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The adolescent brain : unraveling the neural mechanisms of cognitive and affective development

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Chapter 2

Development of cognitive flexibility:

A literature review



This chapter is based on:

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Abstract

Cognitive flexibility is an important aspect of executive functioning, which is essential for successful adaptation to changing environmental demands. Cognitive flexibility is a complex concept that has been measured with many different paradigms. Conceptually, a distinction can be made between instructed flexibility (measured with task switching paradigms) and adaptive flexibility (measured with performance monitoring paradigms). Both types of flexibility are still developing across childhood and adolescence. In this chapter, we describe the behavioral and neural development of these two types of cognitive flexibility. For instructed flexibility, results indicate that performance is generally better in adults compared to children. FMRI-studies point to increased neural activity in adults compared to children in frontal and parietal areas, the basal ganglia and the thalamus. Adaptive flexibility also shows an age-related increase in performance. With development, neural activity patterns show a specialization of frontal and parietal areas for processing different types of feedback, which carry different informative value for future behavior. This indicates that instructed and adaptive flexibility are separable processes with different developmental trajectories. Future studies should focus on the interaction between instructed and adaptive flexibility across development, and include longitudinal, genetic and network analyses in their methods.

Executive functions

An important characteristic of human cognition is that people are constantly looking for ways to improve themselves. Rather than sticking to the status quo, people use flexibility and creativity to successfully adapt to an ever-changing environment. For instance, children in schools have to get used to switching between different subjects for each class. Instead of continuing to speak French during Spanish class, children tend to switch quite easily between classes. In situations like these, most people will recognize when they need to change their approach to adapt to a new environment. For successful adaptation to a changing environment, executive functions are of paramount importance. Executive functions refer to the ability to behave in goal-directed actions in new and challenging situations, and to overcome automatic thoughts and behaviors (Garon, Bryson, & Smith, 2008). Executive functions are thought to consist of at least 3 sub processes: (1) working memory, (2) inhibition and (3) cognitive flexibility (Huizinga, Dolan, & van der Molen, 2006; Miyake et al., 2000), although the exact number of sub processes and their structure remains a matter of debate.

Cognitive flexibility

In this chapter we will focus on cognitive flexibility. Cognitive flexibility is defined as the ability to adapt behavior to changing environmental demands. It is therefore essential for adaptive cognition, creative problem solving and ‘out of the box’ thinking. Without cognitive flexibility, we would be stuck in rigid behavioral patterns and we would be having difficulty adapting to new situations. Cognitive flexibility is, because of its inherently adaptive nature, arguably the most important component of executive functioning, as well as the component that shows the most profound changes across child and adolescent development. However, cognitive flexibility cannot be seen as an entirely distinct executive function, because it relies heavily on two other executive functions: working memory and inhibition (Huizinga et al., 2006). Working memory is important for flexibility because it is necessary to remember your goals and keep relevant information on-line. Inhibition is important because for flexible behavior, automatic responses need to be inhibited in order to choose a response that is better suited to current demands.

Development of cognitive flexibility

Cognitive flexibility undergoes profound changes across child and adolescent development (Cragg & Chevalier, 2012). The development of cognitive flexibility is of considerable importance for successful school performance. For instance, cognitive flexibility scores are related to math scores and phonemic awareness in preschoolers (Blair & Razza, 2007) and task switching performance was found to be related to reading and math scores in a longitudinal study in preschool and primary school (Bull, Espy, & Wiebe, 2008). Furthermore, interventions aiming to improve executive functioning skills (including flexibility) improve school readiness in young children (Bierman, Nix, Greenberg, Blair, & Domitrovich, 2008). Additionally, impairments in cognitive

flexibility are associated with a number of psychiatric disorders, such as autism spectrum disorder (Corbett, Constantine, Hendren, Rocke, & Ozonoff, 2009), obsessive compulsive disorder (Chamberlain, Blackwell, Fineberg, Robbins, & Sahakian, 2005) and anorexia and bulimia nervosa (Tchanturia et al., 2012). Together, these studies highlight that cognitive flexibility is a cornerstone of cognitive development.

Measuring cognitive flexibility: Adaptive and instructed flexibility

Cognitive flexibility has been studied with many different experimental paradigms (Ionescu, 2012). Many researchers have argued for a better conceptual understanding of a complex and multifaceted construct such as cognitive flexibility (Cragg & Chevalier, 2012; Morton, 2010). Conceptually, a distinction can be made between instructed flexibility and adaptive flexibility. For instructed flexibility, individuals need to adapt behavior based on changing task rules, such as in task switching paradigms. Adaptive flexibility, on the other hand, requires an individual to infer rules based on feedback about prior behavior, such as in performance monitoring paradigms.

In this chapter, we describe the development of these two different types of cognitive flexibility: instructed flexibility and adaptive flexibility, by focusing on task switching and performance monitoring paradigms. Our focus will be on the development of school-aged children (6-17 years), a developmental group which can be directly compared with adults using the same paradigms (Cragg & Chevalier, 2012). Even though most of the research to date on the development of cognitive flexibility has focused on preschool years (Blair, Zelazo, & Greenberg, 2005), school-aged development is marked by continuing improvement of many types of cognitive flexibility. A better understanding of these developmental improvements will hopefully contribute to improving education and interventions.

In the search for a more mechanistic understanding of subprocesses involved in cognitive flexibility, researchers have adopted a new approach to complement behavioral research. That is to say, the processes involved in cognitive flexibility and their developmental trajectory have been investigated from a neurocognitive perspective. This approach has proven highly valuable in situations where there are no overt behavioral indices (such as in the case of feedback processing; Crone, Zanolie, Van Leijenhorst, Westenberg, & Rombouts, 2008) or when different subprocesses may result in the same behavioral outcome (Morton, 2010). Therefore, this chapter will focus on the development of both behavioral and neural processes involved in instructed and adaptive cognitive flexibility. We will first provide a brief overview of the neural mechanisms of cognitive flexibility in adults. Next, we describe several studies that investigated the neurocognitive development of cognitive flexibility. These studies are subdivided into instructed flexibility (measured with task switching paradigms) and adaptive flexibility (measured with performance monitoring paradigms).

Neural mechanisms of cognitive flexibility in adults

Using functional magnetic resonance imaging (fMRI), researchers have been able to identify the neural areas that are important for cognitive flexibility. Most studies in this area have focused on instructed flexibility, by using task switching paradigms. FMRI studies of task switching in adults have generally compared neural activity during switch trials with activation during non-switch trials. The underlying rationale is that this subtraction paradigm allows the researcher to isolate the activity that is specific for switch trials. With this approach, it was found that task switching activates an extensive brain network including activity mostly in the lateral and medial prefrontal cortex (PFC), but also in the parietal lobes, cerebellum and other subcortical areas (Monsell, 2003).

A recent meta-analysis analyzed data from different types of cognitive flexibility paradigms to investigate in more detail the specific contributions of these brain areas (Kim, Cilles, Johnson, & Gold, 2012). The main aim was to distinguish brain areas that are domain-general (activate across different types of flexibility) and which areas are specialized for different types of flexibility. Three different types of paradigms were distinguished by the authors: two types of instructed flexibility (perceptual attention switching and response switching) and adaptive flexibility (referred to as ‘context-based switching’ by the authors). In response switching paradigms, participants are trained to make certain stimulus-response mappings (e.g. press left for circles, right for squares). After a switch, the correct stimulus-response mapping is changed (e.g. press left for squares, right for circles). In attention switching paradigms, participants respond with a key press to different dimensions of the same stimuli. For instance, prior to the switch participants could be asked to respond based on the color of the stimuli. After a switch, participants still see the same stimuli, but now they have to attend to a new dimension (e.g., shape) and ignore the previously correct dimension. In adaptive flexibility paradigms, participants are required to switch between task rules or cognitive ‘sets’. The need to switch is inferred from performance feedback.

Kim et al. (2012) found a widespread network for all three switching types that consisted of medial and lateral PFC, but also parietal, temporal and occipital areas, the caudate nucleus and the thalamus were found. This was consistent with previous meta-analyses which did not distinguish between different switching types (Buchsbaum, Greer, Chang, & Berman, 2005; Derrfuss, Brass, Neumann, & von Cramon, 2005; Wager, Jonides, & Reading, 2004). To investigate areas that are domain-general in nature, the researchers investigated which areas were activated for all three types of switching. Regions in the inferior frontal junction and posterior parietal cortex were found. The researchers therefore argue that that these areas are probably involved in representing and updating task sets, because these processes are essential in all three types of switching (Miyake et al., 2000). Subsequently, they examined which areas were specifically activated for the three switching paradigms. The results revealed that in addition to domain-general regions associated with switching, there were also differences in brain activity for the three switching paradigms. For attention switching, compared to the other types of switching, preferen-

tial activity was found in several caudal PFC regions, posterior parietal cortex and inferior temporal areas. For response switching, preferential activity was found in DLPFC, several frontal gyri and posterior parietal cortex. Adaptive flexibility tasks resulted in preferential activation in rostral PFC regions, middle frontal gyrus, cuneus, inferior temporal cortex, occipital areas and sub-cortical structures. In summary, the findings of this meta-analysis indicated that there are several overlapping regions that are important for different types of task switching, but there are also separate neural networks underlying different types of instructed and adaptive flexibility. This illustrates that task switching is not a unitary process and highlights the importance of studying different types of switching.

In the next paragraphs, the behavioral and neural development of cognitive flexibility will be further described, based on the distinction between instructed and adaptive flexibility. It is well-known that at birth, the structure of the brain is not yet fully developed. Both gray matter (consisting of neurons) and white matter (structural connections between areas) are still maturing. This has been investigated with post-mortem studies and, more recently, with structural neuroimaging techniques. During child and adolescent development, linear increases have been observed in white matter connectivity (Barnea-Goraly et al., 2005; Giedd et al., 1999). For gray matter development, a nonlinear pattern has been found (Casey, Giedd, & Thomas, 2000): For the first two postnatal years of development, gray matter volume increases. After that period, gray matter decreases again with different brain areas differing in the rate at which they mature. The lateral PFC is one of the last areas to develop in adolescence (Casey et al., 2000) with estimates that gray matter in the lateral PFC reaches adult levels in the early twenties (Giedd, 2004). Similar results were found for the parietal cortex and the caudate (Giedd, 2004). It therefore seems that the areas that are important for task switching in adults undergo prolonged structural development during childhood and adolescence. This observation, combined with the results of behavioral studies in which increased switch costs for children were found, led a number of researchers to hypothesize that the development of cognitive flexibility may be related to brain maturation. Several studies have investigated the neural development of instructed flexibility, using two versions of task switching paradigms (response switching and attention switching) that were previously briefly described in the section on neuroimaging studies in adults.

Development of instructed flexibility

Behavioral development of instructed flexibility

The task switching paradigm has proven to be a very valuable tool to investigate the development of instructed cognitive flexibility. Task switching paradigms have been developed in different varieties. For example, a distinction can be made between the alternating-runs variant of the task switching paradigm, in which participants are instructed to switch after every n^{th} trial, and the cue-based switching paradigm, in which a switch is indicated by a cue. In both paradigms, the

demand to switch between tasks can result in ‘mixing costs’ (increased reaction times when comparing a task block with switches to a task block without switches), and ‘switch costs’ (increased reaction times when comparing switch trials within a switch block to non-switch trials within a switch block) (Monsell, 2003).

Developmental comparisons have indicated higher switch costs for children compared to adults, both in alternating run paradigms (e.g. Huizinga et al., 2006) and cued switching paradigms (e.g. Crone, Bunge, van der Molen, & Ridderinkhof, 2006). Developmental improvements are most pronounced between ages 7 and 12, although improvements are still observed in adolescence (Huizinga et al., 2006). In a comprehensive review, Cragg and Chevalier (2012) summarized many different processes which may contribute to these developmental differences. First, they mention that developmental differences may result from an improvement in goal setting. For example, in the alternating run paradigm it is necessary to maintain the task set in mind (e.g., Task A, Task A, Task B, Task B, Task A, Task A) and in cued task switching it is necessary to ‘translate’ the cue into the correct task representation. The finding of higher mixing costs (i.e., trials in a switch block compared to trials in a non-switch block) in children relative to adults has been interpreted as developmental differences in goal setting (Chevalier & Blaye, 2009). Second, developmental differences may be related to overcoming the previously relevant rule. For example, Cepeda, Kramer, and Gonzalez de Sather (2001) showed that increasing the time between trials reduced switch costs in adults but not in children, suggesting that children experience larger interference from previous task set activation. Third, developmental differences may be related to interference from overlapping stimulus response mappings. For example, Crone et al. (2006) showed that it is relatively more difficult for children to switch tasks when the switch trial is associated with the same response hand as on the previous trial compared to when the switch trial is associated with the opposite response hand, most likely because they experience more interference from the previous task-response mapping. Taken together, different underlying processes can account for developmental changes in switching, but exactly how and when these processes take place is not well understood. One way to entangle these developmental processes is by studying the neural mechanisms involved in task switching.

Neurocognitive development of instructed flexibility

In response switching paradigms, participants are instructed to switch between different stimulus-response mappings. Rubia et al. (2006) used a response switching task in which adolescents (10-17 years, all males), and adults (20-43 years, all males) were presented with a grid divided into four squares, with either a horizontal or vertical bidirectional arrow in the middle. On each trial, a red dot appeared in one of the quadrants. When the arrow was horizontal, participants had to judge whether the dot was on the left or right side of the grid. When the arrow was vertical, participants had to judge if the dot was in the upper or lower half of the grid. Behavioral results revealed enhanced switch performance in adults compared to adolescents. When compar-

ing switch trials to non-switch trials, adults showed more activation than adolescents in right inferior PFC, left parietal cortex, anterior cingulate cortex and putamen. The same areas were also found to be related to age in a region of interest and whole-brain regression analysis, further confirming these findings. The most robust age correlations were found in the parietal cortex and basal ganglia, which the authors took to suggest that maturation of these areas is most important for the development of task switching capacity.

Researchers from the same laboratory performed a second study using a similar paradigm with a sample of 63 participants between 13-38 years old (38 males) (Christakou et al., 2009). The behavioral results showed that there were switch costs for both adults and adolescents, but no significant age differences were found. Despite the absence of behavioral differences, with increasing age there was more activity in the bilateral inferior frontal cortex, the anterior cingulate cortex, the caudate nucleus, putamen, thalamus and inferior parietal lobe during switching. This was similar to the findings reported in a previous study using only male participants (Rubia et al., 2006).

A third response switching study was performed by Crone et al. (2006). Participants (17 children 8-12 years, 20 adolescents 13-17 years, 20 adults 18-24 years) were taught to associate three different cues with a pre-specified stimulus-response mapping. Cues could be followed by bivalent stimuli (when depending on the rule, the same stimuli could be associated with different response mappings) or univalent stimuli (stimuli that were always associated with the same response). Switching performance was better for adults and adolescents than for children. The pre-SMA was activated in all groups for rule switching compared to repetition. Interestingly, children also recruited this region more for bivalent repetition trials than for univalent repetition trials, indicating this region is not only active for rule switching but also for rule representation. This suggests a less mature activity pattern in pre-SMA for children compared to adolescents and adults.

A potential confound in task switching studies is the performance difference that is often found between children and adults. Thomas et al. (2011) addressed this issue by using an algorithm that adjusts task difficulty to ensure a similar task performance for all age groups. Participants (21 adolescents 10-16 years and 21 adults 22-40 years) were accustomed to a certain stimulus-response mapping (press '1' for 'X', press '2' for 'O'). When cued with a background color change, they were required to inhibit the prepotent response and replace it with an alternate response (press '3'). Despite the fact that the task was designed to equalize accuracy, there were still significant differences in accuracy between adolescents and adults. The fMRI results indicated that when comparing switch to non-switch trials, adults showed more activity in frontal and parietal areas (bilateral precentral gyri, precuneus, inferior and superior parietal lobule, paracentral lobule). To summarize, the developmental fMRI studies investigating instructed flexibility with response switching paradigms generally find increased activation in frontal and parietal

areas as well as the basal ganglia in adults compared to children or adolescents during switch trials.

Developmental fMRI studies of attention switching

A different aspect of instructed flexibility is investigated with attention switching paradigms. In these tasks, participants are required to switch attention between different perceptual aspects of stimuli. Casey et al. (2004) were the first researchers to investigate attention switching in a developmental fMRI study. Adults (18-23 years, $N = 7$) and children (7-11 years, $N = 7$) performed a task in which they were instructed to judge which of three objects was unique. The unique attribute could be either color or shape, and was alternated on each trial without cueing. Performance on these switch blocks was compared with control blocks, in which the relevant attribute was always color or always shape. Adults performed better on this task in terms of accuracy and reaction time than children. However, no switch costs were found, as indicated by similar behavioral performance on the switch blocks versus the control blocks. A possible explanation is that the task does not require deliberate top-down attention switching, but the unique stimulus ‘pops out’, regardless of the dimension that was being attended to in the previous trial. Neural activity during switch trials compared to non-switch trials resulted in activation in the caudate nucleus in both adults and children. Adults showed more activation during switches than children in the superior frontal gyrus, superior parietal cortex and middle temporal gyrus. However, the task seems to require a minimal amount of cognitive control because the ‘pop-out’ effect of the unique stimulus is probably sufficient for participants to successfully perform the task.

Using a more traditional experimental paradigm for attention switching, Morton, Bosma and Ansari (2009) instructed participants (14 children 11-13 years and 13 adults 19-25 years) to perform the Dimensional Change Card Sorting task. In this task, participants were instructed to sort cards according to changing stimulus dimensions (e.g. red and blue boats and flowers that had to be sorted by either color or shape). Before each trial, participants were cued with the correct sorting rule. When comparing switch and non-switch trials, adults showed more activation in the left posterior parietal cortex and the right thalamus compared to children. Children showed more activation than adults in the right superior frontal sulcus. Behavioral performance was similar for children and adults, suggesting that the age differences could not be explained in terms of performance differences. The authors hypothesized that the parietal cortex is less efficient in children than in adults, leading to compensatory recruitment of the frontal sulcus area. The increased recruitment of superior parietal cortex with development concurs with the findings of Casey et al. (2004). An important difference is that Morton et al. (2009) found a frontoparietal network associated with switching, whereas this network was not found in the Casey et al. (2004) study. Possibly, this is due to the limited cognitive control demands in the experimental task of Casey et al. (2004).

The attention switching findings partly correspond to the results from response switching paradigms (Christakou et al., 2009; Crone, Bunge, et al., 2006; Rubia et al., 2006). That is to say, using both approaches, a frontoparietal/subcortical network associated with switching was found, that was generally more pronounced in adults than children. However, the exact loci of activation were slightly different, indicating that response switching and attention switching may rely on different underlying processes. In line with this hypothesis, similar findings were reported in the direct comparison of these two types of switching in the meta-analysis on adult studies by Kim et al. (2012). An unexpected result was that Morton et al. (2009) found increased activation in a frontal area in children relative to adults. Possibly, the dimensional task switching paradigm used in the Morton et al. (2009) study requires additional processes that are not present in response shifting. This may cause strategy differences between children and adults, which in turn can result in different patterns of neural activity. Children may, for instance, resort to more effortful strategies for updating working memory, which explains the increase in frontal activity. Together, these findings demonstrate that specific task demands can result in different patterns of neural activation across development. In the next paragraph, age differences in task specific demands will be further investigated in the development of adaptive flexibility.

Development of adaptive flexibility

Behavioral development of adaptive flexibility

A second type of cognitive flexibility is adaptive flexibility, which is switching based on performance feedback. Rather than switching based on an arbitrary cue, performance feedback indicates whether a switch is necessary in order to maintain optimal performance. This method of studying cognitive flexibility may more closely resemble real-life situations.

The task that has been the most widely used to study performance-based switching is the Wisconsin Card Sorting Task (WCST; Milner, 1963). In the WCST, participants are instructed to sort cards with pictures following different sorting rules (based on number, color and shape). After sorting, positive or negative performance feedback is provided, indicating whether the correct rule was applied. The rule can change without warning; therefore, the switch cue is the unexpected negative feedback after a certain number of correct sorts. When this happens, participants have to use positive and negative feedback to find the correct rule again. Performance on the WCST improves dramatically in school-aged children, and reaches adult levels around the age of 12 years (Crone, Ridderinkhof, Worm, Somsen, & van der Molen, 2004). Interestingly, some authors have suggested that performance of children is similar to that of patients with damage to the lateral prefrontal cortex (Chelune & Baer, 1986). Similar to prefrontal patients, children have difficulty switching to a new rule and persevere in the old rule; even if feedback indicates this is no longer correct.

The WCST has been a promising starting point for experimental research into the development of adaptive cognitive flexibility (performance-based switching). The WCST is a more complex task than the simple task switching paradigm, but it may therefore also more adequately reflect the complex nature of flexibility in daily life. Several different subprocesses are necessary for successful performance-based switching. It is essential to investigate these different processes in isolation to come to a full understanding of the development of performance-based switching.

One of the complications in the study of performance-based switching is that positive and negative feedback can have different meanings in different stages of an experimental task. For instance, Barcelo and Knight (2002) analyzed error types in the WCST and distinguished efficient errors (errors during the search for a new rule) and random errors (mistakes in a series of correct responses, due to distraction or memory errors). Along the same vein, positive feedback can also have different meanings. Zanolie, Van Leijenhorst, Rombouts and Crone (2008) distinguished first positive feedback (the first positive feedback when the new correct rule is found) and correct responses (when participants are continuing to use the correct response). First positive feedback provides new information that is valuable for learning, whereas correct positive feedback merely confirms what the participant already knows. Because of these differences in informative value, it is important to distinguish different feedback types, since they may rely on different neural processes.

A second complication in the study of performance-based switching is that behavioral outcomes cannot be measured until the next trial occurs. fMRI provides an excellent tool to distinguish the processes underlying performance-based switching. An advantage of fMRI studies is that we can focus on the effects of learning signals (i.e., feedback) in the brain, instead of on the subsequent behavioral response. To date, several neuroimaging studies have investigated the neural underpinnings of feedback processing in adults.

The previously mentioned meta-analysis on different types of task switching in adults already indicated that there are both domain-general areas that are activated for all types of switching, as well as specific activations for adaptive flexibility (Kim et al., 2012). Most of the studies analyzed in this meta-analysis on adaptive flexibility used paradigms based on the WCST, but also included semantic classification tasks, letter matching tasks, visual detection tasks and intra-extradimensional switching tasks. The focus in these studies was usually on the differences in activity for switch and non-switch trials. Other studies have specifically investigated activations during the presentation of positive and negative performance feedback. This approach is also crucial for our understanding of adaptive flexibility because it allows researchers to investigate the neural reactions to an adaptive learning signal.

fMRI results in adults have indicated that for feedback processing, a network similar to the task switching network is activated, including DLPFC, medial PFC (particularly SMA/ACC), parietal areas and the caudate (Holroyd et al., 2004; van Veen, Holroyd, Cohen, Stenger, & Carter, 2004; Zanolie et al., 2008). These areas have typically been found when comparing activity for

negative feedback with activity for positive feedback. This contrast is similar to the comparison between switch and non-switch trials, because negative feedback by definition indicates a ‘switch’ in behavior is necessary for optimal performance. However, not all studies have replicated this negative feedback network. For instance, Nieuwenhuis, Slagter, von Geusau, Heslenfeld and Holroyd (2005) failed to find differential activity to negative feedback in the medial prefrontal cortex using a time-estimation paradigm. Possibly, both positive and negative feedback signals are informative for adaptive learning, especially when both can be used to improve performance. Further research is necessary to unravel the exact contributions of the cognitive control network to feedback processing. In the next section, an overview of the developmental fMRI studies on adaptive flexibility will be provided.

Neurocognitive development of adaptive flexibility

The first neuroimaging study to investigate adaptive flexibility in children used a WCST-like paradigm (Crone et al., 2008). The task was child-friendly and instead of the extra-dimensional switches that are required in the WCST, there were three different rules based on only one dimension (location). Participants (17 children 8-11y, 20 adolescents 14-15y and 20 adults 18-24y) were instructed to ‘help a dog find its way home’ (i.e., find the correct location out of four possible options). Different positive and negative feedback types were distinguished. Adults showed more activation in ACC after negative feedback which indicated a switch (and thus violated expectations) and in the DLPFC after error-related negative feedback. In contrast to adults, children did not differentiate between the different negative feedback types in the DLPFC and ACC. The results (see Figure 1) demonstrate that, with development, there is an age-related specialization in the ACC and DLPFC in their contribution to feedback monitoring. This led to the hypothesis that children have difficulty recognizing the informative value for learning in the different feedback types. Together these results indicate that over the course of development, ACC and DLPFC regions become more specialized for different types of feedback.

One of the difficulties with the Crone et al. (2008) study is that negative feedback was unexpected and therefore may have been more salient than positive feedback. Van Duijvenvoorde, Zanolie, Rombouts, Raijmakers and Crone (2008) examined this question by focusing on learning from positive and negative feedback. Participants (18 children 8-9y, 19 early adolescents 11-13y, 18 adults 18-25y) performed a task in which positive and negative feedback were used to find one of two correct sorting rules (sort by color or sort by shape). Two stimuli were always presented in pairs of trials: a guess trial and a repetition trial. On guess trials, the correct sorting rule (e.g. color or shape) was cued, and the participant had to infer the correct answer based on positive or negative feedback (with an expected value of 50% correct). On the subsequent trial, the participant was expected to apply the correct rule based on information retrieved from the guess trial. The behavioral results showed that adults were better at using performance feedback than adolescents, who in turn performed better than children. Additional-

ly, children performed relatively more inaccurately after negative feedback than after positive feedback. This valence difference was reflected in neural activation patterns. For adults, DLPFC and superior parietal cortex were more active after negative feedback, whereas in children (8-9-years), these areas were activated more after positive feedback. The adolescents did not differentiate between positive and negative feedback, suggesting the turning point was around this age (11-13-years). For both adolescents and adults, but not for children, the SMA was more active after negative than positive feedback. Thus, SMA involvement during feedback learning seems to reach adults levels before the DLPFC.

Finally, in a third paradigm feedback processing was studied using a probabilistic learning task. In such paradigms, feedback is correct on approximately 70-80 percent of the trials. These tasks are more complex than tasks that use determinative feedback (which is by definition 100 percent valid) because it requires attending to long term goals. In a study by van den Bos, Guroglu, van den Bulk, Rombouts and Crone (2009) participants (18 children 8-11y, 27 adolescents 13-16y and 22 adults 18-22y) were instructed to respond to one of two pictures. One picture resulted in positive feedback on 70-80 percent of the trials and the other picture resulted in positive feedback on 20-30 percent of the trials. Children, adolescents and adults performed equally well on the task. Interestingly, when exploring alternative rules (the stimuli that do not result in the highest probability of positive feedback), children showed more activity in DLPFC and dACC after positive feedback, whereas adults showed more activation in these areas after negative feedback. Because these differences were only found when exploring alternative rules, this suggests that the developmental difference is not simply a valence effect (van Duijvenvoorde et al., 2008) but the informative value for learning that shows a different neural developmental trajectory.

Taken together, the studies that investigated the development of adaptive flexibility have demonstrated that with increasing age, several brain areas in the cognitive control network become more specialized for different types of performance feedback. Activity in prefrontal areas (DLPFC, ACC) is more differentiated in adults for different types of positive and negative feedback, which suggests that with development, these areas become more sensitive to the informative value of feedback. The question for future research is how the development takes place in learning from positive to negative, and learning from non-informative to informative feedback.

Overall summary

The neural circuits underlying the development of instructed flexibility and adaptive flexibility were reviewed in this chapter. The development of instructed flexibility has been investigated with two types of task switching: response switching and attention switching. For both paradigms, better behavioral performance was generally found for adults compared to children (but see Christakou et al. (2009) and Morton et al. (2009) for exceptions). Concurrent with these behavioral differences, increased activity for adults compared to children for switching was found in

frontal and parietal areas, the basal ganglia and the thalamus. Morton et al. (2009) additionally found increased activity for children in the right superior frontal sulcus, suggesting possible strategy differences between adults and children. Second, for adaptive flexibility a different developmental pattern was found. Performance-monitoring paradigms have found an age-related specialization of frontal and parietal areas for processing different types of feedback (non-informative versus informative, positive versus negative). These findings indicate that instructed flexibility and adaptive flexibility are separable processes that both contribute to cognitive flexibility. How and when these processes interact is an important question for future research.

Future directions

As highlighted in this chapter, over the past decade several researchers have attempted to understand the neural development underlying the development of cognitive flexibility. Although the current body of literature has provided valuable insights into cognitive flexibility, several advancements can be made which will allow us to draw more firm conclusions about the development of cognitive flexibility. We recommend three directions for future research:

Longitudinal studies

To date, only one study has investigated the neurocognitive development of cognitive flexibility with a longitudinal design (Koolschijn et al., 2011). Included in this study on performance monitoring were the same participants that participated in the Crone et al (2008) study (N at follow up after 3.5 years: 10 adults, 12 adolescents and 10 children). The results indicated that the neural networks involved during the WCST-like task changed over the 3.5 year interval: more activity was found in DLPFC, superior parietal cortex and ACC. Intriguingly, these changes were strongly related to performance improvements, more so than to age per se. This suggests that in previous cross-sectional studies, which often found performance differences between age groups, performance differences can possibly partly explain neural differences between age groups.

The findings of this study highlight the importance of longitudinal designs in developmental psychology and developmental cognitive neuroscience. Longitudinal studies have important advantages over cross-sectional studies (where different age groups are compared as a proxy for development). With longitudinal designs, it is possible to truly investigate development within participants. In cross-sectional designs, within-subject development may be masked if between-subject variability in developmental trajectories is relatively large. Cohort effects (generational differences between age groups other than age) are not a confounding factor in longitudinal studies. Given the important behavioral improvements within individuals over time, longitudinal designs will be of critical importance for future research into the development of cognitive flexibility.

Network analyses

Several studies in adults have indicated that, for cognitive flexibility tasks, it is not only important *which* areas are activated, but also how these areas interact with each other (Madden et al., 2010; Stelzel, Basten, & Fiebach, 2011; van Schouwenburg, den Ouden, & Cools, 2010). Interaction between different brain areas can be described as *functional connectivity*. With functional connectivity analyses, it is possible to investigate temporal correlations between neural signals in different brain areas. It is assumed that a temporal correlation means that these regions work in concert. Research into the development of functional connectivity is an important future venture that undoubtedly will provide us with further insights into the neural development of cognitive flexibility (Morton, 2010; Stevens, 2009).

One developmental study that has investigated functional connectivity in adaptive flexibility was performed by Van den Bos, Cohen, Kahnt and Crone (2012). They re-analyzed the data from a study on probabilistic feedback learning (van den Bos et al., 2009). For all trials, the ‘prediction error’ was calculated using a simple reinforcement learning model. When feedback for a stimulus was better than expected, a positive prediction error was generated by the model for that stimulus, which in turn increases the decision weight for that stimulus (i.e., the chance that stimulus will be selected on the next trial is larger). When feedback was worse than expected, a negative prediction error was generated, resulting in a lower decision weight. The researchers found that the representation of the prediction error resulted in robust activation in the striatum, an effect that was similar across age groups. Interestingly, a functional connectivity analysis showed that with increasing age, the connectivity between activity in the striatum and medial PFC increased. The strength of this connection was also related to the tendency to change expectations after negative feedback. These findings demonstrate that focusing on network analyses can provide additional information over focusing on activity in single brain areas.

Genetics

Finally, recent studies have indicated that there are profound genetic influences on executive functioning. This has been found with both quantitative and molecular genetics studies (Morton, 2010). In quantitative genetic studies, family members who share different percentages of their genes are compared in executive functioning skills. For instance, monozygotic twins share 100 percent of their genes, whereas dizygotic twins and siblings share 50 percent of their genes. A comparison of executive functioning in the different family members can provide an estimate of the amount of variation that is explained by genes or environmental influences. With this approach, it was found that executive functions have a surprisingly high heritability factor (Friedman et al., 2008). This means that monozygotic twins who grow up in completely different environments, will still be very comparable in terms of their executive functioning.

Another approach to investigate genetic influences on executive functioning is to examine specific genetic variations in a particular gene. People who have one variation of the gene can

be compared in executive functioning skills to people with another variation of the gene. With this approach, genetic differences that influence dopamine functioning have already been found in adults for learning from errors (Klein et al., 2007) and task switching (Colzato, Waszak, Nieuwenhuis, Posthuma, & Hommel, 2010; van Holstein et al., 2011) and in children for feedback processing (Althaus et al., 2009). Although few studies have investigated genetic influences on the development of cognitive flexibility, the current body of literature provides strong indications that these influences are likely to be found in future studies.

Conclusion

Executive functions in general, and cognitive flexibility in particular, are important aspects of child development. Cognitive flexibility has been studied extensively in children, which has led to important insights on its developmental origins. Two main types of cognitive flexibility were described in this chapter: instructed and adaptive flexibility. Maturation of brain areas involved in cognitive flexibility tasks seems to play an important role in the development of both types of flexibility. Despite the great progress in this area of research, there are also still many open questions. Future studies should focus on combined approaches using different types of cognitive flexibility in the same individuals, to investigate whether they rely on similar neural mechanisms. Additionally, developmental theories have often been inferred from studies on cross-sectional samples. For truly developmental models, longitudinal studies are essential.

To further advance our knowledge, functional connectivity within the cognitive flexibility network should be investigated, as well as possible influences of genetic variations on the development of cognitive flexibility. We expect that, together, these new insights will allow us to better track the developmental trajectory of cognitive flexibility from childhood, through adolescence into adulthood. This knowledge will hopefully help to create better learning environments across childhood development.

