Chapter 1

General Introduction
At the start of the 19th century Stanley Hall (1904) published his work *Adolescence*, which is widely viewed as the beginning of the scientific research field on this developmental phase. Since then, there has been much progress in the understanding of adolescence, with knowledge converging from various research disciplines (Dahl & Hariri, 2005). The World Health Organisation (WHO) identifies adolescence as a critical transition in the life span, characterised by growth and change. Indeed, it is a period of rapid changes in hormones and brain development. Simultaneously, at a behavioural level, it typically involves impulsivity, novelty seeking and heightened emotions, in combination with limited capacities of self-control. This is a cause of vulnerability to unhealthy behaviours, but also creates unique opportunities for learning, flexibility and positive motivations relevant to adolescent development (Crone & Dahl, 2012). Adolescence is, however, a peak time for the onset of several mental illnesses (Costello, Egger, & Angold, 2005). One of the most frequent reasons for referral to mental health services of children and adolescents are behavioural problems (Armbruster, Sukhodolsky, & Michalsen, 2004; Rutter et al., 2011; Rutter, Giller, & Hagell, 1998). Global trends regarding antisocial behaviours have shown to be stable or decreasing since the 1990s in many countries (Collishaw, 2015). However, it has also been shown that mental health care (i.e., outpatient visits to physicians in office-based practice) of children and adolescents in the U.S. has increased, especially with respect to disruptive behaviour disorders (Olfson et al., 2014). In Europe the number of youths with severe antisocial behaviour (i.e., Conduct Disorder) has been estimated at 2.1 million (Wittchen et al., 2011). Notably, early-onset of antisocial behaviour has shown to predict a variety of negative life outcomes in adulthood and brings considerable costs for society (Cohen & Piquero, 2009; Odgers et al., 2007; Scott, Knapp, Henderson, & Maughan, 2001). Because of its high prevalence and societal costs, research on the development of adolescent antisocial behaviours has become a major interest for global researchers, caregivers and policymakers.
Research has paid particular attention to adolescents who show severe antisocial behaviours from an early age and persist well into adulthood. Interestingly, Hall already noted the universal increase in criminality during adolescence in *Adolescence* (1904), as well as the fact that some will continue and others will desist from it as they mature. In this regard, Moffitt (1993) postulated an influential theoretical framework proposing two separate developmental trajectories of antisocial behaviour, consisting of an adolescent-limited and life-course-persistent type. The adolescent-limited type was thought to have a late onset of antisocial behaviour (>10 years old), which gradually decreases over time and as such desists from adolescence into adulthood. The life-course-persistent type on the other hand, was thought to have an early onset (<10 years old) with antisocial behaviours that are persistent into adulthood (Moffitt & Caspi, 2001). According to this theory adolescents desist (the adolescent-limited type) due to the ability to adapt to changing contingencies. It was postulated that social mimicry of life-course persistent adolescents explains the onset of the adolescent-limited type, facilitated by motivational and learning mechanisms. Likewise, these mechanisms are thought to cause the desisting of antisocial behaviour for the adolescent-limited type when delinquent behaviours shift from rewarding to punishing and the adolescent exits the maturity gap (Moffitt, 1993). Neurobiological deficits have been identified specifically in the life-course persistent type, as compared to the adolescent-limited type (Moffitt & Caspi, 2001). However, more recently it has been shown that adolescents with a late onset (adolescent-onset type) often persist into adulthood as well, which may also be partly explained by neurobiological problems (Fairchild, van Goozen, Calder, & Goodyer, 2013). Validity of the adolescent-limited versus life-course persistent subdivision has been further debated, for example, studies showing childhood-limited and varying ‘intermediate’ trajectories of antisocial behaviour (Geluk et al., 2014; Odgers et al., 2007; Piquero, 2008). It remains unclear what the underlying mechanisms are of each trajectory and what factors are able to differentiate between children in these different trajectories (Fairchild, van Goozen, et al., 2013).

Adolescents who show severe, frequent and persistent antisocial behaviours often end up in the juvenile justice system. Such an imposed intervention is often a last resort. However, it does not always lead to a reduction of problematic behaviours, since recidivism rates after incarceration are high (Wartna et al., 2012; Wartna, Kalidien, Tollenaar, & Essers, 2006). In the
Netherlands, a new compulsory residential treatment programme was implemented in 2008 for treatment of highly problematic adolescents. Adolescents in this programme predominantly show externalising problem behaviours (98%), i.e., aggression and delinquent behaviours (Van Dam, Nijhof, Scholte, & Veerman, 2010). The residential treatment programme is based on the social competence-model (Slot & Spanjaard, 1999) and comprises five treatment stages, working from a closed ward towards a more open environment in which the adolescent can function increasingly more autonomously. The main goal of the programme is to offer the adolescents future perspective. It provides a basic stable environment with a daily routine. Education, guided leisure activities and homework assistance are important aspects of the standard treatment programme. Additionally, the adolescents may receive individual complementary interventions, such as cognitive behavioural therapy (CBT), systemic therapy or eye movement desensitization and reprocessing (EMDR) therapy. Promising treatment results have been reported by adolescents and parents involved, however group care workers have reported worsening of problem behaviours (Nijhof, Veerman, Engels, & Scholte, 2011). In a more recent paper evaluating evidence on the effectiveness of compulsory residential treatments, it was concluded that there is evidence for an overall positive effect of such interventions (Souverein, Van der Helm, & Stams, 2013). However, this is a modest positive effect and there is still much room for improvement of treatment programmes offered in residential care. As such, more research towards the development and persistence of adolescent antisocial behaviours is needed in order to better understand its origins and ultimately provide novel treatment targets or help improve existing treatments.

In the Diagnostic and Statistical Manual of Mental Health Disorders (DSM), disruptive behaviour disorders (DBD), typically involving antisocial behaviours, are subdivided into Oppositional Defiant Disorder (ODD) and Conduct Disorder (CD). Both ODD and CD are typically diagnosed in childhood or adolescence. ODD presents itself as a pattern of angry/irritable moods, argumentative/defiant behaviour, and/or vindictiveness. CD involves a repetitive and persistent pattern of behaviour in which the basic rights of others or major age-appropriate societal norms or rules are violated. In a study investigating prior juvenile diagnoses in adults with mental disorders it was shown that CD and/or ODD may be part of the developmental history of virtually all adult mental disorders (i.e., anxiety-, depressive-, eating-, substance
use- and antisocial personality disorder, schizophrenia and manic episode), with 25% to 60% showing a history of CD and/or ODD (Kim-Cohen et al., 2003). This highlights the importance of antisocial behaviours in youth with regards to mental health later in life.

It is acknowledged that the population of children and adolescents diagnosed with CD and/or ODD is rather heterogeneous, both with respect to behaviour and aetiology. In addition to the formal DSM diagnoses many other terms are used to define pathological or problematic antisocial behaviours. Researchers have used many ways of further subdividing antisocial behaviour in children and adolescents in order to create more homogeneous groups e.g., delinquency, psychopathy, conduct problems and reactive versus proactive aggression. The subtyping of antisocial behaviours is thought to be useful for facilitating greater understanding and matching with underlying neurobiological mechanism and constructing more specific interventions and treatments (Blair, White, & Meffert, 2014; Connor, 2012; Vitiello & Stoff, 1997).

One of the common approaches is to subdivide antisocial behaviours, specifically aggression, based on function or motive, into reactive and proactive aggression. Reactive aggression is known as an emotionally charged response or frustration and is also referred to as ‘impulsive’, ‘hot-blooded’ or ‘affective’ aggression (Dodge & Coie, 1987; Kockler, Stanford, Nelson, Meloy, & Sanford, 2006; Stanford et al., 2003). Proactive aggression is conscious and planned, used for personal gain and also referred to as ‘premeditated’, ‘cold-blooded’ or ‘instrumental’ aggression (Blair, Peschardt, Budhani, Mitchell, & Pine, 2006; Blair, 2001; Blakemore & Choudhury, 2006; Dodge & Coie, 1987; Frick & Ellis, 1999). Literature has provided evidence of specific characteristics for reactive and proactive aggression, such as peer status (proactive aggression relates to more positive status), biological measures (higher heart rate for reactive aggression) and social information processing (reactive aggression relates to early stages and proactive to late stages of processing) (for a review see, Kempes, Matthys, de Vries, & van Engeland, 2005). However, it has also been shown that reactive and proactive aggression often co-occur in the same individual and only small groups are characterised as reactive or proactive only (Kempes et al., 2005). Therefore, it remains uncertain how meaningful the distinction between reactive and proactive aggression is at the level of the individual (person-based). A distinction between these subtypes at a dimensional level might be more appropriate (e.g., Blair et al., 2014).
Social-cognitive processes

Cognitive processes are thought to play an important role in the development and persistence of antisocial behaviours and neurobiological mechanisms have recently gained more attention in this respect (Lee et al., 2014; van Goozen, Fairchild, Snoek, & Harold, 2007). Social cognitive processes focus on how people understand the social world around them, by making sense of other people and their actions, including oneself. Such processes are typically researched in the context of how social perceptions translate into (appropriate and inappropriate) social responses. Models of social-cognitive processing assume that a social event (stimulus) leads to social-cognitive processing of the event, which in turn leads to a certain behavioural outcome (response). Individual social-cognitive processing forms a mediator between the stimulus and the outcome produced and the individual becomes able to respond to the stimulus. However, when this is problematic, there might be less rationale or control over the outcome.

The Social Information Processing (SIP) model assumes that in a social situation, the behavioural outcome is achieved by six sequential processing steps: (1) encoding of external and internal cues, (2) interpretation of cues, including attributions, (3) goal clarification or selection, (4) response generation, (5) response decision, including response evaluation, outcome expectancies, self-efficacy, response selection and the last step involving (6) behavioural enactment (Crick & Dodge, 1994). When problems occur in one of these steps, this may lead to problematic behaviour. It has been suggested that the origin of aggressive behaviours lies within one or multiple problems in the processing of social information (Crick & Dodge, 1994). For instance, it has been shown that attributing hostile intent to others (also referred to as the hostile attribution bias) is linked to aggressive behaviour in several antisocial populations (Orobio de Castro, Veerman, Koops, Bosch, & Monshouwer, 2002) and may predict future aggression (Dodge, 2006). However, little research has included all six sequential SIP steps and various methodological instruments have been used.

Social information processing is influenced by mental structures in the ‘database’, which stores memories and past experiences (Crick & Dodge, 1994). This database consists of latent mental structures and schemata’s and is thought to influence the different sequential steps in the SIP model. These social-cognitive structures influence and mediate the online decision-making process,
connecting external situations to the outcome of social or antisocial behaviour (Huesmann, 1998). In this regard social cognitions, specifically ‘self-serving’ cognitive distortions are thought to contribute to harmful acts against others and are typically linked to aggression and delinquency (Barriga, Hawkins, & Camelia, 2008; Barriga, Morrison, Liau, & Gibbs, 2001).

Promising cognitive behavioural interventions aim to produce changes in cognition, feelings and behaviour (Kendall, 2011; Lipsey, Landenberger, & Wilson, 2007), targeting cognitive (antisocial) biases, beliefs, attributions and schemata’s in order to change problem behaviour. The distinction between reactive and proactive aggression seems particularly promising regarding the assumed underlying social-cognitive processes. Reactive aggression is defensive, frustration based and involves hostile attributions, while proactive aggression is instrumental and stems from positive outcome learning (Merk, Orobio de Castro, Koops, & Matthys, 2005). However, little research has investigated whether reactive and proactive aggression involves distinct social-cognitive processes and whether changes in these processes elicit behavioural changes. The current dissertation will investigate social cognitive processes, both social information processing and self-serving cognitive distortions, involved in reactive and proactive aggression in adolescents.

Executive functioning

Adolescence is an important transitional period from childhood to adulthood, a time of increasing cognitive control, i.e., executive functioning (Crone, 2009; De Luca et al., 2003; Huizinga, Dolan, & van der Molen, 2006). Executive functions are cognitive abilities including planning, inhibition, working memory and cognitive flexibility that are involved in more complex cognitions such as decision-making, modifying behaviour and solving problems. They are important for many every-day situations and are involved in adapting one’s behaviour to the constantly changing environments (Jurado & Rosselli, 2007). Research has shown that poor executive functioning is related to various antisocial behaviours (including delinquency, conduct disorder and psychopathy) and it is thought to be a risk factor for the development and persistence of these behaviours (Morgan & Lilienfeld, 2000; Ogilvie, Stewart, Chan, & Shum, 2011).

Executive functioning has traditionally been linked to the frontal lobes of the brain, but it is now understood to involve interconnections between
cortical and subcortical areas (Heyder, Suchan, & Daum, 2004). It has been argued that dysfunctions of the frontal lobe (i.e., orbitofrontal cortex) leads to impaired decision making in antisocial individuals (Blair, 2004). Structural (and functional) disruptions in frontal brain areas might manifest in poorer executive functions, which in turn facilitates poor decision-making and the development of antisocial behaviours. Research exploring the predictive value of executive functioning for behavioural changes and/or treatment resistance in terms of antisocial behaviours is very scarce and results have been contradictory (Cornet, van der Laan, Nijman, Tollenaar, & de Kogel, 2015; Fishbein et al., 2009; Mullin & Simpson, 2007). In this respect, adolescence is of particular interest, as this is a period of rapid developmental changes (i.e., cognitive growth) and disruptions in the neurodevelopmental processes will manifest in the brain (Lee et al., 2014). However, research on the predictive value of executive functioning for behavioural change among antisocial children and/or adolescents is even more limited. As such, the current dissertation will investigate whether executive functioning can predict changes in terms of antisocial behaviour in severely antisocial adolescents.

**Structural brain development**

It has been proposed that executive functions and social cognitions in adolescence are influenced by structural changes in the brain (i.e., development) (Blakemore & Choudhury, 2006). The human brain does not develop fully until early adulthood and regional brain areas undergo different growth trajectories (Shaw et al., 2008; Wierenga, Langen, Oranje, & Durston, 2014). In this regard, Structural Magnetic Resonance Imaging (MRI) techniques (neuroimaging) are able to provide detailed images of the brain. Many neuroimaging studies have reported structural abnormalities related to antisocial behaviours (e.g., aggression, psychopathy and conduct disorder) in the frontal lobes, the temporal lobe and structures in the limbic system (e.g., De Brito et al., 2009; Fairchild et al., 2011; Fairchild, Hagan, et al., 2013; Wahlund & Kristiansson, 2009; Weber, Habel, Amunts, & Schneider, 2008).

The importance of considering the development of the brain when researching adolescent mental health has recently been highlighted, recognising adolescence as a time of vulnerability, but more importantly, as a time of opportunity for treatment (Crone, 2009; Lee et al., 2014). Deviant development
of the brain may represent a vulnerability for developing psychopathology (Di Martino et al., 2014; Shaw, Gogtay, & Rapoport, 2010). It has been proposed as an intermediate phenotype (i.e., a bridge between genetic and phenotypic factors) for neurodevelopmental disorders (Giedd, 2008). In this regard, in attention-deficit/hyperactivity disorder (ADHD) a maturational delay has been shown to normalize which was in turn related to clinical outcome (Shaw et al., 2010). There are some first indications that a delay in brain maturation might underlie antisocial behaviours (i.e., conduct disorder) (De Brito et al., 2009), however longitudinal studies are lacking. Deviant development of the brain during adolescence may be involved in the development and persistence of antisocial behaviours. In this dissertation structural brain development is investigated in relation to antisocial behaviour during adolescence.
The current dissertation

This dissertation aims for a better understanding of the underlying mechanisms of adolescent antisocial behaviours by investigating cognitive and neurobiological processes involved in various degrees of antisocial behaviour, as well as in developmental trajectories of adolescent antisocial behaviour. The ultimate goal is to help provide new insights for prevention strategies and treatment of antisocial behaviours (Lee et al., 2014; Vaske, Galyean, & Cullen, 2011).

In Chapter 2 the study aimed to provide greater insight into the clinical usefulness of subtyping antisocial behaviours in reactive versus proactive aggression in adolescents.

In Chapter 3 it was investigated which Social Information Processing (SIP) problems are differentially related to reactive and proactive aggression, providing more insight into the distinct SIP problems involved.

In Chapter 4 social cognitive distortions were studied in relation to reactive and proactive aggression. Firstly, it was investigated whether reactive and proactive aggression were differentially related to specific types of self-serving cognitive distortions. Secondly, it was investigated whether changes during treatment in these cognitions related to changes in reactive and proactive aggression.

In Chapter 5 it was investigated whether executive functioning was related to conduct problems in severely antisocial adolescents and whether executive functioning could predict behavioural changes.

In Chapter 6 distinct trajectories of conduct problems were related to structural brain development during adolescence.

Finally, in Chapter 7 it was investigated whether white matter integrity was related to severity of conduct problems in adolescence.
References


