Executive Dysfunction in Developmental Psychopathology

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Outline

- Overview of Executive Functions
  - Definition
  - Categories
  - Developmental considerations
  - Presumed neurological localization
- Assessment of Executive Functions
  - Task assessment
  - Behavioral assessment
- Differential Executive Function deficits in developmental psychopathology
  - Caveats and methodological issues
  - Examples from select diagnostic groups
    - ADHD
    - Bipolar Disorder of Childhood
    - Borderline Personality Disorder
  - Future Directions and Implications
“The term Executive Functions refers to a diverse group of cognitive processes that act in a coordinated way to direct perception, emotion, thought and action.”

“Executive functions are responsible for a person’s ability to engage in purposeful, organized, strategic, self-regulated, goal-directed behavior.”

“While the mainstream literature refers to executive functions as the “CEO” of the brain, studies of brain functioning suggest that executive functions are not a unitary trait, but a set of multiple cognitive capacities that act in a coordinated way.”

EF as “The Conductor”

“Orchestration of basic cognitive processes during goal-oriented problem-solving.”

How many Executive Functions are there?

- Some authors choose to capture the nature of EF under broad categories
  - e.g. Adele Diamond says there are three core abilities:
    - **Inhibitory control** (self-control) – the ability to resist a strong inclination to do one thing and instead do what is most appropriate or needed.
    - **Working Memory** – holding information in mind while mentally working with it
    - **Cognitive Flexibility** – being able to easily & quickly switch perspectives or the focus of attention
Others prefer a more detailed description

<table>
<thead>
<tr>
<th>Perceive</th>
<th>Initiate</th>
<th>Modulate/Effort</th>
<th>Gauge</th>
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<tr>
<td>Focus/Select</td>
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<td>Execute</td>
<td>Monitor</td>
<td>Correct</td>
<td>Others....</td>
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Different regions of the brain mature at different ages.

(Thompson et al, 2001 – Image from the UCLA Laboratory of Neuro-Imaging)
When do EF emerge?

- Inhibitory control starts with birth and continues to develop over childhood (and into adulthood)
- Nonverbal working memory starts at about 3 months and continues to develop through two years
- Verbal working memory starts at about two years and develops through 13 years
- Emotional modulation starts around three years and continues to develop into adulthood
- Planning/Organization/Self-Monitoring starts around three years but continues to develop well into the thirties

Isquith, 2010
Developmental Trajectory of EF

Developmental Trajectory of EF

• Brain development really continues from birth through death
• Neuronal migration has typically ended by birth – it is the interconnection between neurons and their subsequent pruning (regression) that is important
• We have normative data on certain kinds of EF, however the range of “normal” is broad
• Interruptions/disturbance in the “normal” processes of development affect critical periods and the subsequent development of skills which require more basic components (e.g. prematurity, abuse, trauma)
• It is important to recognize that EF is a concept that comes from theory, and does not have an exact match to neuroanatomy and neurophysiology.
• Measurement of EF is difficult in that most of the categories of EF are multidimensional, and that behavioral description of EF often doesn’t mesh onto cognitive measures of the same process, which often differ from test to test.
• A behavior that involves EF the first few times it is performed may not as it becomes habitual.
Can’t we use neuroimaging to help?

- Yes, there is evidence of differential volumetric abnormalities in various areas of the brain, across different diagnoses
- Yes, there is evidence of differential white matter abnormalities found in different diagnoses
- Yes, there is evidence of differential activation patterns across different diagnoses.
- However, MRI, fMRI and SPECT scans are inefficient and impractical for the private practitioner
Neurological location of EF

- Multiple areas of the brain are involved in EF, and seem to be specific to specific EF
- Systems involved include the prefrontal cortex, the striatum, thalamic structures and the cerebellum
- EF circuitry interacts with limbic systems to regulate affective arousal and modulation
The five frontal circuits
- Skeletomotor circuit
- Oculomotor circuit
- Dorsolateral prefrontal circuit
- Orbitofrontal circuit
  - Medial
  - Lateral
- Mesial/Anterior Cingulate circuit

(Bradshaw, 2001; Miller & Cummings, 1999)
“The dorsolateral prefrontal circuit is concerned with the highest cognitive or “executive” functions, which include the capacity to operate via self-direction or without external guidance, the organisation of new behaviours, goal direction, strategy, planning, cognitive flexibility, the maintenance or shifting of set and attention, problem solving, and judgement. Damage, not surprisingly, is associated with the “dysexecutive syndrome”.

(Bradshaw, 2001, p. 32)
“The lateral orbitofrontal circuit is involved with social restraint, empathy, inhibition of interference from external cues, self-monitoring, and the social aspects of personality. Damage or dysfunction in one or other direction results in disinhibition, tactlessness, lack of empathy, inappropriate behaviour, sociopathy, hypomania, explosive aggression, and obsessions or compulsions.”

(Bradshaw, 2001, p. 32)
“The mesially located anterior cingulate circuit mediates initiation of action, response intention, and focused attention, with damage resulting in reduced initiative, apathy, disorders of motivation, attention, and exploration.”

(Bradshaw, 2001, p.33)
Zelazo and Mueller (2002) distinguish between the more cognitive (cool) aspects of EF, associated with the dorsolateral-prefrontal cortex, and the more affective (hot) aspects of EF, associated with orbital and medial prefrontal cortex.

“Cool” EF is elicited by relatively abstract, decontextualized tasks such as those typically used in cognitive testing.

“Hot” EF is elicited by problems that involve high affective involvement.

E.G., in ADHD – inattention is a “cool” symptom while hyperactivity/impulsivity is a “hot” symptom.

“Hot” and “Cold” EF
• There is a great deal of overlap between symptoms of various diagnoses.
• There is a great deal of comorbidity among childhood presentations of various diagnoses (e.g. it is estimated that the comorbidity of BP and ADHD ranges from 60-93%)
• “...developing a neurocognitive profile of each disorder would aide in differential diagnosis and avoid the pitfalls of misdiagnosis in youth.”

Walshaw et al

Why study the neuropsychology of developmental psychopathology?
Whenever I think I have the answer, it usually means I didn’t understand the question.

- Growth in the understanding of neurological structures and circuits is growing so rapidly that it is difficult to keep up.
- Focusing upon external or behavioral manifestations of these symptoms allows me to avoid erroneous “localization” of presumed “lesions” which may not be valid.
Overview of Executive Functions
  ◦ Definition
  ◦ Categories
  ◦ Developmental considerations
  ◦ Presumed neurological localization

Assessment of Executive Functions
  ◦ Task assessment
  ◦ Behavioral assessment

Differential Executive Function deficits in developmental psychopathology
  ◦ Caveats and methodological issues
  ◦ Examples from select diagnostic groups
    • ADHD
    • Bipolar Disorder of Childhood
    • Borderline Personality Disorder
  ◦ Future Directions and Implications
Many specific neuropsychological tasks have been developed to measure EF.

Factor analysis of test batteries of EF do not find a “single” EF factor, but rather (at least) five factors:

- Inhibition
- Working memory
- Planning
- Set-shifting
- Fluency

There are multiple measures of each of the above, with seeming differences in required skills even between two measures that purportedly tap the same skill.
# Common tasks of EF

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<thead>
<tr>
<th>EF Domain</th>
<th>Tasks</th>
<th>Tests</th>
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<tr>
<td>Inhibition</td>
<td>Response inhibition</td>
<td>Continuous Performance Tests</td>
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<td>NEPSY Statue</td>
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<td>Interference control</td>
<td>Stroop-like tasks</td>
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<td>Working Memory</td>
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<td>Digit Span Backwards</td>
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<td></td>
<td>Spatial working memory</td>
<td>CANTAB SWM Task</td>
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<td>Spatial Span</td>
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<td>Planning</td>
<td>Strategy development</td>
<td>Tower of London</td>
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<td>CAS Planning, Rey-O</td>
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<td>Set-Shifting</td>
<td>Flexibility, response to</td>
<td>Wisconsin Card Sort Task</td>
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<td></td>
<td>feedback</td>
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<td>Fluency</td>
<td>Phonemic fluency</td>
<td>FAS Test</td>
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<td>Semantic fluency</td>
<td>Categories</td>
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Concerns in EF measurement

- Executive functions are dynamic – if it is executive today, it isn’t tomorrow
- Executive functions are “molar” – there are multiple contributions to performance on any task
- All tasks require both core cognitive abilities (e.g. visual spatial, language) and executive functions
- Many tasks are so highly structured that performance doesn’t really pull for the “executive” aspect of the function
- Consequently the examiner is often the “executive” who must observe how the person takes the test, rather than just relying upon the score
Many complain that a child may be able to perform relatively well on a specific task of a certain skill, and yet shows day to day evidence of impairment in that same skill.

Barkley has suggested that many kids “know what to do, they just don’t do what they know.”

We therefore have a clinical need for external validation of our findings, ecological validity and a “real-world” anchor to our conclusions.

Isquith, 2010
How is behavioral assessment of EF done?

- Interview
- Observations in environments of concern
- Self-report questionnaires
- Other-report questionnaires
• We all know how to do this, but it is important to ask specific questions about areas of EF difficulty on a daily basis
• What does the child experience as primary interference in their efficient management of daily tasks?
• Get specific examples
• What is the environmental response to those difficulties?
Observations

- What are the parent’s and teacher’s primary concerns?
- Can we reinterpret language (e.g. “lazy”) into an EF construct (e.g. “difficulties with initiation”)
- Is the concern consistent across settings? (e.g. some children perform well within the structure of an experienced elementary school teacher’s classroom, but less so when asked to do homework in the distracting, unstructured environment of the home)
- Do both parents see the behaviors in a similar manner?
- Do the reports of others involved with the child (e.g. therapists, tutors, coaches) corroborate presenting concerns?
There are growing numbers of these, however for children the gold standard is the Behavior Rating Inventory of Executive Functions (BRIEF)

Scales include three “Behavioral Regulation” and three “Metacognitive” subscales, which combine to give a “Global Executive Composite”

Behavioral Regulations subscales:
- Inhibit
- Shift
- Emotional Control

Metacognitive subscales:
- Initiate
- Working Memory
- Plan/Organize
- Organization of Materials
- Task Monitor
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• Much of the research on EF in specific diagnoses have involved older children and adults – the developmental process is often not elucidated
• Many studies have diagnostic groups that aren’t clearly defined, or may combine subgroups (e.g. “ADHD” without subgroup specification)
• We are really at the earliest stages of beginning to understand the issues involved
Are endophenotypes based on measures of executive functions useful for molecular genetic studies of ADHD?

“Although the term ‘endophenotype’ has been used in different ways, virtually all conceptualizations refer to a phenotype that is more proximal to the biological etiology of a clinical disorder than its signs and symptoms and influenced by one or more of the same genes that confer susceptibility to the condition.”

Endophenotypes may be particularly useful for understanding the etiology of complex disorders in which several genes and environmental factors influence the phenotype.

What is an endophenotype?
“[There]...is a large literature revealing that individuals with ADHD exhibit relatively poor performance on clinical neuropsychological tests presumed to assess functions associated with frontal systems (Barkley, 1997a; Pennington & Ozonoff, 1996; Tannock, 1998). These functions are deemed ‘executive’ due to their involvement in higher-order cognitive processes including self-regulation and goal-directed behavior (Loring, 1999).

“Although impairments within the general class of EFs are associated with the ADHD diagnosis, the variability of deficits has made a definitive neurocognitive model of ADHD difficult to discern. Given that measures of EF show preliminary evidence of heritability and at least some familial/genetic overlap with ADHD, such deficits are potentially useful as ADHD endophenotypes. Yet, measures of EF appear less heritable than ADHD, and extant studies do not show individual genes accounting for more than 5% of the variance in neurocognitive tests.”
• Bledsoe, Semrud-Clikeman & Pliszka (2010) found that ADHD-C children who had adequate academic functioning (reading, writing, spelling and math calculation skills) still performed below controls on measures of response inhibition (DKEFS Color-Word inhibition subtest), despite having above average general intellectual functioning.

• This suggests that ADHD is characterized by inhibitory challenges independently of academic competence.

Are ADHD EF deficits due to comorbid learning disorders?

• Hypothesized that because girls’ brains mature 1-3 years earlier than boys in areas previously found to be anomalous in boys with ADHD, girls should demonstrate a different pattern of EF findings than boys (relative to controls)

• They expected that boys would show deficits in both earlier developing skills (response inhibition, response preparation, working memory) and later-developing skills (planning, shifting), whereas girls would only show deficits in the “later” skills

**What about girls with ADHD?**
Findings:
- Compared with age-, sex-, and SES-matched controls, children with ADHD manifested consistent and broad dysfunction in response inhibition, response preparation, verbal and spatial working memory, and planning.
- Girls and boys showed similar patterns of weakness on tasks involving working memory and response preparation, but different patterns of executive dysfunction on tasks related to response inhibition and planning.
- The outstanding deficit in girls with ADHD in the girls between 8 – 13 years of age involved strategic planning.
- Implication – girls and boys with ADHD have differing developmental trajectories, and gender needs to be considered in describing the EF deficits in ADHD.
How about ADHD vs Anxiety Disorder?

- Evaluated 60 children between ages 5 and 14 (16 control, 24 ADHD, 20 Anxiety Disorder).
- Battery of tests including WISC, Stroop, WCST, ROCF
- Findings:
  ◦ No diff in FSIQ or PIQ, ADHD had lower Vocab, Similarities and DS
  ◦ ADHD lower on Stroop word, color, and color-word subtests
  ◦ Anxiety group lower on WSCT perseverations
  ◦ ADHD group poor on ROCF organization on copy and immediate recall, Anxiety group poor only on immediate recall organization
  ◦ ADHD lower on inhibition
  ◦ Anxiety group lower on cognitive flexibility
Executive Function in Pediatric Bipolar Disorder and Attention-Deficit/Hyperactivity Disorder; In search of Distinct Phenotypic Profiles

Reviewed 68 studies of ADHD and 16 studies of pediatric Bipolar Disorder (BD)
- 21 of the ADHD differentiated subtypes or included analyses on comorbid learning disabilities (LD)
- All studies examined ADHD children off medications
- Most BD subjects were taking one or medications, but did not find medication effects on target variables. In 4/5 studies where this was examined, the remaining found a decrease in verbal fluency associated with medication.
• Analysis involved calculation of effect size (ES), weighted by sample size, for the following NP measures of EF:
  ◦ Inhibition
    • Response inhibition – CPT and Stop-Signal Task
    • Interference control – Stroop task
  ◦ Working Memory
    • Verbal wm = Digit Span total and Backwards
    • Spatial wm = CANTAB SWM task and Spatial Span
  ◦ Planning
    • Tower of London
  ◦ Set Shifting
    • Wisconsin Card Sort Task
  ◦ Fluency
    • Phonemic fluency - F-A-S test
    • Semantic fluency - Categories
EF comparison of ADHD and BPD

Walshaw, P.D., Alloy, L.B. & Sabb, F.W. “Executive Function in Pediatric Bipolar Disorder and Attention-Deficit Hyperactivity Disorder: In search of distinct phenotypic profiles.” Neuropsychol Rev. 2010 20:103-120
<table>
<thead>
<tr>
<th>Group</th>
<th>CPT</th>
<th>SSRT</th>
<th>Stroop</th>
<th>DS-T</th>
<th>DS-B</th>
<th>SWM-BSE</th>
<th>SSp</th>
<th>ToL</th>
<th>WCST</th>
<th>FAS</th>
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<tr>
<td>BD</td>
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<td>.80</td>
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ADHD and BD are similar in presentation and cognitive profiles, leading to high comorbidity and low differential specificity. However, there does seem to be emerging evidence of distinctive profiles in EF, however:

- ADHD typically involves deficits in verbal and spatial working memory and phonemic fluency.
- BD typically involves problems related to planning, inhibition of distraction from task-irrelevant stimuli, and having flexibility in thinking strategies.

* - combined forwards and backwards

**Average weighted effect sizes**
Conclusions:

- ADHD and BD are similar in presentation and cognitive profiles, leading to high comorbidity and low differential specificity.
- The does seem to be emerging evidence of distinctive profiles in EF, which may assist differential diagnosis.
Borderline Personality Disorder

- Much of the research has focused upon adults, not children.
- Review by Dell’Osso et al (2008) notes that many of the more recent neuropsychological studies, using comprehensive batteries, implicate inhibitory dysfunction, poor decision making, poor planning – reflecting probably orbitofrontal system dysfunction.
- The OFC, with its extensive and reciprocal connections with the amygdala, may be involved in regulating emotional and behavioral responses.
- Nevertheless, BPD is frequently comorbid with a multitude of other diagnoses, confounding understanding of core features.
The literature on EF studies among BPC is sparse. Paris et al (1999) evaluated 41 BPC and 53 controls and found BPC to have abnormal scores on the WCST and the CPT, suggesting difficulties with difficulty learning from feedback, flexibility, and inattentiveness. Coolidge et al (2000), using an experimental parent rating scale, compared 21 BPC with 21 controls, found the BPC to be rated as having more difficulties than controls on an EF scale containing items assessing decision-making difficulties, organizational impairment, troubles with planning, perseveration, and sequencing difficulties.

Borderline Personality Disorder in Children (BPC)
Zelkowitz et al (2004) concluded that

“both psychological trauma and deficits in executive functioning [sustained attention, planning, flexibility] make significant and independent contributions to the variance in borderline pathology of childhood.”
Differential diagnosis of developmental psychopathology, using the DSM, is often difficult, with overlapping symptoms and comorbidity the rule rather than the exception. Research investigations often reveal complex and conflicting findings, in part due to reliance upon diagnoses as independent variables. As we progress, it may be more useful to think dimensionally, rather than categorically. Dimensions of interest may include affective regulation, intellectual and academic abilities, and specific dimensions of executive functioning, for which objective (task) and observational criteria (rating scales) can have enhanced reliability and specificity, particularly as they are linked to neurological circuitry.

What can we deduce?
Thank you for your attention!