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Demystifying cognitive flexibility: Implications for clinical and developmental neuroscience

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Cognitive flexibility, the readiness with which one can selectively switch between mental processes to generate appropriate behavioral responses, develops in a protracted manner and is compromised in several prevalent neurodevelopmental disorders. It is unclear whether cognitive flexibility arises from neural substrates distinct from the executive control network (ECN) or from the interplay of nodes within this and other networks. Here we review neuroimaging studies of cognitive flexibility, focusing on set shifting and task switching. We propose that more consistent operationalization and study of cognitive flexibility is required in clinical and developmental neuroscience. We suggest that an important avenue for future research is the characterization of the relationship between neural flexibility and cognitive flexibility in typical and atypical development.

Significance of cognitive flexibility

Cognitive flexibility is the ability to appropriately adjust one's behavior according to a changing environment [1,2] (see Glossary). Cognitive flexibility enables an individual to work efficiently to disengage from a previous task, reconfigure a new response set, and implement this new response set to the task at hand. Greater cognitive flexibility is associated with favorable outcomes throughout the lifespan, such as better reading abilities in childhood [3], higher resilience to negative life events and stress in adulthood [4], higher levels of creativity in adulthood [5], and better quality of life in older individuals [6]. Despite the widespread repercussions of intact cognitive flexibility throughout development and into adulthood, rigorous examination of this construct has been elusive.

Defining and measuring cognitive flexibility

Cognitive flexibility can be particularly difficult to examine due to the multitude of ways it has been described in the literature. In some instances cognitive flexibility is discussed in the context of processes requiring shifts in attention (e.g., attentional flexibility [7], attention switching [8], attentional set shifting [9]). In others, it is operationalized by the tasks that are used to measure it (e.g., set shifting [10], task switching [11]).

Here we aim to more precisely define cognitive flexibility to accurately operationalize the construct in behavioral paradigms and link the ability to its neural correlates (Figure 1). Cognitive flexibility is a construct that is an emergent property of efficient executive function (EF) and is typically measured in the laboratory using set shifting or task switching behavioral paradigms. A task can be defined as trials with one set of instructions that govern successful completion. In task switching, participants must switch between tasks with different instructions given some stimulus (e.g., [1,11,12]). For example, in the Badre and Wagner (2006) task, participants must respond by categorizing the stimulus as a vowel/consonant

Glossary

Autism spectrum disorder (ASD): a neurodevelopmental disorder characterized by core deficits in social interaction/communication and the presence of RRBs; those with ASD also have impaired cognitive flexibility [65,69,71,72].
Cognitive flexibility: an emergent property of efficient EF; the ability to appropriately and efficiently adjust one's behavior according to a changing environment [1,2], most commonly measured with task switching and set shifting tasks.
Dynamic functional connectivity: functional connectivity refers to temporal correlations between remote neurophysiological events [84]. Dynamic functional connectivity quantifies changes in functional connectivity metrics over time [85].
Executive function (EF): mental control processes necessary to perform goal-directed behaviors, including working memory, inhibition, and shifting [86].
Inhibition: a subdomain of EF; the ability to control one's attention, behavior, or thoughts to override competing cognitions [87].
Set shifting: a type of lower-level cognitive flexibility task that requires individuals to follow one set of rules to complete a task then shift to using a different set of rules to complete the task [13].
Sliding-window approach to dynamic functional connectivity: a strategy for examining dynamics in fMRI data whereby a time window of fixed length is selected and data points within that window are used to calculate the functional connectivity metric of interest. The window is then shifted in time by a fixed number of data points that defines the amount of overlap between successive windows. This process results in quantification of the time-varying behavior of the chosen metric over the duration of data acquisition [85].
Switch cost: a slowing of response time and decrease in accuracy following a switch trial (versus repeated trials) during task switching and set shifting tasks.
Task switching: a type of higher-level cognitive flexibility task that involves shifting between two types of trial where participants: (i) switch between two simple tasks; and (ii) repeat the same task [12].
Working memory: a subdomain of EF; the short-term storage of information and its 'online' maintenance and manipulation [88].

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Keywords: executive function; inhibition; attention; brain network; dynamic functional connectivity; autism.

0166-2236/
 http://dx.doi.org/10.1016/j.tins.2015.07.003

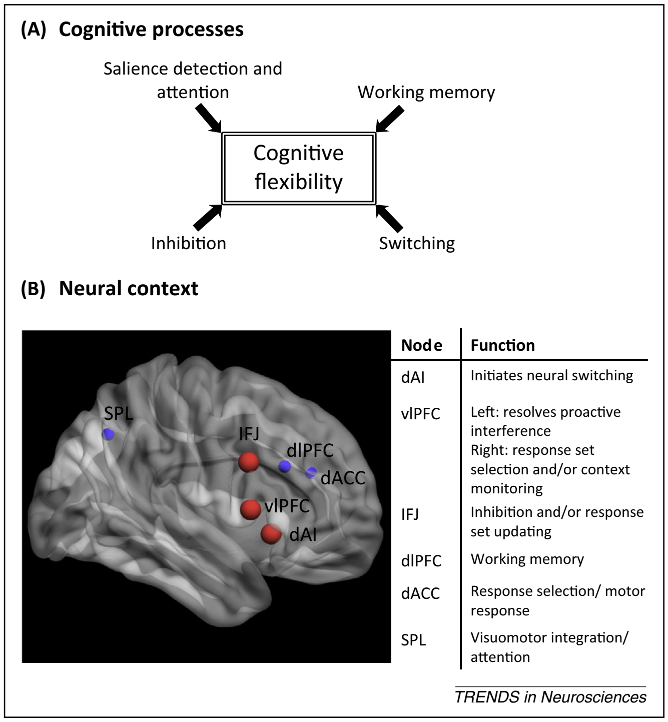

Figure 1. Processes contributing to cognitive flexibility. **(A)** Several cognitive processes work coherently to implement cognitive flexibility. The process of switching has been examined the least because of the difficulty of isolating it from the other processes involved in cognitive flexibility. **(B)** The critical nodes involved in cognitive flexibility (red) in the context of surrounding nodes comprising the executive control network (blue) that work to support component processes such as attention and working memory. The connectivity patterns among nodes may determine which executive function is implemented. The proposed function of each node is listed in the adjacent table. Figure created using BrainNet Viewer (https://www.nitrc.org/projects/bnv/). Abbreviations: dACC, dorsal anterior cingulate cortex [24]; dlPFC, dorsolateral prefrontal cortex [27]; vlPFC, ventrolateral prefrontal cortex (Neurosynth.org 'executive function' query); dAI, dorsal anterior insula [16]; IFJ, inferior frontal junction (Neurosynth.org 'executive function' query); SPL, superior parietal lobule [27].

or odd/even, depending on the cue (e.g., Figure 2A). By contrast, sets comprise different rules within a task that can be used to complete the same overall instruction. Instead of switching between two types of instruction like in task switching, switching between sets may comprise shifting attention between different features of the stimulus to complete the same instruction. For example, in the Casey *et al.* (2004) task, shapes were consistently presented throughout the task and children were instructed to 'pick the unique object' from three stimuli. The children must implicitly determine whether to pick the object based on two perceptual features: shape or color. The instruction (and therefore, the task) is always the same no matter how individuals choose the object. Stimulus–response mapping reversal can also be categorized as a form of set shifting where the goal remains the same (press button x for stimulus y) but simply changing the hand press determines the switch in set (e.g., [13]). Thus, set shifting entails using a new set of rules to complete the same task.

Set shifting is a lower-level form of cognitive flexibility, following the hierarchy of cognitive flexibility outlined by Bunge and Zelazo [14]. These authors conceptualize task switching to be the most complex form of cognitive flexibility and we adopt this view here. Both task switching and set shifting result in slowing of response times and decreases in accuracy, referred to as a 'switch cost'. Switch costs are thought to occur because of the time it takes to inhibit the response set of the previous task as well as the time it takes to reconfigure one's response set to the new task [11,12].

EFs required for cognitive flexibility

Several subdomains of EF act coherently to successfully implement cognitive flexibility (Figure 1). In constantly changing environments, individuals must first identify how their surroundings have changed by directing attention to those elements that are in flux. After ascertaining that a previous strategy is not appropriate in the new environment, individuals must inhibit previous responses and reconfigure a new strategy. Individuals take in information and manipulate it in real time to flexibly switch responses from one scenario to another. Cognitive flexibility is not merely the sum of implementing various EFs but also requires shifting, or the reconfiguration of one's response set to the new goal.

Salience detection

The relative salience of a stimulus determines whether it will capture attention and be processed further. The salience network [including the anterior insula (AI), dorsal anterior cingulate cortex (dACC), and other subcortical and limbic structures] plays a central role in the detection of behaviorally relevant stimuli and the coordination of neural resources [15]. The process of salience detection is the first step toward attention allocation and subsequent implementation of flexible responses. While the posterior and mid-insula act to integrate and transmit interoceptive signals, the AI plays a critical role in orchestrating dynamic interactions between large-scale brain networks for externally oriented and internally oriented attention in neurotypical adults and children [16].

Attention

An influential model of attention posits that the process can be decomposed into goal-directed top-down processing and stimulus-driven bottom-up processing. The dorsal attention network (DAN), composed of the intraparietal sulcus (IPS) and frontal eye fields (FEFs), is thought to underlie top-down processing and the ventral attention network (VAN), composed of the right temporoparietal junction (TPJ) and ventrolateral prefrontal cortex (vlPFC), supports bottom-up attention [17]. Laboratory tasks of cognitive flexibility may involve both of these attentional systems. For example, unexpected stimuli that cue a switch phase direct attention via the VAN. In other tasks, experimenters may provide cues that indicate what rule should be implemented and thus the participant exerts top-down control to orient to the relevant features of the stimulus. These attentional systems may also work synergistically to filter incoming sensory information that is relevant to the goal. Regardless of the extent to which these attentional systems are recruited, the DAN and VAN are critically involved in successful cognitive flexibility.

Working memory

Cognitive flexibility tasks require the maintenance of two or more rule representations for successful completion. Many fMRI paradigms include an additional working memory component over and above this active maintenance of response sets. For example, the cognitive flexibility task developed by Armbruster and colleagues (2012) requires participants to remember a multitude of rules and contingencies with the main objective of using the brighter number presented to determine whether the number is either (i) odd or even or (ii) less than or greater than five, depending on the cue (Figure 2A). In general, task switching paradigms, which are inherently more complex than set shifting tasks, tend to impose greater working memory demands. fMRI studies implementing working memory paradigms generally demonstrate activation of the dorsolateral PFC, vlPFC, and premotor and parietal cortices [18], constituting the ECN. If working memory load is not properly controlled for in task designs, potential confounds can arise when attempting to identify neural correlates of cognitive flexibility.

Inhibition

When actions and goals need to be updated to adapt to a new environment, previously engaged responses must be inhibited. Inhibitory control is thus a crucial aspect of cognitive flexibility [19]. The brain regions most consistently involved in inhibitory control are the right vlPFC [20,21], AI, and inferior frontal junction (IFJ) [22]. Recent studies have aimed to delineate the separable functional roles of these three regions in inhibitory control. Cai and colleagues [23] revealed that the rAI is particularly important for detecting behaviorally relevant events, highlighting its role as a node in the salience network [24]. Sebastian and colleagues [25] demonstrated that the rIFJ is important for detection of behaviorally relevant stimuli, emphasizing its primary involvement as a possible mediator between the dorsal and ventral attention networks. Mirroring the Cai *et al.* (2014) results demonstrating the specific functional role of the right vlPFC in inhibitory control, Sebastian *et al.* (2015) showed that the right vlPFC is involved in response inhibition as it interacts with motor regions to update action sequences.

Brain networks underlying cognitive flexibility

Recent meta-analyses of neuroimaging studies of cognitive flexibility in neurotypical adults have identified a distributed network of frontoparietal regions involved in flexible switching, including high-level cortical association areas (vlPFC, dlPFC, anterior cingulate, right AI), the premotor cortex, the inferior and superior parietal cortices, the inferior temporal cortex, the occipital cortex, and subcortical structures such as the caudate and thalamus [26,27]. Ongoing work is attempting to understand how these brain regions interact to form a coherent network to implement cognitive flexibility. Here we highlight the regions that have been most consistently linked with cognitive flexibility and related processes in the neuroimaging literature.

IFJ

The IFJ may be particularly necessary for the updating of task rule representations during task switching [1]. The IFJ is consistently activated across various paradigms eliciting cognitive flexibility such as set shifting and task switching [26]. Further, inhibitory control tasks, in addition to cognitive flexibility tasks, tend to activate the IFJ [28]. The right IFJ is strongly activated for context monitoring during inhibition [29]. The results of these studies suggest a fundamental role of the IFJ in cognitive flexibility, but it is unclear precisely what cognitive operation is implemented by the IFJ. A survey of the tasks engaging the IFJ suggests that this brain region is either the site of response-set updating of task rules or the site of inhibition

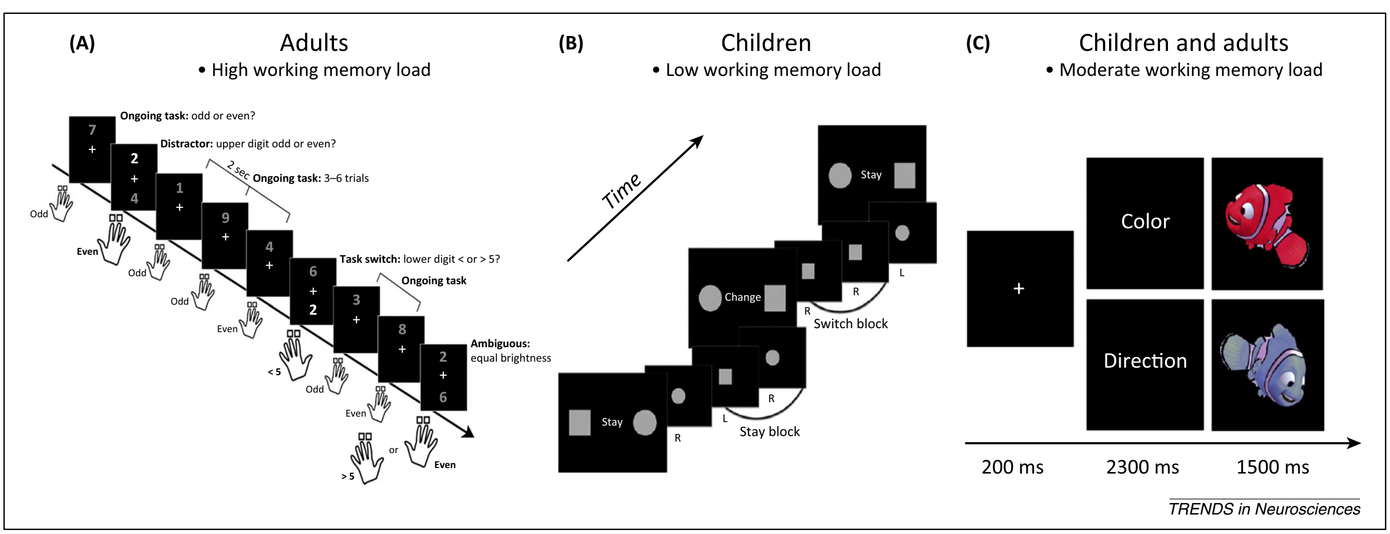

Figure 2. Cognitive flexibility tasks adapted for fMRI. Various task paradigms designed to elicit cognitive flexibility in adults, children, or both cohorts. **(A)** Adult task reprinted from [1], with permission from MIT Press. The task comprises three conditions: the ongoing task, a distractor requiring inhibition, and a task switch. To complete the task, the participant must use the brighter digit if two digits appear. The location of the brighter digit determines whether the condition is the distractor or the task switch. **(B)** Task reprinted, with permission, from [13]. The task comprises stay and switch conditions. Children must respond with their right or left hand based on the spatial mapping of the stimuli on the instruction cue. **(C)** Developmental task reprinted, with permission, from [55]. Participants must respond with either their right or left hand to indicate the color or direction of the Nemo fish, dependent on the instruction cue. Response–stimulus mapping remains constant throughout the task.

of the previous response set. The fact that inhibition is inherently involved in cognitive flexibility may explain why the IFJ is consistently activated across paradigms requiring participants to flexibly switch their response set or task rule representation.

vlPFC

The vlPFC, widely implicated in inhibitory control [20,21,29], is also consistently recruited during cognitive flexibility tasks. Badre and Wagner (2006) surmise a specific role of the left vlPFC in resolving proactive interference from the previous task set. Dippel and Beste [30] argue that the right vlPFC promotes selection of a strategy that hierarchically structures actions during tasks that require complex sequencing of motor actions. Their data suggest that the right vlPFC supports the selection of the most efficacious response set when confronted with a task requiring various possible responses, such as during task switching or set shifting paradigms.

Posterior parietal cortex (PPC)

One of the most robust regions of activation across various cognitive flexibility tasks is the PPC [26]. The PPC is the site of visual attentional processing and visuomotor integration [31], which are likely to drive this region's recruitment during various cognitive flexibility tasks. Parietal cortices tend to show stronger activation than prefrontal areas during cognitive flexibility tasks [32,33], perhaps due to the strong attentional components necessary to successfully switch response sets. Thus, involvement of the PPC may not be specifically related to the shifting processes inherent to cognitive flexibility tasks, which are likely to rely on prefrontal cortices.

Insula and ACC

Other areas consistently reported in cognitive flexibility fMRI studies are the ACC and AI [27,28,34–36], which are key nodes of the salience network [24] or cingulo-opercular network [37]. As discussed in the previous section on executive processes, nodes of the salience network may be critically involved in shifting attention to the new response set.

Delineating a cognitive flexibility network in the context of an ECN

Cognition is achieved through the interplay of anatomically separated and interconnected local networks defining large-scale networks subserving attention, language, memory, and other cognitive processes [38]. Network views of cognition and behavior currently dominate the cognitive neuroscience landscape [39,40]. Cognitive flexibility is likely to emerge from the interplay of specific nodes in the frontal and parietal cortices, all of which are necessary while each provides a relatively specific functional contribution. These nodes may not be specific to cognitive flexibility but are activated across a range of other EFs such as working memory, attention, and inhibition [27]. The neural context in which these nodes operate, such as their connectivity with other nodes [41], may determine which cognitive operation is conducted. We propose that within the domain-general ECN, the specific computations among nodes and their anatomical specificity within the broader frontoparietal networks determine which EF is behaviorally observed. Particularly important for distinguishing brain activity between various EFs may be the temporal dynamics of internode connectivity. In cognitive flexibility, working memory is continuously involved as task representations must be maintained, giving rise to dlPFC activity. With a change in environment (or task cue or response feedback), dorsal and ventral attention networks come online, where FEF–PPC and vlPFC–TPJ activity would be expected. dAI activity may then drive the switch to another neural network involving frontal regions such as the right vlPFC [42] and IFJ, which are required to inhibit the previous task representation and employ the new rule. This model is speculative at this time and remains to be validated with future causal modeling studies.

Development of cognitive flexibility and associated brain regions

Behavioral trajectories

Cognitive flexibility skills begin to develop in early childhood, with a sharp increase in abilities between 7 and 9 years of age. Cognitive flexibility becomes largely mature by 10 years of age [43] but skills continue to improve throughout adolescence and into adulthood [44,45], reaching their peak between the ages of 21 and 30 years [46]. Components of EF involved in cognitive flexibility follow different developmental trajectories (Figure 3). Inhibition develops as early as 12 months and is largely mature by 10–12 years of age. Working memory also emerges early in toddlerhood and continues to improve throughout adolescence [45]. Because component EFs involved in cognitive flexibility do not follow identical developmental trajectories, if measures are not taken to control for inhibitory and working memory demands in

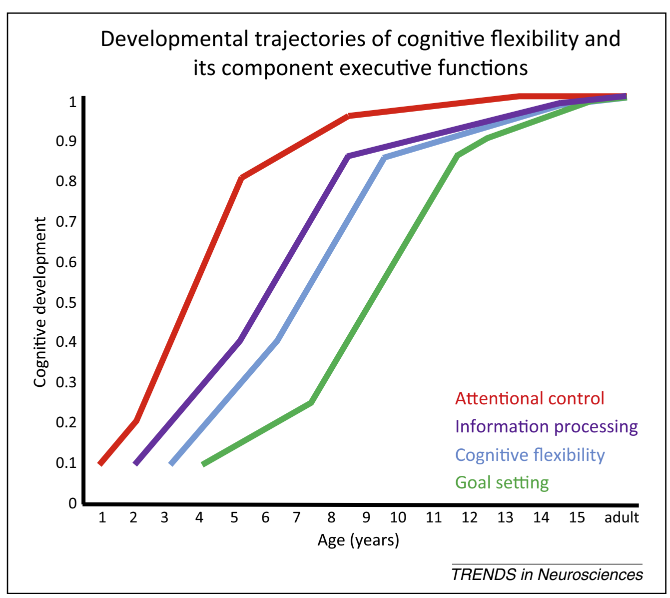

Figure 3. Developmental trajectories of cognitive flexibility and component executive functions. Hypothesized developmental trajectories of attentional control, information processing, cognitive flexibility, and goal setting relative to mature adult levels of cognitive development. Adapted from [44], with permission from Taylor & Francis. (http://www.tandfonline.com).

task design, adults will outperform children on cognitive flexibility tasks.

Behavioral studies suggest that children use qualitatively different strategies from adults to implement flexible cognition [47–49]. Around 8–9 years of age, children change their control strategies from retrieving the task goal by orienting their attention to the relevant stimulus features to using cue–stimulus–response associations [49]. Inhibition and working memory contribute to successful cognitive flexibility beginning around 4 years of age, driven by advances in children's goal-representation abilities [50]. Faster and more accurate cognitive flexibility skills in adulthood may be attributed to improvements in perceptual speed, superior working memory [46], improved resistance to interference from the irrelevant task [46,51], the use of associative processing [49], and improved task set reconfiguration abilities [52].

EF network development

Most studies of cognitive flexibility comparing children and adults find higher levels of, and more specific, activation in the frontal, parietal, and basal ganglia regions in adults and more dispersed activations in children [53,54], whereas others report little difference in brain activation between age groups [55]. One interesting finding is a general increase in activation in right-lateralized regions and decrease in activation in left-lateralized regions with age [54,56,57]. It is unclear whether this is due to the functional segregation of interhemispheric homologs specific to EFs or the spatial demands of most cognitive flexibility tasks, which may preferentially recruit the right hemisphere with development.

Young children (around 5 years of age) tend to have difficulty processing task cues efficiently to determine the relevant task [48,58,59]. Cue monitoring is also an important facet of inhibition [60] that may be subserved by the right vlPFC [29]. Developmental brain network differences between children and adults may be partially explained by improvements in cue monitoring, possibly driven by maturation of the right vlPFC. In support of this view, Rubia *et al.* [54] showed a linear increase in activation of right vlPFC from childhood to adulthood during both inhibition and switching tasks.

Executive dysfunction and cognitive inflexibility

The rudimentary versions of EF that emerge in infancy lay a foundation for the emergence of more mature EFs that underlie self-control. In middle childhood, executive dysfunction that was previously masked may become apparent as children begin to be challenged academically and socially [45]. In particular, decreased levels of cognitive flexibility and working memory are associated with a range of academic deficits from reading to science [3]. In adolescence, intact EF is demonstrated as the ability to think through decisions before acting, requiring the inhibition of automatic responses, and the ability to make effective decisions given a desired goal [45]. As EF skills become increasingly effective as adolescents progress into adulthood, the sum of various executive dysfunctions that have accumulated across time may have the greatest impact during adulthood. In adults, cognitive inflexibility is associated with clinical symptoms such as rumination [61] and longer duration of eating disorder illness [62].

Various neurodevelopmental disorders such as autism spectrum disorder (ASD), attention-deficit hyperactivity disorder, and obsessive–compulsive disorder are accompanied by executive dysfunction [63–65]. Although cognitive flexibility deficits may be present in all three disorders, it may be most profoundly impacted in ASD [66,67] and is specifically linked with the core symptoms of ASD [68,69]. Further, the neurobiology of cognitive flexibility deficits in ASD has been largely neglected by the literature and therefore should be further characterized as a possible model for aberrant neural correlates of cognitive flexibility that may generalize to other disorders. Using ASD as a model, we may be able to better characterize deficiencies in the goal selection, updating, and representation/maintenance subconstructs of cognitive control, as put forward by the Research Domain Criteria [70].

Cognitive inflexibility in ASD

ASD is a neurodevelopmental disorder characterized by core deficits in social interaction and social communication in addition to the presence of restricted and repetitive behaviors (RRBs) [71]. ASD is characterized by a distinct executive dysfunction profile of impaired cognitive flexibility and planning abilities with intact inhibitory control [65,69,72]. Further, cognitive inflexibility in ASD is associated with higher levels of RRBs [68,69]. Despite the clear link between cognitive inflexibility and RRBs in ASD, this core deficit has been underexamined in the neuroimaging literature.

Currently, there are four published neuroimaging studies of cognitive flexibility in ASD [13,36,57,73]. The Schmitz *et al.* (2006) and Yerys *et al.* (2015) studies reported greater activation in frontoparietal regions in children with ASD during a cognitive flexibility task,

Box 1. Developmental and clinical considerations in study design

Tasks should be designed to isolate activations associated specifically with cognitive flexibility while separating the activity from or controlling for working memory and inhibitory control processes. Further, when considering task design researchers must keep in mind the differential development of working memory and inhibition that undoubtedly contributes to cognitive flexibility performance. To control for task difficulty between children and adults, researchers should aim to match accuracy levels between age cohorts. Another approach that has previously been used is to administer tasks of differing difficulty between age cohorts but match groups on accuracy [17], although this approach may introduce confounds due to the inherent differences between tasks. The most valid measures of cognitive flexibility will produce a switch cost, so tasks should be designed with this in mind. To ensure the reliability and validity of cognitive flexibility tasks, psychometric analyses should be conducted prior to development of novel fMRI tasks. Finally, it should be considered that although clinical populations, developmental cohorts, and neurotypical adults may be matched on behavioral performance, this may not be an ecologically valid representation of the real world. In studying ASD specifically, more work should be done to assess the extent of the relationship between neural flexibility, cognitive flexibility, and the diminished behavioral flexibility that presents as RRBs.

whereas Shafritz *et al.* (2008) reported reduced activation in children with ASD that correlated with higher RRBs. Taylor *et al.* (2011) considered developmental effects and found that, although the right insula tended to increase in activation from 7–14 years, in ASD the activation decreased with age. The only consistent finding among this limited literature is the clear differences in activation patterns present in children with ASD while implementing cognitive flexibility. All studies controlled for accuracy; therefore, these altered brain activation profiles could represent compensatory mechanisms required to successfully implement cognitive flexibility in ASD.

To obtain a coherent picture of divergent developmental trajectories, important clinical and developmental issues must be considered (Box 1). To synthesize research findings on this topic and move forward in a coherent manner, the scientific community should adopt a single construct to refer to the appropriate adjustment of behavior in a changing environment: cognitive flexibility.

Future directions: relating neural flexibility and brain dynamics to cognitive flexibility

An emerging literature suggests that brain signal variability, or neural variability, may represent a complex neural system capable of great dynamic range and an enhanced ability to efficiently process varied unexpected external stimuli [74]. Brains of older individuals exhibiting less consistent behavioral performance exhibit reduced variability of blood-oxygen level-dependent (BOLD) signal compared with brains of younger individuals [75]. These findings have led to the proposal that variability in brain function is necessary for optimal responsivity to changing environmental demands [76,77].

It has recently been demonstrated that, in typical development, greater variability of functional connection strengths across time can be seen with increasing age [78]. Although neural variability appears to be beneficial in typical development, excessive neural variability may be maladaptive in clinical disorders such as ASD [79]. Both EEG and fMRI studies of individuals with ASD have reported excessive neural variability compared with controls across primary sensory brain regions [79]. We have recently found evidence for decreased levels of discriminability between evoked and intrinsic functional brain network configurations in children with ASD compared with typically developing (TD) children and further linked this neural flexibility measure with severity of RRBs in ASD [80]. These studies suggest that an optimal level of neural flexibility must be maintained to support cognitive flexibility throughout the lifespan.

A new analytic approach, dynamic functional connectivity, attempts to account for variations in brain network topology as a function of time [81,82]. The functional significance of dynamic functional connectivity in the brain remains under investigation, but there is already evidence to suggest that these brain dynamics have consequences for behavior. Individuals with brain networks exhibiting greater dynamics show enhanced performance on behavioral tasks including measures of sustained attention and fluid intelligence [83]. A natural question is the extent to which brain dynamics or neural flexibility indices can explain individual differences in cognitive flexibility throughout development.

Box 2. Outstanding questions

- How does the brain mature across childhood and adolescence to produce mature EFs?
  - The development of brain networks that support EFs has not been thoroughly characterized, with current developmental studies offering mixed results derived from cross-sectional datasets [53–57].
  - Future studies should employ longitudinal designs to determine how EF networks emerge from childhood to adulthood. See Box 1 for suggestions on the design of a developmental study of EF networks.
- Does cognitive flexibility require a shifting process above and beyond working memory and inhibitory processes, and how is this represented in the brain?
  - Behavioral studies [89] suggest that there are updating and shifting abilities unique from common EF ability. Neuroimaging studies that aim to delineate activation and connectivity specific to shifting, over and above attention, salience, working memory, and inhibitory processes, are needed to confirm the behavioral dissociation of shifting from other EFs.
  - To test this question, researchers should employ cognitive flexibility fMRI studies by administering a battery of EF tasks including attention, inhibition, working memory, and set shifting in the scanner and calculating contrasts of set shifting > other EFs. Psychophysiological interaction analyses can help disentangle connectivity profiles that may be specific to cognitive flexibility.
- What are the connectivity patterns among nodes in the ECN responsible for producing successful cognitive flexibility?
  - Studying the temporal dynamics of the communication among ECN nodes may be necessary to parse how the brain enables cognitive flexibility.
  - Event-related fMRI task designs and BOLD response profile analysis across the duration of a trial may be necessary to tease apart this sequence of internode connectivity that gives rise to cognitive flexibility.
- How do optimal brain dynamics and neural flexibility contribute to cognitive flexibility?
  - A growing literature suggests that moment-to-moment fluctuations in patterns of brain connectivity are relevant for various behaviors.
  - Dynamic functional connectivity approaches to examining typical and atypical development will enable greater insights into the appropriate levels of neural flexibility required for achieving optimal levels of cognitive flexibility.

Concluding remarks

Cognitive flexibility is a critical skill that enables individuals to accurately and efficiently respond in the face of changing environments. The specific interactions among key network nodes that are required to successfully implement cognitive flexibility continue to be characterized (Box 2). Important considerations need to be accounted for as researchers begin to examine the development of cognitive flexibility and its disruption in various disorders such as ASD. Taking into account developmental differences in working memory and inhibitory abilities is a first step toward designing more reliable laboratory tasks of cognitive flexibility. Leveraging advances in the study of brain network dynamics will also move the field forward in a synergistic manner to discover the relationship between neural flexibility and cognitive flexibility in typical and atypical development.

Acknowledgments

This work was supported by awards K01MH092288 and R01MH107549 from the National Institute of Mental Health, a Slifka/Ritvo Innovation in Autism Research Award, and a NARSAD Young Investigator Grant to L.Q.U.

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