Executive Function Impairment in Patients with Medical Illness

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Disclosure

- Clinical Trials: Myriad, Pfizer, GSK, Neurochem

- CLOX and EXIT25 were developed at UTHSCSA
Learning Objectives

- To define executive function and give clinical examples of executive function impairment
- To describe potential causes of executive function impairment in patients with medical illness
- To describe the relationship between executive function impairment and functional status in elders
Executive Function

- The ability to think abstractly and to plan, initiate, sequence, monitor and stop complex behavior

- Two Major Conceptual Themes
  - Frontal lobe function: insight, will, abstraction, and judgment
  - Behavioral regulation of nonexecutive processes
Executive Function

That set of cognitive processes that allow one to behave independent of the environment instead of having behaviors mediated by the environment.

Examples:

- Cooking
- Driving
- Riding a bike
Psychiatric Illness and Executive Impairment

- Dementia
- Depression
- Bipolar Disorder
- ADHD
- Substance Disorders
- Schizophrenia
- Personality Disorders
Medical Illness and Executive Impairment

- Peripheral arterial disease
- Hypertension
- Diabetes
- COPD
- OSA
- CHF
- HIV
- Lung cancer
- ESRD (dialysis)
Executive Function and Behavior

- **Apathy**
  - “Depression”
  - Perseveration
  - Impaired set shifting

- **Disinhibition**
  - Stimulus bound
  - Impulsivity
  - Aggression
  - Imitation Behavior
Examples of Executive Errors

- Perseveration: uncontrollable repetition
- Impulsivity: impaired self regulation
- Set Shifting
- Response inhibition
Bedside Executive Measures

- CLOX: An Executive Clock Drawing Task
- The Executive Interview (EXIT25)
- Controlled Oral Word Association Test
- Design Fluency Task
- Trailmaking Test, Part B
The Executive Interview (EXIT25)

- 25 item bedside scale
- Items derived from frontal lobe sequelae
- 15 minutes, lay interviewers
- Scored 0-50, higher scores worse
- 15/50 best discriminates healthy elderly from demented subjects (ROC, c=.93)
- Normal *young* adults rarely >07/50
Instructions: CLOX1

1) Place the blank side of the CLOX form in front of the subject.

2) State “Draw me a clock that says 1:45. Set the hands and numbers on the face so that a child could read them.”

3) Once the subject begins the task, no further assistance is allowed (i.e. no prompting or repeat instructions)
Grading CLOX

- Subject gets one point for each of the following 15 items
Does the figure resemble a clock?

- 52yr with Depression NOS
Outer circle present?

- 52yr with EtOH Dependence and Major Depression
Diameter greater than one inch?

- 75yr with Vascular Dementia
37yr with Mood d/o secondary to HIV
No sectoring or tic marks?

- 23yr with End-Stage Renal Disease
12, 6, 3, and 9 placed first?

- 43yr with Schizophrenia
52yr with Schizoaffective d/o, bipolar type
Only Arabic numerals?

- 60yr with Schizoaffective d/o, bipolar type
Only numbers 1-12 among the Arabic numerals present?

- 51yr with Schizoaffective d/o
Is the sequence 1-12 intact?

- 77yr with Depression secondary to GMC (bile duct cancer)
Only two hands present?

- 53yr with Depression secondary to GMC (s/p CVA)
All hands represented as arrows?

- 42yr with Heroin Dependence
Hour hand between 1 and 2 o’clock?

- 20yr with Schizophrenia
Minute hand longer than hour hand?

- 37yr with Substance Induced Psychosis
None of the Following:

1). Hand pointing to 4 or 5 o’clock?
2). “1:45” present?
3). Any other notations (e.g. 9:00)?
4). Any arrows point inward?
5). Intrusion from hand or face present?
6). Any letters, words, or pictures?
7). Any intrusion from circle?
61yr with HIV Dementia (pre-printed circle intrusion)
35yr with Delirium/Acute Renal Failure
38yr with HIV Dementia
CLOX1

- ≤10/15 represents the lowest 5\textsuperscript{th} percentile for young adults.

- CLOX1 correlates well with the EXIT25 (r = -0.83).

- CLOX1 is more sensitive to executive function than similar clock-drawing tasks relative to the EXIT25.
ECF Determines Level of Care

% Variance in Level of Care Among N=148 CCRC Residents (Total Model $R^{**} = 0.57$)
Transition to 24-hour Care


### Table 1. Multivariate Analysis of Cognitive Tests With Incident Use of 24-Hour Care

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio (95% Confidence Interval)</th>
<th>Model 1*</th>
<th>Model 2*</th>
<th>Model 3†</th>
<th>Model 4‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CLOX1 score (&lt;12)</td>
<td>2.1 (1.4–3.1)</td>
<td>—</td>
<td>2.0 (1.4–3.0)</td>
<td>2.2 (1.5–3.4)</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>1.0 (1.0–1.1)</td>
<td>1.0 (1.0–1.1)</td>
<td>1.0 (1.0–1.1)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Sex (male)</td>
<td>0.9 (0.6–1.5)</td>
<td>0.9 (0.6–1.4)</td>
<td>1.0 (0.7–1.5)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>MMSE score (&lt;26)</td>
<td>—</td>
<td>1.6 (0.9–1.1)</td>
<td>1.2 (0.7–2.2)</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

*Note:* *Adjusted for age and sex.
†Adjusted for CLOX1, age, sex, and MMSE.
‡Adjusted for CLOX1, age, sex, MMSE, comorbidity, Geriatric Depression Scale score, Tinetti Gait and Balance score, and number of medications.

MMSE = Mini-Mental State Examination; NS = not significant.
Methods:
1. N = 21 subjects were administered the MacCAT modified to assess decision-making capacity to participate in a minimally invasive research protocol.

2. Subjects were administered the EXIT25, CLOX1, CLOX2, and the MMSE

3. A subject was considered to have failed the MacCAT if they failed one or more of the following categories with the following cut-points: understanding (≤4), reasoning (≤3), appreciation of disorder and treatment benefit (0 for each).
Table 1. Demographic and cognitive test means in patients passing and failing the MacCAT-T (standard deviation in parentheses).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pass MacCAT (n=11)</th>
<th>Fail MacCAT (n=10)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>61.3 (5.7)</td>
<td>68.6 (10.7)</td>
<td>p = 0.03</td>
</tr>
<tr>
<td>Education</td>
<td>13.9 (2.5)</td>
<td>11.7 (2.2)</td>
<td>p = 0.02</td>
</tr>
<tr>
<td>EXIT25</td>
<td>11.5 (4.1)</td>
<td>15.5 (5.0)</td>
<td>p = 0.03</td>
</tr>
<tr>
<td>CLOX1</td>
<td>11.5 (2.3)</td>
<td>10.4 (2.6)</td>
<td>p = 0.15</td>
</tr>
<tr>
<td>CLOX2</td>
<td>13.1 (1.3)</td>
<td>13.4 (0.7)</td>
<td>p = 0.26</td>
</tr>
<tr>
<td>MMSE</td>
<td>28.8 (1.5)</td>
<td>27.9 (1.6)</td>
<td>p = 0.10</td>
</tr>
</tbody>
</table>
Results

**TABLE 1. Spearman Correlation Coefficients for Modified MacCAT-T Performance**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Understanding</th>
<th>Appreciation</th>
<th>Reasoning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.43</td>
<td>-0.19</td>
<td>-0.44</td>
</tr>
<tr>
<td>Education</td>
<td>0.64&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.09</td>
<td>0.77&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>EXIT25</td>
<td>-0.64&lt;sup&gt;a&lt;/sup&gt;</td>
<td>-0.44&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-0.54&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>CLOX1</td>
<td>0.25</td>
<td>-0.03</td>
<td>0.43</td>
</tr>
<tr>
<td>CLOX2</td>
<td>-0.12</td>
<td>0.06</td>
<td>0.12</td>
</tr>
<tr>
<td>MMSE</td>
<td>0.45&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-0.02</td>
<td>0.54&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>p < 0.01.  <sup>b</sup>p < 0.05.  Age<sub>n</sub> = 19; Education<sub>n</sub> = 20; EXIT25, CLOX1, CLOX2, and MMSE<sub>n</sub> = 21. EXIT25: Executive Interview; CLOX: Executive Clock Drawing Task; MMSE: Mini-Mental State Examination.
EXIT25 failure (at 15 /50) was 100% accurate in predicting the capacity of elder COPD patients to learn to use an inhaler.
Questions???

- 38yr with HIV Dementia