Etiology and Treatment of Intermittent Explosive Disorder

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Aggression

Behavior by an individual directed at another person or object in which either verbal force or physical force is used to injure / coerce or to express anger
How Much Aggression is “Out There”?  

♦ 13-20% of school aged children engage in bullying  

♦ 90+% of adolescents report being verbally aggressive to their dating partner  

♦ Among young adults, 22% men and 13% women report being physically aggressive in the past year  

♦ 9% of young adults report being hurt in the past year due to physical aggression
Types of Aggression

Premeditated / Instrumental vs. Affective / Reactive
Intermittent Explosive Disorder (IED)
DSM-IV IED Criteria

- Several discrete episodes of failure to resist aggressive impulses that result in serious assaultive acts or destruction of property.
- The degree of aggressiveness expressed is grossly out of proportion to any precipitating psychosocial stressors.
- The aggressive behavior is not better accounted for by another mental disorder and are not due to the direct physiological effects of a substance or a general medical condition.
Epidemiology of IED

- **Prevalence:** ~5% in community samples
- **Onset:** Teens   **Offset:** 40’s – 50’s
- **Course:** Chronic waxing / waning course
- **Gender:** ~ 60 % male
- **Race:** No consistent findings
- **Education:** Without college degree higher prevalence
Phenomenology of IED

- **Typical Outbursts**
  - Rapid onset with increased tension/energy
  - Short lived (~30 minutes)
  - Response to minor provocation by loved one or associate
  - Can include verbal aggression, property assault, violence
  - Guilt, Shame (but sometimes also justification) afterward
A “typical” outburst
Consequences

- Two assaults requiring medical attention
- $\sim 1500-2000$ damage to property
- Poor relationships, work difficulties
- Intergenerational transmission of aggression
## IED and Physical Health ($N = 10,366$)

Table 3

<table>
<thead>
<tr>
<th>Outcome</th>
<th>B</th>
<th>SE (B)</th>
<th>Wald</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart attacks</td>
<td>0.12</td>
<td>0.24</td>
<td>0.26</td>
<td>1.13</td>
<td>0.71–1.81</td>
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<tr>
<td>Heart disease</td>
<td>0.35</td>
<td>0.17</td>
<td>4.07*</td>
<td>1.42</td>
<td>1.01–1.99</td>
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<tr>
<td>Hypertension</td>
<td>0.27</td>
<td>0.10</td>
<td>7.40**</td>
<td>1.31</td>
<td>1.08–1.59</td>
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<tr>
<td>Stroke</td>
<td>0.70</td>
<td>0.23</td>
<td>9.51**</td>
<td>2.01</td>
<td>1.29–3.14</td>
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<tr>
<td>Lung disease</td>
<td>0.42</td>
<td>0.24</td>
<td>2.94</td>
<td>1.52</td>
<td>0.94–2.45</td>
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<tr>
<td>Diabetes</td>
<td>0.29</td>
<td>0.15</td>
<td>3.88*</td>
<td>1.33</td>
<td>1.00–1.77</td>
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<tr>
<td>Cancer</td>
<td>0.29</td>
<td>0.19</td>
<td>2.33</td>
<td>1.33</td>
<td>0.92–1.91</td>
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<tr>
<td>Arthritis</td>
<td>0.27</td>
<td>0.10</td>
<td>7.86**</td>
<td>1.31</td>
<td>1.09–1.58</td>
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<tr>
<td>Neck/back pain</td>
<td>0.33</td>
<td>0.08</td>
<td>17.02***</td>
<td>1.39</td>
<td>1.19–1.62</td>
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<tr>
<td>Headaches</td>
<td>0.49</td>
<td>0.08</td>
<td>38.75***</td>
<td>1.64</td>
<td>1.40–1.91</td>
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<td>Ulcer</td>
<td>0.31</td>
<td>0.12</td>
<td>7.44**</td>
<td>1.36</td>
<td>1.09–1.69</td>
</tr>
<tr>
<td>Other chronic pain</td>
<td>0.23</td>
<td>0.11</td>
<td>4.70*</td>
<td>1.27</td>
<td>1.02–1.58</td>
</tr>
</tbody>
</table>

* $p < .05$.  ** $p < .01$.  *** $p < .001$.  

McCloskey et al., 2010
Co-Morbid Dx in IED Subjects (Epidemiological Study N = 9282)

- Any Dx
- Any Impulse Control Dx
- Any Anxiety Dx
- Any Mood Dx
- Any Substance Dx

* Included ADHD, ODD, CD

Kessler et al, 2006
Etiology of IED
Biological Factors

Affective Aggression

*Serotonin (5-HT)
Androgens
Vasopressin
Nitric Oxide
GABA
Norepinephrine
Dopamine
# Pharmacological Challenge Studies

<table>
<thead>
<tr>
<th>Author(s) and Year</th>
<th>Weighted Pearson Correlations [95% CI]</th>
</tr>
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<tbody>
<tr>
<td>Kahn et al., 1988</td>
<td>-0.30 [ -0.95 , 0.35 ]</td>
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<td>Germine et al., 1992</td>
<td>0.25 [ -0.30 , 0.79 ]</td>
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<td>Krystal et al., 1994</td>
<td>-0.31 [ -0.73 , 0.12 ]</td>
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<td>Bond et al., 1995</td>
<td>-0.47 [ -1.04 , 0.11 ]</td>
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<td>Cherek et al., 1995</td>
<td>-0.91 [ -1.46 , -0.35 ]</td>
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<td>Koreen et al., 1997</td>
<td>-0.10 [ -0.66 , 0.47 ]</td>
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<td>Cherek &amp; Lane, 1999</td>
<td>-0.80 [ -1.30 , -0.30 ]</td>
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<tr>
<td>Cherek &amp; Lane, 2001</td>
<td>-0.66 [ -1.54 , 0.23 ]</td>
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<td>Cherek et al., 2002</td>
<td>-0.39 [ -0.98 , 0.19 ]</td>
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<td>Netter et al., 2006</td>
<td>-0.15 [ -0.60 , 0.30 ]</td>
</tr>
<tr>
<td>Berman et al., 2009</td>
<td>-0.16 [ -0.48 , 0.15 ]</td>
</tr>
<tr>
<td>McCloskey et al., 2009</td>
<td>-0.19 [ -0.47 , 0.09 ]</td>
</tr>
<tr>
<td>Gowin et al., 2010</td>
<td>-0.53 [ -1.13 , 0.06 ]</td>
</tr>
<tr>
<td>Vote Counting Estimate</td>
<td>-0.02 [ -0.18 , 0.14 ]</td>
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<tr>
<td>Weighted Mean Estimate</td>
<td>-0.32 [ -0.47 , -0.16 ]</td>
</tr>
</tbody>
</table>
Cognitive Deficits

- Impulsivity
- Socio-Emotional Information Processing
- Emotion Regulation
Impulsivity

- The general tendency to act on one’s impulses rather than to inhibit them (Joiner, 2005)

- A personality trait characterized by initiation of behavior without adequate forethought as to the consequences of this behavior. OR acting on the spur of the moment without thinking about the consequences of those actions (Connor, 2012).
Gambling Task

Percentage of Cards Selected from Disadvantageous Decks (A & D) Across Time

IED subjects picked significantly more cards from disadvantageous decks over the final 25 trials.

** p<0.01, two-tailed

Best et al., 2002
IED and Impulsivity

- Compared IED, PD and HV groups on self-report (Barratt Impulsivity Scale) and behavioral (Immediate Memory Task, Bechara Gambling Task) measures of impulsivity
  - IED N = 302
  - PD N = 141
  - NV N = 281
IED and Self-Reported Impulsivity

BIS Score

* IED > PD > HV p < .001

McCloskey, et al, in prep
IED and Behavioral (IMT) Impulsivity

**Commission Errors**

- HV
- PD
- IED

* IED > PD, HV ; p < .05

McCloskey, et al, in prep
But.....
A second study compared IED, PD and HV groups on self-report (BIS) and behavioural (Passive Avoidance Task, Go-Stop) measures of impulsivity.

- IED N = 251
- PD N = 80
- NV N = 135
IED and Self-Reported Impulsivity

* IED > PD > HV p < .01

McCloskey, et al, in prep
IED & Behavioral (GO-STOP) Impulsivity

$\text{IED} = \text{PD} = \text{HV} ; \ p > .10$

McCloskey, et al, in prep
Social Information Processing (SIP)

- Encoding / Attention
- Making attributions / interpretations
- Clarifying goals
- Generating responses
- Evaluating responses
- Enacting responses
SIP as a Mediator of Aggression

- Social Information Processing Deficient in Aggressive Children (Dodge et al., 1990, 1994). SIP was found to mediate the relationship between history of child abuse and aggression.
IED and Attention Bias

Emotional Stroop

Stroop Interference (N = 28)

* p < .05

McCloskey et al, in prep
IED and Attribution Bias

You tell a friend something personal and ask your friend not to discuss it with anyone else. However, a couple of weeks later, you find out that a lot of people know about it. You ask your friend why she/he told other people and your friend says: Well, I don’t know, it just came up and I didn’t think it was a big deal.”

* * P < .05

Coccaro, Noblett & McCloskey 2009
Emotional Information Processing

- The ability to accurately identify the emotional valence of stimuli such as facial expressions, vocal intonation, and body posture
Test of Facial Expressions

Number of Errors Made by Each Group for 5 Facial Expressions

IED subjects made significantly more errors for anger, disgust and surprise

** p<0.01, two-tailed

Best et al., 2002
IED and Emotional Information Processing

Number of Times Subjects Labeled Neutral Faces With Each of 5 Expressions

Best et al., 2002
Emotional Regulation

- The capacity to adjust one's emotional arousal level so that an optimal intensity of engagement with one's environment is achieved (Cicchetti, Ganiban, & Barnett, 1991).

- Implicit and explicit efforts to maximize positive and minimize negative moods and feeling states (Westen, 1985 / 1994).

- The processes by which individuals influence which emotions they have, when they have them, and how they experience and express these emotions. (Gross, 1998)

- The processes by which people seek to change their emotional experience or expression. (Gross, 2001)
IED and Anger

McCloskey, Berman, Noblett & Coccaro, 2006
## Emotion Regulation and IED

### Affect Lability Scale

<table>
<thead>
<tr>
<th></th>
<th>HV (n=103)</th>
<th>PC (n = 67)</th>
<th>IED (n = 207)</th>
<th>$F$</th>
<th>$\eta_p^2$</th>
<th>Post-hoc</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Depression</strong></td>
<td>15.44 (4.73)</td>
<td>20.90 (7.27)</td>
<td>25.66 (6.67)</td>
<td>89.29***</td>
<td>0.33</td>
<td>IED &gt; PC &gt; HV</td>
</tr>
<tr>
<td><strong>Hypomania</strong></td>
<td>17.40 (5.66)</td>
<td>22.62 (7.67)</td>
<td>27.48 (7.30)</td>
<td>71.72***</td>
<td>0.28</td>
<td>IED &gt; PC &gt; HV</td>
</tr>
<tr>
<td><strong>Biphasic</strong></td>
<td>11.45 (3.27)</td>
<td>15.48 (5.90)</td>
<td>19.36 (6.21)</td>
<td>70.85***</td>
<td>0.28</td>
<td>IED &gt; PC &gt; HV</td>
</tr>
<tr>
<td><strong>Anxiety</strong></td>
<td>8.35 (2.56)</td>
<td>11.49 (5.04)</td>
<td>14.73 (4.50)</td>
<td>80.49***</td>
<td>0.31</td>
<td>IED &gt; PC &gt; HV</td>
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<tr>
<td><strong>Anger</strong></td>
<td>7.89 (1.99)</td>
<td>10.52 (4.24)</td>
<td>17.84 (5.02)</td>
<td>206.52***</td>
<td>0.53</td>
<td>IED &gt; PC &gt; HV</td>
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<tr>
<td><strong>Anxiety/Depression</strong></td>
<td>9.21 (2.58)</td>
<td>13.25 (5.83)</td>
<td>17.34 (5.98)</td>
<td>82.69***</td>
<td>0.31</td>
<td>IED &gt; PC &gt; HV</td>
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</table>

### Affect Intensity Measure

<table>
<thead>
<tr>
<th></th>
<th>HV (n=103)</th>
<th>PC (n = 67)</th>
<th>IED (n = 207)</th>
<th>$F$</th>
<th>$\eta_p^2$</th>
<th>Post-hoc</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Negative Intensity</strong></td>
<td>13.81 (4.73)</td>
<td>18.70 (7.00)</td>
<td>21.35 (5.62)</td>
<td>60.47***</td>
<td>0.25</td>
<td>IED &gt; PC &gt; HV</td>
</tr>
<tr>
<td><strong>Negative Reactivity</strong></td>
<td>20.65 (4.78)</td>
<td>22.61 (4.87)</td>
<td>21.96 (5.07)</td>
<td>4.89**</td>
<td>0.03</td>
<td>IED, PC &gt; HV</td>
</tr>
</tbody>
</table>

** $p < .01$, *** $p < .001$. **

_Fettich, McCloskey, Look & Coccaro, in prep_
Hypothesized Emotion Information Processing / Regulation Pathway

Slide from Davidson 1999
Mechanism of BOLD Functional MRI

- BOLD = Blood Oxygenation Level Dependent

Brain activity $\uparrow$

Oxygen consumption $\uparrow$

Cerebral blood flow $\uparrow\uparrow$

Oxyhemoglobin $\uparrow$

Deoxyhemoglobin $\downarrow$

![Diagram showing normal and high blood flow with oxyhemoglobin and deoxyhemoglobin](image-url)
fMRI Study of Implicit EIP in IED

Paradigm:
- Block design using the Ekman and Friesen Pictures of Facial Affect.
- 5 minute runs, 6 runs per scan
- Blocks each contained one expression type (Anger, Fear, Digest, Happy, Sad, Surprise, Neutral), a crosshair was used as baseline.
- Subjects were asked to identify gender only.
IED subjects show increased amygdala activation and decreased orbitofrontal activation to angry faces (compared to controls)

"man"

Coccaro, McCloskey, Fitzgerald & Phan, 2008
fMRI Study of Explicit EIP in IED

Paradigm:

• Block design using the Ekman and Friesen Pictures of Facial Affect.
• 4 minute 20 second runs, 4 runs per scan
• Blocks each contained one expression type (Anger, Fear, Disgust, Happy, Sad) interleaved with a crosshair condition that was used as baseline.
• Subjects were asked to identify the valence of the pictures (positive, neutral, negative)
IED again subjects show increased amygdala activation but this time do not show orbitofrontal deactivation to angry faces (compared to controls)

"negative"

McCloskey, Phan, Angstadt, Fettich & Coccaro., in rev
Furthermore, in contrast to HV’s who showed a negative feedback between AMY and OFC, IED subjects showed positive AMY –OFC coupling.
fMRI Study of Emotion Response in IED

Paradigm:

- Block design using the IAPS picture series (5 pics, 4 sec per pic).
- 4 minute runs, 4 runs per scan
- Blocks each contained one valance (Positive, negative, neutral) interleaved with a crosshair condition that was used as baseline.
- Subjects were asked to identify the valence of the pictures (positive, neutral, negative)
fMRI of Emotion in IED (N=20)

- IED subjects show increased amygdala activation but this time also showed increased DLPFC to negative stimuli (compared to controls)

“negative”

McCloskey, et al., 2009
Psychotherapy for IED

- No published studies had directly examined the efficacy of psychotherapy for IED.
- Only one study (Galovski & Blanchard, 2002) has assessed IED in a psychotherapy study:
  - Examined the effectiveness of a brief cognitive-behavioral intervention on aggressive drivers.
  - Overall the treatment was effective in reducing aggressive driving.
  - However, the IED subjects (n=9) showed less improvement than non-IED subjects (n=18).
Cognitive Restructuring, Relaxation and Coping Skills Training (CRCST)

- Developed by Deffenbacher and McKay
- Empirical support as treatment for anger
- 8 treatment sessions
- 3 key components
  - Relaxation
  - Cognitive Restructuring
  - Coping Skills Training (Imaginal Exposure)
CRCST for IED

♦ Modifications of CRCST included
   ♦ Focus on aggression
   ♦ Lengthening the treatment from 8 to 12 sessions
     ♦ Explanation of cognitive restructuring 2 sessions
   ♦ Inclusion of “time out” technique
   ♦ Increased emphasis on relapse prevention
   ♦ Individual and group format
## Anger Distortions / Strategies

<table>
<thead>
<tr>
<th>Anger Distortion</th>
<th>Strategies</th>
</tr>
</thead>
</table>
| Catastrophizing    | • Be *realistically* negative  
                      | • Look at the whole picture                                                 |
| Overgeneralization | • Be specific, accurate  
                      | • Counter-examples/ exceptions to the rule                                  |
| Shoulds            | • Preferences, not shoulds  
                      | • People do what they want, not what I want                                 |
| Name calling       | • Describe the behavior, not the person  
                      | • Visualize the language                                                    |
| Mind reading       | • How do I know what they’re thinking?  
                      | • Think of other explanations                                               |
| Blaming            | • How can I solve this myself?  
<pre><code>                  | • Acknowledge that they’re probably taking care of their needs as best they can. |
</code></pre>
<table>
<thead>
<tr>
<th>Sessions</th>
<th>1-3</th>
<th>Relaxation Training</th>
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<tbody>
<tr>
<td>Sessions</td>
<td>3</td>
<td>Time Out</td>
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<tr>
<td>Session</td>
<td>4-5</td>
<td>Cognitive Concepts</td>
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<tr>
<td>Session</td>
<td>6</td>
<td>Coping Skills (Anticipatory)</td>
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<td>Sessions</td>
<td>7-8</td>
<td>Coping Skills (Medium)</td>
</tr>
<tr>
<td>Sessions</td>
<td>9-10</td>
<td>Coping Skills (High)</td>
</tr>
<tr>
<td>Sessions</td>
<td>11-12</td>
<td>Coping Skills (Highest)</td>
</tr>
</tbody>
</table>
Pilot RCT of CRCST for IED

- **Participants**
  - IED

- **Conditions**
  1. Individual CRCST (12 50-minute sessions)
  2. Group CRCST (4-6 group members, 1-2 therapists, 12 75-minute sessions)
  3. Wait list + self-monitoring control (kept weekly anger log for 12 weeks)

- **Outcome measures**
  - Aggression: Overt Aggression Scale Modified (OASM)
  - Anger: State Trait Anger Expression Inventory 2 – Trait Aggression Scale
  - Depression: Beck Depression Inventory-II (BDI-II)
  - Hostile Bias: Hostile Automatic Thoughts (HAT)

McCloskey, Noblett, Deffenbacher, Gollan & Coccaro, 2008
Efficacy of CBT in Reducing Aggression

McCloskey et al, 2008
Efficacy of CRCST in Reducing Anger

<table>
<thead>
<tr>
<th>Group</th>
<th>Pre</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wait-List</td>
<td>29</td>
<td>27</td>
</tr>
<tr>
<td>CRCST-I</td>
<td>29</td>
<td>20</td>
</tr>
<tr>
<td>CRCST-G</td>
<td>28</td>
<td>19</td>
</tr>
</tbody>
</table>

McCloskey et al, 2008
Efficacy in Reducing Hostile Thoughts

McCloskey et al, 2008

* p < .05
Efficacy in Reducing Depression

**BDI - Total Score**

<table>
<thead>
<tr>
<th>Group</th>
<th>Pre</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wait-List</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>CRCST-I</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>CRCST-G</td>
<td>13</td>
<td>5</td>
</tr>
</tbody>
</table>

* *p < .05

McCloskey et al, 2008
Efficacy of CRCST in Reducing Aggression Among subjects with BPD (N = 12)

McCloskey et al, unpublished
CRCST vs. SUP for IED

■ Participants
  - IED (N = 50)

■ Conditions
  1. Individual CRCST (12 50-minute sessions)
  2. Individual Supportive Psychotherapy (12 50-minute sessions)

■ Outcome measures
  - Aggression: Overt Aggression Scale Modified (OASM)
  - Anger: State Trait Anger Expression Inventory 2 – Trait Aggression Scale
  - Depression: Beck Depression Inventory-II (BDI-II)
  - Hostile Bias: Hostile Automatic Thoughts (HAT)

McCloskey et al, in prep
Efficacy of CRCST vs. SUP in Reducing Aggression

McCloskey et al, in prep
Efficacy of CRCST vs. SUP in Reducing Anger

McCloskey et al, in prep
Efficacy of CRCST vs. SUP in Reducing Hostile Thoughts

McCloskey et al, in prep
Efficacy of CRCST vs. SUP in Reducing Depressive Sx

McCloskey et al, in prep
Conclusions

- IED appears to be associated with deficits in socio-emotional information processing and emotion regulation.
- These deficits appear to be linked to dysregulated corticolimbic circuits.
- Early data supports the efficacy of treatments that focus on correcting these cognitive-affective deficits.
Collaborators

Mitchell Berman, Ph.D.  Mississippi State University
Emil Coccaro, M.D.  University of Chicago
Jerry Deffenbacher, Ph.D.  Colorado State University
Jackie Gollan, Ph.D.  Northwestern University
Kurt Noblett  Hines VAMC
K. Luan Phan, M.D.  University of Illinois at Chicago
MAD LAB  Temple University