reduced competence, or not meeting the inclusion criteria were still eligible for treatment. Thus, the decision to participate did not affect the patient's treatment or care in any way. The protocol was approved by the local medical ethical committee (Commissie Mensgebonden Onderzoek Regio Arnhem-Nijmegen) and the rights of the participants were protected.

2.3 Task and Design

A three-stimulus oddball paradigm was employed in order to investigate both variants of the P3. Subjects were seated at approximately 75 cm from a 100 Hz monitor and the stimuli were presented in the centre of the display in black against a white background. The stimuli consisted of either the letter 'S', the letter 'H' or one of 40 different non-letter ASCII characters with font size 24 and font type Arial. Participants were instructed to use their right index finger to press a designated button on a button box whenever the letter 'S' (Target, 10%) appeared and to withhold responses if the stimulus was either an 'H' (Standard, 80%) or another unique character (Novel, 10%). Participants were not informed about the occurrence of rare novel stimuli in the task. Four hundred trials were presented, divided in 4 blocks of 100 trials. Stimuli were presented for 250 msec and followed by a 1500 msec response window before the next stimulus was presented.

2.4 Apparatus and recordings

Electrophysiological data were collected using 27 active electrodes (ActiCap, Brain Products, Munich, Germany) arranged according to a variation of the 10-20 system. Abralyt 2000 abrasive gel (EasyCap, Herrsching, Germany) was used for the conduction of signals to the electrodes. Vertical eye movements were recorded by placing electrodes above and below the left eye and horizontal eye movements were registered at the outer canthi of the eyes. Electrophysiological data was acquired at 500 Hz without filtering with the QuickAmp amplifier (Brain Products, Munich, Germany) and the electrodes were referenced to the left ear during signal acquisition.

2.4.1 EEG data processing

ERP data were filtered offline using a .02-20 Hz filter and re-referenced to the average of the linked ears. EOG artifacts were removed using Independent Component Analysis [88]. Additional artifact rejection scans were conducted in order to detect other types of artifacts remaining in the data. Amplitudes exceeding ± 50µV were

labeled as artifacts and removed from the dataset and a minimum of 15 artifact-free trials for each participant in each condition was set as a condition for inclusion [212], but artifact rejection yielded an average of 36 novel and 38 target trials per participant. Subsequently, activity associated with each type of stimulus was averaged separately in epochs starting 200 msec prior to stimulus presentation and ending 700 msec after stimulus onset. Segments were baseline corrected to a 200 msec pre-stimulus interval.

The P3s were detected with automatic algorithms at electrode sites FCz and Pz. As the P3a has been reported both at Fz [210] and at FCz [216] in these types of populations, we first explored which of these two frontal electrodes showed larger amplitudes. These were larger at FCz. The most positive peak between 275-575 msec following stimulus-onset was determined for the P3a [211] and between 300-700 msec for the P3b. The responses to the frequently occurring standard stimuli were not included in the analyses because detailed inspection of the data indicated that not all participants had a pronounced electrophysiological reaction to this type of stimulus. Therefore, it was not possible to execute peak detection for the standard stimuli which would yield reliable results for each individual.

2.5 Statistical analyses

For ERP analyses, the individual mean amplitudes were entered in a repeated measures General Linear Model (GLM) with Stimulus Type (Novel, Target) and Location (FCz, Pz) as within-subject factors and Group (Controls, Non-psychopaths, Psychopaths) as between-subjects factor. Behavioral data were investigated by entering reaction times (RTs) to targets in a Univariate GLM with Group as between-subject factor. Accuracy data were divided in correct responses to targets, incorrect button presses to novels (false alarms), and errors to non-targets (commission errors) and analyzed with Kruskal-Wallis tests because the data were not normally distributed.

3. Results

3.1 Behavioral results

RT analyses revealed a main effect for Group [$F(2, 56) = 7.32$, $p = 0.001$]. Healthy controls showed shorter RTs (399 msec; all p's < 0.01; Table 2) than the psychopathic group (470 msec) and the non-psychopathic group (479 msec), while the two patient groups did not differ ($p = 0.902$). The groups did not show any differences in amount of correct hits [χ^2 (2, $N = 59$) = 0.558, $p = 0.757$], false alarms [χ^2 (2, $N = 59$) = 3.04, $p = 0.218$], or in the total number of responses to non-targets [χ^2 (2, $N = 59$) = 0.421, $p = 0.122$].

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Table 2 Behavioral results for the psychopathic, non-psychopathic and the control group.

	Psychopathy (n=20)	Non-psychopathy (n=23)	Healthy controls (n=16)
Reaction time	470 (76)	479 (70)	398 (54)*
Correct hits	39.4 (1)	39.7 (0.6)	39.7 (0.7)
False alarms	0.5 (0.7)	0.17 (0.4)	0.38 (0.8)
Errors to non-targets	0.65 (0.8)	0.22 (0.4)	0.44 (0.8)

Group means are reported with their standard deviation between brackets. Reaction times are reported in msec and accuracy measures in counts. Significant group differences are flagged.

3.2 ERP results

Initial analyses showed that there was a main effect for Location [$F(1, 56)$ = 15.6, $p < 0.001$] indicating higher overall amplitudes at Pz (9.4 µV, SD = 5.0) compared to FCz (7.4 µV, SD = 4.8). There was no main effect for Type [$F(1, 56)$ = 0.422, $p = 0.519$]. As expected, there was a significant interaction for Location × Type [$F(1, 56)$ = 47.2, $p < 0.001$], indicating that the mean P3 amplitude to novels (7.9 µV, SD = 5.0) was larger at FCz compared to targets (6.9 µV, SD = 5.1; $t(58)$ = 2.59, $p = 0.012$), while amplitudes to targets were maximal at Pz (10.0 µV, SD = 5.2) compared to novels (8.7 µV, SD = 4.2; $t(58)$ = -3.1, $p = 0.003$). The main effect for Group revealed smaller overall amplitudes in the offender samples [$F(2, 56)$ = 11.1, $p < 0.001$; Figure 1]. Importantly however, the Location × Type × Group interaction also reached significance [$F(2, 56)$ = 9.79, $p < 0.001$].

To identify the source of the latter significant 3-way interaction, separate GLMs were carried out for each group, with Type and Location as within-subject factors. The results revealed significant Location × Type interactions for both the psychopathic and the control group (all F's > 13.3, all p's < 0.01). Further examination of this two-way interaction revealed that also within these two groups, peaks to novels were significantly larger than targets at FCz, while targets elicited significantly larger amplitudes than novels at Pz (one-sided paired sample t-tests: all p's < 0.05; see Figure 2). In contrast, the Location × Type interaction was not significant for the non-psychopathic offenders, [$F(1, 22)$ = 1.31, $p = 0.265$], indicating that the non-psychopathic group did not differentiate between novels and targets at FCz nor at Pz (see Figures 1 and 2).
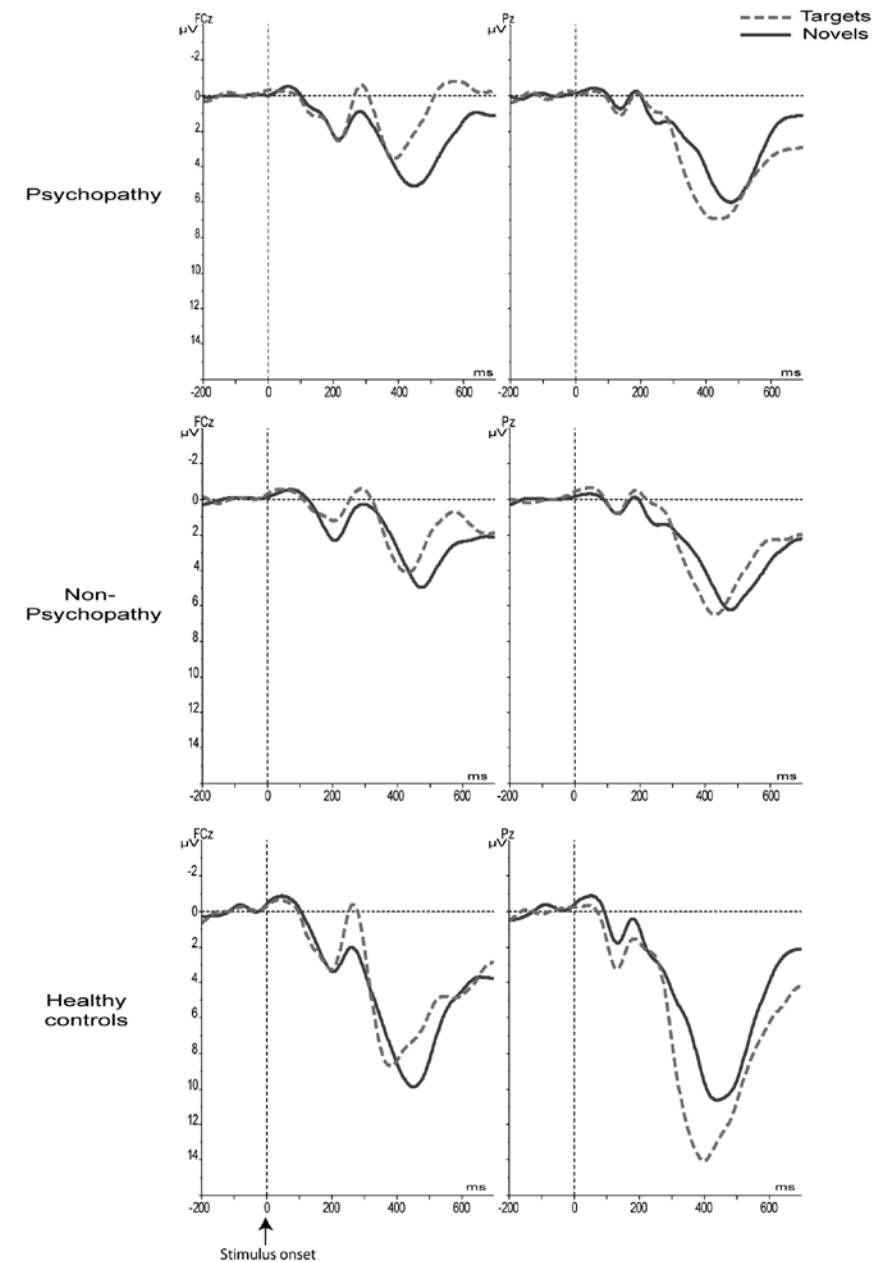

Figure 1 Grand average stimulus-locked waveforms for the P3a at FCz and the P3b at Pz for each group separately.
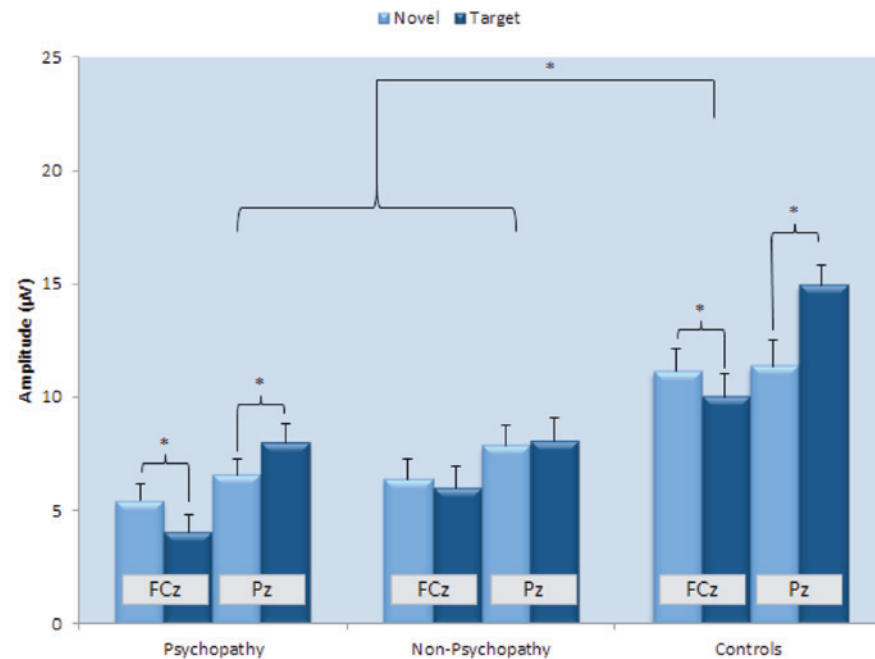
Figure 2 Average peak amplitudes for novels and targets at FCz and Pz for the psychopathic, non-psychopathic and control group, respectively.

4. Discussion

The aims of the present study was to investigate and compare the P3 to novel events (P3a) and the P3 to infrequent targets (P3b) between groups of offenders with and without psychopathy and healthy controls, and to compare the groups on the ability to differentially allocate (late) attention and process various stimulus types at an electrophysiological level. The results show that both psychopathic and non-psychopathic offenders generally exhibit reduced P3a and P3b amplitudes compared to healthy individuals, but do not differ from each other in overall amplitudes. The findings in the non-psychopathic offenders corroborate previous reports of reduced P3s in general (non-psychopathic) antisociality [194]. At first glance, the results on the P3a in the group with psychopathy would seem in contrast to our hypothesis that the amplitude of the P3a should be similar to that of the healthy controls and would also be consistent with previous outcomes showing P3a reductions in psychopathy [199]. Importantly however, the present findings suggest that a more subtle difference exists between the offender groups that is not captured by traditional methods

assessing overall peak estimates. In spite of the overall reduction in P3 amplitudes, the psychopathic group showed a larger P3 to novel relative to target stimuli in frontocentral areas and larger P3 amplitude to targets compared to novels in parietal areas, thus resembling the healthy individuals on this aspect. These findings indicate that psychopathic individuals are capable of monitoring and allocating late selective attention accordingly to various types of infrequent stimuli, even in the light of an overall reduction in deployment of attentional resources. The latter seems not to be the case in the non-psychopathic group of offenders.

The ability to still differentiate novels and targets found in the group with psychopathy is consistent with the claim that psychopathy is related to enhanced processing capabilities [194]. It is plausible that they were showing superior processing capabilities, because their level of processing ultimately leads to the same psychophysiological pattern as healthy controls, while deploying fewer resources. This idea converges with previous claims that the monotonous nature of the oddball task might not be stimulating enough to fully trigger the attentional resources of psychopathic individuals and could also be an explanation for the lack of differences between the two offender groups on overall P3 amplitudes. Future studies using more complex paradigms combined with more fine-grained stimulus-level ERP analyses could shed more light on this issue.

It is also worth considering our results in light of the attention-based RM hypothesis. The traditional formulation of this hypothesis postulates that the abnormal behavior seen in psychopathy is due to abnormalities in the automatic allocation of attention to secondary but meaningful information to current goal-directed behavior [41]. Thus, psychopathic individuals fail to attend to secondary information that competes for the occupation of the focus of attention with information that is central to current goal-directed behavior. Based on this general definition it could initially be predicted that psychopathy should be related to reduced attentional allocation to non-relevant novel events and a tendency to overfocus on the target stimuli in our task, which should be reflected by reduced P3s to novelty relative to the P3s to targets in both frontocentral and parietal areas. Our findings do not seem to support this prediction as the group with psychopathy did not show larger ERPs to targets at both locations. One explanation could be that our task was not suitable to test the mechanisms that have been claimed to be related to the deficient response modulation in psychopathy. Stimuli were presented in succession, which means that there was no competition between peripheral and central information for occupying the focus of attention. Furthermore, recent work within this framework has narrowed down the abnormalities in allocation of attention in psychopathy to an early attentional bottleneck that occurs in a much earlier time-window relative to the P3 [32,217]. Baskin-Sommers et al. [32] found psychopathic inmates to show larger ERP amplitudes implicated in early attentional processing,

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suggesting superior allocation of attention in this early stage. It is possible that this superiority caused an increased deployment of cognitive resources in an early stage of processing in order to differentiate between the stimuli in the group with psychopathy, reducing the need for engaging cognitive resources for differentiation later stages in the timeframe of the P3. Thus, the presence of an anomalous early attention bottleneck as postulated by recent specification of the RM hypothesis could also explain our findings showing intact stimulus differentiation in spite of reduced overall amplitudes in the group with psychopathy.

In contrast to the psychopathic group, non-psychopathic subjects failed to show appropriate type-dependent modulation of attention and seemed to disengage their resources during processing, which was especially evident in the total lack of differentiation in parietal areas (Figure 2). These results are in line with previous evidence linking impairments in cognitive processing and the P3 to non-psychopathic antisociality [194]. Also, one tentative hypothesis is that this deficiency in disentangling information might be related to greater perceived ambiguity in the interpretation of information, which in turn may result in hostile and inappropriate behavior often seen in these types of (non-psychopathic) populations [218]). Future studies specifically designed to address this matter should explore this possibility.

The results also support the notion that although offenders with and without psychopathy clearly show overlap in covert behavior and psychopathology, they may still differ on other aspects (such as the extent to which specific personality traits are present) and in their neurocognitive make-up [219]). The combination of our electro-physiological and our behavioral results add support to this claim. The behavioral findings point out that the healthy control group showed shorter RTs compared to the offender samples, while the offender groups did not differ from each other on any behavioral measure. Also, all groups showed very high levels of accuracy and did not differ on any of these measures. This pattern of performance could be accounted for in terms of a speed/accuracy trade-off, which required the offenders to slow down in order to achieve normal accuracy that is comparable to that of the healthy controls. This interpretation would be consisted with previous reports of poor behavioral performance in both non-psychopathic antisociality and psychopathy [195,220]. However, the group difference in the discrimination of novels and targets reflected by the ERPs indicates group dissimilarities in the neurocognitive processing preceding the observed behavior. In a recent investigation of the interplay between inhibitory control and affective processing in psychopathy and non-psychopathy it was also found that both groups showed comparable behavioral performance while ERPs showed significant group differences in cognitive performance [27]. The absence of group differences in behavior might be due to the simplicity of the tasks used both in the present study and that by Verona et al. [27]. All together, these results converge with previous claims that these groups form two related but separable populations

within the spectrum of antisocial personality disorders [199,219], with non-psychopathic antisociality being more prone to deficient cognitive processing in general relative to psychopathy [194].

One potential limitation is that it could be argued that the size of our samples might have led to insufficient statistical power. However, our samples were large enough to detect between-group effects, within-group effects and the interactions of interest with high levels of significance in our GLMs. Another potential limitation comes from the argument that the diminished cognitive processing (reflected in this case by the reduced P3s) found in the offender groups are related to a more general reduction in cognitive well-being during incarceration [221,222]. As countries differ in their penitentiary regimes, in some countries inmates regularly remain confined to their cells for the great majority of the day or are deprived in other ways. This could debatably lead to less exercising of their cognitive skills. In our case, we believe that it is unlikely that incarceration itself is responsible for our results. The Dutch forensic psychiatric system is unique in that it mimics everyday life outside the forensic clinics, requiring patients to work, participate in therapies, study, exercise, etc., throughout the day. Moreover, some of the offenders were in the resocialization trajectory, meaning that they were working outside the clinic and participated in society on a daily basis while still under surveillance and care of the institute. Therefore, we do not believe that the differences found relative to our healthy control group can be purely attributed to incarceration.

5. Conclusion

In sum, this study directly compared the P3a and P3b in healthy subjects, non-psychopathic offenders and psychopathic individuals. The findings show that both psychopathic and non-psychopathic offenders exhibit reduced P3 amplitudes to rare events in both frontocentral (P3a) and parietal areas (P3b) relative to matched healthy controls. This is generally indicative of a reduced ability to allocate late selective attentional resources to infrequent events. Importantly however, the current study provides evidence for a dissociation between the two offender groups on a more detailed level. While the psychopathic group did show normal differentiation in attentional allocation to infrequent task-relevant and task-irrelevant stimuli, the non-psychopathic sample did not show this pattern. These results also highlight the advantage and importance of assessing electrophysiological processes on a more detailed level when comparing populations known to show deficiencies reflected in specific ERP components. Comparing groups based on grand average ERPs (calculated across all subjects within a specific sample) is very useful in ascertaining whether a specific group shows larger or smaller ERP amplitudes. However, this method conveys

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less information about the health of the cognitive mechanisms that drive the individual ERPs. Future studies employing alternative approaches to data analyses would help disentangle the neurocognitive underpinnings of different psychiatric populations collectively marked as antisocial, in order to increase our understanding of this heterogeneous and relatively opaque class of personality disorders.

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Summary & Discussion

Summary

The research presented in this thesis was conducted with the goal to increase the understanding of psychopathy by examining adaptive behavior and information processing. Chapter 2 dealt with the question whether processing of the outcome of own actions was impaired in psychopathic offenders. Outcome was defined as a response being either correct or incorrect (i.e., an error), and was indexed by the error-related negativity (ERN) and the error positivity (Pe) as markers for early automatic and late controlled processing, respectively. The offenders with psychopathy showed similar ERN amplitudes relative to a comparison group consisting of healthy individuals, indicating intact automatic processing of error-related information in psychopathy. In contrast, the group with psychopathy showed reduced Pe amplitudes, thus reflecting impaired controlled processing of errors. This dichotomy was also present in the behavioral findings. Behavioral measures related to automatic adaptation (e.g. congruency effects, past-error slowing) did not differ between the groups. However, the average signaling rate of errors (the behavioral measure for controlled error processing) was found to be 10% lower in the individuals with psychopathy. Taken together, the converging ERP and behavioral results indicate that automatic aspects of action monitoring are intact in psychopathy, while later stages involved in controlled processing and error awareness are compromised.

Chapter 3 describes an ERP study on the processing of external error-feedback during trial-and-error learning in psychopathy. A reinforcement-learning task was used to investigate how negative feedback indicating erroneous outcomes is processed and whether previously found learning impairments are related to diminished use of information conveyed by errors. The main findings were that individuals with psychopathy processed the error-related feedback appropriately, but the reduced response ERNs point out that they are less capable of using the feedback to create an internal template and learn. Importantly, learning was achieved, yet only after a large amount of trials. These findings indicate that a) psychopathy is related to deficits in learning associative relationships and generalizing predictive contingencies to new situations, b) this impairment is related to a reduced ability to internalize and use valuable information to adapt, c) learning is achieved but only after large amount of trials, and thus follows a much slower time course compared to healthy individuals.

Importantly, people are social beings and therefore a large portion of our actions is executed within a social context. Monitoring the actions of others is important for learning socially appropriate behavior. It could be hypothesized that due to the antisocial tendencies seen in psychopathy, monitoring of others' actions might be impaired. This question was examined in chapter 4, in which the observation of others' actions was investigated. To this end, ERPs indexing motor and action-outcome

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processing were examined for both own and observed actions in psychopathy relative to a healthy control group. The results on monitoring of own actions converged with those described in chapter 2, namely that detecting own actions did not differ between psychopathy and healthy controls. In contrast, the group with psychopathy showed reduced ERPs to the outcome of the observed actions, while the actions themselves were processed properly. The findings were interpreted as evidence that hampered processing of observed action-outcomes might contribute to abnormal social learning and thus the acquisition of disruptive social behavior.

Chapter 5 reports an experiment in which some of the main electrophysiological findings described in chapters 2 and 3 were translated to a behavioral paradigm. The ERP experiments indicated that there is dissociation between intact automatic/ unintentional and hampered controlled/active use of performance-related information in psychopathy. The hypothesis was that this distinction should also be present during response reversal, meaning that individuals with psychopathy should show unaffected response reversal when automatic learning is facilitated and impaired reversal when explicit learning is predominant. The instructions were used to provide a context in which one of these learning mechanisms was facilitated. As predicted, psychopathic individuals were capable of performing a complete response reversal during automatic learning, but failed to do so during controlled learning. Interestingly, the pattern in the results suggests that response reversal might have been achieved if more time had been available. This could indicate that the controlled learning of the reversal mechanism is not impaired as such, but that changes in behavior follow a slower time course compared to automatic learning. This slower rate of adaptation during learning was also evident in the behavioral results discussed in chapter 3. In sum, these findings indicate that deficient response reversal in psychopathy is closely related to the *type* of learning mechanism that is predominant (automatic vs. controlled) and is influenced by the context in which adaptation occurs. They also provide more evidence that it is the active and effortful use of information, rather than (only) learning itself, which is impaired in psychopathy.

Chapter 6 zooms in on the question whether the use of information can be quantified computationally and which psychopathy-related personality traits have explanatory power and covary with these parameters in the general population. Using this approach we succeeded in parameterizing the amount of reward history and social information that was used to achieve learning in an associative learning task. Importantly, this study extends the findings in clinical psychopathy to the general population by showing that psychopathy-related traits (but not generic antisociality) have the largest explanatory potency for the computational parameters. Thus, they point out that reduced use of both social and non-social information seems related to traits relevant to psychopathy in both clinical and non-clinical populations.

Chapter 7 describes a study that was (to some extent) inspired by the long-standing debate concerning the commonalities and differences between psychopathy and generic antisocial behavior. Part of this dispute is based on the overlap in behavioral tendencies observed in antisocial populations with and without psychopathy. However, the observation that two individuals show similar behavior does not necessarily indicate that the underlying cognitive processes are equivalent. The results discussed in chapter 6 also support the claim that psychopathy and generic antisociality differ on the neurocognitive level. Based on this notion, the integrity of late attention processing was examined and compared between individuals with psychopathy, antisocial offenders without psychopathy and healthy controls. Two variants of the P3 were used as indexes of late selective attention. Also, allocation of attention can be regarded as a continuous process in which information travels from frontal to parietal brain regions depending on their relevance and novelty, but there has been no previous investigation of these dynamics in any of the three populations. The findings point out that both groups of offenders show smaller P3 amplitudes relative to healthy controls. Interestingly, despite these reductions the group with psychopathy still differentiated between infrequently occurring (but task-relevant) stimuli and showed a level of deeper processing that was similar to controls. In sharp contrast, the group of generic antisocials did not show the stimulus-dependent differentiation, indicating diminished recruitment of the neurocognitive mechanisms involved. In sum, the findings suggest that psychopathy might be associated with unimpaired modulation of late attention and the deployment of fewer resources, but that general antisociality is related to an overall deficiency in late attention processing.

2. Discussion

2.1 An integration of the main findings

One finding that recurs in each of the five experiments on adaptive behavior is that psychopathy seems to be related to dysfunctions in the active implementation of available information to adapt. These impairments appear to be present during both short-term (chapter 2) and long-term adaptation (chapters 3 and 5). However, these studies only provide indirect evidence that it is the use of information that is impaired, rather than latent deficiencies in other processes. This culminated in the study presented in chapter 6, which aimed to (a) obtain direct evidence that impairments in this aspect of cognition indeed exist by quantifying the amount of reward-history and social information people use to learn, (b) investigate whether the findings in clinical psychopathy are also found in non-clinical personality correlates of psychopathy, and (c) specify which psychopathy-related traits were associated with the dysfunctions. Although this study was conducted in a sample of healthy individuals, the finding that

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only personality traits argued to be linked to core aspects of psychopathy were related to the computational parameters provides support for the notion that aberrant use of information might be typical for psychopathy in both its clinical (i.e. the disorder) and non-clinical (i.e. the presence of tendencies that are not pathological) manifestations.

The results in chapter 6 also point out that the impairments in adapting behavior reported in chapters 2-5 might be specific for clinical psychopathy and cannot be generalized to antisociality. However, I would like to draw this conclusion with a certain cautiousness, due to the lack of a non-psychopathic group of offenders in these experiments. In the same vein, the results described in chapter 7 also show that psychopathy differs from general antisociality in terms of cognitive functioning and that these disorders show divergent impairments in cognitive functioning even when behavior suggests the opposite [27].

2.2 Considering the dominant models of psychopathy
It is important to consider the body of work presented here in the light of the two neurocognitive models of psychopathy that have received the greatest empirical support, namely the RM hypothesis and the IES model. In this section I will highlight how these theories fail to provide an explanation for a selection of the findings described in this thesis. First, the RM hypothesis explains psychopathy in terms of impairments in automatic shifts of attention to accommodate relevant secondary information. A problem in shifting attention implies that maladaptive behavior in psychopathy is a consequence of impaired allocation of attention to incoming sensory information rather than a problem in processing information about motor output. Some of the results obtained in our experiments challenge the prediction that attentional impairments drive behavioral problems in psychopathy. For example, the ERN and the Pe index functions that are tied to motor processing and do not reflect stimulus processing or attentional shifting. So it is unclear what role deficient modulation of attention could play in explaining the finding that automatic action monitoring is intact in psychopathy, while later controlled action-outcome processing is compromised. This problem also arises in relation to the results on response reversal reported in chapter 5. Based on the current formulation of the RM hypothesis it could be reasoned that the information carried by the predictive cues is of secondary nature and that consciously redirecting attention towards the cues (Experiment 2) should indeed lead to impaired response reversal. However, as events were presented serially during the task they did not compete to occupy the current focus of attention. As there is no competition in the early stages of selective attentional processing, individuals with psychopathy should not show response reversal impairments during explicit learning according to the RM hypothesis. An alternative prediction is that a problem in automatically shifting attention could lead to impaired response reversal

during automatic rather than controlled learning. From this perspective, individuals with psychopathy should fail to automatically allocate attention to the cues and the information they carry because this information would be of secondary importance to the primary task, resulting in deficient adaptation of behavior during automatic learning. The finding that the group with psychopathy showed normal adaptive behavior argues against this prediction.

Second, the findings also challenge some of the predictions of the IES model. As discussed in chapter 3, this model predicts intact acquisition learning in psychopathy and therefore cannot account for the disturbed acquisition found in psychopathy during the reinforcement learning task employed. Also, it is unclear how the brain circuitries described in this model can explain the reduced error awareness reported in chapter 2 and the intact modulation of late attention in psychopathy discussed in chapter 7. The same holds for the presence of intact response reversal in psychopathy during automatic learning (chapter 5, Experiment 1), as the current formulation of the IES model seems to predict a general deficiency in response reversal without making a distinction between automatic and controlled learning processes. However, proponents of the IES model could argue that the paradigm and analyses employed did not capture stimulus-outcome (i.e. cue-outcome) learning, but stimulus-stimulus (i.e. cue-stimulus) learning instead. As a result, an intact automatic response reversal would still be consistent with the predictions of the IES model as the reversal would not be driven by stimulus-outcome relearning. However, one important difference with other response reversal tasks previously used (see [59,61]) is that while in these paradigms the stimulus-outcome contingencies were altered during the task in order to trigger response reversal, in our task the stimulus-outcome mappings remained fixed throughout the entire experiment. This means that in our task each stimulus (e.g. the go stimulus) co-occurs consistently with the same response (i.e. the button press) and the same outcome (i.e. positive feedback) during the entire experiment, especially given the near perfect levels of accuracy (defined as percentage of correct responses) that were achieved in each group of participants. The core principle of Hebbian leaning describes that events that co-occur reliably may lead to a common neural representation. In other words, due to learning the neurons that code the occurrence of a specific stimulus and the response and the outcome that follow should start firing together, leading to a unitary stimulus-response-outcome (S-R-O) representation. The net result is that the predictive cue activates the most likely the S-R-O representation, and thus becomes earliest predictor of positive outcome. Even if it were stimulus-stimulus learning that took place, the IES framework could still not explain the reversal impairment found during controlled learning (chapter 5, Experiment 2).

In sum, the findings obtained in the present studies cannot be explained by the currently dominant neurocognitive frameworks of psychopathy. One reason might be that the current formulation of these models encompasses only a portion of the

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dysfunctions that are characteristic of psychopathy. The scope of the RM hypothesis is limited to impaired modulation of early attention, and the IES model is primarily concerned with deficits related to amygdala and orbitofrontal cortex functioning. In the next sections, I will argue that broadening the scope of the fronto-limbic network which the latter cortical structures are part of might offer a better explanation for the present data.

2.3 Current neurobiology in psychopathy
In the recent neurocognitive literature on clinical psychopathy there is a lot of focus on the fronto-limbic network and certain cognitive functions (for a review see[20]). Parsimony is an essential component of scientific reasoning, but it is important to realize that the IES model has generated unique empirical findings than cannot be fully explained by the RM hypothesis, and vice versa. In addition, the present findings do not completely fit within either models, so it seems too optimistic to believe that a disorder as complex and opaque as psychopathy can be explained by one primary neurocognitive deficit.

The need for integration has led Moul and colleagues [57] to propose a neurobiological framework centered on the amygdala that attempts to merge the IES model and the RM hypothesis, and have labeled their model the Differential Amygdala Activation Model (DAAM). One of their main arguments is that psychopathy is related to impaired stimulus-outcome learning due to dysfunctions in the basolateral amygdala (BLA), but that functions carried out by the central nuclei (CeN) are either intact or might even be superior in these individuals. From a general perspective, this model concurs with the IES model by positioning the main loci of impairment in psychopathy within the amygdala. Another core tenet is that the BLA is implicated in automatic shifting of attention and a hampered BLA could explain the deficient attentional shifts predicted by the RM hypothesis. Importantly, besides these commonalities there are marked differences in the predictions made by the DAAM relative to the other two models (for more details see [57,223]).

A strength of this model is that it may foster our thinking about the unification of pre-existing theories, but it suffers from a too narrow scope centered on the amygdala. Furthermore, the model seems to have been developed based on a selected set of studies suggesting impaired BLA and intact CeN functioning, but to me it is unclear how it copes with results showing impairments in autonomic functions believed to be modulated by the CeN (e.g. reduced modulation of startle reflex [95]) or those in action monitoring obtained in the studies reported in this thesis. In all, the DAAM is still in its infancy and needs to gain convincing empirical support for some of its provocative predictions.

Still, one reason to consider the DAAM is that the empirical substantiation of the neurobiological correlates of the RM hypothesis is not abundant, nor are its ties to

relatively well-established general neurobiological networks for cognition [48]. Importantly, I would like to stress that the latter is not an absolute prerequisite for a cognitive model to have good explanatory power, as science has often shown that the presence of profoundly altered neurobiology does not necessarily translate to deficits in all corresponding aspects of cognition or behavior [224]). In other words, altered neurobiology does not always map on to abnormal cognition or behavior.

One question that arises is whether it is possible to define a framework that could accommodate the present results without disregarding the large body of empirical data in favor of the established models. In the following sections, I will use the present results to highlight the value of considering the involvement of the anterior cingulate cortex (ACC) in understanding psychopathy, as well as subregions and functions of the prefrontal cortex that have been less prominent (or maybe even absent) in the literature on psychopathy. Note that my primary goal here is to offer some thoughts on how to reconcile the present findings with existing models, and not to propose a comprehensive explanatory model of psychopathy that includes all the brain regions that might be involved. Also, my line of reasoning assumes that primary neurobiological counterparts of the RM hypothesis lie within the same cortical network as the IES model and the DAAM.

2.4 The anterior cingulate cortex
The notion that a network involving the amygdala and the OFC is impaired in psychopathy seems to be gaining popularity in research in both children and adults. However, this cortico-limbic network also includes other areas such as the ventral striatum [69] and the ACC [51,225]. There is a fair amount of data relating the ACC and the OFC for various cognitive operations that are crucial for changing behavior, such as reward-based decision-making, top-down modulation of attention and social valuation (for reviews see e.g. [51,164,226]). It has been argued that subregions of the OFC drive behavior by coding stimulus-related information about the current value of a choice [51,227]. Importantly, the OFC has few direct connections to motor areas, so in order to drive a change in behavior it needs to relay its signals to other regions directly connected to motor areas. In contrast, the ACC codes action values and has direct access to regions involved in motor control, but has less direct access to stimulus-related information. Thus, change of behavior is dependent on both the OFC and the ACC, as well as on the outcome of their interactions [51,139].

It is important to take into account that the ACC is a relatively large structure that shows differential connectivity patterns and functional interactions with other regions [164,228]. Bush and colleagues [229] have proposed that this area can be subdivided into a dorsal section (dACC) that is mostly connected to areas involved in (non-affective) reward-guided behavior and rostral-ventral section (vACC) involved in social cognition and affective processing, which is strongly connected to the OFC and

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the amygdala. Thus, given the anatomical and functional relevance of the ACC it is unfortunate that this area has been less prominent in research on psychopathy (see also [219,230]), and further studies are needed to assess the exact roles of ACC functioning in psychopathic behavior.

2.5 The frontal pole

As indicated above, the vACC is connected to the OFC. These connections are the strongest between the vACC and medial parts of the OFC [228]. The medial OFC, or ventromedial prefrontal cortex (vmPFC), has repeatedly been associated to behavioral, affective and social impairments in psychopathy [231,232]. It is important to realize that the term vmPFC is an umbrella-term for a specific set of subregions within the prefrontal cortex and cytoarchitectonic decomposition has shown that the vmPFC is mostly occupied by regions pertaining to the rostral frontal cortex (Brodmann area (BA) 10). BA10 is also known as the frontal pole, the frontopolar cortex or the anterior prefrontal cortex. However, one important aspect that is often overlooked in the literature is that the rostral frontal cortex can be subdivided in subregions BA10r and BA10m that are part of the vmPFC, and BA10p that occupies the most anterior part of the rostral frontal cortex (but not exclusively) and is not part of the vmPFC [233]. More recent connectivity-based parcellation has identified a similar subdivision into a subarea that has been termed the lateral frontal Pole (lFP) and a medial subregion (mFP) corresponding to the vmPFC/mOFC (see [234]). The lFP probably corresponds to the same area some refer to as BA10p, and henceforth I will adhere to the term lFP (see Figure 1). The lPF is remarkable in that it is the only cortical area that is exclusively interconnected to the OFC, temporal cortex and ACC (and not directly to the amygdala), and is only involved in higher-order cognitive processing [234,235]. The vmPFC has been very prominent in the literature on psychopathy, while the lFP has received much less attention (if any). There are reports on frontal pole functioning in psychopathy [137], but the term 'frontal pole' is often used to denote either the entire BA10 and adjacent areas (e.g. BA9) or just the subregions that occupy the vmPFC and not the most anterior part of the rostral frontal cortex. This lack of precision in the nomenclature together with methodological limitations might be some of the reasons why the lFP has not received a lot of consideration in the literature.

The lFP has been implicated in various complex cognitive tasks, such as prospective memory, reallocation of attention and cognitive branching, introspection, and considering multiple relationships simultaneously [235]. It has been proposed that these tasks involve integrating and coordinating information from multiple cognitive operations in order to adapt behavior optimally, and that this is the overarching function of the lFP [235,236]. That is, the lFP coordinates and integrates simultaneous cognitive operations (e.g., during multi-tasking) and uses the resulting information to
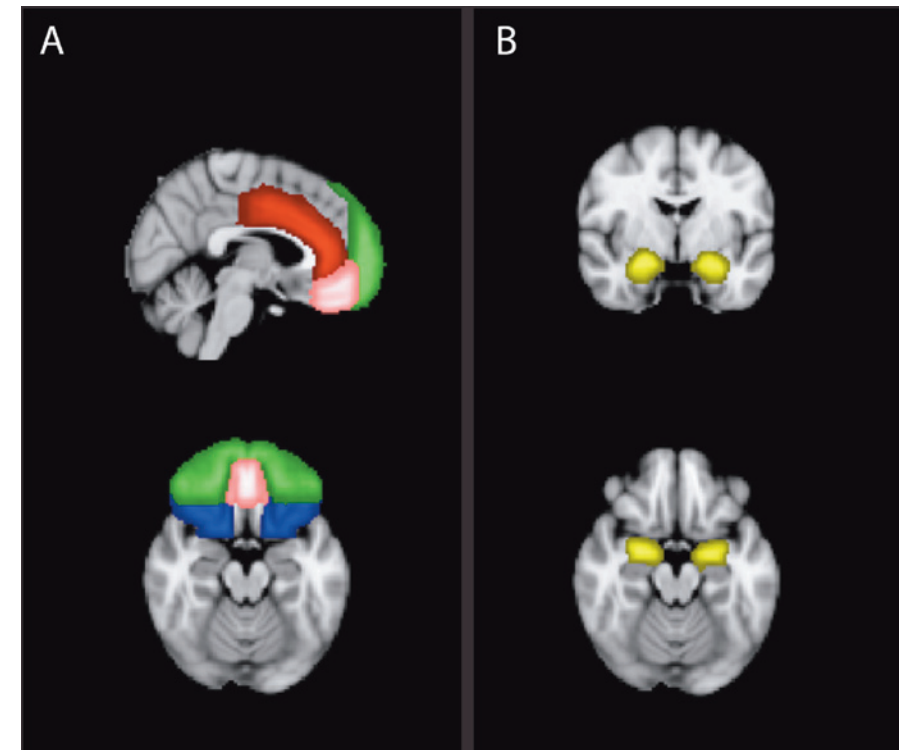

Figure 1 A. Location of the anterior cingulate cortex (red), lateral frontal pole (green) and ventromedial prefrontal cortex (pink). **B.** Location of the amygdala.

guide other areas within the network to change ongoing behavior if necessary. Thus, the lFP plays a pivotal role in adaptive behavior and given its functional and anatomical relationships to areas such as the ACC it seems a likely candidate for being involved in maladaptive behavior in psychopathy (see also Figure 2). Next, I will use the data presented in this thesis to illustrate the importance of the ACC and potentially the lFP for understanding change of behavior in psychopathy.

2.6 The anterior cingulate cortex, frontal pole, and psychopathy

The work presented in this thesis highlights the importance of broadening the focus of neurocognitive research in psychopathy beyond the amygdala and the OFC. For instance, the deficient processing of the outcomes of observed actions is consistent with the idea that the processing of specific aspects of action-evaluation in the ACC is impaired in psychopathy. The evaluation of action-values is important for quickly
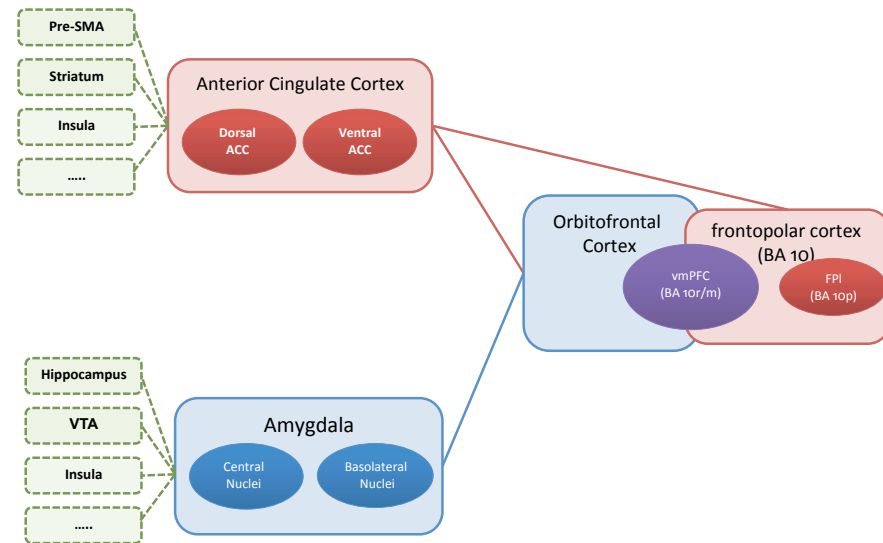
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Figure 2 Simplified schematic depiction of the proposed expansion. Blue shadings indicate areas traditionally studied in psychopathy, red indicates areas speculated to be involved based on present findings, green denotes other areas of (potential) relevance for psychopathy not discussed here.

selecting an optimal response, and this information is propagated within the same network as the amygdala and the OFC [51]. Importantly, impairments such as intact response-outcome but hampered action-outcome observation could be accounted for by considering the subregions of the ACC and their functional segregation. By doing so it would be possible to formulate hypothetical explanations for the diverging findings on monitoring own and others' action in psychopathy. Note that more detailed cytoarchitectonic decomposition has revealed as many as nine substructures within the ACC [228], but for the sake of simplicity I will adhere to the division into dACC and vACC.

The intact response ERN in psychopathy indicates that this component might be generated in subregions of the ACC that are outside the 'affective' network with the OFC and amygdala. This would correspond with the cognitively oriented dACC according to Bush et al. [229]. The dACC is believed to be involved in processing and using non-social reward information to guide behavior [164], which converges with views on the role of the dACC in monitoring self-generated choices [139]. In contrast, observing the outcomes of others' actions serves a social function and therefore it could be expected that these computations are carried out by subareas of the ACC

located in the social-affective network, as is the case for the vACC [164]. Thus, the intact response ERN in psychopathy discussed in chapters 2 and 4 indicate that the dACC appears to be functionally intact in psychopathy with respect to action monitoring. On the other hand, the smaller ERPs for observed action-outcomes in psychopathy could be because the generator of these components is located in the in more ventral regions in the ACC. However, in a recent study de Bruijn et al. [131] found that ACC activity did not differ for own and observed errors, but this could have been a consequence of the methodological and analytical approach employed. A more recent study in macaques found that there are specialized neurons in the ACC for coding own and observed errors, respectively [237]. These results support the notion that two distinct circuits exist in the ACC, one for coding the outcome of own actions and another for others' actions. Furthermore, an impaired vACC in psychopathy would also be consistent with fMRI findings showing hypoactivity in this area in both children [238] and adults with psychopathy [239].

At first glance, the reduced response ERN in psychopathy found in the reinforcement learning study seems to contradict the prediction that the dACC is intact in psychopathy. However, one important aspect to take into account is that the amplitude of the response ERN might reflect a different process during these types of tasks. That is, in reinforcement learning tasks the response ERN reflects the formation of an internal template of the action-outcome mappings that is driven by the use of the information conveyed by external feedback cues [119]. This requires the integration and use of more information relative to the action monitoring in non-learning tasks such as the Flanker task. My hypothesis is that the mechanisms involved in integrating and using information are impaired in psychopathy, and the diminished response ERN during reinforcement learning is a consequence of less information reaching the dACC rather than a functional deficiency in the dACC itself. Holroyd and Coles [240] conducted a study using computer simulations combined with electrophysiological recordings (ERPs) and interpreted the findings as evidence that the dACC integrates reinforcement-history information. But, as they did not use fMRI it is not possible to ascertain whether it is the dACC itself that carries out these computations or if it receives input from other areas involved in tracking and integrating action-related information. Given the role of the lFP in monitoring, coordinating and implementing information to guide behavior, it is also possible that this area is the one in charge of carrying out the integration of reinforcement-history and then relays the information to other areas such as the dACC. In the following section I will theorize on how the involvement of the lFP might be useful in (partly) explaining aspects of maladaptive behavior psychopathy.

The role of the lFP in integrating and using information to initiate changes in behavior resonates with the findings discussed in chapters 2-6 (see Figure 3). Reduced error awareness could be a consequence of diminished integration of the negative

action-outcome (ERN) and the increasing availability of additional contextual information. As the processing of an error transitions from automatic to controlled stages, the information carried by the ERN must be combined with information resulting from computations in other brain regions in order to initiate voluntary behavior. However, to my knowledge there is currently no direct empirical support for this prediction.

Also, the three learning studies (chapters 3, 5 and 6) consistently point out that clinical psychopathy and psychopathy-related traits in the general population are associated with diminished use of information during slow-paced adaptation (i.e., learning). These findings argue in favor of disturbed functioning of the IFP from various perspectives. First, each of the learning experiments in which impairments were found required using information resulting from multiple simultaneous computations in order to perform optimally, for instance, tracking and maintaining information about alternative choices due to the probabilistic nature of the predictive relationships (see also [227]), or considering both history of reward and social advice to reach a decision.

Second, impaired acquisition was found in the reinforcement learning study (chapter 3), but not in the study on response reversal during controlled learning (chapter 5). These results may appear to be conflicting, but could in fact be accounted for by assuming abnormal functioning of the IFP. Previous studies have shown that the IFP becomes more active as the complexity of the relational processing increases [241]. The discrepancies between the results in chapters 3 and 5 can be explained in terms of task complexity. That is, study 5 required tracking of probabilistic relationships for only two stimuli, while study 3 was much more complex as it involved monitoring contingencies for twenty-four stimuli. Therefore, it can be expected that the complex nature of the latter study should lead to greater recruitment of the IFP, and a deficiency in this area in psychopathy may lead to deficient coordination and use of information and could account for the impaired performance observed. Alternatively, it could be argued that it is not an impairment in the IFP but rather in the OFC that might account for the discrepancies. It has been proposed that the lateral part of the OFC (lOFC) is in charge of attributing an outcome to the corresponding stimulus [242]. Therefore, the more stimulus there are, the greater the chance of the lOFC attributing the outcome to an incorrect stimulus. This faulty attribution process may also account for impairments in response reversal [242,243], as it would lead to the attribution of a positive outcome to the stimulus that previously lead to this reward based on the initial contingencies learned during acquisition instead of the novel predictive stimulus after reversal of the contingencies occurs. However, in a recent study it has been pointed out that only the mOFC/vmPFC is compromised in psychopathy and not the lOFC [230]. Also, an imaging study in children with psychopathic tendencies found reduced vmPFC activation during a reversal learning task while the lateral OFC

showed normal activation [244]. Taken together, these findings argue in favor of an impairment in the IFP rather than the lOFC.

Third, a dysfunction in this brain region should lead to reduced coordination of cognitive operations within a trial and diminished integration of information, resulting in less use of the available information to adapt. The findings in chapter 6 confirm this prediction and indicate that there is an exclusive relationship between psychopathy-related traits and computational parameters capturing the use of information during learning. Future studies will need to establish whether these findings translate back to clinical psychopathy. Still, the results from chapter 2 clearly show that learning followed a much slower time course in clinical psychopathy relative to healthy controls, and the same pattern was found after the probabilistic contingencies were reversed during explicit learning as described in chapter 5. These findings provide strong indications that the computational parameters quantifying use of information should be much lower in clinical psychopathy relative to non-psychopathic samples. Finally, during Experiment 1 of chapter 5 automatic learning was predominant and it is hypothesized that the unimpaired response reversal found in psychopathy was because '*automatic processing is assumed not to rely on the integrity of the (prefrontal) brain system regulating cognitive control*' (chapter 5, p. 88). The assumption is that automatic and controlled learning are believed to rely on distinct neurocognitive circuitries and this claim has also received empirical support [245,246]. If the prefrontal system regulating cognitive control is equated with the IFP, it follows that in this study the execution of response reversal bypassed the IFP during automatic learning and therefore was not reliant on complete functional integrity of the IFP, resulting in intact automatic response reversal in psychopathy. It is worth noting that it has been claimed that the IFP (referred to as aPFC in the original paper) '*..is also involved in implicit processing of environmental changes, in the absence of awareness*' (p.90 in [247]). However, examination of the areas activated during this experiment shows that BA10 was not engaged, but that the activation was found in areas pertaining to the neighboring BA9. So it seems that other regions of the rostral frontal cortex other than the BA10 are involved in processing implicit information, but not the specific area being referred to here as IFP (or BA10p).
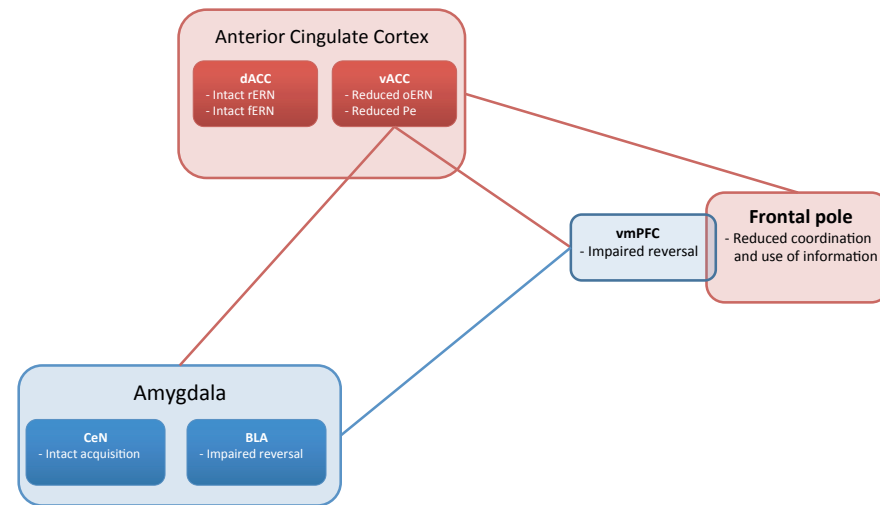
8

Figure 3 Functional embedding of the present findings in the proposed expansion.

2.7 Expanding the scope of research on psychopathy

The present findings were obtained using electrophysiology and behavioral paradigms. Therefore, some of the predictions formulated here, especially those concerning the lFP, still need to receive direct empirical support using computational modeling and neuroimaging techniques. Still, extant literature and the body of work presented in this thesis point towards functional impairments in specific subregions of the ACC and maybe in the lFP in psychopathy. The involvement of the lFP in cognitive branching and reallocation of attention might also explain some findings obtained within the framework of the RM hypothesis. Decision-making often involves maintaining primary goals online while attention is reallocated to search for significant secondary information. An impaired lFP in psychopathy could result in reduced integration of primary and secondary information, ultimately manifesting itself as a relative tendency to focus attention excessively on the established primary goals.

Finally, I would like to argue that there is a relative overfocus on the OFC and the amygdala and their functions in the literature on psychopathy, and argue that taking functions carried out by other brain structures pertaining to the same fronto-limbic network into account allows a broader and more cohesive understanding of the various neurocognitive impairments seen in psychopathy. It is also important to consider functional and anatomical segregation *within* this network because this will contribute to a broader view on cognition in psychopathy and accommodate a larger set of conflicting findings, therefore increasing explanatory power. Note that the expansion proposed here (see Figure 2) would not necessarily conflict with the

primary predictions and findings supporting the RM hypothesis, the IES model or the DAAM, but would instead complement these theories. This framework accommodates a fair portion of the findings presented in this thesis within the neurobiological framework put forth in the IES model, broadens the amygdala-centered formulation of the DAAM, and at the same time embeds the RM hypothesis in a broader and more ecologically plausible neurobiological network than the DAAM. As the areas discussed here (amygdala, OFC, ACC, lFP) are all part of the same network relevant for adaptive behavior, this notion advocates a more nuanced approach and accentuates that behavioral impairments can also be caused by variations in the interactions between several areas involved in adaptive behavior and not only of the individual brain structures (see also [51,164]). It additionally offers novel research questions regarding cognitive deficiencies in psychopathy, which should translate to impairments in various types of operations such as the modulation of prospective memory and long-term integration of and use of information relevant for adapting behavior. Future studies should investigate the integrity of these cognitive operations in clinical and non-clinical psychopathy, but also focus more on the structural integrity within the ACC and lFP in these populations, for example, using high-resolution structural imaging.

3. Treatment: the value of context for changing behavior

One primary goal of most clinical interventions within forensic psychiatry is to treat pathological behavior and cognition in order to reduce the chance of recidivism. Ideally, a patient following treatment should shift away from disruptive behavior and develop (novel) prosocial behavioral repertoires that are beneficial for their daily functioning in society. This change in behavior is not achieved in a vacuum, but occurs within a certain context. For instance, a patient could learn to control certain impulses within the safe and familiar confinements of his ward, but might fall back on previous behavioral tendencies after being transferred to a ward with less structure or even recidivate when confronted with the large amount of freedom of choice in life outside of detention. Although there may be a translational gap between the scientific work presented here and clinical practice, I believe that is useful to reflect and make inferences about how the present results might inform us about ways to develop interventions that are fine-tuned to the characteristics of psychopathy. For this purpose, I will define context as a situational property that provides additional knowledge needed to adapt optimally and that is not present or rapidly accessible within the internal knowledge structures of the individual. This situational source of information can be cognitive (e.g. instructions), social (e.g. another individual giving advice, others' non-verbal behavior), or both.

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The study described in chapter 2 investigated the ERP correlates of monitoring of one's own actions, which can be regarded as an introspective process. The finding that error awareness is disturbed in psychopathy indicates this aspect of short-term adaptive behavior is impaired when there is no obvious context providing additional information. Interestingly, the error positivity has also been related to the motivational significance of the error [94]. This presumably requires error awareness as well as information about the context in which the error occurred so that its significance can be evaluated, thus stressing the importance of context in guiding behavior. Similarly, other aspects of the same monitoring mechanism were assessed in a social context and processing impairments were found that were specific to information originating from the external environment. In the reinforcement-learning experiment we tapped into neurocognitive abnormalities pointing towards a reduced ability to generalize learning rules and applying them to new stimuli. In essence, this parallels the clinical observation that patients have problems in extrapolating newly acquired behaviors to novel contexts. The response reversal study showed how subtle variations in the amount of information provided can change the context and influence change of behavior and the computational modeling study also showed that learning from a social context is linked to traits conceptually related to psychopathy.

The present findings emphasize the importance of considering the context in which behavior must be adapted, as it might provide crucial information during treatment sessions. The first suggestion is that clinicians should be aware of the way information is provided during therapeutic sessions. Interventions promoting recruitment of automatic neurocognitive mechanisms involved in behavioral adaptation may be effective in psychopathy. One way to do this is by using computer-based approaches that stimulate automatic learning and adaptation. The second suggestion is that reducing the ambiguity in the information that is provided might have beneficial effects on treatment. This could be achieved through implicit mechanisms because patients are not aware of all the information available and experience less ambiguity, but also by doing the opposite and making the information very explicit. It has been shown that individuals with psychopathy show unimpaired decision-making when forced to stop and reflect on ongoing behavior for a few seconds [47]. This converges with the finding that individuals with psychopathy need more time to process information before a change in behavior occurs. On way to implement this would be to create protocols aimed at standardizing the context in which information is provided to promote the acquisition of prosocial behavior and to give patients with psychopathy enough time to process the information received so that it becomes very explicit and less ambiguous.

Closing remarks

The work presented in this thesis offers novel insights into the dynamics of adaptive behavior in psychopathy. It highlights the importance of exploring and translating general neuroscientific approaches to studies in (forensic) clinical populations and vice versa. Although it may take a lot of time before results obtained with this type of fundamental research can be incorporated in daily clinical practice, I believe that the body of work presented here contributes to this end. I think that (good) neurocognitive science always contributes to understanding behavior in one way or another, in the same way that every drop of water has an essential contribution to the existence of an ocean.

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Nederlandse Samenvatting
Veranderen is niet makkelijk; adaptief gedrag in psychopathie.

Bij het horen van het woord 'psychopaat' denken de meesten aan bloederige taferelen, oncontroleerbare lust voor moord en meedogenloosheid. Dit beeld van de psychopaat is ook terug te vinden in fictieve karakters zoals Hannibal Lector en Freddy Krueger. Zoals vaak het geval is, blijkt het in de praktijk anders in elkaar te zitten. Er blijken verschillende types psychopathische mensen bestaan; sommige hebben de neiging om impulsief te handelen, terwijl anderen juist goed in staat zijn om hun gedrag in de meeste situaties onder controle te houden. Het bestaan van deze subtyperingen heeft tot veel discussie geleid over de vraag wat psychopathie eigenlijk is. Daarnaast toont psychopathie veel overlap met de antisociale persoonlijkheidsstoornis, waardoor nog meer onduidelijkheid ontstaat. Tot de dag van vandaag is hierover geen overeenstemming bereikt. Wel is het zo dat er een dominante definitie is ontstaan, waarin afvlakking op sociaal-emotioneel gebied centraal staat, in combinatie met een antisociale levensstijl. Dit is dan ook de definitie die op het moment in de forensische psychiatrie wordt gehanteerd.

In Nederland bestaan er Forensisch Psychiatrische Centra, beter bekend als TBS-klinieken, waarin behandeling wordt geboden aan individuen die geweldsdelicten hebben gepleegd, en tegelijkertijd lijden aan 'een gebrekkige ontwikkeling of ziekelijke stoornis van de geestesvermogens'. Het uiteindelijke doel is om door middel van verschillende interventies het (zelf-)destructieve gedrag van deze patiënten bij te sturen, zodat ze na hun vrijlating goed kunnen functioneren in de maatschappij. Hoewel het TBS-systeem successen kent bij het behandelen van patiënten met allerlei soorten psychiatrische problematiek, blijft het een uitdaging om het gedrag van patiënten met psychopathie te veranderen. Om beter te begrijpen waarom dit zo is, is het nodig om inzicht te krijgen in wat de onderliggende mechanismen zijn van de afwijkingen van deze groep patiënten. Een manier om dit te krijgen is door te onderzoeken of het brein anders omgaat met informatie die aangeeft dat huidig gedrag aangepast moet worden, zoals fouten en negatieve feedback. Deze gedachtegang vormt de basis van dit proefschrift. De eerste 3 hoofdstukken betreffen studies waarin systematisch is gekeken naar het verwerken van fouten en feedback. In mijn studies heb ik fouten gedefinieerd als negatieve uitkomsten veroorzaakt door verkeerd handelen, denk bijvoorbeeld aan een situatie waarin u een email verstuurd heeft en u zich meteen daarna realiseert dat de bijlage niet is bijgevoegd.

Er bestaat dus een systeem in ons brein dat in gaten houdt wat de resultaten zijn van onze acties, de zogenaamde action monitoring systeem. De verwerking van dit systeem kan met behulp van hersengolfmetingen (elektro-encefalografie of EEG) worden onderzocht. Vlak nadat het systeem een fout detecteert, treedt er een piek op in de elektrische breinactiviteit, de zogenaamde *error-related negativity* (ERN).

Zoals de naam het al weggeeft gaat het hier om een signaal met een negatieve elektrische lading die gerelateerd is aan de detectie van een fout. Deze ERN reflecteert de automatische verwerking van fouten door ons cognitieve systeem. De ERN treedt op wanneer we zelf een fout maken, maar ook wanneer we negatieve feedback krijgen (dit wordt dan wel de fERN genoemd) en wanneer we andermans fouten detecteren (de oERN).

In hoofdstuk 2 wordt een studie beschreven waarbij de verwerking van eigen fouten is onderzocht bij patiënten met psychopathie ten opzichte van een groep gezonde vrijwilligers. Daarnaast is ook onderzocht in hoeverre deze patiënten zich bewust waren van de fouten die optraden. Voor de bewustwording van fouten wordt vaak een andere breinpotentiaal als maat gebruikt, genaamd de error positivity (Pe). De resultaten toonden aan dat patiënten met psychopathie en gezonden geen verschillen lieten zien in de amplitude van de ERN en dat psychopaten dus goed in staat waren om hun fouten te detecteren. Er is wel een groepsverschil gevonden voor de Pe, wat aangeeft dat ze zich minder bewust waren van het feit dat ze een fout hadden gemaakt. Dit patroon was ook in de gedragsmatige resultaten zichtbaar. Er bleek dus een onderscheid te bestaan tussen intacte automatische verwerking van fouten (de detectie) en verstoring in de bewustwording van de gemaakte fout en het aanpassen van het eigen gedrag hierop. In hoofdstuk 3 heb ik bij dezelfde groep patiënten het vermogen om gebruik te maken van negatieve feedback (de fERN) tijdens leren van straf en beloning onderzocht. De bevindingen van dit hoofdstuk laten zien dat patiënten met psychopathie moeite hebben om van negatieve feedback te leren, maar laat wel zien dát ze in staat zijn om te leren. Deze bevindingen staan haaks op de gangbare opvatting dat patiënten met psychopathie niet in staat zijn om nieuw gedrag aan te leren en mede hierdoor niet behandelbaar zijn. Wel heeft deze groep patiënten meer tijd nodig, omdat ze minder goed in staat zijn om negatieve feedback te gebruiken om hun gedrag aan te sturen. In hoofdstuk 4 wordt vervolgens een studie beschreven waarin gekeken is naar EEG-activiteit tijdens het observeren van andermans fouten. De verwachting was dat de psychopathiegroep kleinere hersenpotentialen (gemeten als de oERN) zouden vertonen na het zien van fouten die door iemand anders zijn gemaakt dan mensen zonder psychopathie. Uit de resultaten bleek echter dat ze niet alleen voor geobserveerde fouten kleinere hersenpotentialen lieten zien, maar ook voor geobserveerde handelingen die correct waren uitgevoerd. Er is als het ware sprake van verminderde verwerking van de uitkomsten van andermans acties. Dit zou mogelijk een rol zou kunnen spelen bij het ontstaan van antisociaal gedrag, maar toekomstig onderzoek zal dit moeten uitwijzen.

In het tweede deel van dit proefschrift wordt een aantal studies beschreven die voortborduren op de resultaten uit het eerste deel van mijn proefschrift. De elektrofysiologische bevindingen in deel één zijn als basis gebruikt in een aantal gedragsexperimenten. Het onderzoek in hoofdstuk 5 sluit aan op de resultaten uit hoofdstukken 2

en 3, en probeert de patroon van resultaten uit te breiden naar andere aspecten van gedragsaanpassing. Eerder onderzoek suggereert dat individuen met psychopathie in staat zijn om te leren dat bepaalde prikkels tot straf of beloning leiden. Maar in tegenstelling tot gezonde deelnemers, zijn ze niet in staat zijn om hun gedrag aan te passen als de prikkels die eerst beloond werden opeens niet meer belonend zijn. Het aanpassen van gedrag nadat de associatie tussen stimulus en bekrachtiging is veranderd is een vorm van leren die bekend staat als het uitvoeren van een response reversal. In de studie in hoofdstuk 5 is gekeken of het probleem met response reversal in psychopathie onder invloed staat van het onderscheid tussen automatische en gecontroleerde verwerking (hoofdstuk 2). Met de instructies is er geprobeerd om automatische of gecontroleerde verwerking te faciliteren in twee experimenten. De bevindingen laten zien dat patiënten met psychopathie geen moeite hebben met response reversal als leren automatisch/impliciet plaatsvindt, maar wel wanneer leren doelbewust en gecontroleerd moest plaatsvinden (expliciet leren). Kort gezegd, wanneer ze niet werden geïnstrueerd dat ze iets moesten leren konden ze hun gedrag goed aanpassen wanneer het nodig was. Dit was echter niet het geval wanneer ze de instructie kregen dat ze een leertaak aan het uitvoeren waren en ze hierdoor doelbewust om moesten gaan met informatie tijdens het uitvoeren van de taak. Deze bevindingen geven aan dat de rigiditeit die vaak aan psychopathie wordt toegekend niet per se op een leerprobleem hoeft te wijzen, maar ook kan voortkomen uit een probleem om bewust relevante informatie te gebruiken om gedrag aan te passen. In hoofdstuk 6 wordt op dit laatste dieper ingegaan. In deze studie is er gekeken of het mogelijk is om te kwantificeren hoeveel informatie mensen gebruiken om te leren. Tijdens leren combineren we verschillende bronnen van informatie en het eindresultaat is o.a. afhankelijk van hoeveel waarde we hechten aan elke bron. Het principe is dus dat als een bepaalde bron belangrijke informatie biedt, deze informatie ook een groter aandeel heeft in het leerproces. In de studie in hoofdstuk 6 heb ik gekeken in hoeverre mensen gebruik maken van sociaal advies en beloning tijdens leren. Met computationeel modelleertechnieken is er voor elk van deze twee bronnen van informatie afzonderlijk uitgerekend wat haar bijdrage was in het leerproces. Deze studie is niet bij patiënten uitgevoerd, maar bij gezonde deelnemers die geselecteerd waren op basis van persoonlijkheidstrekken die aan psychopathie zijn gerelateerd. Door deze benadering was het mogelijk om te bepalen welke persoonlijkheidstrekken gerelateerd waren aan het gebruik van sociaal advies en beloning. Uit de resultaten komt naar voren dat er inderdaad een relatie bestaat tussen een aantal aan psychopathie gerelateerde persoonlijkheidstrekken en het verminderde gebruik van zowel sociaal advies als bekrachtiging. Ook geven resultaten aan dat niet (alleen) leren, maar andere factoren de rigiditeit in het aanpassen van gedrag zouden kunnen verklaren. Toekomstig onderzoek zal uit moeten wijzen of patiënten met psychopathie dezelfde effecten laten zien.

Als laatste wordt er in hoofdstuk 7 een studie gepresenteerd die aansluit op de discussie over het verschil tussen het hebben van antisociale persoonlijksheidsstijl en psychopathie. In het experiment is er met behulp van hersenpotentialen onderzocht of deze twee groepen van elkaar verschillen wat betreft prestaties op een selectieve aandachtstaak. Tevens is een vergelijking gemaakt met mensen zonder psychopathie. In deze taak kregen de deelnemers in 80% van de gevallen de letter H te zien op het scherm (de 'standaard' stimulus), in 10% van de gevallen de letter S (de 'target') en in 10% van de gevallen telkens een nieuw leesteken (bijv. #, @, !). Bij het zien van de target moesten ze reageren door een knop in te drukken op een knoppenkast en bij het zien van een nieuwe stimulus hoefden ze niet te reageren. In dit paradigma gaan proefpersonen automatische hun aandacht richten op de target stimulus en de categorie met de nieuwe stimuli. Elke categorie veroorzaakt een karakteristieke patroon in het EEG-signaal, dat verbonden is aan het selectief richten van aandacht. Vergeleken met de gezonde deelnemers, vertoonden de twee patiëntengroepen verminderde activiteit tijdens het verwerken van de target en de nieuwe stimuli. Uit gedetailleerdere analyses blijkt echter dat de groep met psychopathie ondanks de verminderde activiteit nog steeds in staat was om de twee stimuli goed te verwerken. Dit was niet het geval bij de groep deelnemers die gekenmerkt werd door antisociaal gedrag. De conclusie is dan ook dat er bij psychopathie geen sprake lijkt te zijn van een verstoring van bepaalde vormen van aandacht en dat deze individuen met minder inzet van cognitieve capaciteit even goed de stimuli kunnen verwerken als gezonde deelnemers. Patiënten met een antisociale persoonlijkheidsstijl daarentegen laten een algemeen probleem zien in het verwerken van prikkels.

In samenvatting, het werk dat in dit proefschrift is gepresenteerd geeft nieuwe inzichten over hoe het brein omgaat met informatie bij patiënten met psychopathie. De resultaten laten zien dat deze groep patiënten moeite heeft met het verwerken van informatie die cruciaal is voor de succesvolle aanpassing van gedrag, maar ook dat dit niet voor alle aspecten van verwerking geldt. Daarnaast benadrukt een deel van de resultaten het belang van de context waarin leren en aanpassing plaats moeten vinden. De bevindingen zouden op termijn handgrepen kunnen bieden voor het ontwikkelen van behandelvormen die aangepast zijn aan de cognitieve verwerkings-stijl van patiënten met psychopathie. Wellicht heeft deze groep patiënten baat bij behandelinterventies die zich richten op automatische/impliciete leermechanismen, of andere vormen waarin de context waarin informatie wordt aangeboden is geopti-maliseerd voor deze patiënten.

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Curriculum Vitae

Inti Brazil was born on December 22nd 1982 on Curaçao, an island in the Caribbean Sea. For most of his childhood he attended Kolegio Erasmo, the only school on the island to teach in the local language Papiamentu and according to the basic principles of the humanist movement. He got his VWO (Higher Scientific Secondary Education) diploma at the Radulphus College in 2001. That year he moved to the Netherlands to study psychology at Leiden University. After obtaining his Master's degree in cognitive psychology in 2005, he worked as a junior researcher and policy officer at the Pompekliniek, a forensic psychiatric center in Nijmegen. He also held a formal appointment at the department of psychiatry of the Radboud University Medical Center during this period. After spending the first few years setting up a lab in the Pompekliniek and conducting initial studies in forensic offenders, he was successful at obtaining the NWO Mosaic grant in 2009. This grant was intended to stimulate the participation of talented non-native individuals in academia by funding a PhD studentship. For his PhD project he moved to the Department of Neuropsychology & Rehabilitation psychology at the Radboud University but also continued working as a researcher in the Pompekliniek. His project was focused on investigating the electro-physiological correlates of performance monitoring in psychopathy. In 2011, halfway through the project, he received the Koningsheide award, a prestigious prize for outstanding and innovative contribution to Dutch forensic psychiatry. During the last 2 years of his PhD project he had the opportunity to be a collaborator on various national and international projects. In May 2013 he started working as an assistant professor at the Radboud University in Nijmegen.

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