Social Anxiety with Dr. Cummings

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In today's episode of the podcast, we discuss social anxiety disorder, its clinical manifestations and therapeutic treatment methods.

Introduction

Social anxiety disorder is one of the more common psychiatric disorders with a prevalence of 12%, although this number may be an underrepresentation because of how few patients actually seek treatment (Schneier, 2006). The disorder starts to present in teenage years, but most patients live with their symptoms for 10 or more years until they finally pursue treatment.

Individuals with social anxiety disorder tend to avoid important events and activities, such as classes, meetings, or public speaking. The disorder is essentially the fear of rejection by a group one would like to be part of. This is different from shyness because of the intensity and pervasiveness of the symptoms. Social anxiety disorder is collectively due to one's genetics and environment. For example, growing up in a home with overbearing or overprotective parents can increase the chances of developing the disorder.

Cognitive behavioral therapy and pharmacotherapy provide treatment for social anxiety disorder. The goal of treatment is to *reduce* social anxiety to manageable levels. CBT targets the negative thoughts and behaviors that increase situational anxiety and maladaptive behaviors. First-line pharmacotherapy for social anxiety disorder includes selective serotonin-reuptake inhibitors (e.g., fluoxetine, paroxetine, fluvoxamine, citalopram, escitalopram, sertraline, vilazodone, vortioxetine) and serotonin-norepinephrine-reuptake inhibitors (e.g., venlafaxine, desvenlafaxine, duloxetine, milnacipran, and levomilnacipran).

DSM and Social Anxiety Disorder

The DSM-V has restructured its way of organizing the different classes of anxiety disorders. It removed obsessive-compulsive disorder and post traumatic stress disorder from the anxiety disorder category and created individual categories for each. It added separation anxiety and selective mutism to specific phobias; generalized anxiety disorder and social anxiety disorder now comprise the anxiety disorders category.

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DSM-5 Criteria for Social Anxiety Disorder:

1. Intense fear or anxiety regarding one or more social situations where the individual is worried they will be judged by others.
2. The individual fears that he or she will act in a way that will be negatively evaluated (i.e., will be humiliating or embarrassing, lead to rejection or be offensive to others).
3. The social situations are avoided or endured with intense fear or anxiety.
4. The fear or anxiety is out of proportion to the actual threat posed by the social situation and to the sociocultural context.
5. The fear, anxiety, or avoidance is persistent, typically lasting for 6 months or more.
6. The fear, anxiety, or avoidance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
7. The fear, anxiety, or avoidance is not attributable to the physiological effects of a substance (e.g., drug abuse, medication) or another medical condition.
8. The fear, anxiety, or avoidance is not better explained by the symptoms of another mental disorder such as panic disorder, body dysmorphic disorder, or autism spectrum disorder.
9. If another medical condition (e.g., Parkinson's disease, obesity, disfigurement from bums or injury) is present, the fear, anxiety, or avoidance is clearly unrelated or is excessive.

What diagnostic questions are important when evaluating SAD?

- Ask the patient if there are any situations, such as public speaking or gatherings with strangers, that make them anxious enough that they avoid them. This allows the patient to discuss freely what they avoid in their life.
- Ask about comorbid disorders such as depression or comorbid anxiety disorders, such as panic disorders or agoraphobia (extreme end of SAD).
- Ask about simple phobias.

Cognitive Behavioral Therapy vs. Psychodynamic Therapy

For social anxiety disorder, various methods within cognitive behavioral therapy have shown to be slightly more effective than psychodynamic therapy. This needs to be taken into the context that therapy is more dependent on the therapist's alliance, empathy, and the patient's

expectation than the modality (Episode 077). In Leichsenring et al., 2013, the study tested the effectiveness of psychodynamic therapy and CBT in social anxiety disorder.

In both CBT and psychodynamic therapy, up to 25 individual 50-minute treatment sessions were conducted. The study found higher remission rates and response rates in patients from the CBT group when compared to the psychodynamic therapy group and the waiting list group. The remission rates of CBT were 36% compared to 26% of the psychodynamic group. The response rates were 60% for CBT when compared to 52% from the psychodynamic group. CBT was found to have a slight win over psychodynamic therapy. Overall, both treatment methods were found to be effective.

During the COVID-19 pandemic and lockdown period, there was great curiosity regarding the impact of social isolation among social anxiety disorder patients that were undergoing treatment. It was wondered whether these patients would revert back to their original states during isolation or if therapy would help them overcome the fears and phobias related to COVID-19. A study compared CBT with psychoeducational-supportive therapy on medical students with social anxiety disorder. These patients had undergone therapy just before the COVID-19 pandemic. The study aimed to follow-up and establish whether treatment effects of CBT were maintained given the social restrictions during the pandemic. The study found that treatment effects of CBT were significantly better and maintained over PST after a 14-month follow up period.

Table 2

SPIN at different time periods.

		SPIN pre-treatment		SPIN post-intervention		SPIN post-lockdown	
	n	Mean	SD	Mean	SD	Mean	SD
CBT	33	38.67	6.21	28.91	10.52	30.69	10.52
PST	32	36.72	7.09	35.63	5.89	38.07	6.33

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Note: SPIN = Social Phobia Inventory; CBT= Cognitive behavioral therapy; PST = Psychoeducational-supportive therapy.

Cognitive behavioral therapy can be a useful tool in helping re-conceptualize an individual's anxiety so that it can be a useful “monitoring” system in the environment.

Exposure therapy, part of CBT, is another useful behavioral therapy mode. In this model, the patient is exposed to the feared stimulus gradually so that they can master the anxiety. It is an alternate approach to train the brain centers to not be overly active when faced with the things that make the individual anxious.

High Comorbidity in SAD

It is fairly common for patients with social anxiety disorder (SAD) to also be diagnosed with other mood disorders. Patients with SAD may also have major depression, specific phobias, bipolar disorder or obsessive-compulsive disorder. However, major depression is the most common comorbid disorder among social anxiety disorder patients. These patients tend to present worse, with increased severity of symptoms, increased risk of relapse and decreased functionality (Koyuncu et al., 2019). Patients with SAD fear negative judgment from others, but someone with SAD and major depression would be worried about being negatively judged because they are not deserving or worthy of being liked.

The challenge with comorbidity in SAD is figuring out what therapeutic regimen works best for the patient. One specific study focused on comparing vortioxetine, an SSRI, to a placebo in a group of individuals that had MDD comorbid with SAD. The study found vortioxetine-treated patients did significantly better than those on placebo, and also found improvement in depression before they saw improvement in the social anxiety disorder (Liebowitz et al., 2017).

Neurobiological Associations and Changes in Social Anxiety Disorder

There is a lot of new research aimed at understanding the neurobiology of social anxiety and the neurological components at play. A comprehensive and recent literature review by Mizzi et al., 2021, takes a look at insights on some key neurobiological models of SAD. The most commonly studied region of the brain was the amygdala. Across the studies, high connectivity was found between frontal-amygdala regions, frontal-parietal regions, and temporal-amygdala.

Functional Significance

- **Amygdala and prefrontal cortex:** Plays a role in controlling attention to stimuli and emotion regulation with the presence of disturbed top-down control (prefrontal cortex unable to inhibit the amygdala response) or increased bottom-up processes (hypersensitive amygdala leading to increased activity in the prefrontal cortex) in maintaining anxiety.

- **Superior frontal gyrus:** Involved in the initiating responses and is activated during shifts of attention. Altered connectivity between these regions and frontal areas may be linked to impairment in socio-cognitive processes that are seen in social anxiety disorder.
- **Fusiform gyrus:** Involved in facial visual processing. Increased activity between this region and the amygdala may reflect constant hypervigilance to social threats (e.g., angry faces) in people with SAD.
    - During a face processing task, a study tested the neural responses of patients with social anxiety disorder to fearful vs. neutral faces and the connectivity between the specific brain regions. The study found that there was greater reactivity in the fusiform gyrus and right amygdala in SAD patients compared to the control group (Frick et al., 2013). Patients with SAD attribute anger and hostility to even the neutral faces, which indicates an overattribution to the idea that these patients feel they are being scrutinized or judged.

- **Parahippocampal region:** Hyperactivity has been associated with disruptions in perceptual analysis of scene layouts. Hyperconnectivity between the amygdala and this region may be associated with dysfunction in post-event processing.
- **Amygdala- frontal connectivity:** The most common finding was changes in positive connectivity between the amygdala and frontal areas. However, disturbances in the fear circuitry are specific to subregions of the amygdala. For example, the centromedial complex of the amygdala (rather than the basolateral or superficial complex) had increased connectivity with the prefrontal cortex.

Some significant neuroanatomical changes have also been studied in SAD patients. A whole-brain voxel-wise analysis compared the brains of SAD patients to a control group and found significantly decreased gray matter volume in the right thalamus, bilateral putamen and the left parahippocampal region of the SAD patients. The study also found a negative correlation between the decreased gray matter in the bilateral putamen and the duration of SAD and positive correlations between the dysfunctional resting state-functional connectivity of the right thalamus with limbic lobe/ACC or cerebellum and SAD duration.

This is a significant finding because the functional changes play a role in the pathophysiology of SAD. The neuroanatomical changes also help assess symptom severity in these patients.

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Pharmacological Therapies and Anxiety-related Disorders

Dr. Cummings discusses the different pharmacological treatments for SAD and states that, essentially, the role of the medications is to help reduce the anxiety to a manageable level so that the patient can be made more available for psychotherapy.

Anxiety can be effectively treated with the balance of medications and therapy. The main medications used for treatment of SAD are SSRIs and SNRIs.

The use of benzodiazepines has been debated and can be seen from a positive and negative angle, depending on the patient population being treated. Clinicians that generally treat patients with addiction related problems don't like to use benzodiazepines. However, clinicians that treat anxiety-related disorders have to weigh the benefits vs. side effects of use. One study included SAD patients that had already undergone a 10-week treatment plan with sertraline, but lacked positive effects. These patients were divided into 3 different groups. The groups were sertraline plus clonazepam, sertraline plus placebo, and venlafaxine. The treatment plan was 12 weeks long and at the end, results found that the group treated with sertraline and clonazepam did much better than the patients in the other two groups. However, it is well known that there can be significant cognitive issues with use of benzodiazepines (Episode 11), and sometimes they can interfere with the work of therapy.

Other Pharmacological Treatments

Aside from SSRIs and SNRIs that are the mainstay of treatment methods for SAD, researchers have started trialing different pharmacological approaches to help reduce anxiety. More recently, research has started on cannabidiol, a psychoactive component of marijuana, and its effects on anxiety. In animal studies, the maze test in rats found that CBD helped them perform better. Cannabidiol enhancement of exposure therapy in treatment refractory patients with social anxiety disorder and panic disorder with agoraphobia: A randomized controlled trial, found that CBD did not improve outcomes in the patients. Nonetheless, research is still needed in this area to better understand how cannabinoids can help modulate the amygdala and other associated areas.

Another approach that still needs research is oxytocin, a neurohormone. In animal studies, it has been shown to reduce anxiety-like behavior and in humans it has been shown to increase human interaction and bonding (Jones et al., 2017).

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Drugs vs. Placebo

The power of placebo can be pretty meaningful. In a randomized clinical trial by Frick et al., 2021, 27 patients with social anxiety disorder were divided into two groups. One group was verbally told that they were going to receive the effective drug escitalopram (Lexapro) while the other group was told they would receive a non-effective neurokinin-1-receptor antagonist, that would give them the side effects of Lexapro® without any of it effects.

In reality, both groups received escitalopram (Lexapro®) 20 mg to test:

1) Would expectancy to get treated have an effect on the dopamine and serotonin levels as measured by PET scans with radiotracers.
2) Would both groups have equal decreases in symptoms

Findings were:
Individuals that were told they were receiving the real medication:

1. Had significantly lower dopamine transporter binding by the radiotracer in the striatal and thalamic brain (meaning the actual dopamine in the brain was releasing slower from the dopamine transporters, leading to better outcomes due to expectancy).
2. Had equal serotonin transporter changes as seen by a radiotracer
3. Had a larger change in effect size d = 2.33 compared to d =0.93 over 9 weeks of treatment

Overall, this study highlights the significance of expectancy and belief and how treatment is highly influenced by the faith one has in a given treatment. For the patient, the thought that taking the drug will make them “safe” has an important impact on the circuitry between the hippocampus, amygdala, and caudate nucleus.

Overview of Pharmacology for Anxiety Disorders:

Pharmacotherapy of Anxiety Disorders: Current and Emerging Treatment Options
Below is a chart with an overview of all the medications with their therapeutic doses for anxiety-related disorders.

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TABLE 1 | Current treatments for anxiety disorders.

Medication class	Mechanism of action	FDA approvals for anxiety disorder	Off-label uses	Therapeutic dose ranges (mg/day)
SSRIs:				
Fluoxetine	Selective 5-HT reuptake inhibitor (20)	PD	GAD, SAD	20–60
Sertraline		PD, SAD	GAD	50–200
Citalopram		None	GAD, PD, SAD	20–40
Escitalopram		GAD	PD, SAD	10–20
Paroxetine		PD, SAD, GAD	None	20–60
Paroxetine ER		PD, SAD	GAD	27–75
Fluvoxamine		None	GAD, PD, SAD	100–300
SNRIs:				
Duloxetine	5-HT, NE (and DA) reuptake inhibitor (17)	GAD	PD, SAD	30–60
Venlafaxine (XR)		GAD	PD, SAD	75–300
Desvenlafaxine		None	GAD, PD, SAD	50–100
TCAs:				
Clomipramine	NE and 5-HT reuptake inhibitor (20)	None	GAD, PD, SAD	100–250
Imipramine		None	GAD, PD, SAD	100–300
Desipramine		None	GAD, PD, SAD	100–200
Nortriptyline		None	GAD, PD, SAD	50–150
MAOIs:				
Phenelzine	MAO inhibitor (21)	None	GAD, PD, SAD	30–90
Mixed antidepressants:				
Mirtazapine	5-HT_2, 5-HT_3, α_2, H_1 antagonist (27)	None	Anxiety, GAD, PD, SAD	15–45
GABAergic drugs:				
Pregabalin	Unclear, may modulate Ca channels (51)	None	GAD, SAD	150–600
Gabapentin		None	GAD, SAD, PD	600–2,400
Benzodiazepines:				
Clonazepam	GABA-A agonist (44)	PD	Anxiety, GAD, PD, SAD	1–2
Alprazolam		Anxiety, PD	GAD, PD, SAD	1–4
Lorazepam		Anxiety	GAD, PD, SAD	2–6
Chlordiazepoxide		Anxiety	GAD, PD, SAD	20–100
Oxazepam		Anxiety	GAD, PD, SAD	30–60
Antipsychotics:				
Trifluoperazine	D_2 antagonist (84)	Anxiety	GAD, PD, SAD	2–6
Olanzapine	D_2, 5-HT_2 H_1 antagonist (85)	None	Anxiety, GAD	5–15
Quetiapine	D_2, 5-HT_2 H_1 antagonist (85)	None	Anxiety, GAD	50–300
Beta-blockers:				
Propranolol	β-1, β-2 antagonist (77)	None	Anxiety, PD, SAD	60–120
Antihistamines:				
Hydroxyzine	H_1 antagonist (76)	Anxiety	GAD, PD, SAD	25–100
Other anxiolytics:				
Buspirone	5-HT_{1A} partial agonist (22)	Anxiety	GAD	15–60

Key: 5-HT, Serotonin; AGP, Agoraphobia; DA, Dopamine; D_2, dopamine-2 receptor; ER, XR, Extended Release; FDA, Food and Drug Administration; GAD, Generalized Anxiety Disorder; GABA, Gamma Aminobutyric Acid; H_1, Histamine 1 receptor; MAO, Monoamine Oxidase; MAOI, Monoamine Oxidase Inhibitors; NE, Norepinephrine; PD, Panic Disorder; SSRI, Selective Serotonin Reuptake Inhibitor; SNRI, Serotonin Norepinephrine Reuptake Inhibitor; SAD, Social Anxiety Disorder; TCA, Tricyclic Antidepressants.

More Information on CBT

If you are curious, here are more details regarding CBT and what it entails:

Cognitive behavioral therapy for social anxiety disorder aims to target the painful cycle of negative thoughts (“I won’t have anything to say, people will think I’m stupid.”) and behaviors (e.g., changing jobs to avoid giving presentations) that lead to increased situational anxiety. The goal is to change the individual's thinking and behavioral patterns.

These strategies include:

- Learning to recognize one's malformed ways of thinking that create problems and reevaluating them (see episode 2 for more on cognitive distortions).
- Gaining a better understanding of the behavior and motivation of others.
- Using problem-solving skills to cope with difficult situations.
- Learning to develop a greater sense of confidence in one's own abilities.
- Facing one's fears instead of avoiding them.
- Using roleplay to prepare for potentially problematic interactions with others.
- Learning to calm one's mind and relax one's body.

CBT typically consists of 12 to 16 weekly sessions, each lasting 60 to 90 minutes. The therapist and the patient create a list of feared situations, used as a guide for exposure practices. The therapist helps the patient restructure their cognitive thoughts and alter their expectations of certain situations. For example, individuals that fear social gatherings with strangers because they believe they will be scrutinized or judged are helped to recognize that people are unlikely to notice or care and that most people are paying attention to themselves.

Patients also learn methods to use to replace unhelpful expectations ("I shouldn't be anxious at a party.") with positive behavioral goals ("I'll start two conversations at the party."). They practice using these methods while being exposed to feared situations in roleplaying with the therapist.

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References:

Frick, A., Howner, K., Fischer, H., Kristiansson, M., & Furmark, T. (2013). Altered fusiform connectivity during processing of fearful faces in social anxiety disorder. *Translational psychiatry*, *3*(10), e312. https://doi.org/10.1038/tp.2013.85

Hjorth, O. R., Frick, A., Gingnell, M., Hoppe, J. M., Faria, V., Hultberg, S., Alaie, I., Månsson, K. N. T., Rosén, J., Reis, M., Wahlstedt, K., Jonasson, M., Lubberink, M., Antoni, G., Fredrikson, M., & Furmark, T. (2021). Expectancy effects on serotonin and dopamine transporters during SSRI treatment of social anxiety disorder: a randomized clinical trial. *Translational Psychiatry*, *11*(1). https://doi.org/10.1038/s41398-021-01682-3

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Jones, C., Barrera, I., Brothers, S., Ring, R., & Wahlestedt, C. (2017). Oxytocin and social functioning. *Dialogues in clinical neuroscience*, *19*(2), 193–201. https://doi.org/10.31887/DCNS.2017.19.2/cjones

Kwee, C. M., Baas, J. M., van der Flier, F. E., Groenink, L., Duits, P., Eikelenboom, M., van der Veen, D. C., Moerbeek, M., Batelaan, N. M., van Balkom, A. J., & Cath, D. C. (2022). Cannabidiol enhancement of exposure therapy in treatment refractory patients with social anxiety disorder and panic disorder with agoraphobia: A randomised controlled trial. *European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology*, *59*, 58–67. https://doi.org/10.1016/j.euroneuro.2022.04.003

Koyuncu, A., İnce, E., Ertekin, E., & Tükel, R. (2019). Comorbidity in social anxiety disorder: diagnostic and therapeutic challenges. *Drugs in context*, *8*, 212573. https://doi.org/10.7573/dic.212573

Liebowitz, M. R., Careri, J., Blatt, K., Draine, A., Morita, J., Moran, M., & Hanover, R. (2017). Vortioxetine versus placebo in major depressive disorder comorbid with social anxiety disorder. *Depression and anxiety*, *34*(12), 1164–1172. https://doi.org/10.1002/da.22702

Leichsenring, F., Salzer, S., Beutel, M. E., Herpertz, S., Hiller, W., Hoyer, J., Huesing, J., Joraschky, P., Nolting, B., Poehlmann, K., Ritter, V., Stangier, U., Strauss, B., Stuhldreher, N., Tefikow, S., Teismann, T., Willutzki, U., Wiltink, J., & Leibing, E. (2013). Psychodynamic Therapy and Cognitive-Behavioral Therapy in Social Anxiety Disorder: A Multicenter Randomized Controlled Trial. *American Journal of Psychiatry*, *170*(7), 759–767. https://doi.org/10.1176/appi.ajp.2013.12081125

Mizzi, S., Pedersen, M., Lorenzetti, V., Heinrichs, M., & Labuschagne, I. (2021). Resting-state neuroimaging in social anxiety disorder: a systematic review. *Molecular Psychiatry*, *27*(1), 164–179. https://doi.org/10.1038/s41380-021-01154-6

Samantaray, N. N., Kar, N., & Mishra, S. R. (2022). A follow-up study on treatment effects of cognitive-behavioral therapy on social anxiety disorder: Impact of COVID-19 fear during post-lockdown period. *Psychiatry research*, *310*, 114439. https://doi.org/10.1016/j.psychres.2022.114439

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Manal Piracha, Michael Cummings, M.D., David Puder, M.D.

Schneier, F. R. (2006). Social Anxiety Disorder. *New England Journal of Medicine*, *355*(10), 1029–1036. https://doi.org/10.1056/nejmcp060145

Zhang, X., Suo, X., Yang, X., Lai, H., Pan, N., He, M., Li, Q., Kuang, W., Wang, S., & Gong, Q. (2022). Structural and functional deficits and couplings in the cortico-striato-thalamo-cerebellar circuitry in social anxiety disorder. *Translational Psychiatry*, *12*(1). https://doi.org/10.1038/s41398-022-01791-7

Hunter, L. E., Meer, E. A., Gillan, C. M., Hsu, M., & Daw, N. D. (2022). Increased and biased deliberation in social anxiety. *Nature Human Behaviour*, *6*(1), 146-154.