Summary

Brain mechanisms and antisocial behavior

Neurobiological research and issues concerning the explanation, reduction and prevention of criminality

Introduction

Reducing crime continues to be high on the social agenda, and how to reduce or stop criminal behaviour is an important question in this respect. In recent years, there has been a great deal of investment in the development of effective behavioural interventions aimed at reducing the chance of recidivism. Scientists have concluded that while some interventions are reasonably effective, even the most effective interventions have unsatisfactory results for many children, adolescents and adults. A number of these people may benefit from more refined diagnostic techniques and new intervention methods. Prevention is another important issue, as many criminal careers develop from serious problematic behaviour during childhood. The question is how such a development can be recognised in time and how children can be prevented from going off the rails and exhibiting criminal behaviour. The growing scientific consensus is that the approach to such issues should involve biological factors as well as social, societal, legal and psychological factors.

In recent decades, there has been tremendous growth in research providing insights into biological processes, which are part of the basis for antisocial behaviour, including criminal behaviour. Recent technological developments are an obvious reason for this. Knowledge of how the human brain works has developed rapidly thanks in part to new brain scanning techniques, such as Magnetic Resonance Imaging (MRI), which enable us to image the brain with increasing accuracy and study the brain 'in action' for the first time. In addition, molecular genetics provide many new insights on certain gene variants, which constitute risk or protective factors for antisocial behaviour. Another reason is that the formulation of theories has developed further as a result of the growing number of studies. Hypotheses on, for example, the relationships between genetic factors, child-rearing conditions, emotional and cognitive problems and the development of antisocial behaviour are more precise today than they were roughly 20 years ago.
As far as the ministry of Justice is concerned, it is important for research, policy and practice to include the development of neurobiological knowledge in addition to the existing predominantly social science and legal knowledge. In the first place, this is needed to keep up with knowledge development, fitting with the idea that policy should be increasingly knowledge-oriented and scientifically supported. Neurobiological, neuropsychological and behavioural genetic research is still relatively unknown in judicial circles. Secondly, scientific developments in neurobiology and genetics will have consequences for

keeping up-to-date and further developing diagnostics and judicial interventions. Knowledge of social and psychological diagnostics and interventions, as well as diagnostics and interventions relating to biological factors, is needed in order to (continue to) utilise the available resources for the implementation of criminal sanctions as effectively as possible. Thirdly, the development of neurobiological knowledge has implications for the prevention of criminality. In particular, this concerns the prevention of the development of antisocial behaviour which can cause serious nuisance and/or lead to criminal conviction.
Fourthly, research on the interface between social psychology and neuroscience can contribute to knowledge about factors that can promote or interfere with social cohesion. A relevant question is how we can ensure that the neurobiological research conducted in the coming years provides knowledge and insights that fit with policy and practical issues concerning crime prevention and reduction. Another important question is how knowledge on relevant developments in the field of neurobiology and genetics can be transferred to professionals, such as judges, and to study programmes in law.

This literature study has two objectives. The first is to provide a number of examples of lines of neurobiological research according to themes in the areas of sanctions and crime prevention. The reason for this is to provide an impression of where this type of knowledge fits or can fit in with issues concerning the implementation of sanctions and the prevention of antisocial behaviour, including violent crime. The second objective is to begin defining the directions in which future research could lead.

The following themes are addressed in the different sections: 'child abuse and neglect', 'problem children, dangerous adolescents and violent adults', 'sex offenders', 'judicial intervention and the reduction of recidivism' and 'neuroscience and social cohesion and conflict'. The structure of each section is the same: first, the policy context of the theme in question is outlined and research questions, which are important in the scientific support of the policy in the relevant field, are named. Then, an impression is given of neurobiological research that is relevant to the theme in question. The lines of neurobiological research discussed have been selected in consultation with experts in this area and on the basis of literature research.

The terms criminality, behaviour that transgresses moral standards, antisocial behaviour and violent behaviour overlap each other, in some areas. For example, not all convicted offenders are diagnosed with antisocial personality disorder (ASP), and not everyone diagnosed with ASP will commit criminal offences. In this study, *antisocial behaviour* is used as a collective term for the phenomena referred to above.

Findings

Child abuse and neglect

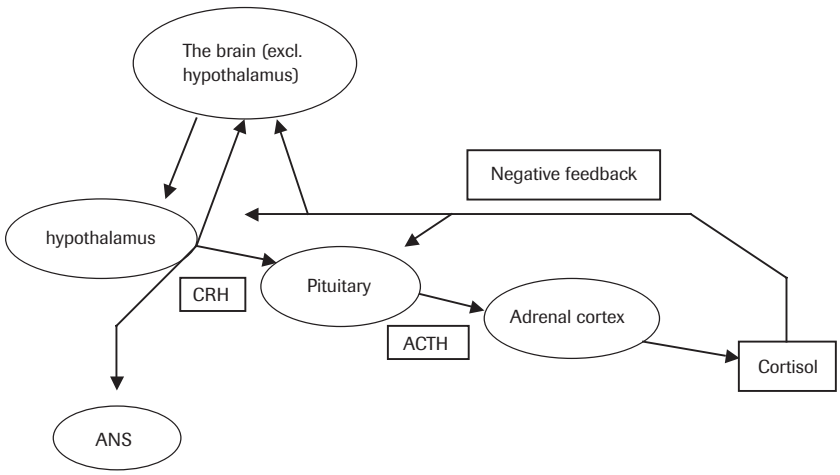
The problem of domestic violence, including child abuse and neglect, is high on the political agenda worldwide, including the Netherlands. Abuse (physical, emotional, sexual) or neglect at an early age can lead to a variety of psychological and social problems, and numerous studies have found these factors to be predictors of antisocial behaviour later in life. In order to develop effective prevention strategies and interventions, a better understanding is needed of the underlying mechanisms that create the link between childhood abuse and antisocial behaviour later in life. Knowledge is growing on the neurobiological effects of abuse and neglect. Studies show that abuse and neglect have consequences for the development and regulation of the hormonal stress system (an overactive stress system can lead to depression, while an underactive stress system can lead to antisocial behaviour), for social information processing (for example, being too quick to interpret situations or other people's behaviour as threatening or hostile). They also influence the capacity to produce chemical messengers in the brain, which play an important role in positive social behaviour and social attachment. Finally, they have negative effects on cognitive development, such as executive functioning, like impulse controlling urges and being able to adjust behaviour flexibly when the situation changes.

Not all abused or neglected children display antisocial behaviour, and the research focuses on the question of why some children do go on to display antisocial behaviour and violence while others do not. This appears to be linked to a genetic vulnerability. Studies have looked at whether the MAOA gene, which has a significant influence on the concentration of chemical messengers in the brain, plays a role. This gene occurs in both a short form and a long form. It turned out that only children who had the short variant of the MAOA gene *and* were abused had an increased chance of exhibiting antisocial and violent behaviour as adults. Abused children with the long form of the MAOA gene had the same chance of displaying such behaviour as non-abused children. Scientists wanted to know which mechanisms caused the MAOA gene to lead to an increased risk of antisocial behaviour. Research suggests that people with the short form of the gene are more sensitive to unpleasant social experiences, with the concentrations of neurotransmitters in the brain probably affecting the susceptibility to react. Neurotransmitters are chemical messengers that have significant effects on the brain and on communication between the different areas of the brain. They have a major influence on personality and social behaviour.

Other genes have also been found to be linked to an increased risk of antisocial behaviour. Besides MAOA, these include the COMT gene, the DRD4 gene and the 5HTT gene. All of these genes influence brain development, in particular the neurotransmitters and their receptors.

'Problem children, dangerous adolescents and violent adults'
The prevention and reduction of crime is high on the agenda of the ministry of Justice. Many criminal careers begin with serious antisocial behaviour and other problem behaviour during childhood. Designing and expanding effective prevention strategies requires knowledge on the development processes involved. Which mechanisms are involved in the development of antisocial behaviour, and how can children and adolescents be prevented from going off the rails and turning to crime? In addition, a greater understanding is needed of the best aspects on which to focus interventions and risk management for criminal juveniles and adults.

Figure s1 De hypothalamus-pituitary-adrenal axis (HPA-axis)



The HPA-axis (hypothalamus-pituitary-adrenal axis). In reaction to a stressor the hypothalamus produces corticotropine releasing hormone (CRH). CRH stimulates the pituitary gland to release adrenocorticotropic hormone (ACTH). ACTH induces the adrenal cortex to produce the 'stress hormone' cortisol. Cortisol prepares the body to cope with stress for an extended period of time (for instance through an increased energy supply from glucocorticoids) but can cause harm in the long run (Kahn, 2006). The elevation of cortisol levels in the blood induces the hypothalamus and pituitary via a negative feedback system to reduce the release of CRH and ACTH respectively. In this way the stress reaction declines. The activation of the HPA-axis is under the influence of brain structures such as the amygdala, and the products of the HPA-axis have effects on the brain (cortisol for instance affects mood in this way). The hypothalamus affects the autonomic nervous system (ANS) for example via CRH, which leads to an increase of heart rate and of sweat gland activity (galvanic skin response).

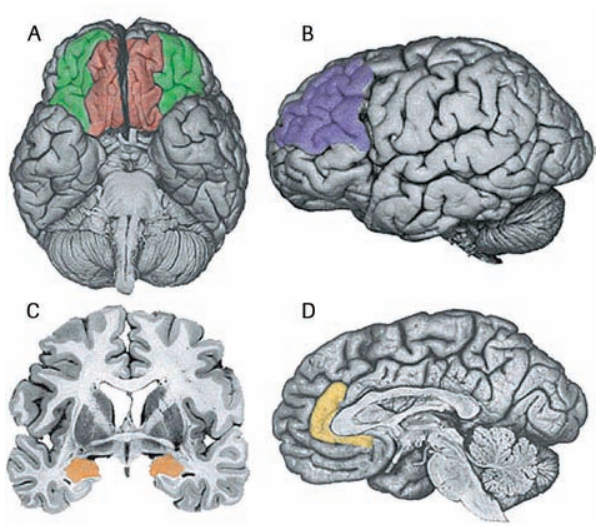
More and more research data are becoming available on the connection between a number of interrelated neurobiological systems, emotional and cognitive problems and persistent antisocial behaviour (see Figure s1). These systems are the hormonal stress system: the hypothalamus-pituitary-adrenal (HPA) axis, the autonomous nervous system (ANS), messengers in the brain (neurotransmitters, including serotonin) and a circuit of brain structures involved in emotion regulation.

The HPA axis runs from the hypothalamus to the adrenal gland via the pituitary gland. In reaction to a stressor, the hypothalamus produces CRH (corticotropin-releasing hormone), which instructs the pituitary gland to release ACTH (adrenocorticotropic hormone), which in turn stimulates the adrenal cortex to produce the stress hormone cortisol. Cortisol enables the body to cope with stress for longer periods of time (for example, by increasing the availability of energy).

The autonomous nervous system is the part of the nervous system which responds automatically to stimuli such as hunger, thirst, cold and also to stress. The ANS regulates functions such as heart rate, dilation and constriction of blood vessels, and sweat gland activity. Reactions of the ANS are prompted by activity in the higher brain areas, particularly the hypothalamus.

Emotion regulation is the extent to which emotions are experienced, expressed or suppressed. Among other structures, the emotion-regulating circuit comprises the prefrontal cortex (PFC), including the orbitofrontal cortex (OFC), the amygdala, hippocampus, hypothalamus, anterior cingulate cortex (ACC), the insula and the ventral striatum (see Figures s2 and s3). The forebrain (PFC, OFC) plays an important role in 'executive functioning', such as planning, cognitive flexibility and abstraction, and the ability to control and manage one's own behaviour (for example, emotional impulses). The amygdala is involved in emotions like fear and may also be involved in impulsive aggressive behaviour.

Figure s2 Brain structures involved in emotion regulation



Key structures in the circuitry underlying emotion regulation. (**A**) Orbitoprefrontal cortex in green and the ventromedial prefrontal cortex in red. (**B**) Dorsolateral prefrontal cortex. (**C**) Amygdala. (**D**) Anterior cingulate cortex. Each of these interconnected structures plays a role in different aspects of emotion regulation, and abnormalities in one or more of these regions and/or in the interconnections among them are associated with failures of emotion regulation and also increased propensity for impulsive aggression and violence (source: Davidson, Putnam & Larson, 2000).

Figure s3 The regulation of emotional impulses

How are emotional impulses regulated in the brain? Buckholtz and Meyer-Lindenberg (2008) conclude on the basis of results from fMRI studies, that it is plausibel that the ventromedial prefrontal cortex (VMPFC) activates the cingulate cortex (CC) which subsequently has an attenuating influence on amygdala activity, leading to the suppression of emotional impulses. In people carrying the short variant of the MAOA-gene this affect regulation circuitry may be more labile than in people with the long variant (source: Buckholz & Meyer-Lindenberg, 2008).

The aforementioned systems are closely related. The ANS and the HPA axis are activated by the hypothalamus. The hypothalamus is connected to many other brain areas involved in emotion regulation. Areas from this circuit (such as the amygdala) can also activate the HPA axis via the hypothalamus. One of the ways the brain areas influence one another is by means of neurotransmitters. Neurotransmitters are chemical substances that transmit signals from one brain cell to another, leading to increased or decreased activation of a particular function or circuit. Various areas of the emotion-regulating circuit contain numerous receptors for the neurotransmitter serotonin. Seeing a frightening situation, for example, will normally activate the amygdala, which influences the hypothalamus, which activates the HPA axis, resulting in the production of cortisol. The hypothalamus also activates the ANS, resulting in an increased heart rate and sweat gland activity.

Many studies have found a link between low autonomous nervous system activity (measured as a low heart rate and low skin response)

and reduced hormonal stress system activity (measured as a low cortisol level in reaction to stressors like frustration and provocation) on the one hand, and antisocial behaviour on the other. In addition, research on the interaction between the prefrontal brain regions and the amygdala plays a significant role in neurobiological theories on antisocial behaviour. Several studies have shown that a poorly functioning prefrontal cortex (particularly the OFC and MFC) is associated with a previous history of (impulsive) aggressive behaviour. Furthermore, dysfunctions of the amygdala and the closely related hippocampus appear to be associated with aggressive and/or violent behaviour. Among other things, the hippocampus is involved in the (emotional) long-term memory and regulation of hormonal stress system activity. Finally, there appears to be a connection between relatively low prefrontal cortex activity compared to amygdala and hippocampus activity on the one hand, and impulsive aggressive and/or violent behaviour on the other.
Several studies have found decreased levels of the neurotransmitter serotonin among people with antisocial behaviour. Neurotransmitters, including serotonin, play a role in the connections between these areas of the brain. Serotonin has 14 different receptor types, and the emotion-regulating circuit comprises many serotonin receptors. Serotonin is presumed to have an inhibiting effect on reactive aggression, partly by reducing impulsivity.

The developmental processes that lead to antisocial behaviour are diverse, and there are many different theories on the dysfunctions associated with antisocial behaviour. According to some scientists, different types of aggression may involve different neurobiological factors. Models that distinguish between reactive or impulsive aggressive behaviour and premediated or instrumental aggressive behaviour assume that persistent impulsive behaviour is related to deficits of executive functioning (prefrontal cortex), as a result of which the individual is less capable of regulating his/her own behaviour and, for example, controlling urges. Instrumental aggression is more likely to involve a dysfunction of the amygdala, as a result of which the individual is less capable of recognising emotional signals like someone else's fear and sadness, and is less sensitive to learning from the negative consequences of his/her behaviour.

Sex offenders
Sexual offences against adults and against children in particular cause a great deal of suffering and lead to social unrest. An understanding of the underlying neurobiological, psychological and social mechanisms that lead to problem sexual behaviour may contribute to (further) development of prevention and intervention strategies for sexual offences.

Several scientists suggest that paedophilia could be caused by a developmental disorder that dates back to the early childhood years or even before birth. They support this theory with a variety of data, including the results of fMRI studies. Some studies conclude that childhood head injuries occur more frequently among paedophiles, and recent studies have reported structural abnormalities in the regions of the brain involved in sexual development. Some sex offenders have been found to have more general neuropsychological deficiencies that are not specifically related to sexual offences, such as poor impulse control. There have been relatively few studies on the endocrinological aspects of sexual crime. More insight in this area could be useful with regard to risk management. For example, a recent study found that the testosterone level measured at admission to a treatment clinic could predict the chance and severity of future recidivism.

Judicial intervention and the reduction of recidivism
The reduction of recidivism is one of the spearheads of the policy of the ministry of Justice. In recent years, the prison system, the TBS (placement under hospital order) sector, the probation and aftercare service and the judicial youth policy department have increasingly opted for evidence-based diagnosis, risk assessment and behavioural interventions with the aim of reducing the recidivism risk. Time and again, meta-analyses of large numbers of efficacy studies have shown that while some of the current interventions are reasonably effective, many children, adolescents and adults receive little or no benefit from these interventions.

Research demonstrates the importance of taking into account neurobiological and neuropsychological characteristics associated with the processing of social and emotional information, the functioning of the stress system, and the regulation of one's own behaviour when developing and planning interventions. Adult detainees and children with persistent antisocial behaviour who had deficits in the functions mentioned responded poorly to a cognitive behavioural therapeutic programme. More sophisticated diagnostics, involving social and psychological aspects as well as neuropsychological and neurobiological factors, are needed in order to provide a better choice of interventions and to develop new interventions for those who do not benefit from existing intervention techniques. New intervention techniques can be based on techniques used in neurology to stimulate brain function or to suppress excess activity of certain brain cells. Examples of such techniques are Transcranial Magnetic Stimulation (TMS) and Deep Brain Stimulation (DBS). Increasingly, research is being conducted on the applications of such methods for psychological problems such as mood and anxiety disorders which are characterised by emotional problems. The suitability of TMS to stimulate certain brain functions in forensic psychiatric patients with

psychopathic personalities is being studied on a small scale. Pharmacological research on human aggression is still in its infancy, although medication against aggression is regularly applied in practice. For more long-term treatment, drugs that act on (certain receptors of) the serotonin neurotransmitter system are thought to be promising as they can have specific effects on aggression without affecting other behaviour. Scientists regard pharmacotherapy as an important part of the treatment for (subgroups of) sex offenders. Psychopharmaceuticals targeting the serotonin system (SSRIs) are frequently prescribed and have fewer side effects than hormonal libido suppressants. However, there have been hardly any controlled efficacy studies on the use of SSRIs to reduce libido and recidivism among sex offenders, and little is known about the drugs' mechanisms of action.

More has become known recently about the effects of psychological interventions on neurobiological processes. A number of examples relating to obsessive-compulsive disorders, phobias and depression have been described, which give more insight into the effects of the therapy at brain level. An example is how the reduction of anxiety during therapy is accompanied by changes in regions of the brain involved in emotion regulation.
The extent to which the neurochemical and neuroanatomical pathways involved in the regulation of emotions and aggressive behaviour are influenced by seeing aggression (on television for example) and by other 'everyday activities' is a relevant question. It has been known for some time that violent films, television and video games can increase the chance of aggression and violence among viewers or players in the short term. However, less is known about the long-term effects, partly because they are more difficult to research. The effects of violent video games may be greater than those of films because games are played actively and interactively, which is likely to involve the neural circuits more intensively. Studies show that the brain activity patterns in children who play violent video games resemble those of individuals with a disturbed aggression regulation. Whether (frequently) playing violent videogames has long-term effects on the development of neural circuits for aggression regulation would have to be investigated in a longitudinal study.

Research also shows that deficiencies of certain nutrients prenatally and in childhood can be connected to antisocial behaviour later in life. A possible mechanism by which the deficiencies could lead to an increased risk of antisocial behaviour is the disturbed development of the serotonin neurotransmitter system, which disrupts the development of emotion and stress regulation. Several studies underline the importance of early prevention through good prenatal care, which could help prevent diseases and developmental disorders as well as antisocial behaviour. Among

other things, this concerns the prevention of smoking and alcohol use and stress by the expectant mother.
Enriching the environment of children who grow up in poverty, by providing proper nutrition and activities, can also help reduce the chance of future antisocial behaviour. There is some evidence to suggest that nutritional supplements can help reduce aggressive behaviour among young adult offenders.

Neuroscience and social cohesion and conflicts
In addition to growing knowledge on the neurobiological aspects of antisocial behaviour, there is a great deal of research focusing on the neurobiological basis of positive social behaviour, such as empathy and cooperation. The discipline that specialises in this area is called social neuroscience. This is another important area of expertise for the ministry of Justice, because knowledge about factors that promote pro-social behaviour, like cooperation or complying with social standards, may help define strategies to prevent and reduce antisocial behaviour and improve social cohesion.

Empathy is an important concept in criminological theories, and there has been much psychological research on the subject. Recent studies have shed more light on the underlying neurobiological processes, showing that empathy also involves 'mirror neurons'. Mirror neurons are activated by seeing a targeted action, as well as by carrying out such an action oneself. Empathising with social emotions such as feelings of guilt, shame, pride, pleasure and disgust involves mirror neurons located in the insula. The insula is involved in processing emotional information (such as aversion, fear, anger or love) and receives input from the amygdala and other structures. The insula is thought to identify physical stimuli associated with emotions, thus contributing to the awareness of the emotional experience. More knowledge on the neurobiological factors that are important in empathy may provide a better understanding of the underlying problem of disorders such as psychopathy and autism for which one of the characteristics is a lack of empathy.
Role-play paradigms are used to study the conditions under which people are inclined to cooperate, support the common good, comply with social standards, act out of self interest and punish others who do not comply with social standards. Such experiments can at the same time reveal which processes occur in the brain, for example: which aspects of the social situation in question are rewarding or painful. In addition to social psychological and sociological research, such studies may provide more insight into the possibilities of preventing antisocial behaviour by learning more about the underlying mechanisms of pro-social behaviour and the situations in which people are inclined to behave pro-socially. Studying social processes that can lead to antisocial behaviour is

also part of social neuroscience. For example, research is conducted on the neurological aspects of social processes like stereotyping and preconception. Studies suggest that the amygdala is involved in (subconscious) preconception and also provide insight into methods to present information in such a way that the chance of preconceptions being activated is reduced. Social exclusion or ostracism is the subject of social, psychological and neurobiological research. According to scientists, there is evidence to suggest that social exclusion causes the same reactions in the brain as physical pain. People tend to use two general coping strategies when they feel excluded. The first is to seek and strengthen social connection and self-confidence, which is a relatively pro-social strategy. However, individuals who employ this strategy appear to be more sensitive to social acceptance and are willing to pay a higher price for it. The second strategy focuses on gaining recognition and restoring or controlling the social situation in some way. According to the scientists involved in this research, this strategy is more likely to lead to antisocial and aggressive behaviour than to pro-social behaviour. Ostracised individuals may be more susceptible to recruitment by extremist groups who show an interest in them.

Limitations
This study is necessarily limited. The neurosciences are rapidly developing, and the information presented here must be considered from that perspective. Only a broad outline of the different areas of research is given. This study has made extensive use of a number of important review articles and other key publications. Readers who wish to learn more about the subjects addressed should refer to these articles.
Important subjects in research on the prevention and reduction of antisocial behaviour, which have not been addressed in this study, include the neurobiology of addiction and the neurobiology of various psychiatric disorders (such as schizophrenia, anxiety disorders, obsessive-compulsive disorders and depression). This study also does not address the significance of the neurosciences in the administration of justice and law enforcement and the ethical aspects of neurobiological research in relation to antisocial behaviour.

Possible directions of research

Based on the lines of research discussed above, a number of suggestions for overall directions of research and possible applications are made.

Development and prevention of antisocial behaviour
Scientists conclude that, on the whole, we are only moderately successful in the prevention and treatment of antisocial and violent behaviour. Even

the most effective interventions do not work sufficiently for a substantial number of children, adolescents and adults. One reason for this is the lack of knowledge about underlying cognitive and emotional problems and their neurobiological causes.
An important theme for research is the relationship between genetic characteristics, stressful child-rearing conditions, functioning of the emotion-regulating circuit in the brain, the development of the stress system and the development of antisocial behaviour. Scientists propose an integrative model in which they link family factors (including genetic influences and unfavourable child-rearing conditions due to e.g. abuse or neglect) with negative behavioural effects (antisocial behavioural problems and criminality). Neurobiological deficiencies that are characterised by disinhibition (for example, abnormalities in the serotonin system, the hormonal stress system or the amygdala) and cognitive and emotional problems (such as learning and memory problems, deficiencies of the executive functions or hostile attribution processes) are mediating factors in this respect. Such a model provides good points of departure for practical scientific research.
Most of the existing research on neurobiological factors and antisocial behaviour is correlational: usually a study examines whether neurobiological deficiencies occur in a population of children or adolescents with behavioural disorders, or offenders or forensic psychiatric patients displaying antisocial or violent behaviour. No conclusions can be drawn from such studies about whether the antisocial behaviour is in fact caused by neurobiological deficiencies. However, this could be done by means of experimental studies in which, for example, medication is used to influence specific neurobiological deficiencies in order to determine whether this also causes changes in the antisocial behaviour. Another example is to influence behaviour by means of psychological treatment and verify whether this is associated with changes in neurobiological factors.
Longitudinal studies can be used to investigate whether changes in certain variables can predict changes in other variables, for example: whether unfavourable child-rearing conditions and genetic factors can bring about neurobiological, emotional and cognitive problems, which in turn combine to result in antisocial behaviour.

Diagnosis and subtyping
More use should be made of neurobiological factors in the short term, to study their value in subtyping and refinement of diagnostics supplementary to the usual psychological and psychiatric diagnostics. Diagnosis and subtyping prior to an intervention could assist in finding the most suitable intervention for an individual. They can also be used to indentify individuals for whom a particular intervention is not (yet) suitable because, for example, the individual lacks certain basic

skills needed to complete the intervention. Following an intervention, subtyping could take place to identify the individuals for whom the intervention was effective as well as those for whom it was not. This could include neurobiological parameters related to reactivity of the stress system (heart rate, sweat gland activity, cortisol reaction), functioning of the amygdala (tasks involving recognition of facial expressions, sensitivity to frightening stimuli, learning through negative consequences) and the executive functioning (such as tasks in which one's own behaviour must be adjusted or corrected).

In addition to subtyping, the neurobiological parameters could also be used to investigate the extent to which treatment objectives are achieved. Results of standardisation and validation studies of neurobiological parameters could be obtained in the short term. Some neurobiological factors, such as testosterone level, may also have added value in risk assessment.
Supplementary neurobiological instruments can also provide methodological benefits. In the context of judicial interventions, adolescents and adults are diagnosed mainly on the basis of questionnaires and interviews. These methods are sensitive to distortion, such as when individuals provide certain answers because they think they are socially acceptable. Supplementary neurobiological instruments are not as prone to such difficulties, although they do have their own limitations.
More and more is being learned about the relationship between genetic profiles and the risk of specific psychological and behavioural problems, including antisocial behaviour. Research shows that genetic characteristics can provide important information in psychiatry concerning the chance of success and side affects of the application of medication. Several scientists expect that genetic profiles will play a more significant role in the needs assessment for (behavioural) interventions in the future. It is important to consider how and under which conditions such information can be used with regard to needs assessment and evaluation of judicial interventions. Subtyping on the basis of genetic profiles in order to acquire more knowledge through research could be an initial step in this.

Renewal of interventions
Firstly, neurobiological factors can contribute to the further development of interventions already used in the judicial context, such as cognitive behavioural therapeutic programmes and pharmacological treatment. Secondly, they can contribute to the development of new interventions, including interventions already developed and studied for efficacy in other settings, but not yet applied in the judicial context, such as neuropsychological tasks used in a teaching and education context, which

stimulate certain brain functions that are also important in relation to antisocial behaviour. The possibility of training subconscious thought processes is being studied in addiction research. This may be also useful for children or adults with antisocial behaviour who express a 'hostility bias', the tendency to interpret ambiguous situations as hostile. Research is also being conducted on the possibility of influencing the sensitivity to punishment and reward by means of neuropsychological tasks or neurological techniques like TMS. Furthermore, the use of reward paradigms may be an alternative in behavioural interventions and parent training for (young) offenders who are less sensitive to punishment but who are strongly reward-oriented.

Increasing knowledge on the mechanisms behind the effects of neglect and abuse on (later) behaviour may eventually provide a basis for the renewal of interventions. This could include interventions that support the development of social information processing and cognitive functions, such as training executive functions. Some scientists also recommend researching whether the administration of oxytocin could help people who do not produce enough oxytocin themselves. A link is also being made between low reactivity of the hormonal stress system, as found in children who exhibit a lot of antisocial behaviour, and cognitive and emotional problems (such as an increased tendency to interpret social situations as hostile). Scientists argue that the cortisol peak that occurs in normal test subjects in response to a stressful event may be necessary in order to assess the nature of a conflict and respond in a proportional manner. Such a cortisol peak is *not* found in children with antisocial behaviour. A hormonal stress system that does not function as well as it should, as seen among antisocial children, may hinder the cognitive and emotional information processing needed for behavioural therapeutic interventions. In that case, treatment of children with reduced base cortisol levels or a reduced physiological reaction to stressors may be more effective if the operation of the hormonal stress system is normalised medicinally first, before offering behavioural interventions. More scientific research could be conducted on the dysfunctions and pharmacological treatment possibilities of the HPA axis in children and adults with antisocial behaviour.

Pharmacological treatment in addition to and in combination with psychological interventions may also be beneficial, particularly for severe aggression. Pharmacotherapy of human aggression is an area in which relatively little research has been conducted. Research into the neurobiological factors associated with antisocial behaviour and the models for different types of abnormal human aggression can undoubtedly form an important source of inspiration. There are examples of research in which imaging techniques are used to gain more

insight into the active mechanisms of medication therapy for aggressive behaviour.
On the basis of current data, pharmacotherapy is regarded as a promising part of interventions for boundary-transgressing sexual behaviour, in addition to psychological treatment and supervision. Although medication is applied specifically to these aspects, little is known about the neurobiology and endocrinology of different types of boundary-transgressing sexual behaviour. For example, it could be important to investigate if and in which parts of the hypothalamus-pituitary-gonadal (HPG) axis and the HPA axis abnormalities may occur among sex offenders. A better understanding of these mechanisms could contribute to an increase in the efficacy of (pharmacological) interventions.
There is a great shortage of methodologically sound efficacy studies on pharmacotherapy in humans with severe aggression as well as libido-suppressing medication in sex offenders, even though such medication is regularly used in practice.

More and more research is being conducted on candidate genes that may be considered risk factors for specific problems, including psychiatric disorders, addiction and persistent antisocial behaviour. The suspected likelihood of the importance of interactions between genetic predisposition (such as variants of the MAOA gene, DRD4 gene, COMT gene or 5HTT gene; see Appendix 3 for explanation), brain development and environmental factors (unfavourable child-rearing conditions) in the development of antisocial behaviour has been discussed above. Medication tailored to the patient's genetic profile is used for different somatic diseases (for example, in breast cancer treatment), and 'pharmacogenetics' are also being used increasingly in research and treatment of psychiatric illnesses. These developments may also be important in research on interventions for antisocial behaviour, for instance with respect to variants of MAOA and other genes that affect brain development.

An increasing number of studies use imaging techniques such as fMRI to show that psychological treatment can affect biological processes in the brain. Such research is important because it can increase our understanding of the active mechanisms of psychotherapy. It is advisable to acquire such knowledge on psychological treatments aimed at reducing antisocial behaviour as well, which knowledge could then be used to develop the most effective psychological treatments possible.

Broadening and interdisciplinarity
Many of the neurobiological studies discussed in this study involve violent offenders, forensic psychiatric patients or children or adolescents with behavioural disorders. It would be useful to extend this research to other

populations to determine whether the findings concerning neurological processes associated with antisocial behaviour can be utilised in a broader perspective. An example is the possibility of customising measures imposed on people who commit traffic offences involving aggression or reckless behaviour. Another example is (lighter) forms of antisocial behaviour, such as vandalism and hooliganism.

The discussed research is also relevant to cooperation of the judicial authorities at local level, for example with municipal authorities, partly because the discussed insights are relevant for promoting social cohesion as well as identifying and reducing antisocial behaviour. Furthermore, the discussed research is relevant to areas such as youth care and mental and general health care. Examples include the problem of aggression in regular psychiatry, the relationship between stress and aggression, the relationship between stress and depression, and the importance of early prevention and prenatal care. In addition, the neurobiological insights and lines of research addressed are important in education. These subjects should be given more attention in university and post-university education in law. Neurobiological research on antisocial behaviour is also important in primary and continuing education because, for example, this can lead to a greater understanding of how to deal with antisocial behaviour among students.

Many scientists agree that researchers from different disciplines should work together to study complex issues like antisocial behaviour at multiple levels. Better use could be made of adjoining fields of research, for example in collaborative projects, when studying issues with regard to crime prevention and reduction. This applies for instance to fields, such as health care, education and studies on animals. Cause and effect relationships can often be researched in animals using experimental studies that cannot be performed on humans for practical and/or ethical reasons.

Conclusions

Neurobiological and behavioural genetic scientific research has had a significant influence on general psychiatry in the last decade. It has contributed substantially to the understanding of psychiatric disorders such as schizophrenia and depression. Neurobiological and behavioural genetic research is still relatively unknown in legal circles, and it is still underused in policy, practice and scientific research with regard to judicial interventions. This applies to forensic psychiatry, behavioural interventions and forensic care in the prison system and juvenile institutions, outpatient treatment and (probation) supervision.

In summary, the lines of neurobiological research discussed in this study can aid in:
- Gaining a better understanding of the underlying mechanisms and driving forces of antisocial behaviour
- Keeping existing behavioural interventions up to date
- Keeping up to date and further developing diagnostic tools and risk management tools
- Selecting the most suitable interventions (subtyping)
- Developing new interventions for individuals who do not respond to traditional interventions
- Gaining further insight into the underlying mechanisms of the development, maintenance and discontinuation of antisocial behaviour
- The further development of knowledge on protective factors against the development of antisocial behaviour
- Gaining more insight into the possibilities of preventing children and adolescents from turning to antisocial behaviour
- Influencing the (Dutch) research agenda to ensure that neurobiological research relevant to (future) judicial applications is conducted.

Finally, the following four recommendations are made:
1 The underlying principle should be that biological parameters should be just as involved in research, diagnosis and treatment as psychological and social parameters. Without the biological factors, we will miss important underlying mechanisms and driving forces of (antisocial) behaviour.
2 Ensure interdisciplinary research involving social, psychological and biological factors as well as scientists from different disciplines.
3 Involve practitioners (for example, care providers in custodial institutions) in the development of research plans and questions from the start, and do not wait to involve them until scientific findings are ready for application in practice.
4 Ensure the transfer of knowledge to society, and to study programmes for lawyers and others who are active in judicial policy and in practice.

The main conclusion of this literature study is that the studies discussed support the argument that neurobiological factors deserve a structural place in research into the causes, prevention and reduction of antisocial behaviour.