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# CHAPTER 7

## Child Development and the Neuroscience of Medical Decision-Making

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(under review)

## Abstract

**Background:** Various international laws and guidelines stress the importance of respecting the developing autonomy of children and involving minors in decision-making regarding treatment and research participation. However, no universal agreement exists as to at what age minors should be deemed decision-making competent. Minors of the same age may show different levels of maturity. In addition, patients deemed rational conversation-partners as a child can suddenly become noncompliant as an adolescent. Age, context and development all play a role in decision-making competence. In this chapter we adopt a perspective on competence that specifically focuses on the impact of brain development on the child's decision-making process.

**Discussion:** We believe that the discussion on decision-making competence of minors can greatly benefit from a multidisciplinary approach. We adopted such an approach in order to contribute to the understanding on how to deal with children in decision-making situations. Evidence emerging from neuroscience research concerning the developing brain structures in minors is combined with insights from various other fields, such as psychology, decision-making science and ethics. Four capacities have been described that are required for (medical) decision-making: (1) communicating a choice; (2) understanding; (3) reasoning; and (4) appreciation. Each capacity is related to a number of specific skills and abilities that need to be sufficiently developed to support the capacity. Based on this approach it can be concluded that at the age of 12 children have the capacity to be decision-making competent. However, this age coincides with the onset of adolescence. Early development of the brain's reward system combined with late development of the control system diminishes decision-making competence in adolescents in specific contexts. We conclude that even adolescents possessing capacities required for decision-making, may need support of facilitating environmental factors.

**Summary:** This chapter intends to offer insight in neuroscientific mechanisms underlying the medical decision-making capacities in minors and to stimulate practices for optimal involvement of minors. Developing minors become increasingly capable of decision-making, but the neurobiological development in adolescence affects competence in specific contexts. Adequate support should be offered in order to create a context in which minors can competently make decisions.

## Background

Various international guidelines stress the importance of involving children in decision-making regarding medical treatments and research participation. According to article 12 of the UN Convention on the Rights of the Child, "children shall be provided with the opportunity to be heard in any judicial or administrative proceeding affecting the child directly" (Unicef, 1989) . More specific medical guidelines include The Second Directive by the European Parliament and the Council of the European Union, which states "A clinical trial on minors may be undertaken only if […] the minor has received information according to its capacity of understanding" (EU, 2001) . In addition, many countries have laws specifying at what age children should be involved in decisions about medical treatment or scientific research. In the Netherlands for example, children from the age of 16 may take treatment decisions independently, and children from the age of 12 are allowed to give informed consent for research participation or treatment together with their parents. In the US a minimum age of 7 years old is defined for asking assent (as opposed to legal consent) from children (NIH, 2005). In the UK, children under the age of 16 cannot be treated without parental consent, unless they prove to be mature according to the Gillick ruling (Tait, Voepel-Lewis, Zikmund-Fisher, & Fagerlin, 2010) .

These laws and guidelines underline the importance of respecting the developing autonomy of children. However, they also show that there is no universal agreement as to at what age it is appropriate for children to be considered competent for decision-making. Empirical evidence demonstrates that children have an emerging competence at a very young age. Weithorn & Campbell found children as young as 9 years old to have the capacity to make informed choices (Weithorn & Campbell, 1982). In addition, some studies conclude that children at age 14 or 15 are as competent as adults (Mann, Harmoni, & Power, 1989; Steinberg, 2013; Weithorn & Campbell, 1982). A recent study demonstrated that generally children older than 11.2 years are competent to consent to clinical research (Hein, Troost, & Lindeboom, 2014). Yet in most countries, children are considered incompetent until the age of 18 or 21, when they officially have reached legal adulthood.

In medical practice it is not clear-cut whether a child of a certain age is sufficiently competent for medical decision-making. Different children of the same age may have a different level of maturity. Young children, who have demonstrated sufficient competence for decision-making in a certain situation, can lack adequate competence in another. Furthermore, children who have shown to be reasonable conversation partners during their treatment, can (temporarily) be noncompliant in adolescence (see box 1), especially in chronic illness where factors as denial and the wish to be the same as the peer group influence treatment adherence (Dinwiddie & Muller, 2002). Age, context, and development all play a role in determining decision-making competence. In this chapter we explore a way in which insights in brain development can contribute to insights in decision-making competence of children at various ages.

**Box 1: The story of Elsa**

Elsa is a 16 year old adolescent who was diagnosed with diabetes type I at the age of 6.

When she was a girl, Elsa was very eager to learn about her daily diabetes care. From a very young age she was taught how her insulin pump worked. At school, as well as at home, she was able to manage her diabetes well. She could calculate the insulin dose needed during meals, and she showed profound insight in how to adjust her insulin pump settings when her blood glucose levels were not optimal. At age 10, Elsa was so well informed and experienced that she was able to handle her diabetes with her parents only exerting global supervision.

When Elsa turned 12 and went to secondary school things changed. She started to exert less self-control. She did not measure glucose levels and did not inject insulin for meals at school. Her school friends were unaware of her diabetes because Elsa did not inform them. Elsa tried to deny her diabetes at school, and often even took off the insulin pump, for example during physical exercise at school.

When at the pediatrician´s office, Elsa was always friendly, showing remorse and promising improvement. At age 14 however, she had to be admitted to the Intensive Care Unit because of severe dysregulation of her diabetes and an acute life-threatening situation. At age 16, the same happened after drinking large amounts of alcohol.

**Box 1.** The story of Elsa: an example of how competency seemingly fluctuates in adolescence.

### Decision-making competence and capacity

A certain level of competence is required for medical decision-making in order to balance the respect for autonomy with the protection of vulnerable patients (Appelbaum, 2007). In order to be sufficiently *competent*, one needs to have the *mental capacity* to make decisions, but also should be accountable of the decision in the specific situation. That is, one can in theory have the mental ability to make a reasonable decision, but a certain situation can render a person incompetent, e.g. due to stress or peer pressure (Miller, Drotar, & Kodish, 2004). *Decision-making capacity* is thus necessary, but not sufficient for being *decision-making competent*.

Decision-making capacity is defined by four standards: (1) expressing a choice; (2) understanding; (3) reasoning; and (4) appreciation (Appelbaum & Grisso, 2001; Appelbaum & Roth, 1982; Grisso, Appelbaum, & Hill-Fotouhi, 1997). The first standard means that a person should be able to demonstrate a choice of treatment or research participation. The second standard, understanding, requires that a person has adequate understanding of the relevant information of the medical situation and the treatment options, as well as awareness that one needs to make a choice. The third standard requires the capacity to reason about possible risks and benefits of the decisions in light of its consequences. Fourth, appreciation of the impact of the decision on one's own life is required. In order to be considered competent to make a decision all four capacity standards should be met (Appelbaum & Grisso, 2001; Grisso et al., 1997).

However, decision-making competence is not an on-or-off phenomenon (Ganzini et al., 2004). It is relative to the specific decision in the specific situation (Bolt & van Summeren, 2014; Ganzini et al., 2004). A person can thus have the competence to make one decision, but not another. Complementarily, some propose that the more gravity and the more risks related to the decision, the higher the capacities required in order to be competent to decide (Bolt & van Summeren, 2014; Buchanan, 2004). This is based on the idea of proportionality between autonomy to choose and the well-being of a person. If the consequences of a decision may have a high impact on someone's well-being, a higher capacity is required in order to grant that person the autonomy to make the decision (Buchanan, 2004). Furthermore, certain diseases, medical as well as mental, can affect competence, either temporarily (e.g. when a patient loses consciousness) or in a chronical manner (as is the case in progressing Alzheimer's disease (Marson, Ingram, Cody, & Harrell, 1995)).

The ultimate competence is thus dependent on capacities, but also specific to a certain context and certain decision. There are thus many factors that play a role in decision-making competence. The most important factor in children is development. As children grow older, their capacities to comprehend information and therefore competence to make a decision increase. Therefore, insight in the development of various abilities related to medical decision-making may contribute to understanding at what age children could be considered decision-making competent.

### Aim

We reviewed the evidence emerging from neuroscience research concerning the impact of developing brain structures on children's decision-making capacities and competence. We subsequently combined insights from neuroscience with various other fields: psychology, decision-making science, ethics and medical practice. We believe that the discussion about decision-making competence of minors can greatly benefit from a multidisciplinary approach, as the issue has many aspects. It is not our aim to quantify specifically at what age exactly children should be considered decision-making competent, but rather to contribute to insights on how to deal with children in medical decision-making, and to add to the general discussion on children and decision-making.

In this chapter, we will discuss the aforementioned four standards of medical decision-making capacity as defined by Appelbaum and Grisso (Appelbaum & Grisso, 2001). We will discuss the development of the various skills and abilities required for each standard, as well as describe the brain areas that are involved in these skills. Relating brain areas, development and decision-making abilities can contribute to an understanding of child behavior and competence. However, we will only be able to provide a simplified insight in the neuroscience background, as each ability requires the contribution of numerous brain areas and structures and we aim to keep this discussion readable for clinicians without a background in neuroscience. For a more elaborate overview of brain structures involved in decision-making, we want to point the reader to the paper of Rosenbloom et al. (Rosenbloom, Schmahmann, & Price, 2012). In addition, neuroscience insights in relating specific brain areas to specific abilities is still developing, and the field is currently just starting to gain knowledge about the specific development of these abilities in the brain (Weber & Johnson, 2009). As neuroscience is a relatively new and developing science, this chapter will give an initial insight in the issue, but evolving neuroscience will lead to further insights.

Next to relating the four standards to brain development, we will discuss what happens in the brain during adolescence and how this influences decision-making. Adolescents often seem to have a reduced ability to make reasonable decisions (Dinwiddie & Muller, 2002; Steinberg, 2004), and this phenomenon can be related to the developmental events happening in the brain during this period. The paragraph on adolescents will enlighten why many adolescent patients will consent to treatment in the clinic but do not do as asked when they return to normal day-to-day life.

## Brain development reflected in children's decision-making competence

The four standards of medical decision-making capacity will be discussed in association with neurological skills and brain areas. In order to aid the reader, an overview of the location and function of the discussed brain areas can be found in figure 1.

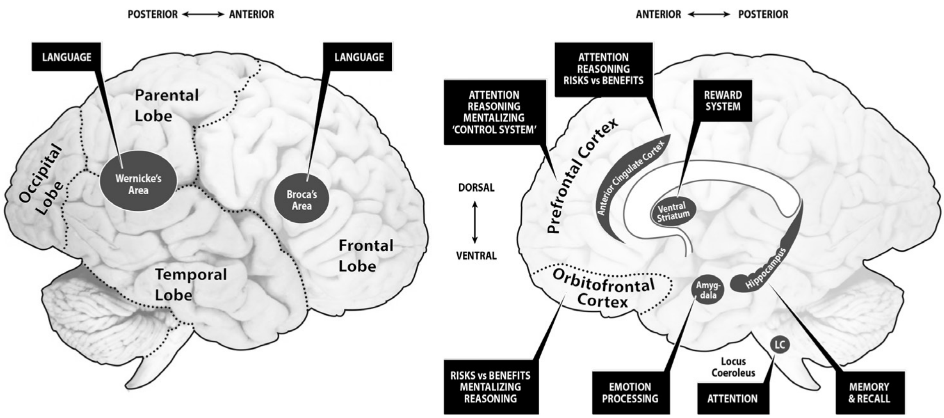


Figure 1. Overview of the brain areas discussed. This is a simplified illustration of the locations of the brain areas discussed and the decision-making capacities associated with these areas.

### 1. Expressing a choice

The first and least rigorous standard for decision-making capacity is the ability to express a choice. This standard implies that someone can communicate a preference of treatment or research participation. The required neurological skill for this standard is being able to **communicate**, either in spoken language or nonverbally (Appelbaum & Grisso, 1988,

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2001). Although nonverbal communication is used much earlier in life than spoken language, medical decision-making is legally restricted to spoken or written language. Nonverbal communication can be used as an indication of dissent or of implicit consent, but not as a legal form of consent. Therefore this discussion will focus on verbal language development.

Language development starts very early in life and continues to develop through adolescence into adulthood. At an early age, spoken language develops in close relation to gestures, spoken language on its own becomes more dominant in early childhood (Reed & Warner-Rogers, 2008). At age 4, children are already capable of producing a substantial degree of language proficiency and an extensive vocabulary (Nolen-Hoeksema, Fredrickson, Loftus, & Wagenaar, 2009; Reed & Warner-Rogers, 2008).

The main brain structures responsible for language production and comprehension are Broca's area and Wernicke's area (Nolen-Hoeksema et al., 2009). By the age of 6, the language regions are already active (Friederici, Brauer, & Lohmann, 2011), but the connections between the different regions still need to mature. Children use different brain pathways within these brain areas than adults, as they need complementary structures to support the language processing in the still immature pathways (Brauer, Anwander, & Friederici, 2011). During language development, the various areas are alternating between increased and decreased involvement (Nolen-Hoeksema et al., 2009). At age 5, children can produce quite complex sentences and have a reasonable understanding of the language they hear (Shaffer & Kipp, 2007). Between the ages of 5 and 9, children improve their grammar and start to master more sophisticated sentences. From 6 years old, pronunciation becomes adult-like, vocabulary and grammar increases (Shaffer & Kipp, 2007). This grammar refinement continues throughout adolescence.

## 2. Understanding

The second standard requires the ability to understand the information provided about the proposed medical treatment or research. In addition, a person should comprehend the fact that a choice needs to be made. Understanding requires a combination of neurological skills (Appelbaum & Grisso, 1988, 2001): one first needs to have sufficient **intelligence** and **language** proficiency to process the information. Further, one needs to be able to **orient** and direct **attention** towards the information. In addition, understanding requires **memory** and **recall** skills, in order to process and integrate information beyond the short-term moment.

**Intelligence**, although not an uncommon concept, is hard to define, as there are many different psychological perspectives (Nolen-Hoeksema et al., 2009). For the purpose of assessing decision-making capacity it suffices to state that the child needs to have a certain baseline of thinking skills, processing capacity, and creativity; a low intelligence might hinder understanding and further processing of information. Intelligence consists of various skills and therefore numerous brain areas, as well as connections between those areas play a role in maturing intelligence. Various IQ tests are available to measure someone's intelligence from the age of about 2.5 years old. IQ scores become relatively stable at the age of 4, but the IQ of an individual may still increase or decrease over time as a result of education and environment (Shaffer & Kipp, 2007). IQ scores could be used in the determination whether someone is sufficiently intelligent to make a decision, when this is uncertain.

**Attention** is necessary to identify the information that should be processed and the context of this information (Weber & Johnson, 2009). There are three skills involved in attention: alerting, orienting, and executive control (Petersen & Posner, 2012; Posner & Petersen, 1990; Rueda et al., 2004). Although they work together, these three skills develop at different speed independent of each other and are separate systems in the brain (Anderson, 2002; Rueda et al., 2004).

**Alerting** is simply the ability to maintain an alert and conscious state and direct attention to incoming stimuli (Petersen & Posner, 2012; Rueda et al., 2004; Waszak, Li, & Hommel, 2010). The ability to alert is related to a number of areas in the brain and an arousal system in the brain stem. The brain areas associated to alerting are mostly located in the right hemisphere, more specifically in the right frontal cortex and the right lateral parietal cortex (Mezzacappa, 2004). The neuromodulator norepinephrine secreted in the locus coeruleus is also related to the alerting system (Petersen & Posner, 2012). Norepinephrine influences a number of areas in the frontal cortex and parietal areas, thereby stimulating processes required to alert (Petersen & Posner, 2012). The ability to alert develops relatively late in life: it emerges at the age of 12 months, but continues to develop until the age of 10 and even beyond (Mezzacappa, 2004; Rueda et al., 2004).



**Orienting** means to guide the attention towards a certain stimulus, such as looking in the direction of a person entering the room (Posner & Petersen, 1990). There are two main brain systems involved in orienting: a dorsal system for visual-spatial input, and a ventral system for bottom-up reorienting to shift orientation (Petersen & Posner, 2012). The neurotransmitter acetycholine is involved specifically in stimulating orienting, but not in alerting. The ability to orient is fully developed at late childhood, with the evidence for maturity varying from the ages of 6 to 10 (Rueda et al., 2004; Waszak et al., 2010).

**Executive control** is necessary to focus on the information provided and to prevent distraction by other thoughts or irrelevant information, such as a song playing in the background. The Anterior Cingulate Cortex (ACC) plays an important role in top-down control in the brain, together with the Medial Frontal Cortex (Posner & Petersen, 1990). It is thought that there are two separate executive networks; the first one is the cingulo-opercular system which focuses on maintaining a stable task performance. The second network, the frontoparietal system initiates and adjusts control, therefore influencing task initiation and task switching (Dosenbach, Fair, Cohen, Schlaggar, & Petersen, 2008). Both systems consist of a number of different brain areas contributing to executive control. This ability for executive control is already present at a young age; even children of 3 years old can inhibit irrelevant information and focus on a specific stimulus (Anderson, 2002). For relatively simple situations, the ability to control attention conflicts rapidly develops and becomes stable after age 7, while the skill to control complex situations continues to develop until the ages of 10 to 15 (Reed & Warner-Rogers, 2008; Rueda et al., 2004; Waszak et al., 2010). In addition, early education and training can influence executive attention skills as can environment during development (Mezzacappa, 2004; Rueda, Rothbart, McCandliss, Saccomanno, & Posner, 2005).

**Memory and recall** are essential for understanding information, as they are involved in the processing of that information in the brain. Information can be retained for a short moment in the short-term memory (Reed & Warner-Rogers, 2008). This short storage of information is useful for instant recall and to process the information before it is stored more permanently. When information is actively processed, it will proceed to be stored either for an intermediate-term or for the long-term. Intermediate-term storage is for temporarily relevant information (e.g. street names of the neighborhood where you live, or information on a treatment procedure). Long-term storage is (semi)permanent, for information such as date of birth. In order to access the stored information, it can be **recalled** and used in the working memory (Nolen-Hoeksema et al., 2009; Reed & Warner-Rogers, 2008). An important brain structure in creating new memories is the hippocampus, which is involved in encoding new information and consolidation of the information from short-term memories into long-term memories. In addition, the amygdala plays a role in memory for emotional situations and information and in consolidation of these memories. The hippocampus and related brain systems are already in place before birth, but rapidly develop during the first year of life and continues to improve during childhood (Reed & Warner-Rogers, 2008).

During childhood the ability to remember information and the amount that can be remembered develops. The way in which children use their memory and in which they recall information changes during this development, leading to more accurate and more efficient storage (Guillery-Girard et al., 2013; Rhodes, Murphy, & Hancock, 2011). In addition, as more experiences are stored, memory can be used better to interpret new information (Weber & Johnson, 2009). Children are able to **recall** information from memory at an early age, but with time the ability increases and children can provide more information and details about a certain event (Dionne & Cadoret, 2013).

**Memory** specifically increases between the ages of 6 and 12, and then goes on to slightly increase during adolescence (Guillery-Girard et al., 2013; Thaler et al., 2013). Short-term memory develops in a linear fashion with age and becomes stable after the age of 11 (Goldstein et al., 2014; Thaler et al., 2013). Long-term memory develops very rapidly between the ages of 6 and 8, then from the age of 9 it develops more slowly, in order to reach a stable point at the age of 12 (Goldstein et al., 2014; Thaler et al., 2013)). The two types of memory thus develop in a different pattern, but reach maturity at the same age. In addition, studies on retrieval tasks demonstrate that at the age of 10-12, children appear to have recall ability comparable to adults (Czernochowski, Mecklinger, & Johansson, 2009; Rhodes et al., 2011; Sprondel, Kipp, & Mecklinger, 2011).

### 3. Reasoning

The third standard is that, next to understanding the factual information, someone should be able to reason about risks, benefits and possible consequences of the treatment or research options presented (Appelbaum & Grisso, 1988, 2001; Grisso et al., 1997). This standard is a step further from factual understanding and requires the ability for logical **reasoning** and **weighing risks and benefits**.

**Reasoning** is the process by which information that we possess is used to create new insights about information that we do not have. Three systems in the prefrontal cortex that are connected to each other play a role in reasoning: the orbitofrontal cortex (OFC), the ACC and the dorsal lateral prefrontal cortex (DLPFC) (Rosenbloom et al., 2012). The OFC has connections with limbic pathways, among which the aforementioned amygdala, which is involved in emotion processing. The OFC plays a role in reasoning for a decision related to rewards, punishments and emotions. The ACC is involved in reasoning for complex decisions, such as when there are conflicting options. The third system, the DLPFC, can integrate multiple sources of information, which is important for more complicated reasoning, using working memory and emotion processing, while also being connected to the OFC and ACC.

There are two main types of reasoning: deductive, or logical reasoning, and inductive, or probabilistic reasoning (Nolen-Hoeksema et al., 2009). Deductive reasoning is based on logical premises, for example: if it rains, the grass becomes wet → it rains → so the grass is wet. Inductive reasoning is based on the likelihood that something will happen, for example: I have seen many swans but never a black one, so black swans probably do not exist. These two types of reasoning are based on different processes in the brain, with different underlying networks (Parsons & Osherson, 2001). Inductive reasoning is performed by a network of brain areas involved in recall of information and evaluation of knowledge on the world, both necessary to assess the probability of an outcome. Deductive reasoning, on the other hand, relies on a logic-specific neural network that holds rules for deduction. Processes related to inductive reasoning seem to mostly take place in the left hemisphere, whereas for deductive reasoning mostly brain areas in the right hemisphere are activated (Parsons & Osherson, 2001).

There is evidence that people use different reasoning approaches for the same task, depending on working memory strength. When someone has a strong working memory, a more deductive approach will be used, whereas in case of weaker working memory efficiency, a person will rely more on probabilistic information (Markovits, 2013; Verschueren, Schaeken, & d'Ydewalle, 2005). In addition, the preference for either logic or intuitive reasoning shifts with age (Reyna & Brainerd, 2011). Young children prefer logic reasoning and may even outperform adults in deductive tasks. From adolescence on, intuition starts to play a bigger role in reasoning, sometimes leading to logical fallacies, but in general improving most reasoning outcomes (Reyna & Brainerd, 2011).

Children at the age of 6 to 8 already demonstrate the ability for logic reasoning (Markovits, 2013; Pillow, Pearson, Hecht, & Bremer, 2010). Around the age of 8 or 9 children will understand the differences between deductive and inductive reasoning and guesses (Markovits & Thompson, 2008; Pillow, 2002; Pillow, Hill, Boyce, & Stein, 2000). Then, between the ages of 8 and 11, children's reasoning skills improve significantly, mainly due to improved use and access to their own knowledge (Markovits, Fleury, Quinn, & Venet, 1998). In addition, children's insights in good and bad reasoning and thinking quality improve between the ages of 6 and 10 (Amsterlaw, 2006). Complex reasoning about alternative causal relations needs more time to develop, in adolescence it has become more accurate, but even adults often make mistakes (Markovits, 2013).

**Weighing risks and benefits** of various decisional options requires identification of these risks and benefits, and the ability to attribute a value to them. The ACC (also involved in executive control) plays a role in evaluating risks and uncertainty and the likelihood of success of a plan (Cohen, Heller, & Ranganath, 2005). The ACC works together with the orbitofrontal cortex (OCF) and a large network of other regions, working together in decision-making. The OFC is involved in evaluating the reward and related emotions of certain outcomes and is related to other brain areas that are involved in emotional processing (Rosenbloom et al., 2012).

In a study with children between 6 and 10, it was found that older children were able to identify more risks for a hypothetical situation than younger children (Hillier & Morrongiello, 1998). However, there was no difference between younger and older children with respect to the overall risk rating of the situations (Hillier & Morrongiello, 1998). Adults are better in identifying risks than adolescents (Mann et al., 1989). It has been observed that adults are much better than children of ages 11-15 to identify risks in medical decision-making, but there was no difference in identification of benefits (Halpern-Felscher & Cauffman, 2001). Still only 50% of the adults in the study would mention both a risk and a benefit of the decision.

So even though with increasing age the identification of risks in a situation improves, this does not necessarily mean that the situation will be weighed differently. Risk perception can be influenced by emotional factors, such as feeling vulnerable or feeling safe, and cues from others in the situation (Morrongiello & Rennie, 1998). In addition, as will be discussed later in this chapter, even though risk identification is mature in late adolescence, the way people of this age will deal with risks still differs from that of adults.



### 4. Appreciation

The strictest standard of decision-making capacity is appreciation. The appreciation of the nature of a situation implies that someone will not only understand the various options, but also the relevance of these options for the personal situation. In order to appreciate the situation and personal relevance of the decision at hand, one needs to have the ability of **abstract thinking**, which includes being aware that others have a mind of their own, which is called **theory of mind** (Appelbaum & Grisso, 2001; Appelbaum & Roth, 1982).

**Abstract thinking**, or the ability to think about things that are intangible, is necessary in order to understand the consequences of a decision. There are many different skills an brain areas involved in this skill. Thinking about situations that are not present in the current reality requires creating a mental representation (Markovits, 2013). Subsequent manipulation of this mental model can be used to think about the consequences of various options, e.g. compare burden and benefits of one treatment with another. Between the ages of 3 and 4, the ability to manipulate a mental model increases significantly (Markovits, 2013). Improvement of the efficiency of working memory with age, necessary to hold the mental model, further increases the ability of abstract thinking (Markovits, 2013; Pike et al., 2010). In addition, experience and knowledge play a role in hypothetical representations. The ability to create mental models is also closely related with understanding the perspective of others, as conceptualized in 'theory of mind'.
**Theory of mind** is the ability to understand the perspective or mental states of others and own-mental states (Nolen-Hoeksema et al., 2009; Reed & Warner-Rogers, 2008). The terms **theory of mind** and **mentalizing** are often used interchangeably, while strictly spoken the first indicates a more factual comprehension and the latter an affective understanding. Both aspects play a role in medical decision making situations. Mentalizing about others means an understanding that someone has another mind and understanding how someone will feel in a hypothetical situation, or someone else's intentions or knowledge. Mentalizing about oneself is understanding oneself, being aware of own thoughts, and cognitive processes. This skill requires a number of brain structures, such as memory, emotion, emotion regulation, empathy, language and executive functions (Korkmaz, 2011; Pfeifer & Blakemore, 2012; Rosenbloom et al., 2012). Mentalizing requires the ability to 'decouple' thought from reality: one needs to be able to think about a situation, rather than to respond to current sensory input from that situation itself. This decoupling involves the medial prefrontal cortex, which can responds differently between physical responses to a situation and mental representations of that situation (Frith & Frith, 2003). In addition, the OFC (also involved in weighing risks and benefits), is involved in mentalizing, as it plays a role in emotional processing and affects the ability for empathy (Rosenbloom et al., 2012). Therefore, the development of mentalizing is a process that takes a long time as all involved brain regions need to mature and not do so in a synchronically fashion (Pfeifer & Blakemore, 2012). Already at elementary school age, children are developing a theory of mind (Schwanenflugel, Henderson, & Fabricius, 1998).There are studies indicating the emergence of mentalizing at an age as young as 1,5 years old (Frith & Frith, 2003).

Between 3 and 4 years old children start to recognize their own beliefs and desires, which contribute to the development of personal norms and values, and start to understand how these influence their own actions and how the beliefs and desires of others motivate the other person's actions. From the age of 4 children begin to understand that the perspective of others can be different from their own, and at an age of 6 most children show this understanding in certain tasks (Abu-Akel, 2003; Frith & Frith, 2003; Shaffer & Kipp, 2007). Mentalizing capacity continues to develop at least until the age of 11 and refines until the age of 16 (Abu-Akel, 2003; Korkmaz, 2011). In adolescence there is a significant improvement in mentalizing about others, which will be discussed further on in this chapter (Blakemore & Mills, 2014).

### Model

Below, the discussed abilities and their developmental trajectories are visualized in a model (see figure 2). This overview shows that the necessary abilities and relating brain areas do not develop synchronically; some aspects of capacity are mature much earlier than other. This illustrates that decision-making competence is not an on-or-off concept, but rather a growing skill with age.

### Recent developments

Results of a recent study on children's competence to consent to clinical research showed that it could be assessed validly and reliably using a tool. The MacArthur Competence Assessment Tool for Clinical Research was studied in a population of pediatric patients between 6 and 18 years of age (Hein et al., 2014). The study demonstrated that age limits for children to be deemed competent to decide on research participation could be estimated as follows: children of 11.2 years and above generally appeared to be competent, whereas children of 9.6 years and younger were generally not competent. A change-over occurred between 9.6 and 11.2 years, and the cross-over point was estimated at 10.4 years (Hein et al., 2014). In the same study, the four domains representing competence in most jurisdictions (understanding, appreciation, reasoning, and expressing a choice) appeared to constitute a single trait in children. These results correspond well with the model in figure 2. Below the age of 10, too many abilities are still in their (early) development and overall competence cannot be expected.

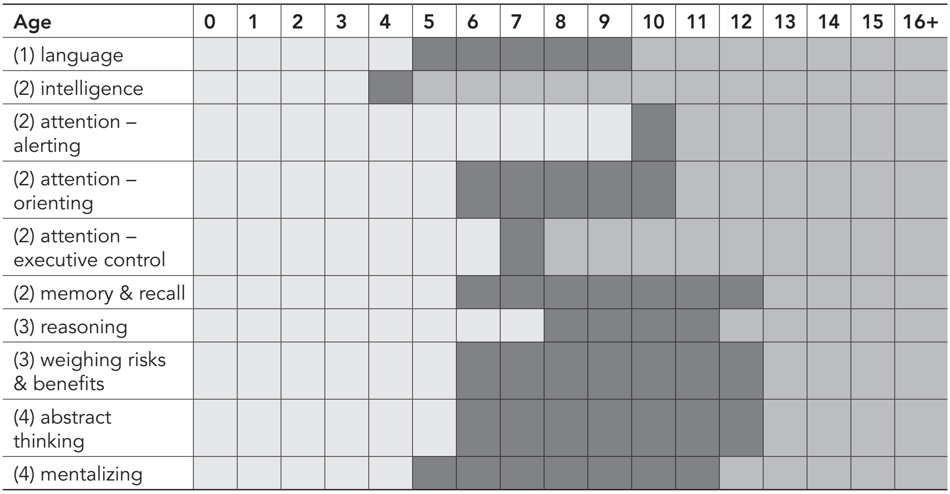


Figure 2. Development of decision-making capacity. In this figure the critical developmental period (darkest) for each of the discussed abilities is reflected. Each box indicates one year of life: e.g. the box under 0 indicates the period between birth and reaching the age of 1. The development of each ability starts at an early age, and continues to mature to a small or larger extent into adolescence or even beyond.

## Adolescence and decision-making competence

The demonstrated model might suggest a linear pattern in development and a corresponding linear increase in decision-making competence with age. However, due to differences in cross-talk between the various brain structures over the course of brain development, competence might fluctuate. A period in which this is especially pronounced is adolescence. In this period, great changes and developmental leaps take place in the brain, which can have a profound effect on decision-making competence.

Adolescence is a period associated with a number of health issues and increased mortality (Dahl, 2004; Steinbeck, Towns, & Bennett, 2014). Adolescents often have increased appetite and therefore a change in diet; in addition adolescence is typically the time when tobacco addiction initiates and a time of emerging alcohol and substance (ab)use (Braams, Van Leijenhorst, & Crone, 2014; Steinbeck et al., 2014). Further, for chronically ill children, this is a time where the disease management approach can change, sometimes creating risky of even life-threatening situations. The increased mortality seen in adolescence is mostly associated with risky behavior, sensation-seeking and peer influences affecting decision-making (Dahl, 2004).

Adolescence starts around the age of 12 and the neurologic developments initiated can continue beyond the age of 18, into early adulthood (Crone, 2008; Steinberg, 2013). The brain in adolescence differs significantly from the brain in childhood and in adulthood (Blakemore & Robbins, 2012; Casey, Jones, & Hare, 2008; Crone, 2008; Steinberg, 2010). In order to gain more insight in the effect of adolescence on decision-making, it is important to have an understanding of this period. The most significant changes in the brain are associated with processing rewards and risks, self-regulation, and the effect of peers on decision-making. The neurologic changes affect decision-making in general and, depending upon context, can affect medical decision-making to a certain extent as well.

### Risk, sensation-seeking and self-regulation

Adolescents are prone towards increased risk-taking and this is associated with the development of a number of brain-structures. Two brain systems are especially important: the prefrontal cortex (PFC), which is the control system; and the ventral striatum, the reward system. The control system is involved in impulse control, the ability to stop a certain urge or action, and thus involved in self-regulation. The ability for self-regulation develops mainly from the age of 12 until the age of 18 (Crone, 2008), but continues to improve into early adulthood (Steinberg, 2013). In addition, the prefrontal cortex also becomes better at other functions that require control, such as planning ahead, weighing risks and benefits and in making complicated decisions. The cross-talk between the control system and the reward system and associated emotional regulation is not fully developed before early adulthood (Steinberg, 2013). This means that even though an adolescent can have intellectual maturity, this does not automatically imply the presence of emotional and social maturity (Casey et al., 2008; Steinberg, 2013).

The reward system involves a structure that creates dopamine in response to rewards. Dopamine gives a feeling of pleasure, which can lead to learning and the urge to repeat the experience. During adolescence, the reward system becomes hyperresponsive; the dopamine response to a reward is much higher (Van Leijenhorst et al., 2010). This is associated with increased reward-seeking and sensation-seeking (Blakemore & Robbins, 2012; Steinberg, 2008; Van Leijenhorst et al., 2010). The increased responsiveness of the reward system even applies to small rewards, making the positive effect of a small 'success' of a decision more pronounced for adolescents than for children or adults (Van Leijenhorst et al., 2010). Thus in a dilemma in which there is a small chance of a reward, this reward can be attributed such a high value that the situation is no longer perceived as a dilemma by the adolescent and there is only one path to choose (Steinberg, 2004).

The development of the control and the reward systems do not follow a linear pattern, as different brain areas mature at different stages in life (Gogtay et al., 2004). In general, brain development follows a pattern where first lower-order areas develop before higher-order areas mature. Initially it starts with maturation of the sensorimotor areas, and then will follow areas responsible for spatial orientation, speech, language, and attention. The last brain areas to mature are those involved in executive function and attention, located in the prefrontal cortex (Gogtay et al., 2004). Based on structural brain development research, there appears to be a 'mismatch' between the development of various regions, specifically the amygdala and the prefrontal cortex. The amygdala, responsible for emotion processing and input in the reward system, starts to mature in late childhood and stabilizes at mid- to late adolescence (Mills, Goddings, Clasen, Giedd, & Blakemore, 2014). However, the PFC starts to mature in early adolescence and it is not until young adulthood that this area is mature. In addition, the nucleus accumbens in the ventral striatum, appears to develop early in some and later in others, which might explain a 'mismatch' in some adolescents, but more research should lead to further insights in this development (Mills et al., 2014).

As a result of the nonlinear maturation of brain structures, the control system (PFC) develops slowly, even into early adulthood whereas the reward system (amygdala and possibly the nucleus accumbens) already changes in early adolescence (Steinberg, 2013). This nonlinear development accounts for the risky decisions often observed in adolescents, such as binge drinking or drunk driving (Steinberg, 2004). This is however not to say that adolescents are incapable of estimating risks or making responsible decisions. Evidence from laboratory experiments demonstrates that adolescents have a decision-making capacity similar to adults (Braams et al., 2014; Casey et al., 2008; Crone & Dahl, 2012; Steinberg, 2013). Adolescents thus have better insight in decision-making than children do, consistent with our proposed model. Yet do they end up in precarious and risky situations and their behavior is often not consistent with their capacity.

This inconsistency can be explained with the distinction between 'hot' and 'cold' contexts. An emotional context is called a 'hot' situation, whereas in 'cold' situations, decisions are not or only minimally emotionally loaded (Steinberg, 2004). When emotions play a role in a situation, this can significantly influence the decision-making process and outcome (Blakemore, 2012; Braams et al., 2014). Whether a situation is hot or cold is not predefined: it can vary per individual to what extent a context is perceived as emotionally loaded (Blakemore & Robbins, 2012). Research has shown that during adolescence, risk-taking in decisions in cold situations is similar to that of children and adults (Blakemore & Robbins, 2012). However, when in a hot, emotionally-loaded situation, risk-taking is increased, affecting decision-making severely (Blakemore & Robbins, 2012; Braams et al., 2014; Steinberg, 2013). This explains the often risky decisions that adolescents make, seemingly only thinking about short-term rewards, even though afterwards they can reasonably assess their leap in judgment.

One particular type of emotionally loaded situation is the presence of peers. As adolescence is essentially a process to develop the capacity to navigate the social landscape, social cues become increasingly important (Crone & Dahl, 2012). During adolescence, the acceptation by peers becomes an important purpose in everyday life and guides decision-making (Blakemore & Mills, 2014). Correspondingly, the ability to understand the perspective of another person and predict that person's behavior increases (Blakemore & Robbins, 2012). As discussed, this ability for mentalizing develops until late adolescence and it modulates decision-making. In addition, self-awareness increases during adolescence (Blakemore & Mills, 2014).

Accordingly, decision-making in the presence of peers is substantially different from individual decisions (Albert, Chein, & Steinberg, 2013). When with peers, the brain sensitizes even more towards rewards and possible rewarding outcomes are higher valued. The adolescent can show an adequate understanding of the situation and its risks involved, but the developing control system can become overruled by the emotional cues in this 'hot' context (Casey et al., 2008). As a result of the hot context, adolescents are more prone towards making risky decisions, even when only a small reward can be expected (Dahl, 2004). This also explains why adolescents' risk-prone tendencies are mostly observed in group situations, especially when there is a certain form of excitement present ('hot') (Steinberg, 2004).



### Strengths and vulnerabilities of adolescents in medical care

The developing brain in adolescence thus demonstrates lower cognitive control and is more prone towards risk-taking, especially when together with peers. These characteristics can affect decision-making competence during adolescence. The competence of adolescents to make a decision can vary per situation. Some medical decisions can be considered 'cold', with minimal influence of social or emotional factors (Steinberg, 2013), providing a good context for a competent decision. Treatment and research decisions are generally not impulsive decisions, and a certain amount of time for consideration is provided. This will reduce impulsive and unreasoned decisions in adolescents (Casey et al., 2008). However, this does not mean that an adolescent will necessarily live up to the decision in the long run, as context might change. For example, a diabetes patient can be very aware of the benefits of a regular and structured diet and discuss this wisely in a hospital setting. However, living up to the treatment pattern can be much harder when the same person is with a group of friends who decide to skip class and go for a snack. Now the context of the decision turned into a hot, peer-influenced and exciting situation, which affects the decision-making rationale and possibly the outcome, as also illustrated in the example in box 1. Some adolescents are more susceptible to such an effect than others, and thus the outcome of the dilemma is not necessarily the same for each young patient, making practice very unpredictable.

Especially in treatment situations, adolescents can demonstrate this type of seemingly decreased competence for responsible decisions (Steinbeck et al., 2014). Short-term rewards become more important than long-term rewards, even when choosing for an immediate reward can mean a loss on the long-term (Blakemore & Robbins, 2012; Crone & Dahl, 2012). This can make it complicated to stick to a healthy lifestyle or treatment pattern, which usually does not deliver immediate rewards, but is meant to increase long-term health. Another factor playing a role might be the expectation of the long-term reward. It appears that adolescents over-estimate their risk of dying soon (Fischhoff, Bruine de Bruin, Parker, Millstein, & Halpern-Felsher, 2010). This over-estimation of a chance on a short life automatically diminishes the value of any long-term rewards, as the chance of living long enough to receive the reward is considered relatively low.

Although these characteristics render adolescents more vulnerable towards risky situations and their consequences, they also are an important aspect of developing into an adult. During adolescence, the brain shows a high amount of plasticity, resulting in vulnerabilities, but also in opportunities (Dahl, 2004). The sensitivity to rewards together with increased value of social cues creates a perfect situation for learning new skills that are important to function in a social context (Blakemore & Mills, 2014; Crone & Dahl, 2012). Adolescents can learn very quickly and can sometimes even outperform adults when it comes to problem-solving and creativity (Crone & Dahl, 2012). In addition, adolescence is a time in which health behavior can be stimulated to consolidate, or when behavior can easily be altered, if the adolescent is motivated to do so (Steinbeck et al., 2014). Therefore, adolescence offers an opportunity to target health behavior and disease management and teach the brain new behavior (Galvan, 2014; Steinbeck et al., 2014).

# Discussion

In this chapter we have analyzed the neurological development of decision-making capacities based on the four standards from Appelbaum & Grisso; expressing a choice, understanding, reasoning, and appreciation (Appelbaum & Grisso, 2001). The development of the brain demonstrates a nonlinear pattern and therefore decision-making competence does not increase in a linear fashion with age. Based on our model, it might be expected that children around the age of 12 already have the competence to make medical decisions. However, this age coincides with the onset of adolescence, which is associated with altered decision-making patterns. Adolescents are prone towards increased risk-taking, especially in emotional situations and when with peers. This affects their decision-making competence, mostly in 'hot' or emotional situations, such as compliance decisions in everyday life at school, but less so in 'cold' situations such as deciding upon treatment in the hospital. As a result, decision-making competence in adolescence can vary greatly between moments and contexts. It is thus complicated to pinpoint a certain age at which a child should be considered fully competent to make medical-decisions based on brain development. Even more so since brain development can vary between individuals and gender.

In addition, in this chapter we mainly discuss the neurological background of decision-making competence, with the aim to contribute to insights about the age at which the brain is mature enough to be capable of making a decision. However, mature neurological capacity does not automatically mean that a child is competent for any medical decision. There are many factors that influence decision-making competence, either temporarily or chronically. Miller has proposed a model on children's capacity in which initial predisposing factors are identified, followed by four groups of factors that influence decision-making competence, namely child, parent, clinician, and situational factors (Miller et al., 2004). Predisposing factors include the discussed cognitive development, as well as experience. Factors related to the child are personality (Alderson, 1992), emotional state of the child that can affect capacity and serve as a spotlight or motivator for information and preferences (Alderson, 1992; Mann et al., 1989; Weber & Johnson, 2009). In addition, disease severity can affect understanding, as well as retention of information and reasons to consent (Schaeffer et al., 1996). Parent and clinicians can influence the child's competence with their attitude towards the child and the attention and support provided in the decision-making process (Alderson, 1992; Hein et al., 2012; Mann et al., 1989). Finally, situational factors such as the type and complexity of the decision, the setting and time constraints play a role (Miller et al., 2004). Therefore, it is impossible to define a cut-off point at what age children should be presumed competent to make medical decisions based on neuroscience.

Nevertheless, based on empirical research, indications for a just age limit for alleged competence to consent in children are estimated. In the clinical research context, children of 11.2 years and above are generally competent. In the treatment context initial indications point into the direction of comparable age limits for alleged competence, around the age of 12, but more research is needed to confirm these findings. This leads to the recommendation of a double consent procedure (child and parent) for minors from the age of 12 until 18. Taking into account that parents are generally provided with the legal authority to raise their children, they are assigned with rights and responsibilities. A double consent procedure could achieve an adequate consideration between the legal position of the child and that of the parents. A double consent procedure will do justice to both, the developmental aspects of children and the specific characteristics of the parent-child dyad. The parental role offers extra protection by creating the context for the child's competent decision-making and by facilitating the child's long term autonomy.

It is evident that decision-making competence increases with age, rather than being an on-or-off trait (Ganzini et al., 2004). In accordance with this development, and out of respect for children's autonomy, children should be increasingly informed and involved in the decision-making process (De Lourdes Levy, Larcher, & Kurz, 2003; Kurz et al., 2006; Weithorn & Campbell, 1982). Attention should be paid to providing the child with adequate information, as decision-making competence is *'only as good as the provided information'* (Ganzini et al., 2004; Hein et al., 2012). This means that the supplied information needs to be adapted to the child's level of communication and understanding, for example by providing separate sheets for the child and offering oral explanations (De Lourdes Levy et al., 2003; Gill et al., 2003). As long as there is no adequate information, it is certain that children cannot meaningfully be involved in the decision-making process (Alderson, 2007; Appelbaum, 2007; Bos et al., 2013; de Vries & van Leeuwen, 2008; Martenson & Fagerskiold, 2008).

## Conclusion

Currently, medical laws and regulations reflect the belief that child development is of influence on children's decision-making process to such an extent that age limits are presented at which children are deemed incompetent or competent. In problematic cases, child psychiatrists and –psychologists are consulted to assess the decision-making capacities of a child, the clinical operationalization of the legal concept of competence. In this chapter we adopt a perspective on such competence assessment that specifically focuses on the impact of brain development on the child's decision-making process. Taking this perspective opens up the opportunity to implement results from an emerging field in neurobiological research on how developing brain structures may affect a child's decision-making capacities. The insights provided in this chapter are intended to aid insight in the practice of dealing with minors in medical situations, and to stimulate further discussion about decision-making capacity and competence in children.

In neuroscience, changes in brain structures have been detected that are related to changes in decision-making capacities. The authors are aware that this is a rapidly developing field, with many questions left to be answered. Future neuroscientific research could be helpful if decision-making about treatment or research participation could be specifically targeted in the study designs. Such research will be valuable with respect to our understanding of brain development related to children's capacities. Furthermore, it would enable more detailed assessment of children's competence to consent in questionable situations.

Summary

Various international laws and guidelines underline the importance of respecting the developing autonomy of children. However, they also show there is no universal agreement as to at what age children are considered competent for decision-making. In this chapter we adopt a perspective on competence that specifically focuses on the impact of brain development on the child's decision-making abilities. Neuroscience research is related to the four capacities required for medical decision-making, which are communicating a choice, understanding, reasoning, and appreciation. Based on this approach it can be concluded that at the age of 12 children have the capacity to be decision-making competent. However, this age coincides with the onset of adolescence. Early development of the brain's reward system combined with late development of the control system diminishes decision-making competence in adolescents in specific contexts. We conclude that even adolescents possessing capacities required for decision-making may need support of facilitating environmental factors.