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MEDICINE

Treating Anxiety and Depression Through the Lifespan

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Learning Objectives

- Identify signs and symptoms of mood and anxiety disorders and differentiate them from features of autism spectrum disorder (ASD)
- Recognize pharmacologic and psychosocial interventions
- Appreciate age-related changes

Clinical Example

- Justin: 15-year-old male who is bullied by classmates in general education, feels sad and lonely, uncertain of the future, lives at home with his parents.
- Diagnosis: major depressive disorder and generalized anxiety disorder
- Treatment: Sertraline initiated, engaged with peer group, referral to DORS for transition planning

Clinical Example

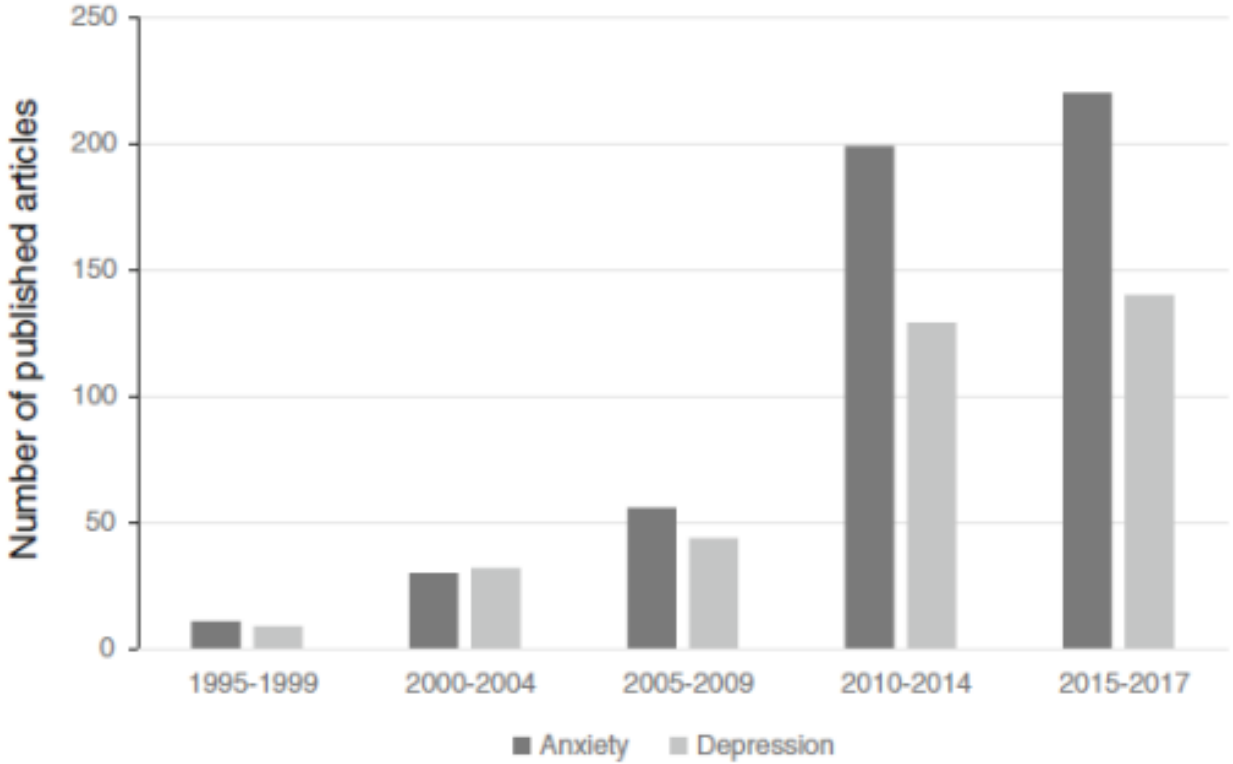
- Paul: 62-year-old male with language impairment, intellectual disability who has times of appearing unhappy, less willing to discuss love of maps with his sisters, increase in hand-biting, lethargy
- Diagnosis: major depressive disorder
- Treatment: becomes more irritable on SSRI so it is discontinued; low-dose aripiprazole improves hand-biting and lethargy; bolstered support systems, referred to occupational therapy

Dr. Leo Kanner (1943)

- "Anxiously obsessive desire for the maintenance of sameness ..."
- Fear of mechanical things (e.g., vacuum, elevator)
- Fear of changing things (e.g., wind and large animals)
- Fear of running water, gas burner

Kanner, 1943, *Nervous Child*

Increase in Research on Anxiety and Depression



White et al. 2018

TABLE 1

Prevalence of *DSM-IV* Disorders

Disorder	3-Mo Point Prevalence/100	95% CI
Any disorder	70.8	58.2–83.4
Any main disorder[a]	62.8	49.8–75.9
Any emotional disorder[b]	44.4	30.2–58.7
Any anxiety or phobic disorders[c]	41.9	26.8–57.0
Generalized anxiety disorder	13.4	0–27.4
Separation anxiety disorder	0.5	0–1.6
Panic disorder	10.1	0–24.8
Agoraphobia	7.9	3.0–12.9
Social anxiety disorder	29.2	13.2–45.1
Simple phobia	8.5	2.8–14.1
Obsessive-compulsive disorder	8.2	3.2–13.1
Any depressive disorder	1.4	0–3.0
Major depressive disorder	0.9	0–2.3
Dysthymic disorder	0.5	0–1.4
Oppositional or conduct disorder	30.0	14.9–45.0
Oppositional defiant disorder	28.1	13.9–42.2
Conduct disorder	3.2	0–7.1
Attention-deficit/hyperactivity disorder	28.2	13.3–43.0

10-13.9 years

Mostly male

Population derived sample

Simonoff et al., 2008

J Am Acad Child and Adolesc Psychiatry

Psychiatric Illness and ASD

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- Anxiety and mood disorders are common co-occurring psychiatric illnesses in adults with ASD
- Some studies have reported rates as high as 70%
- Meta-analysis:
  - Any *current* anxiety: 27%
  - *Lifetime* anxiety: 42%
  - Any *current* depression: 23%
  - *Lifetime* depression: 37%

Charlot et al. 2008; Mazefsky et al. 2008; Lever and Geurts 2016; Hollocks et al. 2019

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Changes in prevalence with aging: Different developmental risk periods

	ASD								
	All ages		Young		Middle		Older		Young versus middle versus older
	N	%	N	%	N	%	N	%	Fisher's χ^2
Any psychiatric disorder	109	79.0	38	82.6	41	87.2	30	66.7	6.02*
Mood disorders	79	57.2	24	52.2	35	74.5	20	44.4	9.30**
Depression	74	53.6	19	52.2	31	66.0	19	42.2	5.24^{+}
Dysthymia	25	18.1	6	13.0	13	27.7	6	13.3	4.04
PDysD (only females)	9	20.9	3	18.8	3	16.7	3	33.3	5.16
Anxiety disorders	74	53.6	30	65.2	25	53.2	19	42.2	4.81^{+}
Panic disorder	21	15.2	11	23.9	6	12.8	4	8.9	4.01
Agoraphobia	29	21.0	10	21.7	9	19.1	10	22.2	0.20
Social phobia	21	15.2	10	21.7	10	21.3	1	2.2	10.23**
Specific phobia	16	11.6	5	10.9	7	14.9	4	8.9	0.84
PTSS	4	2.9	1	2.2	3	6.4	0	–	4.66
OCD	30	21.7	13	28.3	10	21.3	7	15.6	5.85
GAD	22	15.9	8	17.4	9	19.1	5	11.1	3.12

Lever and Geurts, 2016

Impact of Anxiety and Depression

- Exacerbates ASD symptoms
- Interferes with treatments for ASD
- Irritability, outburst, self-injury, GI symptoms
- Increases parental stress and anxiety
- Risk for long-term psychopathology
- Influences transition planning to adulthood
- Interferes with relationships and employment

Diagnosis can be Challenging

- Self-report is difficult
- Diagnostic overshadowing
- Overlapping symptoms
- Lack of standardized measures

Overlapping Symptoms

- Social avoidance in ASD also present in social anxiety
- Social indifference in ASD may seem like social isolation associated with depression
- Repetitive behaviors could be mistaken for symptoms of OCD
- Emotion dysregulation (stemming from cognitive rigidity, sensitivity to change, difficulty reading social cues) may be interpreted as anxiety symptoms
- Sleep difficulties, atypical affect, cognitive rigidity in both ASD and depression

Rosen et al. 2018

When making a diagnosis…

- Important to take a thorough history of baseline history
- Look for a change in baseline
- Look for triggers

Clinical Presentations of Anxiety in ASD

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- **Traditional disorders (based on the DSM-5)**

  Generalized anxiety disorder – general worries
  Separation anxiety disorder – fear of being away from loved ones
  Social anxiety disorders – worries about being judged
  Specific phobia – fear of specific objects
  Obsessive-compulsive disorder – uncomfortable thoughts/rituals
  Posttraumatic stress disorder – mood/behavioral reaction to trauma

- **Ambiguous presentations**

  Excessive fears of change
  Fears about special interest
  Social confusion
  Unusual phobias

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Assessing Anxiety in ASD

- General symptoms – fear, restlessness, avoidance, irritability, worsening ASD symptoms, physical symptoms, worry
- Look for triggers (contexts, stimuli)
- Has there been a change in baseline?

Clinical Presentations of Depression

- **Typical presentations (based on DSM-5)**
  - Sadness
  - Loss of interest in activities
  - Poor concentration
  - Changes in sleep, appetite, energy
- **Atypical presentations**
  - Increase in core ASD symptoms
  - Regression in adaptive skills
  - Increase in aggressive and self-injurious behaviors

Rosen et al. 2018

Assessing Depression in ASD

- Changes in sleep patterns (increased sleep, insomnia)
- Changes in eating habits (decrease in appetite, food refusal), weight loss
- Easy fatigue, loss of energy, increased or unusual physical complaints
- More time spent in bed than usual
- Sudden unexpected crying spells OR laughing spells
- Loss of interest for previously satisfying activities

Ghaziuddin et al. 2002; Stewart et al. 2006; Underwood et al. 2015

Assessing Depression in ASD

- Preoccupations may change in content or character
- Aggravation of hand flapping, echolalia
- Restlessness
- Self-harm
- Loss of daily routines, decrease in self-care, regression of skills (i.e., incontinence episodes)

Perry et al. 2001; Stewart et al. 2006

Assessing for Suicidal Ideation

- Increased rates of suicidal ideation and suicide attempts
  - One study of individuals receiving Kaiser healthcare found risk of suicide attempts was 5-fold higher in adults with ASD compared to general population
- Elevated risk due to co-occurring psychiatric disorders, social isolation, lack of access to appropriate mental health care

Cassidy et al. 2014; Croen et al. 2015; Hirvikoski et al. 2016

Assessing for Comorbidities

- ADHD
- Substance use disorders
- Medical illness

Hofvander et al. 2009; Joshi et al. 2013

When Might an Individual Seek Treatment?

- Academic difficulties
- Meltdowns/withdrawn/avoidance at home
- Life experiences – bullying, change in family structure
- Times of transition - Entering employment, leaving home
- Losses - Death of a parent or sibling, loss of employment
- Other major changes
  - Emergence of medical or surgical illnesses (especially chronic diseases that involve lifestyle changes)

Treatments

- Medications
- Psychosocial
  - Therapy: Cognitive Behavioral, Mindfulness
  - Education, employment support
  - Changes in home environment
- Medical Care
- Access

Increasing Medication Use with Age

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TABLE 1 Medicaid-Reimbursed Psychotropic Medication Use Among Children With ASDs ($N = 60\,641$)

Parameter	Any Psychotropic Medication, %	≥3 Concurrent Psychotropics, %	Psychotropic Medication Class, %					
			Antidepressant	Neuroleptic	Anxiolytic	Mood Stabilizer	Sedative	Stimulant
Total ($n = 60\,641$)	56	11	25	31	12	21	3	22
Gender								
Female ($n = 13\,435$)	55	10	25	28	14	24	4	17
Male ($n = 47\,205$)	56	11	25	32	11	20	3	24
Age, y[a]								
0–2 ($n = 1009$)	18	0.1	2	2	6	5	8	1
3–5 ($n = 10\,119$)	32	2	9	12	7	8	3	13
6–11 ($n = 27\,545$)	56	9	23	29	10	18	2	28
12–17 ($n = 17\,164$)	67	17	34	42	15	29	3	23
18–21 ($n = 4804$)	73	20	39	49	23	39	6	9

Mandell et al. 2008

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Medication Use Among Adults

Table 3 Medication usage among participants

Description	N = 129	%
Any medication[a]	101	78.2
Any prescription medication	91	70.5
Psychotropic prescription medication	76	58.9
Antipsychotic	46	35.6
Typical	11	8.5
Atypical	41	31.7
Antidepressant	46	35.7
Anxiolytic/benzodiazepine (non-SSRI)	30	23.2
Alpha 2 agonist	5	3.9
Anticonvulsant	45	34.9
Sedative–hypnotic (non-benzodiazepine)	17	13.2
Lithium	5	3.9
Other	9	6.9
2 or more medications	50	38.8
3 or more medications	33	25.6
4 or more medications	18	14.0

[a] Includes over the counter agents, vitamins, and herbal supplements

Buck et al. 2014

Medication Use Among Older Adults

Table 4 Individuals with ASD diagnoses and at least one prescription of psychotropic drugs (antipsychotics, anxiolytics, hypnotics and sedatives, antidepressants)

	No ID diagnosis (n = 345) n (%)	ID diagnosis (n = 256) n (%)
At least one prescription of		
Antipsychotics	217 (63)	214 (84)
Anxiolytics	204 (59)	198 (77)
Hypnotics and sedatives	172 (50)	145 (57)
Antidepressants	171 (50)	152 (59)
No of psychotropic drugs		
0	46 (13)	12 (5)
1	65 (19)	26 (10)
2	69 (20)	49 (19)
3	99 (29)	91 (36)
4	66 (19)	78 (30)

Nylander et al. 2018

Antidepressant/Anti-Anxiety Medications

Few studies of use in adolescents and adults for depression and anxiety

Buchsbaum et al. 2001; Williams et al. 2013; Hollander et al. 2014; Taylor et al. 2016

Commonly Prescribed Antidepressants

SSRIs	SNRIs	Other
Citalopram	Duloxetine	Bupropion
Escitalopram	Venlafaxine	Buspirone
Fluoxetine		Mirtazapine
Sertraline		
Fluvoxamine		
Paroxetine		

SSRI Dosing in ASD

Medication	Starting Dose	Maximum Dose
Sertraline	12.5-25mg	200mg
Fluoxetine	2.5-5mg	60mg
Citalopram	2.5-5mg	40mg
Escitalopram	1.25-2.5mg	20mg

Vasa, et al., 2015
Pediatrics

Side Effects of Various Medications

Nausea

Weight gain

Diarrhea

Paradoxical agitation

*Caution with drug-drug interactions

Medications for Anxiety-Specific Symptoms

Medication	Indication
Insomnia	Melatonin, Clonidine, Trazodone
Physiological arousal	Clonidine, Guanfacine (short and long acting preparations)
Behavioral dysregulation	Clonidine, Guanfacine Atypical Antipsychotics
Situational anxiety	Lorazepam, Propranolol

Vasa, et al., 2015
Pediatrics

Antipsychotics

- Risperidone and aripiprazole have been FDA approved for use in children/adolescents
- Targets: Irritability, aggression, self-injury, repetitive behavior
- Sedation, weight gain, risk for diabetes and high cholesterol

McDougle et al. 1998, Hellings et al. 2006; Anagnostou et al. 2016; Lord et al. 2018

Other Medications

- Mood stabilizers
  - Lithium
  - Valproic acid
  - Carbamazepine, oxcarbazepine
- No evidence for medical marijuana or cannabidiol (CBD) at this time

Guidelines

- Start medications at low doses
- Gradually increase dose with regular monitoring for side effects and response to targets
- Stop if ineffective
- Continuously assess whether to continue or stop the medication

Psychotherapy

- Evidence for cognitive behavioral therapy (CBT) in ASD
- CBT: exposure, modeling, parental involvement
  - Several studies have found moderate to large treatment effects for use in anxiety; fewer studies have focused on its use in depression
- Adults with ASD are less likely to receive talk therapy than adults without ASD

Maddox et al. 2018; White et al. 2018

Modified Cognitive Behavioral Therapy

- ASD, FSIQ >70
- Social anxiety, generalized anxiety, and separation anxiety disorder
- 12-16 weeks
- Modifications:
  - General concepts of stress and feeling upset
  - Identifying anxious situations
  - Graduated exposures with reinforcement
  - Self-regulation strategies
  - Limited cognitive restructuring
- Response rates 38 – 71.4%

Vasa et al., 2014 *J Autism Dev Disord;* Ung, et al., 2015.. *Child Psychiatry Hum Dev*
Kreslin, et al., 2015, *Child Adolesc Psychiatry Ment Health*

Cognitive Behavioral Therapy in Adults

- Not as much data as in children/adolescents
- Pilot studies of adults without ID using group CBT
- One study found clinically significant improvement of OCD symptoms
- Randomized controlled trial for OCD and anxiety: good treatment response and maintenance over 12 months

Langdon et al. 2016; Russell et al. 2009; Russell et al. 2013

Mindfulness Based Interventions

- Paying attention to experiences in the present moment in a nonjudgmental and accepting way (acceptance without analysis)

  → Can lead to improved emotion regulation and increased emotional awareness

- Body scan, mindful eating exercises, mindful breathing meditation, movement exercises

Spek et al. 2013

Mindfulness Based Interventions

- Adolescents: small studies without a control group
- Adults: studies have used group modality approach, modified protocol for ASD (avoided use of metaphors or ambiguous language)
- Reduced anxiety, depression, rumination
- Treatment effects may last up to 9 weeks
- May be equally as effective as CBT
- May decrease autism symptoms (based on Social Responsiveness Scale for adults)

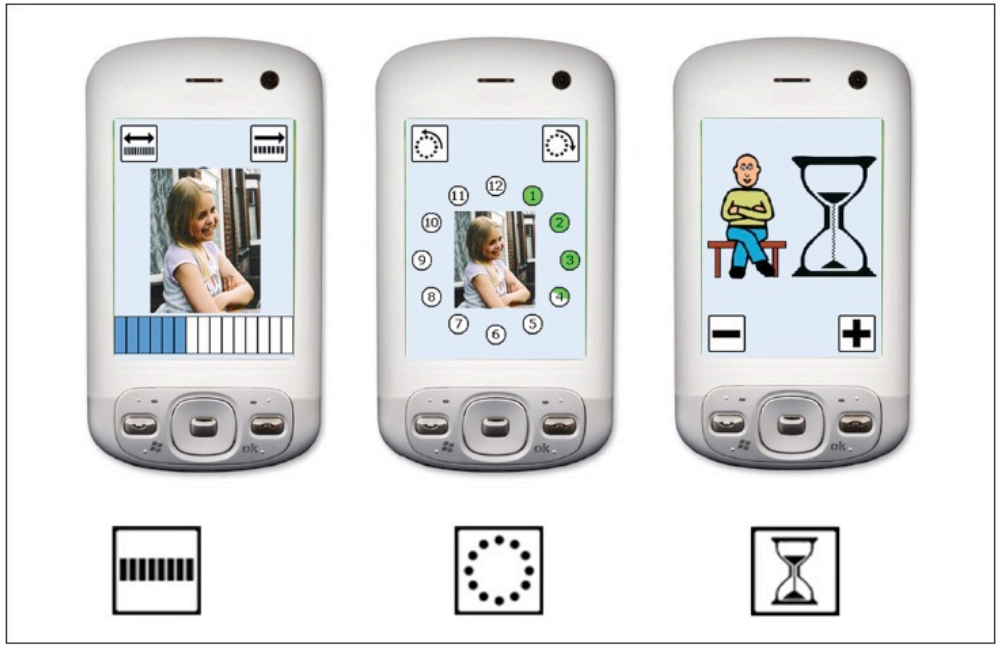
Spek et al. 2013, Kiep et al. 2015; Sizoo & Kuiper, 2017

Technology-based Interventions

- Computer programs, touch-screen apps, virtual reality
  - Technology highly preferred in many with ASD
  - Visual medium
  - Allow individuals to have control to work at their own pace
- Sidekicks! App
- Real-time stress management (RTSM) techniques (guided relaxation, attention shifting, deep breathing, positive self-talk)

Kuo et al. 2014; Birtwell et al. 2018; Hare et al. 2016

Technology-based Interventions



Tic-Tac software: alternative system for representing time

Reduced anxiety-related behaviors in waiting situations

Campillo et al. 2014

Other Interventions

- Social skills interventions
  - One study showed self-reported improvements on depression and anxiety inventories
- Supported employment
- Occupational therapy for sensory differences
- Wellness: healthy diet, exercise, leisure programs
- Support the individual and improve the person-environment fit

Hillier et al. 2011; Lai and Baron-Cohen 2015; Sizoo and Kuiper 2017; Garcia-Villamisar and Dattilo 2010

Summary

- Anxiety and depression are frequent co-occurring disorders in individuals with ASD throughout the lifespan
- Emerging evidence base for use of psychotherapies particularly in children (CBT and MBI), yet often underutilized
- Medications are frequently prescribed, yet there are limited data and their use should be monitored with caution