Seasonal Affective Disorder
Diagnosis and Treatment

Scott Crow, M.D.
## Disclosures

### Research Support
- Eli Lilly
- Abbott
- Pfizer
- Bristol-Myers Squibb
- GlaxoSmithKline
- Ortho-McNeill

### Consultant
- Pfizer
- Eli Lilly
- Ortho-McNeill
How is SAD Diagnosed?
What causes SAD?
What is the impact of SAD?
How is SAD treated?
One out of Five Patients with Diagnosed Depression* Meets the SPAQ Criteria for SAD

N = 13,358
*Self-reported, physician-diagnosed depression
SPAQ = Seasonal Pattern Assessment Questionnaire

SAD Criteria

- Regular Temporal Relationship between episode onset and a particular time of year.
- Full remissions at a particular time of year.
- In past 2 years, 2 episodes at characteristic time and none outside of that time.
- Seasonal episodes substantially outnumber non-seasonal across the lifetime.
### Symptom Characteristics: Nonseasonal MDD vs SAD

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Nonseasonal</th>
<th>MDD</th>
<th>SAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mood</td>
<td>↓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy level</td>
<td>↓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interest in daily activities</td>
<td>↓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep length</td>
<td>↓ or ↑</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appetite</td>
<td>↓ or ↑</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>↓ or ↑</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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SAD Studies: Typical Historical Sleep Duration Reported by Patients in Winter vs Summer

SAD Studies: Severity of Historical Seasonal Changes

Proportion of Patients Rating Historical Seasonal Changes in These Clinical Parameters “Marked” or “Severely Marked”

- Mood
- Energy level
- Sleep length
- Social activity
- Appetite
- Weight

Patients (%)

0 10 20 30 40 50 60 70 80

SAD Screening

Seasonal Pattern Assessment Questionnaire
Initial Description of NES

$n = 25$ obese

“Large amounts of food during evening & night”

“At least $\frac{1}{4}$ of total calories …. Following the evening meal”

“Sleeplessness”

“Morning anorexia”

Night Eating Syndrome

- Delayed circadian eating pattern
  - > 25% of calories after evening meal
  - ≥ 3 nocturnal wakenings with eating per week
NES in Psychiatric Patients

Lundgren et al
Am J Psychiatry 2006 163:156-8
What Causes SAD?
Environmental and Demographic Predictors of SAD: Study Design

- Nationwide, population-based, cross-sectional, US survey\(^1,2\)
- Sampled 30,000 adults (≥18 years) using a validated questionnaire (SPAQ*) assessing self-reported prevalence of SAD\(^1,2\)
- 13,358 surveys were completed and used in this analysis\(^1,2\)
- SAD prevalence correlated with demographic information that included:
  - Lifetime history of diagnosed depression\(^1\)
  - Local latitude\(^2\)

*SPAQ = Seasonal Pattern Assessment Questionnaire

Latitude and Seasonality Are Highly Predictive of SAD Prevalence

Evidence of Serotonergic Involvement in SAD

- Altered photic entrainment in 5HT$_{1b}$ knockout mice (Sollars et al, 2006).
- Association of 5HT$_{2A}$ (Lee et al, 2006)
Seasonal Mood Disorder and 5HT 2A Receptor

Lee et al, J Affective Disorders 2006 (95) 145-8
Why is SAD a bad thing to have?
MOS: Can - SAD Study

Michalak E, et al, Psychological Medicine, 2006
Q-LES-Q: Can – SAD Study

Michalak E, et al, Psychological Medicine, 2006
SAD Studies: *Reported Historical Seasonal Changes*

![Graph showing seasonal changes in SAD patients](image)

- **Window to initiate preventive therapy**
- **Worst month**
- **Socialize least**
- **Weight gain**
- **Eat most**
- **Sleep most**

SAD Treatment Approaches

1. Bright Light Therapy
2. Activity
3. Medications
4. (Moving?)
Bright Light Therapy for SAD

1. Standard Approach
   - 10,000 Lux Full Spectrum
   - 2-3 Feet distance
   - Facial Contact
   - a.m. exposure
   - Other formats may work
Remission rates (posttreatment Structured Interview Guide for the Hamilton Depression Rating Scale-Seasonal Affective Disorder Version score \( \leq 8 \)) for the 4 light treatment groups (morning [M] or evening [E]) across periods 1 and 2.

Percent of patients with nearly complete remissions, defined as achieving both a 50% decrease (from baseline) in the 24-item Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorder Version (SIGH-SAD) and a score of 8 or lower.

Bright Light Therapy for SAD

2. Side Effects
   • Headache
   • Eyestrain
   • Insomnia
3. Timing
   • a.m. versus p.m.?
   • When to start and when to stop
SAD Studies: Reported Historical Seasonal Changes

Patients (%)

Window to initiate preventive therapy

Month

- Worst month
- Socialize least
- Weight gain
- Eat most
- Sleep most

## Controlled Antidepressant Trials in SAD

<table>
<thead>
<tr>
<th>Author</th>
<th>Drug</th>
<th>n</th>
<th>Duration</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lingaerde et al 1993</td>
<td>Moclobemide</td>
<td>34</td>
<td>3 weeks</td>
<td>+/-</td>
</tr>
<tr>
<td>Lam et al 1995</td>
<td>Fluoxetine</td>
<td>68</td>
<td>5 weeks</td>
<td>+/-</td>
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<tr>
<td>Martiny et al 2004</td>
<td>Citalopram</td>
<td>282</td>
<td>15 weeks</td>
<td>+</td>
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<tr>
<td>Moscovitch et al 2004</td>
<td>Sertraline</td>
<td>187</td>
<td>8 weeks</td>
<td>+</td>
</tr>
<tr>
<td>Modell et al 2005</td>
<td>Bupropion XL</td>
<td>1042</td>
<td>5 months</td>
<td>+</td>
</tr>
<tr>
<td>Lam et al 2006</td>
<td>Fluoxetine &amp; Dim light vs BLT &amp; Placebo</td>
<td>96</td>
<td>8 weeks</td>
<td>BLT quicker o/w similar</td>
</tr>
<tr>
<td>Partonnen &amp; Lonqvist 1996</td>
<td>Moclobemide vs Fluoxetine</td>
<td>32</td>
<td>6 weeks</td>
<td>equivalent</td>
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</table>
## Placebo Controlled Melatonin Trials in SAD

<table>
<thead>
<tr>
<th>Author</th>
<th>Drug</th>
<th>n</th>
<th>Duration</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lewy et al 1998</td>
<td>Melatonin</td>
<td>10</td>
<td>3 weeks</td>
<td>+</td>
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<tr>
<td>Leppamaki et al 2003</td>
<td>CR Melatonin</td>
<td>58</td>
<td>3 weeks</td>
<td>+ (subsyndromal SAD)</td>
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<tr>
<td>Lewy et al 2003</td>
<td>a.m. Melatonin Vs p.m. Melatonin Vs Placebo</td>
<td>282</td>
<td>3 weeks</td>
<td>-</td>
</tr>
</tbody>
</table>
## Controlled Trials of Miscellaneous Agents in SAD

<table>
<thead>
<tr>
<th>Author</th>
<th>Drug</th>
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<th>Duration</th>
<th>Results</th>
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</thead>
<tbody>
<tr>
<td>Rosenthal et al 1988</td>
<td>Atenolol</td>
<td>19</td>
<td>1 wk crossover</td>
<td>–</td>
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<tr>
<td>O’Rourke et al 1989</td>
<td>D-Fenfluramine</td>
<td>18</td>
<td>4 wk crossover</td>
<td>+</td>
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<tr>
<td>McGrath et al 1990</td>
<td>L-Tryptophan BLT</td>
<td>13</td>
<td>1 wk crossover</td>
<td>+ (L-Trypt) + (BLT)</td>
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<tr>
<td>Schlager et al 1994</td>
<td>Propranolol</td>
<td>23</td>
<td>2 wks</td>
<td>+</td>
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<tr>
<td>Lingaerde et al 1999</td>
<td>Gingko biloba</td>
<td>27</td>
<td>10 wks</td>
<td>–</td>
</tr>
<tr>
<td>Ghadirain et al 1998</td>
<td>Tryptophan vs BLT</td>
<td>13</td>
<td>2 wks BLT 4 wks Trypt (crossover)</td>
<td>equivalent</td>
</tr>
</tbody>
</table>
BLT or Meds?
Can – SAD Study

BLT + Placebo vs Fluoxetin + Dim Light
Lam et al, American Journal of Psychiatry, 2006
Prophylactic treatment  
or  
Watchful waiting?
WELLBUTRIN XL® (bupropion HCl extended-release tablets)
SAD Study Design: Studies 1, 2, and 3

Randomization

WXL 150 mg or placebo

Preventive Therapy*

WXL 150–300 mg or placebo

Follow-up (every 4 weeks)

Taper

WXL 150 mg or placebo

Follow-up

First week of spring†

Fall enrollment (Sept–Nov)

Week 0

Week 1

Week 2

Week 4

2 weeks

8 weeks

N = 1042
*Treatment duration was approximately 4 to 6 months for the majority of patients
†First week of spring: March 20–26, 2003 for studies 1 and 2; March 22–28, 2004 for study 3

WELLBUTRIN XL® (bupropion HCl extended-release tablets) for Prevention of Seasonal Major Depressive Episodes

Study 1
2002–2003

Study 2
2002–2003

Study 3
2003–2004

Pooled Analysis

P=0.026
30%

P=0.049
21%

P<0.001
31%

P<0.001
28%

19% (n=140)

13% (n=156)

16% (n=238)

16% (n=534)

28% (n=508)

30%

21%

31%

28%

44% reduction in recurrence of SAD vs placebo

Patients with SAD recurrence (%)

WELLBUTRIN XL

Placebo


Data on file, GlaxoSmithKline.
Conclusions

- SAD is a fairly common and important aspect of depression – especially as you travel farther from the equator
- SAD pathophysiology is partially understood and relates in part to light/circadian rhythm
- Bright light therapy, activity, and pharmacotherapy are treatment options
- Prophylactic treatment should be the focus