Social Anxiety Disorder Guidelines

Stéphane Bouchard, Ph.D.
John Walker, Ph.D.
Pierre Bleau, M.D, FRCP
Overview of the symposium

1. Brief review of basic concepts in social anxiety disorder.
2. Epidemiology of social anxiety disorder.
4. Psychology of social anxiety disorder.
5. Pharmacological treatment of social anxiety disorder.
7. ADAC/ACTA Guidelines.
1. Brief review of basic concepts
Social Phobia / Social Anxiety Disorder

Fear of scrutiny, negative evaluation by others or fear of humiliation and embarrassment
Social Anxiety Disorder (Social Phobia)

- Marked fear of performance or social interaction situations.
- Excessive fear of scrutiny or negative evaluation.
- Fear of acting in a way (or showing anxiety symptoms) that will be humiliating or embarrassing.
- Results in avoidance or endurance with distress.

DSM-IV summarized
Social Phobia “Subtypes”

**Generalized**
- “Most” social situations (DSM IV)
  - performance
  - interactional
- Overlaps with avoidant personality disorder
  - 80-90%

**Nongeneralized** (discrete, specific)
- 1 or 2 social situations
- Usually performance
  - writing in front of others
  - eating in front of others
  - telephone public speaking

Most probably more on a continuum of severity (quantitative) rather than different entities (qualitative). Stein et al., 2000.
Signs and Symptoms: Cognitive Symptoms

- Fear of negative evaluation or disapproval
- Negative evaluation of one’s own performance
- Perfectionist standards
- Expectations that others will be critical
- Expectations that social situations will go badly (trigger bad habit or poor social skills)
- Post-mortem thoughts
Signs and Symptoms: Physical Symptoms

- Blushing
- Stuttering or stammering
- Sweating
- Gastrointestinal symptoms (embarrassing)
- Dry mouth
- Palpitations
- Trembling
- Urgency of micturition
- Panic attacks
Signs and Symptoms: Behavioral Symptoms

- Avoidance of difficult social situations
- Being in situations but not participating (speaking)
- Use of *alcohol* in social situations
- Non-verbal behaviour – eye contact, shaking hands, interpersonal distance
- Relying on family and friends
- Leave the situation
Examples of feared social situations

**Social Interaction**
- Going to a party
- Lunch with peers
- Dating
- Asking a teacher for help
- Speaking to a boss at work
- Asking a salesclerk for help
- Asking for directions

**Performance**
- Public speaking
- Meeting new people
- Fear of eating, drinking or writing in public
- Fear of using a public washroom
- Fear of using a telephone in public
- Playing an instrument, sports
- Entering a room
Differential Diagnosis

Vs Other Anxiety Disorders

Characteristics of social anxiety disorder are:

- Childhood or adolescent onset
- Impairment restricted to social situations
- Blushing (Not present in Panic Attacks)
- Unique cognitions (such as fear of scrutiny by others) (Different from fear to become fool)
- No improvement with TCA
### Rating Scales for Social Anxiety Disorder

<table>
<thead>
<tr>
<th>Evaluation</th>
<th>Rating Scale</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Severity</td>
<td>Clinical Global Impression (CGI) for Severity of Illness</td>
<td>Non-specific</td>
</tr>
<tr>
<td></td>
<td>Liebowitz Social Anxiety Scale</td>
<td>Specific</td>
</tr>
<tr>
<td></td>
<td>Clinical Global Improvement</td>
<td>Non-specific</td>
</tr>
<tr>
<td></td>
<td>Hamilton Rating Scale for Anxiety</td>
<td>Non-specific</td>
</tr>
<tr>
<td></td>
<td>Hamilton Rating Scale for Depression</td>
<td>Non-specific</td>
</tr>
<tr>
<td></td>
<td>Social Anxiety and Distress Scale</td>
<td>Specific</td>
</tr>
<tr>
<td>Functional Disability</td>
<td>Sheehan Disability Scale</td>
<td>Non-specific</td>
</tr>
<tr>
<td></td>
<td>Mini International Neuropsychiatric Interview (MINI)</td>
<td>Non-specific</td>
</tr>
<tr>
<td></td>
<td>Duke Brief Social Phobia Scale</td>
<td>Specific</td>
</tr>
<tr>
<td></td>
<td>Global Assessment of Functioning</td>
<td>Non-specific</td>
</tr>
</tbody>
</table>
### Rating Scales for Social Anxiety Disorder (Cont’d)

#### Patient Self-Administered Scales

<table>
<thead>
<tr>
<th>Evaluation</th>
<th>Rating Scale</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Severity</td>
<td>Social Phobia Inventory (SPIN)</td>
<td>Specific</td>
</tr>
<tr>
<td></td>
<td>Fear Questionnaire</td>
<td>Specific</td>
</tr>
<tr>
<td>Functional Disability</td>
<td>Liebowitz Disability Self-Rating Scale</td>
<td>Specific</td>
</tr>
<tr>
<td>Quality of Life</td>
<td>WHO Quality of Life - 100</td>
<td></td>
</tr>
</tbody>
</table>
2. Epidemiology of social anxiety disorder
Presentation lead by:

John R. Walker, Ph.D.
University of Manitoba
THE EPIDEMIOLOGY OF SOCIAL PHOBIA

John R. Walker, Ph.D.
University of Manitoba
Why is epidemiology important?
Why is epidemiology important?

| Informs us about the impact of a problem on the problem on the population as a whole. |
| Knowledge of prevalence helps in planning service, education, and research. |
| Research on risk factors helps in our understanding of etiology. |
| Basis for developing and evaluating preventative procedures and public health practices |
### Lifetime Social Fears In Young People (EDSP, Munich – Ages 14-24)

<table>
<thead>
<tr>
<th>Situation</th>
<th>Lifetime Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eating or drinking in public</td>
<td>4.4%</td>
</tr>
<tr>
<td>Writing while someone watches</td>
<td>2.2%</td>
</tr>
<tr>
<td>Participating in social events</td>
<td>4.6%</td>
</tr>
<tr>
<td>Performance/test situations</td>
<td>18.2%</td>
</tr>
<tr>
<td>Public speaking</td>
<td>13.2%</td>
</tr>
<tr>
<td>Talking with/to others</td>
<td>6.4%</td>
</tr>
<tr>
<td>Any social fear (from these questions)</td>
<td>27.3%</td>
</tr>
</tbody>
</table>
# Lifetime Rates of Social Phobia

<table>
<thead>
<tr>
<th>Location</th>
<th>Rate</th>
<th>Age, Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Winnipeg</td>
<td>7.1%</td>
<td>18+, Stein et al, 1994</td>
</tr>
<tr>
<td>USA (NCS)</td>
<td>13.3%</td>
<td>15-54, Kessler et al, 1994</td>
</tr>
<tr>
<td>Ontario (OHS)</td>
<td>6.7%</td>
<td>15-64, Boyle et al, 1996</td>
</tr>
<tr>
<td>EDSP, Munich</td>
<td>7.3%</td>
<td>14-24, Wittchen et al, 1999</td>
</tr>
<tr>
<td>Alberta/Winnipeg</td>
<td>7.2%</td>
<td>16+, Stein et al, 2000</td>
</tr>
<tr>
<td>Paris</td>
<td>7.3%</td>
<td>18+, Pelissolo et al, 2000</td>
</tr>
</tbody>
</table>
### Canadian Community Health Survey (2003) Females, 12 Month Prevalence

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Age 15-24</th>
<th>Age 25-64</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social Phobia</td>
<td>6.2%</td>
<td>3.4%</td>
<td>3.4%</td>
</tr>
<tr>
<td>Panic Disorder</td>
<td>3.3%</td>
<td>2.2%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Agoraphobia</td>
<td>1.2%</td>
<td>1.2%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Maj. Depression</td>
<td>8.2%</td>
<td>5.8%</td>
<td>5.5%</td>
</tr>
</tbody>
</table>
### Canadian Commun. Health Survey (2003) Males, 12 Month Prevalence

<table>
<thead>
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<tbody>
<tr>
<td>Social Phobia</td>
<td>3.3%</td>
<td>2.7%</td>
<td>2.5%</td>
</tr>
<tr>
<td>Panic Disorder</td>
<td>1.2%</td>
<td>1.2%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Agoraphobia</td>
<td></td>
<td></td>
<td>0.4%</td>
</tr>
<tr>
<td>Maj. Depression</td>
<td>4.3%</td>
<td>3.5%</td>
<td>3.4%</td>
</tr>
</tbody>
</table>
What are the causes of anxiety and depressive disorders?

- Biological / genetic factors?
- Conditioning or learning?
- Adverse experiences during childhood?
- Life stress close to the time of onset?
Genetics of Social Anxiety Disorder

Kendler’s study of female twin pairs

<table>
<thead>
<tr>
<th>Concordance rates of:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- 15.3% for dizygotic pairs</td>
</tr>
<tr>
<td>- 24.4% for monozygotic pairs</td>
</tr>
<tr>
<td>- Heritability index of 30%</td>
</tr>
</tbody>
</table>
## Childhood Adversity and SAD

**Ontario Health Survey (Chartier, Walker, Stein, 2001)**

<table>
<thead>
<tr>
<th>Adverse Experience</th>
<th>O.R.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Juvenile Justice Involvement</td>
<td>1.82</td>
</tr>
<tr>
<td>Child-welfare involvement</td>
<td>2.70</td>
</tr>
<tr>
<td>Running away from home</td>
<td>3.40</td>
</tr>
<tr>
<td>Lack of close adult relationship</td>
<td>2.63</td>
</tr>
<tr>
<td>Marital conflict – parents</td>
<td>1.82</td>
</tr>
<tr>
<td>Parental history of mental disorder</td>
<td>2.13</td>
</tr>
<tr>
<td>Severe physical abuse</td>
<td>2.54</td>
</tr>
<tr>
<td>Severe sexual abuse</td>
<td>1.72</td>
</tr>
</tbody>
</table>
## Childhood Adversity and SAD - 2

Ontario Health Survey (Chartier, Walker, Stein, 2001)

<table>
<thead>
<tr>
<th>Adverse Experience - School</th>
<th>O.R.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Special education before grade 9</td>
<td>2.97</td>
</tr>
<tr>
<td>Special education after grade 9</td>
<td>2.71</td>
</tr>
<tr>
<td>Failing a grade before grade 9</td>
<td>1.99</td>
</tr>
<tr>
<td>Dropping out of high school</td>
<td>2.08</td>
</tr>
</tbody>
</table>
Social phobia is often the first disorder in the history for individuals with comorbid disorders

Magee et al (1996)
What about childhood?
Concept of Behavioral Inhibition

• Generally shy demeanour
• Tendency to approach new situations with restraint, avoidance, and distress
• Measured in different ways from infancy to early school years
• Moderate levels of stability
• Consistent Inhibition related to later anxiety
Early Developmental Stages of Psychopathology Study

- Munich Germany
- Ages 14 – 24
- Baseline interview and follow up 20 or 40 months afterward
- Parents also provided some information
- First interview covered 12 month and lifetime, follow up interviews covered intervening time
Early Developmental Stages of Psychopathology Study

- Longitudinal design allows an evaluation of risk of future disorders among individuals who have one disorder at the start of the follow up period.

- Previously most of the data available have been from cross sectional studies where researchers must rely on the accuracy of retrospective reports.

- Are retrospective reports influenced by today’s mood? OR, is there under reporting of past experiences?
**Social Anxiety Disorder and Risk of Major Depression (Stein et al., 2001)**

<table>
<thead>
<tr>
<th>Baseline Diagnosis</th>
<th>Depressive Disorder Over Follow-up</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Mental Disorder</td>
<td>8%</td>
<td></td>
</tr>
<tr>
<td>SAD – No Depression</td>
<td>24%</td>
<td>3.5</td>
</tr>
<tr>
<td>Depression – No SAD</td>
<td>25%</td>
<td>3.8</td>
</tr>
<tr>
<td>Depression + SAD</td>
<td>44%</td>
<td>8.7</td>
</tr>
</tbody>
</table>
Social Anxiety Disorder and Risk of Major Depression (Stein et al., 2001)

- Presence of both social anxiety disorder and depression was also related to increased severity of depression (number of symptoms, presence of suicide attempts, duration)

- Other anxiety disorders likely follow a similar pattern

- May not be a causal relationship, third factor may be involved
### Selected Risk Factors For Anxiety and Depressive Disorders (Wittchen et al., 2000)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Depression</th>
<th>SAD</th>
<th>GAD</th>
<th>Panic</th>
<th>Agora</th>
<th>Specific Phobia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edu. Probs.</td>
<td>1.7</td>
<td>2.7</td>
<td></td>
<td></td>
<td>3.6</td>
<td></td>
</tr>
<tr>
<td>Early Sep.</td>
<td>2.0</td>
<td>2.4</td>
<td>2.3</td>
<td>2.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parent Alc.</td>
<td>1.4</td>
<td>2.4</td>
<td></td>
<td></td>
<td></td>
<td>1.4</td>
</tr>
<tr>
<td>Parent Anx.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.3</td>
<td>2.4</td>
</tr>
<tr>
<td>Parent Dep.</td>
<td>2.1</td>
<td>1.9</td>
<td>2.2</td>
<td></td>
<td></td>
<td>1.6</td>
</tr>
<tr>
<td>Behav. Inhib.</td>
<td>10.0</td>
<td>6.4</td>
<td>10.0</td>
<td></td>
<td>18</td>
<td>4.2</td>
</tr>
</tbody>
</table>
Important Research Questions

• Can we intervene early to reduce the impact?

• Will prevention or early intervention applied to anxiety problems reduce other disorders?

• What prevention approaches could be considered?

• How cost effective would various intervention programs be?
Desirable Characteristics for Prevention Approaches

- Community and school based rather than clinic based
- Reaching out to families rather than waiting for referrals
- Non stigmatizing – of children and of parents
- Support parents in their role rather than blaming
- Use change agents who will be available at the community level
- Highly structured program to facilitate dissemination
- Based on sound knowledge of child development
Social Phobia
Why the Strong Interest?

- Most common anxiety Disorder
- Early age of onset
- High rates of comorbidity
- Significant personal morbidity
- High financial burden
- Treatable although under-recognized
3. Neurobiology of social anxiety disorder
Presentation lead by:

Pierre Bleau, M.D.
McGill University
Psychobiology of FEAR

Amygdala
Central Nucleus

- Central Gray
  - Freezing
- Lateral Hypothalamus
  - Blood Pressure
- Paraventricular Nucleus
  - Stress Hormones
- Reticulo pontis
  - Startle Reflex

Conditioning of the Anxiety/Fear Response

Fear conditioning

– Coincidences between stimuli that trigger the fear response and the activation of the amygdala are connected together through hardening of synapses in the basolateral nucleus of the amygdala. These are arguably the formation of ‘emotional memories’

LeDoux J. Biol Psychiatry 1998; McKernan & Shinnick-Gallagher Nature 1997; Davis M Biol Psychiatry
AMYGDALA

Sensory Cortex
(objects)

Rhinal (transitional) Cortex
(memories)

Hippocampus
(memories and contexts)

Sensory Thalamus
(stimulus features)

Medial Prefrontal
(extinction)

FEAR
(responses and experiences)

Conditioning of the Anxiety/Fear Response

Avoidance conditioning

- Dysphoric experiences associated with the activation of the fear/anxiety responses are avoided. This involves prefrontal cortical and limbic interconnections

LeDoux J. Biol Psychiatry 1998; McKernan & Shinnick-Gallagher Nature 1997; Davis M Biol Psychiatry 1998
Conditioning of the Anxiety/Fear Response

Contextual conditioning

– Stimuli associated with cues that trigger the fear anxiety response result in increased vigilance. This involves declarative memory circuits mediated through the hippocampus.

LeDoux J. Biol Psychiatry 1998; McKernan & Shinnick-Gallagher Nature 1997; Davis M Biol Psychiatry

AMYGDALA

- Sensory Cortex (stimulus features)
- Sensory Thalamus
- Rhinal (transitional) Cortex (memories)
- Hippocampus (memories and contexts)
- Medial Prefrontal (extinction)

FEAR (responses and experiences)
Increased Amygdala Response to Angry/Fearful Faces in Normals: Impact of Short vs. Long Allele of the Serotonin Transporter Gene (SERT)

Amygdala Responses: Group > 1 Group

First Cohort (N = 14)

Short Allele SERT

Second Cohort (N = 14)

Long Allele SERT

Hariri et al. Science 2002:297:400-403
Stress results in decreased dendritic branching of neurons in the CA3 region of the hippocampus.

BDNF = brain-derived neurotrophic factor; NE = norepinephrine.

Neurobiology of Anxiety

Cognitive Conspiracies

Afférent pathways

Efferents pathways

PROCESSING

Adapted from Charney and Deutsch 1996
Afférent pathways

Cognitive Functions

Cognitive conspiracies

Cingulate g.

Amygdala

Hippocampus

PROCESSING

Adapted from Charney and Deutsch 1996
And from Gray’s theory 1982, 2000
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Cognitives conspiracy

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Amygdala

Hippocampus

PROCESSING

Lateral Hypothalamus
Dors.Motor N. Vagus
Nucleus Ambiguus
Parabrachial Nucleus
Ventral Tegmental Area
Locus Ceruleus
Dorso-lateral Tegmental N
N. Reticularis Pontis Caudalis
Central Grey or Striatum
Trigiminal, Facial N
Paraventricular N (Hypothal.)

Adapted from Charney and Deutsch 1996
Neurobiology of Anxiety

Cognitive Functions

Cognitives conspiracy

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Lateral Hypothalamus
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Hippocampus

PROCESSING

Adapted from Charney and Deutsch 1996
Neurobiology of Anxiety

- Lateral Hypothalamus
- Sympathetic Activation
- Dors. Motor N. Vagus
- Parasympathetic Activation
- Nucleus Ambiguus
- Increased Respiration
- Parabrachial Nucleus
- Increased Reflexes
- Ventral Tegmental Area
- Cessation of Behavior or Flight
- Locus Ceruleus
- Mouth open, jaw movements
- Noradrenaline
- Dorso-lateral Tegmental N
- Acetylcholine
- N. Reticularis Pontis Caudalis
- Increased Refluxes
- Central Grey or Striatum
- Cessation of Behavior or Flight
- Trigiminal, Facial N
- Mouth open, jaw movements
- Paraventricular N (Hypothal.)
- ACTH Release

Adapted from Charney and Deutsch 1996
Neurobiology of Anxiety

- Lateral Hypothalamus
  - Sympathetic Activation
- Dors. Motor N. Vagus
  - Parasympathetic Activation
- Nucleus Ambiguus
- Parabrachial Nucleus
- Paraventricular N (Hypothal.)
  - ACTH Release
- Ventral Tegmental Area
  - Increased Respiration
  - Activation of Dopamine
    - Noradrenaline
    - Acetylcholine
- Locus Ceruleus
- Dorso-lateral Tegmental N
- N. Reticularis Pontis Caudalis
- Central Grey or Striatum
- Trigeminal, Facial N
  - Increased Reflexes
  - Cessation of Behavior or Flight
  - Mouth open, jaw movements

Adapted from Charney and Deutsch 1996
Neurobiology of Anxiety

- **Lateral Hypothalamus**: Sympathetic Activation
- **Dors.Motor N. Vagus**: Parasympathetic Activation
- **Nucleus Ambigus**: Increased Respiration
- **Parabrachial Nucleus**: Increased Reflexes
- **Ventral Tegmental Area**: Activation of Dopamine (Noradrenaline, Acetylcholine)
- **Locus Ceruleus**: Cessation of Behavior or Flight
- **Dorso-lateral Tegmental N**: Mouth open, jaw movements
- **N. Reticularis Pontis Caudalis**: ACTH Release
- **Central Grey or Striatum**: Cessation of Behavior or Flight
- **Trigimal, Facial N**: ACTH Release
- **Paraventricular N (Hypothal.)**: ACTH Release

Adapted from Charney and Deutsch 1996
Neurobiology of Anxiety

- Lateral Hypothalamus → Sympathetic Activation → Tachycardia, BP elevation
- Nucleus Ambiguus
- Parabrachial Nucleus → Increased Respiration → Respiratory Distress
- Ventral Tegmental Area → Activation of Dopamine
- Locus Ceruleus → Noradrenaline
- Dorso-lateral Tegmental N → Acetylcholine
- N. Reticularis Pontis Caudalis → Increased Reflexes
- Central Grey or Striatum → Cessation of Behavior or Flight
- Trigimal, Facial N → Mouth open, jaw movements
- Paraventricular N (Hypothal.) → ACTH Release → Cortisol (Stress response)

Increased vigilance, behavioral & EEG, facial expression of fear, startle response, freeze or flight, respiratory distress, ulcers, tachycardia, BP elevation, urination, defecation, Bradych.

Adapted from Charney and Deutsch 1996
**Neurobiology of Anxiety**

- **Lateral Hypothalamus** → Sympathetic Activation → Tachycardia, BP elevation
- **Dors. Motor N. Vagus** → Parasympathetic → Urination, defecation, Bradych.
- **Nucleus Ambiguus** → Activation → Ulcers
- **Parabrachial Nucleus** → Increased Respiration → Respiratory Distress
- **Ventral Tegmental Area** → Activation of Dopamine → Behavioral & EEG
- **Locus Ceruleus** → Noradrenaline → Arousal
- **Dorso-lateral Tegmental N** → Acetylcholine → Increased vigilance
- **N. Reticularis Pontis Caudalis** → Increased Reflexes → Startle response
- **Central Grey or Striatum** → Cessation of Behavior or Flight → Freeze or Flight
- **Trigiminal, Facial N** → Mouth open, jaw movements → Facial expression of Fear
- **Paraventricular N (Hypothal.)** → ACTH Release → Cortisol (Stress response)

*Adapted from Charney and Deutsch 1996*
Neurobiology of Anxiety

- Lateral Hypothalamus
  - Sympathetic Activation
  - Tachycardia, BP elevation

- Dors. Motor N. Vagus
  - Parasympathetic Activation
  - Urination, defecation, Bradych.

- Nucleus Ambiguus

- Parabrachial Nucleus
  - Increased Respiration
  - Respiratory Distress

- Ventral Tegmental Area
  - Activation of Dopamine
  - Behavioral & EEG

- Locus Ceruleus
  - Noradrenaline
  - Arousal
  - Increased vigilance

- Dorso-lateral Tegmental N
  - Acetylcholine

- N. Reticularis Pontis Caudalis
  - Increased Reflexes
  - Startle response

- Central Grey or Striatum
  - Cessation of Behavior or Flight
  - Freeze or Flight

- Trigimonial, Facial N
  - Mouth open, jaw movements
  - Facial expression of Fear

- Paraventricular N (Hypothal.)
  - ACTH Release
  - Cortisol (Stress response)

Adapted from Charney and Deutsch 1996
Functional Neuroanatomy of Fear and Anxiety

( Charney & Deutsch 1996 )

Fear and Anxiety Response Patterns

Fight or flight response

Fear-induced skeletal motor activation

Facial expression of fear

Facial hyperventilation

Facial motor nuclei

Facial expression of fear

Fear-induced sympathetic nervous system activation

Fear-induced parasympathetic nervous system activation

Fear-induced sympathetic nervous system activation

Fear-induced parasympathetic nervous system activation

Tachycardia

Increase BP

Sweating

Piloerction

Hormonal stress response

Bradycardia

Ulcers

Defecation

Urination

Hyperventilation

Increased BP

Sweating

Piloerction

Hormonal stress response

Fear and Anxiety Response Patterns

Fight or flight response

Fear-induced skeletal motor activation

Facial expression of fear

Facial hyperventilation

Facial motor nuclei

Facial expression of fear

Fear-induced sympathetic nervous system activation

Fear-induced parasympathetic nervous system activation

Fear-induced sympathetic nervous system activation

Fear-induced parasympathetic nervous system activation

Tachycardia

Increase BP

Sweating

Piloerction

Hormonal stress response

Bradycardia

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Urination

Hyperventilation

Increased BP

Sweating

Piloerction

Hormonal stress response
Neurobiology of Social Anxiety Disorder
Biology of Social Phobia

- Central dopaminergic involvement?
- Central serotonergic dysregulation?
- Peripheral autonomic mediation

Generalized

Nongeneralized
Social Anxiety Disorder Spectrum-Continuum

“Normal”

Shy

Performance - Social Anxiety Disorder

Generalized - Social Anxiety Disorder

Avoidant Personality Disorder
Age At Onset of Social Anxiety Disorder In Subjects Without Agoraphobia or Simple Phobia

(N=106)

Age (years)

Number of Subjects

0-5 6-10 11-15 16-20 21-25 26-30 31-35 36-40 41-45 46-50 51-55 56-60 61-65 66-70 71-75

Schneier 1992
### Serotonergic Function in SAD

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment/Challenge</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knutson, 1998</td>
<td>SSRI treatment</td>
<td>Increased sociability in healthy controls</td>
</tr>
<tr>
<td>Various studies</td>
<td>SSRI treatment</td>
<td>Beneficial effect in Patients with SAD</td>
</tr>
<tr>
<td>Hollander, et al. 1998</td>
<td>m-CPP challenge (partial 5-HT agonist)</td>
<td>Significantly greater cortisol response vs. controls</td>
</tr>
<tr>
<td>Tancer, 1993</td>
<td>Fenfluramine challenge</td>
<td>Increase in cortisol Response</td>
</tr>
<tr>
<td>Moskowitz et al. 2001</td>
<td>Tryptophan Challenge</td>
<td>Increased sociability in healthy controls</td>
</tr>
<tr>
<td>Arbell et al, 2003</td>
<td>5-HTPRL polymorphism</td>
<td>Association between shyness and I allele</td>
</tr>
<tr>
<td>Kang Seob Oh, 2003</td>
<td>5-HTPRL polymorphism</td>
<td>higher proportion of the I allele in SAD patients</td>
</tr>
<tr>
<td>Stevens et al, 2004</td>
<td>5-HTT binding</td>
<td>greater binding potential in patients with SAD</td>
</tr>
<tr>
<td>Nutt et al, 2004</td>
<td>TRP depletion</td>
<td>Reverse SSRI treatment</td>
</tr>
</tbody>
</table>
Neurobiology of SAD

Serotonergic systems

- Increased 5HT associated with dominant social status associated with affiliative behavior
- Decreased 5HT associated with subordinant status

Neurobiology of SAD

Dopaminergic systems
– Modulates approach behavior
– Reduces dopaminergic function in patients with SAD
  • Reduced striatal dopamine reuptake binding
  • Reduced D2 receptor binding density


Evidence for dopaminergic dysfunction

- Atypical antipsychotic olanzapine is effective in social anxiety disorder monotherapy (Barnett et al, 2003)
- High rates of social anxiety disorder in patients with Parkinson’s Disease (Stein et al, 1990)
- Healthy subjects with a detached personality show lower density of the dopamine D$_2$ receptors (Laakso et al, 2000; Farde et al, 1997)
Individual values (n = 24) for D$_2$-dopamine-receptor density plotted against KSP detachment scores. To adjust for the effect of gender, the scores were transformed to T scores using normative data. The T scores have a mean (± s.e.m.) of 50 (±10) in the normal population.

Dopamine Transporter

4 hr after 185 MBq

$^{123}$I-ß-CIT.

24 hrs after 185 MBq

$^{123}$I-ß-CIT and 20 mg paroxetine
Dopamine transporter binding in the basal ganglia of SAD patients and controls

β-CIT binding ratio

Stevens et al, 2004
D₂ Receptor Binding Potential

[123I] IBZM binding potential ml/gr

P < 0.05

Controls

Subjects With Social Anxiety Disorder

Conclusions imaging studies

Increased dopaminergic tone in SAD is consistent with:

- Higher DAT binding potential (Stevens et al, 2004)
- Lower $D_2$ binding potential (Schneier et al, 2000)
- Lower $D_2$ binding in healthy subjects with detached personality (Farde et al 1997)
- Efficacy of atypical antipsychotics in SAD (Barnett et al 2003)

Decreased dopaminergic tone in SAD is consistent with:

- Lower DAT binding (Tiihonen et al 1997)
- Higher prevalence of SAD in Parkinson’s patients (Stein 1990)
Identification
Production
Regulation autonomic resp.

Integration
Executives functions
Regulation - effortful (of affective states)

Dorsal system
- Dorsolateral prefrontal cortex
- Dorsomedial prefrontal cortex
- Dorsal anterior cingulate gyrus
- Hippocampus

Ventral system
- Ventrolateral prefrontal cortex
- Orbitofrontal cortex
- Ventral anterior cingulate gyrus

Amygdala
Insula

Thalamus
Ventral striatum
Brainstem nuclei

Phillips et al., 2003.
4. Psychology of social anxiety disorder
Presentation lead by:

Stéphane Bouchard, Ph.D.
Université du Québec en Outaouais
A cognitive model to guide our understanding

Social situation

Activates assumptions

Perceived social danger

Self-focused attention

Safety behaviours

Somatic and cognitive symptoms

From Clark & Wells, 1996

See also critics from Stravinski et al., 2004.
Dysfunctional beliefs often found in social anxiety disorder

High standards of social performance
– As if in social situations they were in danger of behaving in an inept and unacceptable fashion.

Social evaluation is dangerous
– As if their behaviors will have disastrous consequences (loss of status, loss of worth, rejection).

Unconditional negative beliefs about the self when in social situations.
– Low social self-esteem.
Thoughts content after a social interaction.

(Stopa & Clark, 1993)

-5  5  15  25  35  45

Percent of negative thoughts

Social phobics  Anxious CTRL  Normal CTRL

-5  5  15  25  35  45

Thoughts evaluating oneself  Thoughts about being evaluated by others
Even positive social events...
Walace & Alden (1997)

- 32 generalized social phobics and 32 controls had (manipulated) positive and negative social interactions.
- Successful social interaction produced a more negative response in SP: more self-protective social goals, negative affect and the perception that others would expect more in the future.

PANAS scores

- Social phobics
-Ctrls
Emotional Stroop task.

(Hope et al., 1990)
Abnormal processing of facial expressions.
(Horley et al. 2004)

- Social phobics displayed hyperscanning (increased scanpath length) and avoidance of the eyes (reduced foveal fixations), especially of neutral ($p < .05$) and angry ($p < .01$) faces.
- $N = 22$ generalised social phobics and 22 ctrls.

Fig. 1. Control subjects showed an increasing fixation to eyes across happy, neutral, sad and angry faces, whereas social phobia subjects showed an increasing avoidance of eyes across these emotions. Social phobia subjects also showed extensive scanning of non-features. Scanpaths are representative of a typical subject from each group.
Negative social thoughts are anxiety provoking.

(Hirsch et al., 2003)

- 16 social phobics participated twice in a conversation, once while holding in mind their negative self-image and once while holding a control self-image.

![Bar chart showing STAI-sanx Behavioral ratings](chart.png)

- Measure administered:
  - STAI-sanx
  - Behavioral ratings

- Negative image: Red bars
- CTRL image: Orange bars

- p < .001
Social situations are anxiety provoking in part because social phobics perceive their emotional symptoms as being out of control.

N = 144 social phobics.
SCQ Social Cost Q. «How bad if x happened ?», Performance and Non-performance subscales
ACQ Anxiety Control Q. Reaction and Event subscales.

38 generalized social phobics had to give a speech while focusing on self or others.
5. Pharmacological treatment of social anxiety disorder
Presentation lead by

Pierre Bleau, M.D.
McGill University
# Guidelines for Remission of Social Anxiety Disorder

<table>
<thead>
<tr>
<th>Subjective Goal</th>
<th>Objective Goal</th>
<th>Time Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abolish core symptoms</td>
<td>Little or no fear or avoidance of social situations as measured by functional improvement on standardized scale*</td>
<td>6–12 wk</td>
</tr>
<tr>
<td>Minimize anxiety</td>
<td>HAM-A score ≤7 or 70% improvement on patient-rated scale</td>
<td>3–12 mo</td>
</tr>
<tr>
<td>Eliminate depression</td>
<td>HAM-D score ≤7 or 70% improvement on patient-rated scale</td>
<td>3–12 mo</td>
</tr>
<tr>
<td>Resolve functional impairments</td>
<td>Sheehan score ≤1 (mildly disabled)</td>
<td>3–12 mo</td>
</tr>
</tbody>
</table>

*e.g., Score < 30 on the Liebowitz Social Anxiety Scale

Ballenger 1999
Treatment of Social Anxiety Disorder

- SSRI’s/SNRI’s
- Monoamine Oxidase Inhibitors
- High Potency Benzodiazepines
- Beta Blockers
- Other Agents
- Cognitive-Behavioral Therapy
SSRIs: Controlled Studies

Response rate (%)

- Sertraline
- Fluvoxamine
- Paroxetine
- Placebo

Liebowitz, 2003; Katzelnick 1995; Westenberg, 2004; van Vliet 1993;
Stein et al 1999; Davidson, 2003; Stein 1998; Baldwin, 2000
Paroxetine in Social Anxiety Disorder
LSAS (ITT/LOCF)

P<.05 vs placebo.
Mean dose = 36.6 mg/d at endpoint

Stein et al. 1998
Fluvoxamine in social anxiety disorder

Stein et al, 1999

---

**Placebo** vs. **fluvoxamine**

LSAS over weeks:

- **Placebo** line shows a steady decrease in LSAS over weeks.
- **Fluvoxamine** line also shows a decrease, but it starts lower and remains lower compared to placebo.

Weeks 0 to 12, with marked significant differences at weeks 9, 10, and 11.

---

Stein et al, 1999
Fluvoxamine CR SAD study
LOCF-ITT analysis, change from baseline

Davidson, 2004
# Other SSRIs

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Duration</th>
<th>Response rates (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Paroxetine</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baldwin et al 1999</td>
<td>290</td>
<td>12</td>
<td>66*</td>
</tr>
<tr>
<td>Allgulander et al 1999</td>
<td>96</td>
<td>12</td>
<td>70*</td>
</tr>
<tr>
<td>Stein et al 1998</td>
<td>187</td>
<td>12</td>
<td>55*</td>
</tr>
<tr>
<td><strong>Sertraline</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Katzelnick et al 1995</td>
<td>12</td>
<td>10</td>
<td>50*</td>
</tr>
<tr>
<td>Liebowitz et al 2003</td>
<td>211</td>
<td>12</td>
<td>47*</td>
</tr>
<tr>
<td><strong>Fluoxetine</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kobak et al 2002</td>
<td>60</td>
<td>14</td>
<td>ns</td>
</tr>
</tbody>
</table>

* significantly different to placebo
Venlafaxine XR in Social Anxiety Disorder

Study 1

- Placebo (n=138)
- Venlafaxine (n=133)

Response rate at 12 weeks (%)

Study 2

- Placebo (n=135)
- Venlafaxine (n=136)

Response rate at 12 weeks (%)

Response=CGI score of 1 or 2. *P<0.05 vs placebo; modified ITT/LOCF.

(Liebowitz and Mangano 2002)
Social Anxiety Disorder
Venlafaxine XR vs. Placebo (28 weeks)
LSAS Total Scores (LOCF)

Adjusted Mean Change from Baseline

Week

1 2 3 4 6 8 12 16 20 24 28

Placebo (n=126)
VEN XR 75 mg (n=119)
VEN XR 150-225 mg (n=119)
VEN XR Combined

*p < 0.05 VEN XR 75 mg vs. placebo
† p < 0.05 VEN XR 150-225 mg vs. placebo
‡ p < 0.05 Combined vs. placebo

LOCF = Last Observed Carried Forward

Stein MB & R Mangano. Presented at the American College of Neuropsychopharmacology, Puerto Rico, December 8-12, 2002.
Comparison of Venlafaxine XR and Paroxetine in the Short-Term Treatment of SAD

LSAS Total Score (LOCF) Study 2

Leibowitz et al., ACNP 2002

Adjusted Mean Change from Baseline

Week

Placebo
Venlafaxine XR
Paroxetine

* p < 0.01 Venlafaxine XR vs placebo
† p < 0.01 Paroxetine vs placebo

LOCF = Last Observed Carried Forward
Treatment of Social Anxiety Disorder

- SSRI’s/SNRI’s
- Monoamine Oxidase Inhibitors
- High Potency Benzodiazepines
- Beta Blockers
- Other Agents
- Cognitive-Behavioral Therapy
## Monoamine Oxidase Inhibitors in SAD

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Duration (wks)</th>
<th>% Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liebowitz et al., 1992</td>
<td>74</td>
<td>8</td>
<td>Phenelzine 64</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Atenolol 30</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Placebo 23</td>
</tr>
<tr>
<td>Gelernter et al., 1991</td>
<td>65</td>
<td>12</td>
<td>Phenelzine 69</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Alprazolam 38</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CBT Group 24</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Placebo 20</td>
</tr>
<tr>
<td>Versiani et al., 1992</td>
<td>78</td>
<td>16</td>
<td>Phenelzine 91</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Moclobemide 82</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Placebo 43</td>
</tr>
</tbody>
</table>
### Monoamine Oxidase Inhibitors in SAD

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Duration (wks)</th>
<th>% Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van Vliet et al., 1992</td>
<td>74</td>
<td>8</td>
<td>Brofaromine 80</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Placebo 14</td>
</tr>
<tr>
<td>Humble et al., 1991</td>
<td>65</td>
<td>12</td>
<td>Brofaromine 79</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Placebo 26</td>
</tr>
</tbody>
</table>
RIMAs: Controlled Studies

Response rate (%)

- Placebo
- Phenelzine
- Brofaromine
- Moclobemide

Fahlen et al 1995
Van Vliet et al 1992
Versiani et al 1992
Schneier et al 1998
Noyes et al 1997
Burrows et al 1997
Treatment of Social Anxiety Disorder

- SSRI’s/SNRI’s
- Monoamine Oxidase Inhibitors
- High Potency Benzodiazepines
- Beta Blockers
- Other Agents
- Cognitive-Behavioral Therapy
Benzodiazepines in SAD

Placebo-controlled studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Duration (weeks)</th>
<th>N</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ALPRAZOLAM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gelernter et al. 1991</td>
<td>20</td>
<td>65</td>
<td>Alprazolam: 38% CBT: 24% Placebo: 20%</td>
</tr>
<tr>
<td><strong>CLONAZEPAM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Davidson et al. 1993</td>
<td>10</td>
<td>75</td>
<td>Clonazepam: 78.3% Placebo: 20%</td>
</tr>
</tbody>
</table>

Clonazepam in Social Anxiety Disorder

Clonazepam Mean=2.4 mg/day

78.3

CGI Response = 1 or 2 (%)

(Davidson 1993)
Treatment of Social Anxiety Disorder

- SSRI’s/SNRI’s
- Monoamine Oxidase Inhibitors
- High Potency Benzodiazepines
- Beta Blockers
- Other Agents
- Cognitive-Behavioral Therapy
Propranolol in Social Anxiety Disorder
Scholastic Aptitude Test (SAT)
and Performance Anxiety

(N=32)

On retest

- Expected improvement 14 points
- With propranolol (40 mg) 130 points

Faigel, 1991
Treatment of Social Anxiety Disorder

• SSRI’s/SNRI’s
• Monoamine Oxidase Inhibitors
• High Potency Benzodiazepines
• Beta Blockers
• Other Agents
• Cognitive-Behavioral Therapy
### Other Pharmacotherapies in SAD

<table>
<thead>
<tr>
<th>Study</th>
<th>Duration (weeks)</th>
<th>N</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TCA</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simpson et al. 1998</td>
<td>8</td>
<td>15</td>
<td>20-22% response with imipramine in open-labeled study</td>
</tr>
<tr>
<td>Emmanuel et al 1997</td>
<td>8</td>
<td>41</td>
<td>Imipramine no more effective than placebo</td>
</tr>
</tbody>
</table>

Emmanuel et al
Tricyclic Antidepressants in Social Anxiety Disorder

Double-blind, placebo-controlled trial
- N=41, 8-week trial
- Mean dose: 149 mg/day of Imipramine
- Results: Imipramine no more effective than placebo

Emmanuel 1997
## Other Pharmacotherapies in SAD

<table>
<thead>
<tr>
<th>BUSPIRONE</th>
<th>Duration (weeks)</th>
<th>N</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>van Vliet et al. 1997</td>
<td>12</td>
<td>30</td>
<td>Buspirone = placebo in double-blind study</td>
</tr>
<tr>
<td>Van Ameringen et al. 1996</td>
<td>8</td>
<td>10</td>
<td>Buspirone augmentation useful for SSRI partial responders in open-label study</td>
</tr>
<tr>
<td>Schneier et al. 1993</td>
<td>12</td>
<td>10</td>
<td>Modest efficacy in open-label study</td>
</tr>
<tr>
<td>Munjack et al. 1991</td>
<td>8</td>
<td>17</td>
<td>Modest efficacy in open-label study</td>
</tr>
<tr>
<td>Clark and Agras 1991</td>
<td>6</td>
<td>29</td>
<td>CBT + buspirone &gt; buspirone = placebo for performance anxiety</td>
</tr>
</tbody>
</table>

Buspirone in Social Anxiety Disorder

2 open-label studies
- 50% response rate at mean dose 45-50 mg/d\(^1,2\)
- Mean dose higher in responders (57 mg/d) than non-responders (38 mg/d)\(^2\)

- Negative double-blind, placebo-controlled study of buspirone (mean dose: 32 mg/d) with and vs. CBT\(^3\)
- Response rate: 70% with buspirone augmentation (mean dose: 45 mg/d) of SSRIs\(^4\)

Gabapentin in Social Anxiety Disorder: Efficacy Results

- LSAS
- BSPS
- SPIN
- MMFQ
- HAM-A
- HAM-D
- GCIC

** P<0.01 vs placebo
* P<0.05 vs placebo
ns = not significant

** P<0.01 vs placebo
* P<0.05 vs placebo
ns = not significant

Pande 1999
Treatment of Social Anxiety Disorder

- SSRI’s/SNRI’s
- Monoamine Oxidase Inhibitors
- High Potency Benzodiazepines
- Beta Blockers
- Other Agents
- Cognitive-Behavioral Therapy VS Rx
Response Rates for CBGT, Phenelzine, Pill Placebo and ES at 12 Weeks

Heimberg, et al. 1998
Relapse for CBGT and Phenelzine in Maintenance and Untreated FU

Summary:
- CBGT and Phenelzine were compared for relapse percentages.
- The graph shows the relapse percentage for Maintenance, Follow-Up, and Overall periods.
- Phenelzine has a higher relapse rate compared to CBGT across all periods.

Data Source:
Liebowitz 1999
Potential Anxiolytics in the Future

- CRF antagonists
- Substance P antagonists
- GABAergic agents
- Glutaminergic modulators
- Serotonin receptor subtype agonists/antagonists
6. Psychotherapeutic treatment of social anxiety disorder
Presentation lead by:

Stéphane Bouchard, Ph.D.
Université du Québec en Outaouais
&
John Walker, Ph.D.
University of Manitoba
Role of Psychotherapy

Cognitive-behavioural group therapy
- exposure
- cognitive restructuring
- homework

Social Effectiveness Training (SET)
- skills training
- individualized exposure

Psychodynamic or other traditional psychotherapies are not recommended, although psychosocial support/education is helpful
## Controlled trials of CBT for Social Phobia

<table>
<thead>
<tr>
<th>Study</th>
<th>Length of Follow-up (months)</th>
<th>Treatments</th>
<th>Percentage clinical improvement of completion (if available)</th>
<th>Other treatments (Yes/No)</th>
<th>Wait list (Yes/No)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Butler et al. (1984)</td>
<td>6</td>
<td>AMT &amp; E (N = 15)</td>
<td>Yes: E</td>
<td>Yes: E</td>
<td>Yes</td>
</tr>
<tr>
<td>Mattick &amp; Peters (1988)</td>
<td>3</td>
<td>E &amp; CR (N = 11)</td>
<td>86: E = 52%</td>
<td>Yes: E</td>
<td>Yes</td>
</tr>
<tr>
<td>Mattick et al. (1989)</td>
<td>3</td>
<td>E &amp; CR (N = 25)</td>
<td>Yes: E</td>
<td>Yes: E</td>
<td>Yes</td>
</tr>
<tr>
<td>Heimberg et al. (1990)</td>
<td>6</td>
<td>CBGT (N = 20)</td>
<td>81: ES = 47%</td>
<td>Yes: ES = (most)</td>
<td></td>
</tr>
<tr>
<td>Heimberg et al. (1993)¹</td>
<td>54-75</td>
<td>CBGT (N = 10)</td>
<td>Yes: ES = (most)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hope et al. (1990)</td>
<td>6</td>
<td>CBGT (N = 13)</td>
<td>No: E</td>
<td>Yes: ES = 24%</td>
<td>Yes</td>
</tr>
<tr>
<td>Gellernter et al. (1991)</td>
<td>2</td>
<td>CBGT (N = 20)</td>
<td>No: PH, AL, PL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lucas &amp; Telch (1993)</td>
<td>PT</td>
<td>CBGT (N = 18)</td>
<td>61: ES = 24%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>CBTI</td>
<td>50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heimberg et al. (1998)</td>
<td>PT</td>
<td>CBGT (N = 28)</td>
<td>75: PH = 77%</td>
<td>Yes: PL = 41%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yes: ES = 35%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yes: ES = 27%</td>
<td>No: PH</td>
</tr>
<tr>
<td>Liebowitz et al. (1999)²</td>
<td>6-12</td>
<td>CBGT (N = 14)</td>
<td>Yes: ES = 27%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

From Nathan & Gorman (2002),
AL = alprazolam; AMT = anxiety management therapy; CBGT = cognitive behavioral group treatment, CBTI = cognitive behavioral treatment – individual; CR = cognitive restructuring; E = exposure; ES = educational supportive group psychotherapy (placebo treatment; PL = pill placebo; PH = phenelzine; PT = post-treatment. ¹Follow up study of Heimberg et al. (1990), ²Follow up study of Heimberg et al. (1998)
Individual vs group treatment.  
*(Stangier et al., 2003)*

Individual is better than Group at post and follow-up (*p* < .05)

Note: ANCOVA, no Bonferroni!
Individual vs group treatment.
(Stangier et al., 2003)

Social Interaction Anxiety Scale

Individual = Group at post and follow-up.

N = 71
CT vs Expo and changes in self-perception
(Hofmann et al. 2004)

Self-focused statements during 3 social tasks

Other-focused statements during 3 social tasks

Significant reduction in neg. $p < .01$ [and increased in neutral, not shown]
The difference with WL is significant only for self-focused statements.
Some hints of treatment processes

• Changes in the interpretation of negative social events are correlated with changes in symptomatology (Wilson & Rapee, In press).

• Changes in beliefs that:
  – Others would perceive me negatively
  – Event are indication of negative self-characteristics
  – Event would have adverse long-term consequences

• Client’s expectancy that they will benefit from their treatment significantly predict improvement (sr = .07**), after severity has been statistically accounted for (sr = .26***). Safren et al. 1997.
Effectiveness (real life CBT).
(Lincoln et al., 2003)

Intent to treat. All $p < .0001$

N = 217

Measure administered

Pre Post
Cognitive-behavior strategies

- Self-monitoring
- Cognitive restructuring
- Exposure
- Problem solving
- Relapse prevention
- Modeling
- Transmission of information
In VR exposure for anxiety disorders

The aim of exposure is to help the patient to confront the feared stimulus in order to correct the dysfunctional associations that have been established between the stimulus and perceived threat (e.g., it is dangerous, I can’t cope).
The process of exposure

- **Avoidance** (safety seeking behavior, neutralization)
- **Functional exposure**

![Graph showing the process of exposure with increases in anxiety over time](image-url)
The treatment of social phobia – 100 years ago

- Paul Hartenberg published in 1901 a book where he described a disorder very similar to Social Phobia and suggested treatment strategies that were very close to actual CBT techniques (such as exposure).

Fairbrother, 2002.
Virtual reality

Integration of API evaluation with Design of Virtual Environments

From B. Wiederhold
VR and CBT (in virtuo exposure)
Klinger, Bouchard, Légeron, Roy et al. (submitted)

N = 36, 12 sessions. CBT in group.
Subjects: 43 fear of public speaking patients
- Randomly assigned to one of three groups, distinguished by the type of virtual audience
- Subjects have to talk in front of the virtual audience, at least twice.

Scenario: 8 formally dressed avatars, seated around a table

Three variables:
2 designed to assess the degree of self-reported anxiety generated by experience
The other to measure the speaker’s assessment of their performance.
(With a modified form of the Personal Report of Confidence as a Speaker - MPRCS)
Pertaub, Slater & Barker

**MPRCS**

Type of audience
- Neutral
- Positive
- Negative

**Satisfaction towards the performance**

Type of audience
- Neutral
- Positive
- Negative

ANCOVA (estimated from data in the paper)
Type of audience, p < .05
Negative > positive = neutral.

Anova
Type of audience, p < .05
Neutral > Positive = Negative, p < .05
CBT vs Fluoxetine.

(Clark et al. 2003)

N = 66

At mid and post: CBT < FLU + ex = PLA + ex
At the end of the booster: CBT < Flu + exp
At follow-up: CBT < Flu + exp (Flu was withdrawn 3 to 6 weeks after booster)
CBT vs Fluoxetine

(Clark et al. 2003)

At post: CBT < FLU + ex = PLA + ex
At the end of the booster: CBT < Flu + exp
At follow-up: CBT = Flu + exp (Flu was withdrawn 3 to 6 weeks after booster)
There have been criticisms

• Some points have been raised about comparisons studies.
• The «best» medication may not have been used.
• By the time this type of study is completed, the gold standard treatments might have evolved so much that the comparisons are less useful than expected.
Problems with routinely combining medication treatment and CBT

- Often you do not get the best of both worlds – effects not additive.
- Difficulty telling what aspect of the treatment is having an impact.
- High rate of return of symptoms on discontinuation of medication.
- Why? Does not appear to be due to attribution of change to medication.
Alternative approach to combining treatments

- Informing people about treatment options.
- People start with strong treatment preferences.
- Inform of advantages and disadvantages of each treatment (written material would be best).
- Allow time to decide.
- Implement preferred option, evaluate, add alternative treatments if necessary.
Important research questions

• What is the optimal duration of treatment?
• How do individuals who do not improve with the first treatment respond to a second and third treatment?
• How do relationships change with treatment?
• Can we intervene early to reduce the impact?
• Will early intervention or prevention efforts reduce other disorders?
Cooperation in providing services

- Need to know about what treatments are available and the evidence for them in answering consumer questions.
- Need to know about the treatments to encourage clients to take treatment appropriately.
- Not wise to undermine or create doubts about another treatment - supportive stance works better.
7. ADAC/ACTA Guidelines
Guidelines

- Social Phobia is chronic and important.
- High rates of comorbidity.
- Significant personal morbidity.
- High financial burden.
- Treatable although under-recognized.
  - Cognitive-behavior therapy
  - Pharmacotherapy (see next tables)
<table>
<thead>
<tr>
<th>Place in Therapy</th>
<th>Medication</th>
<th>Starting Dose</th>
<th>Recommended</th>
<th>Usual Maximum Dose Range*</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Line (1 or 2)</td>
<td>Fluvoxamine</td>
<td>25 mg OD</td>
<td>100-300 mg OD</td>
<td>150-300 mg OD</td>
</tr>
<tr>
<td></td>
<td>Gabapentin</td>
<td>300 mg HS</td>
<td>600-3600 mg Divided BID-QID</td>
<td>600-3600 mg Divided BID-QID</td>
</tr>
<tr>
<td></td>
<td>Moolobemide</td>
<td>75 mg BID</td>
<td>300 mg BID</td>
<td>300-450 mg BID#</td>
</tr>
<tr>
<td></td>
<td>Paroxetine</td>
<td>10 mg OD</td>
<td>20-50 mg OD</td>
<td>20-60 mg OD</td>
</tr>
<tr>
<td></td>
<td>Paroxetine CR</td>
<td>12.5 mg OD</td>
<td>12.5-37.5 mg OD</td>
<td>12.5-75 mg OD</td>
</tr>
<tr>
<td></td>
<td>Sertraline</td>
<td>25 mg OD</td>
<td>100-200 mg OD</td>
<td>100-200 mg OD</td>
</tr>
<tr>
<td></td>
<td>Venlafaxine XR</td>
<td>37.5 mg OD</td>
<td>75-225 mg OD</td>
<td>150-375 mg OD</td>
</tr>
</tbody>
</table>

*Based on Clinical Experiences and a review of the literature

#Recommended daily dose of Moolobemide is up to 600mg. However, usage of higher doses has been reported, and in these cases dietary management as if on a MAOI is required.

+While Benzodiazepines may be effective anxiolytic, the potential risk of abuse and suggests use of these adjunctive treatments only. The risk of addiction may be lessened by prescribing them on a regular dose and not using a PRN or as needed basis.

See table at the end of the chapter for definitions of levels of evidence.
# ADAC/ACTA Guidelines for pharmacological treatment - Adults

<table>
<thead>
<tr>
<th>Second Line (Level 3)</th>
<th>Buspirone</th>
<th>10-15 Mg/day</th>
<th>30-60 mg/day</th>
<th>30-60 mg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Citalopram</td>
<td>10 mg OD</td>
<td>20-40 mg OD</td>
<td>40-60 mg OD</td>
</tr>
<tr>
<td></td>
<td>Fluoxetine</td>
<td>10 mg OD</td>
<td>20-60 mg OD</td>
<td>40-60 mg OD</td>
</tr>
<tr>
<td></td>
<td>Mirtazapine</td>
<td>30 mg HS</td>
<td>30-60 mg HS</td>
<td>30-60 mg HS</td>
</tr>
<tr>
<td></td>
<td>Olanzapine</td>
<td>2.5 mg OD</td>
<td>2.5-20 mg OD</td>
<td>5-20 mg OD</td>
</tr>
<tr>
<td></td>
<td>Valproate</td>
<td>250 mg BID</td>
<td>500-2500 mg/Day</td>
<td>500-2500 mg/Day</td>
</tr>
<tr>
<td>Third Line (Level 4 or Clinical issues)</td>
<td>Phenelzine</td>
<td>7.5-15 mg BID</td>
<td>15-45 mg BID</td>
<td>15-45 mg BID</td>
</tr>
<tr>
<td></td>
<td>Clonazepam+</td>
<td>0.5 mg BID</td>
<td>0.5-2 mg BID</td>
<td>0.5-2 mg BID</td>
</tr>
<tr>
<td></td>
<td>Alprazolam+</td>
<td>0.25-1 mg TID</td>
<td>0.25-3 mg BID</td>
<td>3 mg BID</td>
</tr>
</tbody>
</table>
# ADAC/ACTA

**Guidelines for pharmacological treatment**

**Children and adolescents**

<table>
<thead>
<tr>
<th>Place in Therapy</th>
<th>Medication</th>
<th>Starting Dose</th>
<th>Usual Dose Children 6-11 years</th>
<th>Usual Dose Adolescents 12-18 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Line (Level 1 or 2)</td>
<td>Fluvoxamine</td>
<td>50 mg/day</td>
<td>Max. 200 mg/day</td>
<td>100-300 mg/day</td>
</tr>
<tr>
<td></td>
<td>Fluoxetine</td>
<td>5 mg/day</td>
<td>20 mg/day</td>
<td>40 mg/day</td>
</tr>
<tr>
<td>Second Line (Level 3)</td>
<td>Serraline</td>
<td>25-50 mg/day</td>
<td>100-150 mg/day</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Paroxetine</td>
<td>10-20 mg/day</td>
<td></td>
<td>20-50 mg/day</td>
</tr>
<tr>
<td>Third Line (Level 4)</td>
<td>Nefazodone</td>
<td>50-100 mg BID</td>
<td></td>
<td>150-250 mg BID</td>
</tr>
</tbody>
</table>

*Note: Health Canada warning about SSRI*
Social Phobia Treatment - Generalized Subtype

Two Mainstay Forms of Treatment

1. Cognitive Behavioral Therapy (CBT)
   - group
   - individual

2. Pharmacotherapy

Other - social skills/assertiveness training
   - self-help groups/practice (toastmasters)
   - individual, couples, family therapy
Why Has Pharmacotherapy Been Underutilized in Social Anxiety Disorder

- Lack of awareness about the illness (public, professionals)
- Nature of the illness preventing visits to doctor
- Trivialization ("phobia", shyness, avoidant PD)
- Lack of awareness of comorbidity & disability
- At least until recently, few controlled drug treatment trials showing efficacy
- Improvement takes more than 8 weeks
Social Phobia Treatment - Nongeneralized (performance) Subtype

- phobic situations *predictable*
- take medication one hour before

• *Autonomic* symptoms most prominent
  - propranolol 20 - 160 mg.

• *Cognitive* symptoms most prominent
  - alprazolam 0.25 - 1 mg.
Social Anxiety Disorder
Why the strong interest?

Most common anxiety disorder

- Most common anxiety disorder
- Early age of onset
- High rates of comorbidity
- Significant personal morbidity
- High financial burden
- Treatable although under-recognized