

Overcoming psychiatric barriers to effective Hepatitis C treatment

Glenn J Treisman MD PhD
Johns Hopkins University

Mental Illness

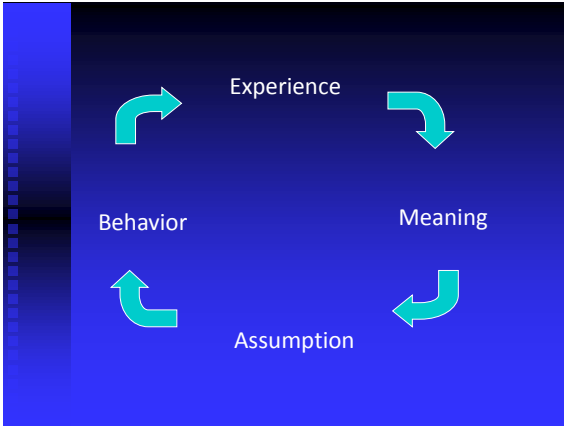
HIV+HEP C Illness and treatment

depression
demoralization
substance abuse
cognitive impairment

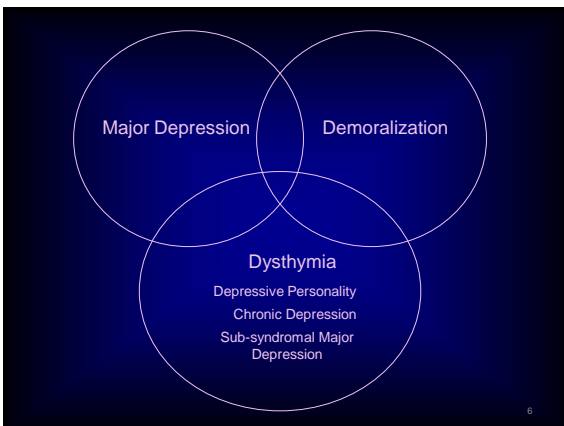
impulsivity
depression
demoralization
substance abuse
cognitive impairment

■ Psychiatric conditions that increase risk for Hepatitis C and complicate treatment

- ◆ Diseases-Depression (Bipolar/Schizophrenia)
- ◆ Temperament (Personality disorders/MR)
- ◆ Behaviors (Addiction)
- ◆ Life experiences (Distrust/Avoidance)



- Psychiatric conditions that increase risk for Hepatitis C and complicate treatment
 - ◆ Diseases-Depression (Bipolar/Schizophrenia)
 - ◆ Temperament (Personality disorders/MR)
 - ◆ Behaviors (Addiction)
 - ◆ Life experiences (Distrust/Avoidance)



Depression diminishes

- Mood-the sense of baseline state of happiness that is usually present
- Vital sense-the sense of being well, healthy, energetic, alert and able
- Self Attitude-the sense of being good, of doing well, of effectiveness and utility to others

Anhedonia

- Loss of reward (pleasure, satiation or satisfaction) associated with behaviors
 - ◆ Appetite Directed Behaviors
 - ◆ Sleeping
 - ◆ Eating
 - ◆ Sex
 - ◆ Function Directed Behaviors
 - ◆ Work
 - ◆ Hobbies
 - ◆ Exercise

Disturbance of Neurophysiology

- Sleep
 - ◆ EARLY MORNING AWAKENING
 - ◆ Difficulty falling asleep
 - ◆ Disrupted sleep architecture
- Appetite
 - ◆ Change in food taste
 - ◆ Weight loss or gain
 - ◆ Immune function
- G.I. function

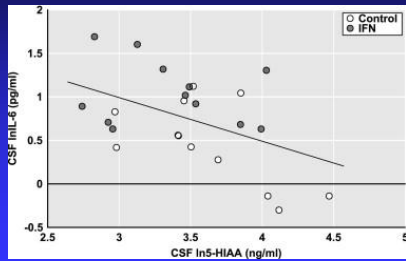
Hepatitis C and Depression

- Depression in 40-50%
 - ◆ Probably both as a consequence of depression induced risk as well as depression caused by Hepatitis C
- Interferon treatment causes depression
- Antidepressant treatment is effective
- Prophylaxis with antidepressants may be effective



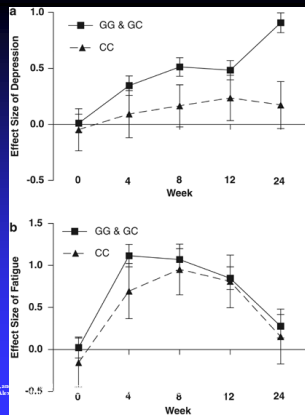
- Depression is associated with immune activation, the stress system (HPA), and genetic vulnerability of monoamine neurotransmission
- Depression is a disease of subcortical brain function and causes cognitive impairment as well as mood changes and other physiologic symptoms

IL-6 and 5-HIAA correlate with INF administration and depression



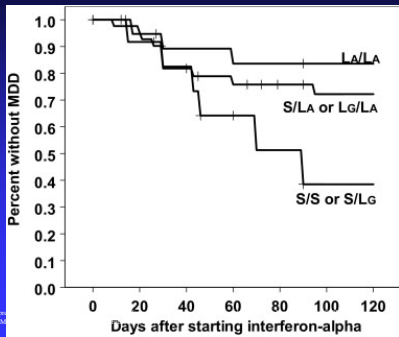
Assessment of central nervous system inflammatory responses by interferon-alpha-1b treatment in major depressive disorder. Kasperk CL, Brunner AM, Maser M, Drake DP, Pogreban D, Wootton AB, Yang GJ, Manning B, Miller AH. *Int J Psychiatry*. 2009 Jun;195(6):506-10.

IL-6 and serotonin polymorphisms correlate with INF-induced depression



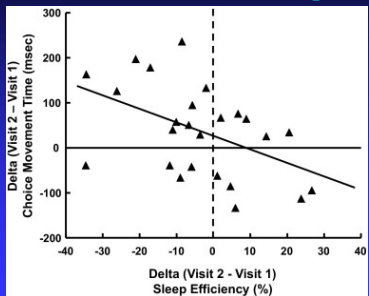
Functional polymorphisms in the interleukin-6 and serotonin transporter genes are associated with depression in patients with major depressive disorder. P. Hervas-Terres, E. B. Fowler, J. F. Caldes, G. Roglich, C. Mendrick, C. Moya, L. N. Alcazar, C. M. Forner.

Alleles for decreased Serotonin transporter are associated with increased risk of INF-induced depression



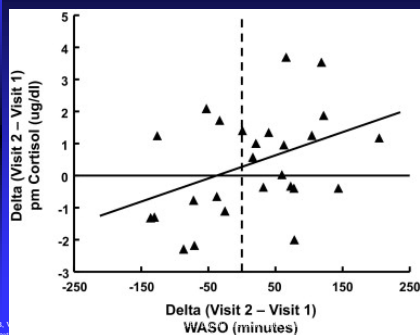
Risk for depression in patients with major depressive disorder treated with interferon-alpha. Rasmussen, S.

Interferon induced decreased sleep efficiency is associated with decreased motor speed



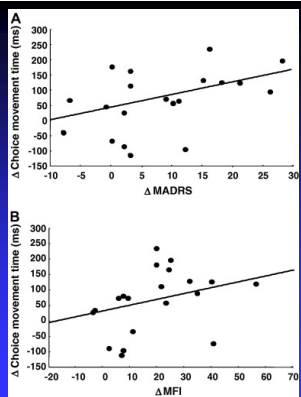
Raison CL, Rye DB, Woolwin BJ, Vogt GL, Bantista RM, Speyer JR, Miller AH. Chronic Interferon-Alpha Administration Disrupts Sleep Continuity and Depth in Patients with Hepatitis C: Association with Fatigue, Motor Slowing, and Increased Evening Cortisol. *Biol Psychiatry*. 2010 May 22

Interferon-induced decreased sleep is associated with increased evening cortisol



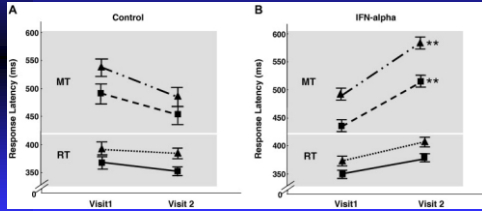
Raison CL, Rye DB, Woolwin BJ, Speyer JR, Bantista RM, Miller AH, et al. Interferon-Alpha Administration Disrupts Sleep Continuity and Depth in Patients with Hepatitis C: Association with Fatigue, Motor Slowing, and Increased Evening Cortisol. *Biol Psychiatry*. 2010 May 22

Depression correlates with subcortical deficits in patients receiving INF



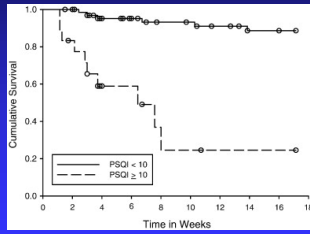
IFN-alpha-induced motor slowing is associated with increased depression and fatigue in patients with chronic hepatitis C. Major M, Woolberg LA, Caporaso L, Pagnoni G, Raison CL, Miller AH. *Brain Behav Immun*. 2008 Aug 22;23(9):970-80.

Interferon treatment effect on subcortical speed



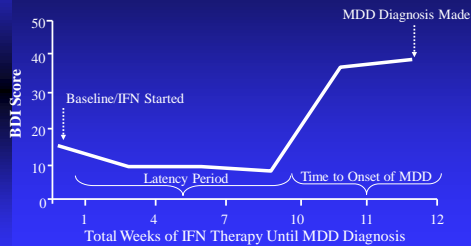
IFN-alpha-induced motor slowing is associated with increased depression and fatigue in patients with chronic hepatitis C. Major M, Welberg LA, Caporin N, Paauw G, Ranson C, Miller AH. *Brain Behav Immun*. 2008 Aug;23(10):70-80.

Poor sleep predicts development of major depression



Fassone PI, Buysse DJ, Rahnouzi M, Pollock BG, Lorch FE. Poor sleep quality predicts onset of other major depression or subthreshold depression with instability during interferon-alpha treatment. *Psychiatry Res*. 2010 May 15;177(1-2):2.

Rapid Escalation of IFN-Induced Depressive Symptoms: Threshold Effect



IFN, interferon; MDD, major depressive disorder. Hauser et al. *Mol Psychiatry*. 2002;7:942-947. N=39

Prophylactic Citalopram PEG IFN/RBV-related Depression

	History	Prophylactic antidepressant	On-therapy antidepressant	Depression rate
(n = 11)	Psych history (-)	None	None	64%
(n = 11)	Receiving methadone substitution	None	None	55%
(n = 14)	Receiving methadone substitution	Citalopram 20 mg QD initiated	Citalopram 20 mg QD continued	14%

P = .028

2 weeks prior to PEG IFN/RBV PEG IFN/RBV initiated PEG IFN/RBV Tx Month 4

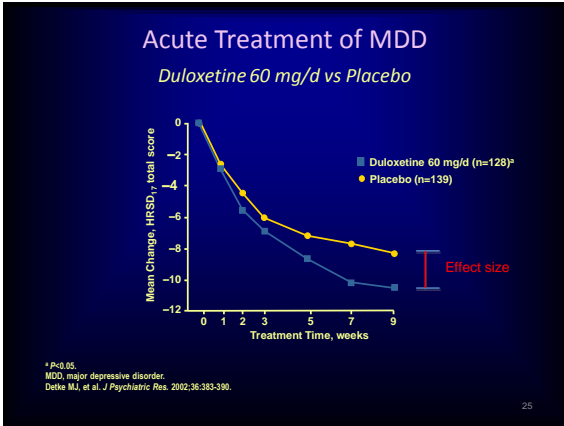
Schaefer et al. AASLD, October 24-28, 2003; Boston, Mass.

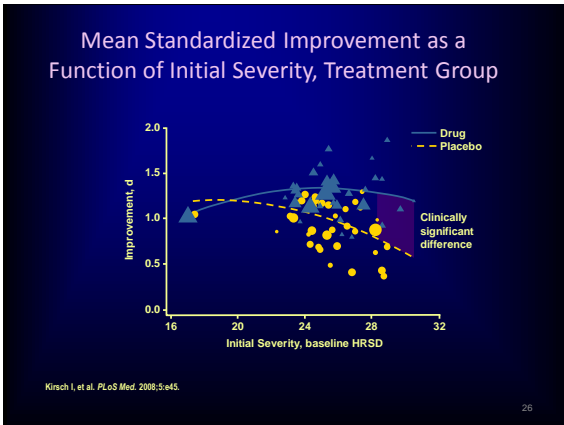
Prophylaxis for depression with INF/RBV therapy

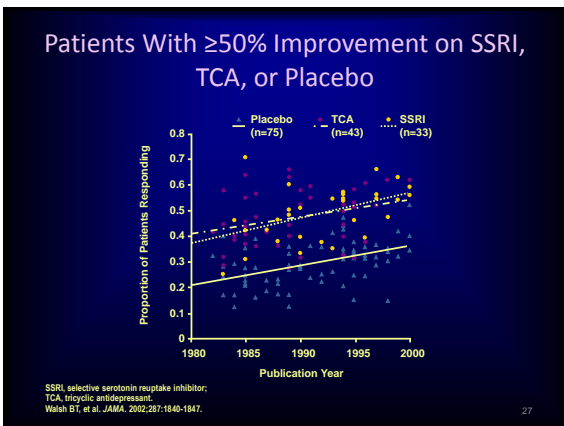
Author (N)	Study Type	Outcome
Gleason et al. 2007 (N=10)	OLT	Escitalopram prevented depression in at risk subjects
Raïsson et al. 2007 (N = 61)	Prospective, DBPC	Paroxetine prevented depression in at risk subjects

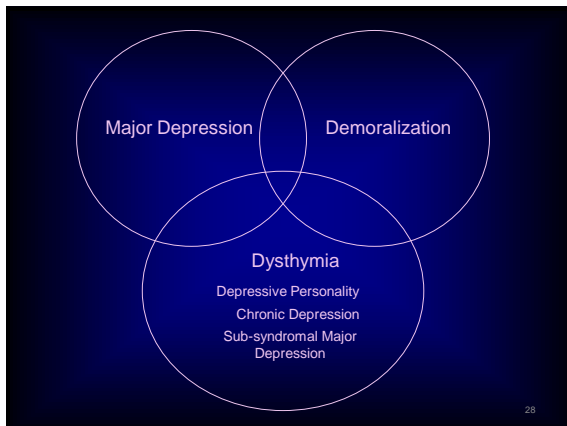
Antidepressants with demonstrated efficacy in the treatment of depression in Hepatitis C

- Fluoxetine
- Sertraline
- Citalopram
- Escitalopram
- Imipramine
- Nortriptyline
- Bupropion
- Mirtazepine
- ECT









It is much more important to know what sort of patient has a disease than what sort of disease a patient has.

William Osler

