General introduction
The start of a new chapter in one’s life is an exciting time filled with personal, social, cognitive and environmental changes. Transitioning into adolescence is such a period that begins between the ages 9 and 12 with biological maturation related to the onset of puberty (Dahl, 2004). This stage is accompanied by increased identity exploration and importance of peers (Pfeifer & Peake, 2012). During these years, children pursue middle education and show great advancements in learning (Steinberg, 2005). The transition out of adolescence is marked by independence from parents (Casey, Duhoux, & Cohen, 2010). In modern society, the start of adulthood is commonly delayed since many young people have prolonged academic trajectories. The period around 18 to 25 years can therefore be considered a separate developmental phase in which new relationships are formed, financial responsibility is reached and a college degree might be obtained (Arnett, 2004). Since the past decade, there has been a lot of research attention for neural changes that underlie behavior throughout adolescence (Galván, Van Leijenhorst, & McGlennen, 2012). Previous functional Magnetic Resonance Imaging (fMRI) studies mostly used samples that were small or encompassed a wide age range (Paus, 2005). The objective of this thesis is to gain more insight into development of brain regions subserving social and cognitive processes, specifically from late childhood to early adolescence and from late adolescence to young adulthood.

**Structural brain maturation**

When girls are about 11 years old and boys are about 14 years old, total volume of the cortex peaks (Lenroot & Giedd, 2006). Over the course of adolescence, gray matter volume decreases while white matter volume increases. These patterns are thought to result from myelination of neurons, improving processing speed, and the loss of unused synapses, increasing neural efficiency (Toga, Thompson, & Sowell, 2006). Concurrently, connections are formed between distinct parts of the brain which leads to enhanced control of behavior (Asato, Terwilliger, Woo, & Luna, 2010). Different brain regions change at varying rates, with higher-order areas maturing later than sensory ones (Gogtay et al., 2004). There are individual differences in development, e.g., males show larger decreases in gray matter volume than females (Koolschijn & Crone, 2013) and intelligent children have a more
plastic cortex (Shaw et al., 2006). Brain maturation continues until young adulthood, particularly in prefrontal and parietal areas important for cognition (Giedd & Rapoport, 2010). In freshman students aged 18 and 19, anatomical changes have been related to the environmental transitions of entering higher education and moving away from home (Bennett & Baird, 2006). It appears that structural development of the cortex is associated with functional brain changes that characterize adolescence (Blakemore & Choudhury, 2006; Casey, Tottenham, Liston, & Durston, 2005).

Social development

For operating in the social world, it is crucial to understand one’s own and others’ personality traits, preferences and beliefs. The ability to encode the mental states of others has been termed ‘mentalizing’ or ‘theory of mind’ (Frith & Frith, 1999). Recent evidence indicates that this ability already emerges in the first year of life (Kovács, Téglás, & Endress, 2010). Social development starts to accelerate after late childhood, as adolescents focus on being popular, spend much time with friends and are sensitive to rejection (Nelson, Leibenluft, McClure, & Pine, 2005). Fine-tuning of the capacity to take someone else’s perspective continues at least until late adolescence (Dumontheil, Apperly, & Blakemore, 2010). At a neural level, the medial prefrontal cortex, medial posterior parietal cortex and temporoparietal junction have been implicated in social cognition (Van Overwalle & Baetens, 2009). The medial prefrontal cortex is particularly activated during self-processing while the medial posterior parietal cortex and temporoparietal junction are preferentially engaged during other-processing (Qin et al., 2012; Saxe, 2006). The roles of these regions change with age, suggesting the use of different strategies in children, adolescents and adults (Blakemore, Den Ouden, Choudhury, & Frith, 2007; Pfeifer, Lieberman, & Dapretto, 2007).

Cognitive development

Performing well in everyday settings requires ‘cognitive control’, the skill of regulating behavior in a goal-directed manner. Cognitive control includes
subcomponents such as inhibition, switching and monitoring, also named ‘executive functions’ (Alvarez & Emory, 2006; Jurado & Rosselli, 2007). These functions come online during infancy while great improvements occur throughout adolescence (Luna, 2009). Separate executive functions mature at different ages (Huizinga, Dolan, & Van der Molen, 2006). As demonstrated by fMRI research, developmental changes in cognitive control are linked to increased recruitment of the medial and lateral prefrontal cortex, lateral parietal cortex and striatum (Bunge & Wright, 2007). A meta-analysis implied that prefrontal activation may increase or decrease over adolescence, depending on the task and context (Crone & Dahl, 2012). Notably, studies using sensitive methods indicate that young adults still demonstrate subtle difficulties with inhibition and switching that are evident in children (Diamond & Kirkham, 2005; Leroux et al., 2009).

**Individual differences**

Social and cognitive developmental paths vary widely between adolescents. There are clear individual differences associated with sex, intelligence, personality and culture. Some research has focused on male/female differences as a source of between-subject variation. For example, it has been observed that mentalizing speed increases during adolescence and that across age, girls are faster than boys (Keulers, Evers, Stiers, & Jolles, 2010). An fMRI study on perspective taking found that female adults engage more emotion-relevant brain regions and male adults recruit more cognitive areas (Derntl et al., 2010). Christakou and colleagues (2009) examined sex differences in the maturation of cognitive control in 13 to 38 year olds. Stronger prefrontal activation with age was seen in females while males showed age-related parietal activation. In the current thesis, individual differences are taken into account by a) investigating the effects of age and sex on social and cognitive processes or b) using homogeneous groups with respect to age, sex and academic performance.

**Relevance for education**
Knowledge about the neural bases of social and cognitive development is of interest for educational practice. Understanding how the brain works can help teachers with instruction and guidance of children (Carew & Magsamen, 2010; Goswami, 2006). Teachers would benefit from more insight into the acquisition of domain-general abilities, e.g., cognitive control, that affect learning of specific skills including math and reading (Ansari & Coch, 2006; Immordino-Yang & Fischer, 2010). Executive functions such as inhibition and monitoring are needed to ignore distractions and concentrate on school assignments. Additionally, it is important to realize that social and emotional processes greatly influence academic performance. This becomes particularly apparent at the start of adolescence, when changes in self-concept and other-evaluations take place (Lieberman, 2012). For example, doing homework is not perceived positively by peers which may affect teenagers’ mental effort. It is clear that the new interdisciplinary field of ‘educational neuroscience’ can answer questions that are difficult to address using behavioral measures alone (McCandliss, 2010). Especially during late adolescence, developmental differences might be small and not easily captured in reaction times or accuracy data. Research on the maturation of students’ brains could lead to findings that are relevant for higher education.

**Thesis aim and outline**

The aim of this thesis was to investigate brain development during the transition into and out of adolescence using fMRI. Participant groups with small age ranges were used, differences between males and females were explored and academic performance was assessed. In the first part, studies on social development are presented while the second part consists of studies on cognitive control framed in an educational context.

*Chapter 2* focuses on changes in brain connectivity during the transition from late childhood to early adolescence. We show results from longitudinal research conducted at the University of California, Los Angeles (UCLA) and the University of Oregon (UO). Children performed a task involving self- and other-appraisals of the social or academic domain at the age of 10 as well as the age of 13. As described in *chapter 3*, a similar task was administered to students aged 18 to 19.
and 23 to 25 at Medical College of VU University Amsterdam and University of Amsterdam (UvA). Sex and age differences in brain activation during self-, other- and reflected self-appraisals were examined. In **Chapter 4**, an fMRI paradigm is reported that distinguishes perspective (Self versus Other) and content (Emotion versus Behavior) of mentalizing. For this study, a homogeneous sample of female students 18 and 19 years old from the first academic year of Medical College at Maastricht University (UM) was included.

**Chapter 5** describes research on development of the neural correlates of cognitive control in the same sample as used for chapter 3. Differences between late adolescents (18 to 19 year olds) and young adults (23 to 25 year olds) as well as differences between males and females were investigated on a combined cognitive and emotional Stroop task. In **Chapter 6**, we included the freshman medical students aged 18 or 19 of chapters 3 and 5 to explore the link between brain activation during cognitive control and academic performance.

**Chapter 7** provides concluding remarks of this thesis with implications and suggestions for future research.

**References**


