

Johns Hopkins TM Regional Symposium: Neuro-Psychiatric Aspects of TM/MS

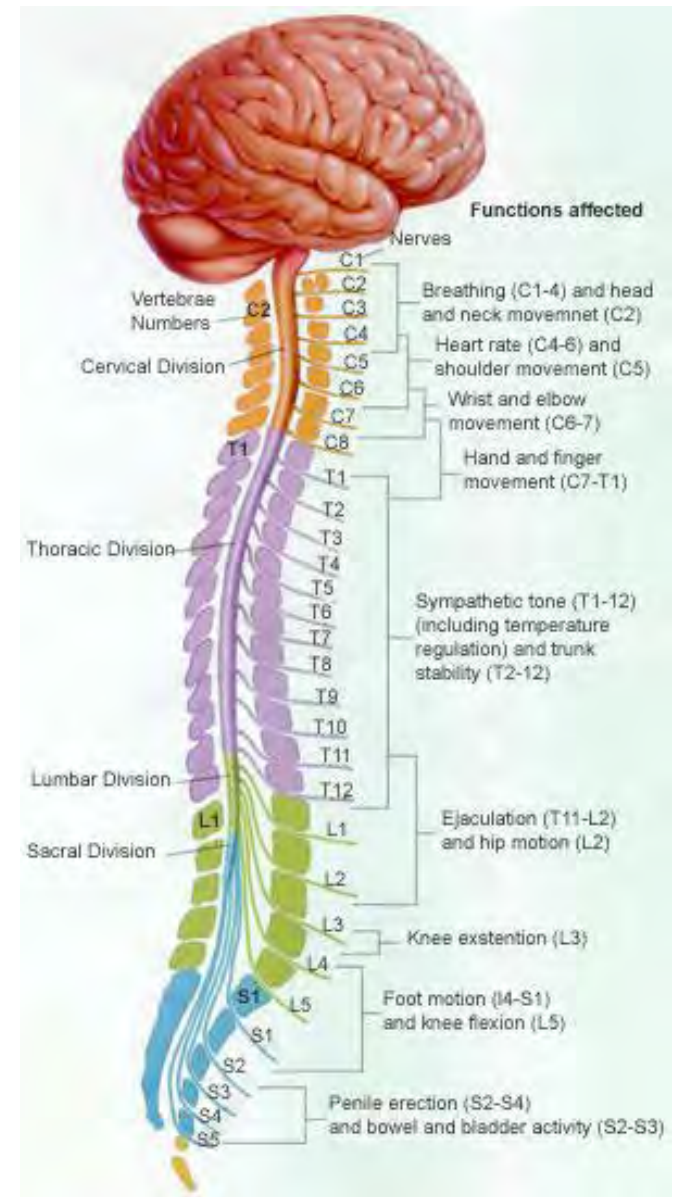
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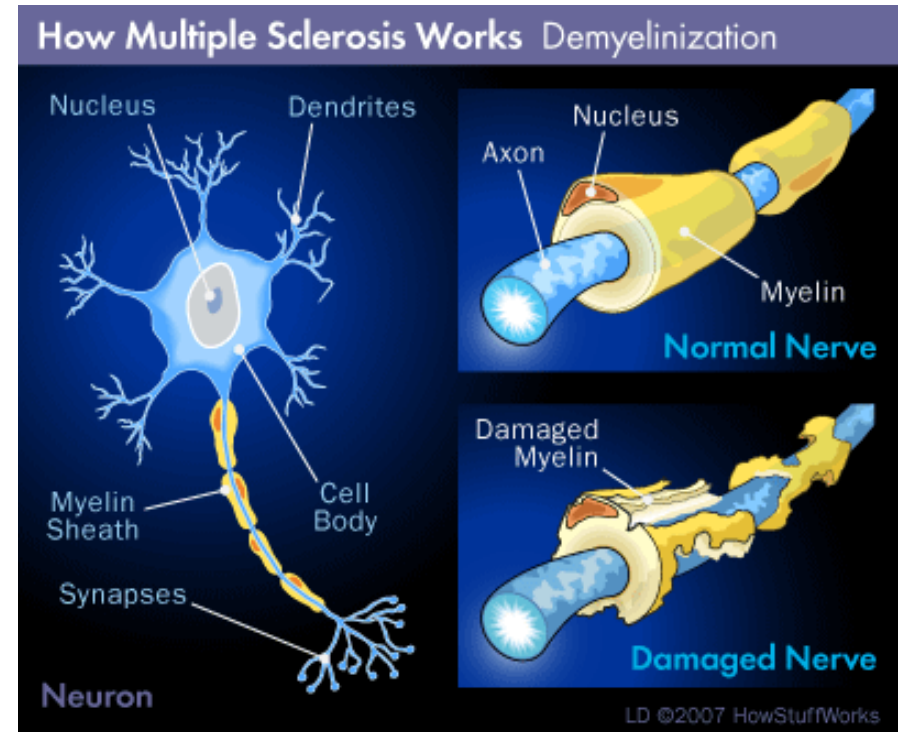
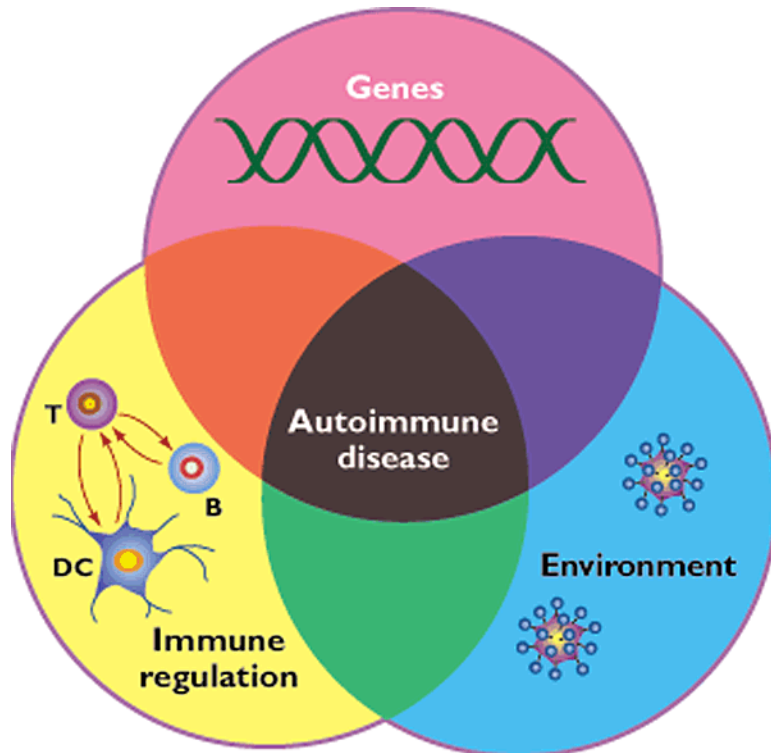
Introduction to Transverse Myelitis (TM):

TM Defined

- **Transverse:**
 - Lying or being across, or in a crosswise direction;
 - often opposed to longitudinal.
- **Myelitis:**
 - An inflammation or infection of the spinal cord.



What is Multiple Sclerosis (MS)?



Psychosocial Impact of Multiple Sclerosis: Exploring the Patient's Perspective

- Phone interviews were used to explore psychosocial functioning, defined as intrapersonal or interpersonal processes, excluding physical symptoms.
- Demographics: 100% RRMS, Northern CA; 75% women; Average: 43 years old, 63% married, 55% employed.
- Psychosocial impact of MS clustered into 3 factors:
 - Deterioration in Relationships: endorsed overall by 20%.
 - Demoralization: endorsed overall by 30%.
 - Benefit-Finding: endorsed overall by 60%.

Benefit-Finding: Percent Endorsing

- Relationships:
 - My friends and family have become more helpful (77%); I am closer to my family (70%); I am closer to my significant other (51%); I keep in better touch with my family (44%).
- Interpersonal Skills:
 - I have learned to be more compassionate (67%); to be more respectful of others (58%); express more feelings (55%); communicate better (48%); be a better friend (48%).
- Perspective:
 - I appreciate the importance of being independent (83%); I appreciate life more (74%); I am more introspective (72%); more conscientious and self-disciplined (60%); more motivated to succeed (59%); more spiritual (45%); more independent in many ways (38%); less inhibited (33%).

Increase in state suicide rates in the USA during economic recession

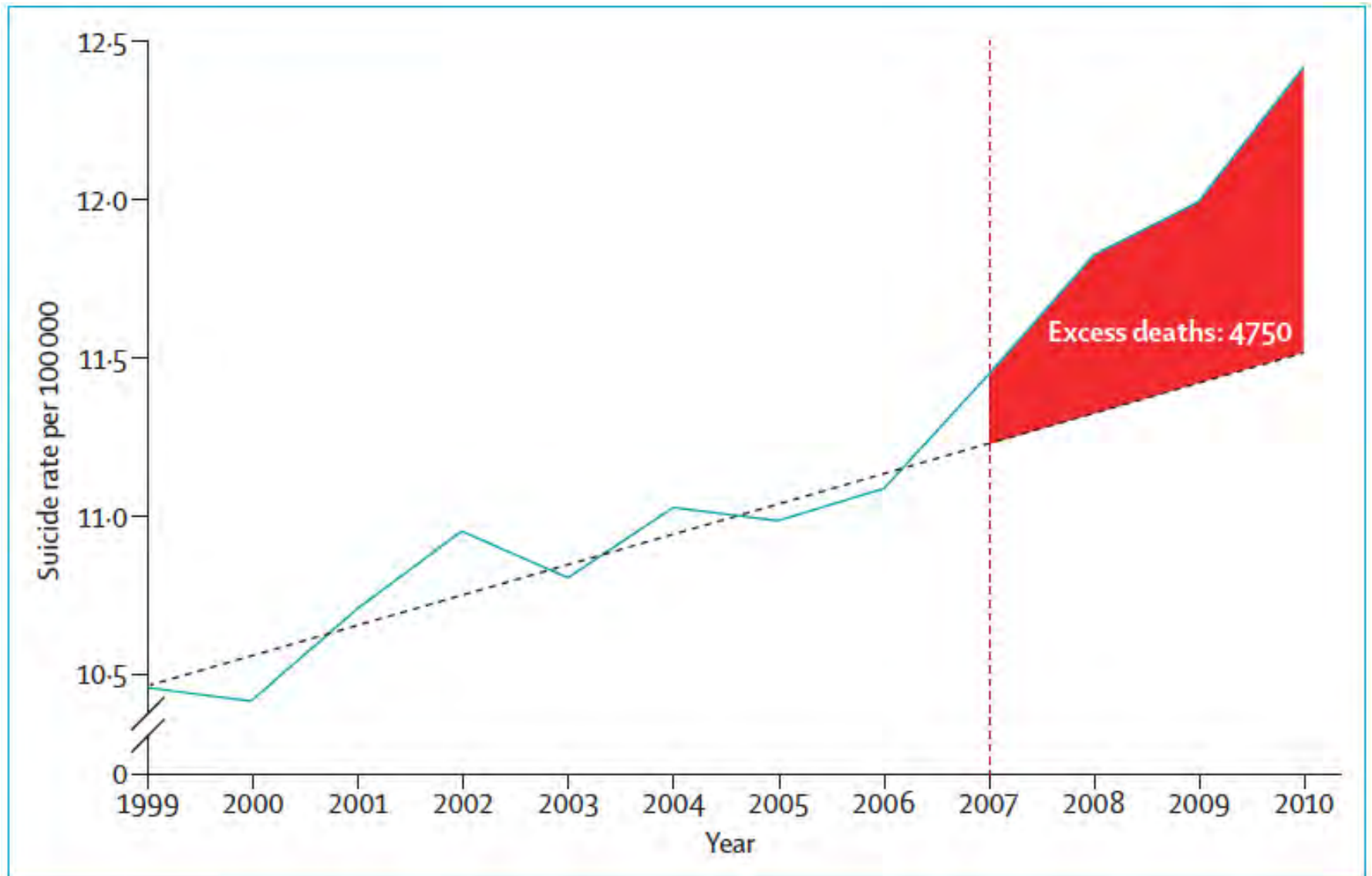


Figure: Time trend analysis of suicide rate in 50 US states and District of Columbia between 1999 and 2010

Vertical line shows onset of recession.

10 Leading Causes of Death by Age Group, United States – 2008

Rank	Age Groups										Total
	<1	1-4	5-9	10-14	15-24	25-34	35-44	45-54	55-64	65+	
1	Congenital Anomalies 5,638	Unintentional Injury 1,469	Unintentional Injury 835	Unintentional Injury 1,024	Unintentional Injury 14,089	Unintentional Injury 14,588	Unintentional Injury 16,065	Malignant Neoplasms 50,403	Malignant Neoplasms 104,091	Heart Disease 495,730	Heart Disease 616,828
2	Short Gestation 4,754	Congenital Anomalies 521	Malignant Neoplasms 457	Malignant Neoplasms 433	Homicide 5,275	Suicide 5,300	Malignant Neoplasms 12,699	Heart Disease 37,892	Heart Disease 66,711	Malignant Neoplasms 391,729	Malignant Neoplasms 565,469
3	SIDS 2,353	Homicide 421	Congenital Anomalies 170	Suicide 2,255	Suicide 4,298	Homicide 4,610	Heart Disease 11,336	Unintentional Injury 20,354	Chronic Low. Respiratory Disease 14,042	Chronic Low. Respiratory Disease 121,223	Chronic Low. Respiratory Disease 141,090
4	Maternal Pregnancy Comp. 1,765	Malignant Neoplasms 394	Homicide 113	Homicide 207	Malignant Neoplasms 1,663	Malignant Neoplasms 3,521	Suicide 6,703	Suicide 8,227	Unintentional Injury 12,782	Cerebro-vascular 114,508	Cerebro-vascular 134,148
5	Unintentional Injury 1,315	Heart Disease 186	Heart Disease 97	Congenital Anomalies 161	Heart Disease 1,065	Heart Disease 3,254	Homicide 2,906	Liver Disease 8,220	Diabetes Mellitus 11,370	Alzheimer's Disease 81,573	Unintentional Injury 121,902
6	Placenta Cord Membranes 1,080	Influenza & Pneumonia 142	Benign Neoplasms 59	Heart Disease 132	Congenital Anomalies 467	HIV 975	HIV 2,838	Cerebro-vascular 6,112	Cerebro-vascular 10,459	Diabetes Mellitus 50,883	Alzheimer's Disease 82,435
7	Bacterial Sepsis 700	Septicemia 93	Chronic Low. Respiratory Disease 55	Chronic Low. Respiratory Disease 64	Influenza & Pneumonia 206	Diabetes Mellitus 574	Liver Disease 2,562	Diabetes Mellitus 5,622	Liver Disease 8,526	Influenza & Pneumonia 48,382	Diabetes Mellitus 70,553
8	Respiratory Distress 630	Cerebro-vascular 63	Cerebro-vascular 41	Cerebro-vascular 56	Diabetes Mellitus 204	Cerebro-vascular 539	Cerebro-vascular 2,035	Chronic Low. Respiratory Disease 4,392	Suicide 5,465	Nephritis 39,921	Influenza & Pneumonia 56,284
9	Circulatory System Disease 594	Chronic Low. Respiratory Disease 54	Influenza & Pneumonia 40	Influenza & Pneumonia 49	Cerebro-vascular 189	Liver Disease 423	Diabetes Mellitus 1,854	HIV 3,730	Nephritis 4,803	Unintentional Injury 39,359	Nephritis 48,237
10	Neonatal Hemorrhage 556	Perinatal Period 51	Septicemia 25	Septicemia 36	Complicated Pregnancy 169	Congenital Anomalies 379	Septicemia 892	Viral Hepatitis 2,732	Septicemia 4,552	Septicemia 27,028	Suicide 36,035



Centers for Disease Control and Prevention
National Center for Injury Prevention and Control

Source: National Vital Statistics System, National Center for Health Statistics, CDC.

Produced by: Office of Statistics and Programming, National Center for Injury Prevention and Control, CDC.

CS227502

Major Depression Versus Sadness

- Major depression is a syndrome.
- It is not just severe sadness.
- Sadness is to major depression what cough is to pneumonia.
 - Cough can be an indicator of pneumonia.
 - Not every cough is the result of pneumonia.
 - Sometimes pneumonia presents without a cough.
 - Consider the company the cough keeps.
 - Productive sputum, tachypnea, fever, consolidation

DSM IV Inventory: SIGEMCAPS

- Sleep (↓ / ↑)
- Interest (or pleasure)
- Guilt (or worthlessness)
- Energy (fatigue)
- Mood
- Concentration
- Appetite (↓ / ↑ or weight loss or gain)
- Psychomotor retardation (or agitation)
- Suicidal ideation (or thoughts of death)
- $\geq 5/9$ Sx for ≥ 2 weeks

Medical Causes of Depression:

- **Neurologic disorders:** CVA (30-50%), subdural hematoma, epilepsy (45-55%), brain tumors (30%), **Multiple Sclerosis (37-62%)**, Parkinson's disease (40-50%), Huntington's disease (40%), syphilis, Alzheimer's disease (15-50%)
- **Autoimmune disorders:** **Multiple Sclerosis (37-62%)**, rheumatoid arthritis (30-50%), DM (30%), SLE (25-44%).
- **Drug induced:** reserpine (15%), **interferon-alpha** (10-57%), β -blockers, corticosteroids, estrogens, benzodiazepines, barbiturates, ranitidine, Ca^{2+} -channel blockers
- **Substance induced** (25%): EtOH, sedative-hypnotic, cocaine & psychostimulant withdrawal
- **Metabolic:** hyper/hypothyroidism, Cushing's syndrome, hypercalcemia, hyponatremia, diabetes mellitus
- **Nutritional:** vitamin B12 deficiency
- **Infections:** HIV, HCV (25%), mononucleosis, influenza
- **Cancer** (20-45%): especially pancreatic CA (40-50%)

Burden of Depression in MS Patients

(Patten & Metz, Psychother Psychosom, 1997, 66:286-92)

- Lifetime Prevalence:
 - 37-62% MS
 - 17% General Population (NCS)
- Current Prevalence:
 - 14-27% MS
 - 5% General Population (NCS)
- Cognitive Impairment in MS:
 - Lifetime prevalence 45-65%

SIGEMCAPS → MS/TM

- Sleep (↓ / ↑) → Insomnia (sedative)
- Interest (or pleasure) → Adjustment to new normal
- Guilt (or worthlessness) → Barrier to rehab and Tx
- Energy (fatigue) → MS Fatigue (stimulant)
- Mood → Sadness
- Concentration → MS memory loss
- Appetite → Weight loss
- Psychomotor retardation → MS memory loss,
- Suicidal ideation → Hopelessness, death
- Magnification of suffering → Chronic Pain (marijuana)

Depression and MS

- Depression is **common** in patients with MS and is associated with considerable **morbidity** and **mortality**.
- The available evidence suggests that **depression** in MS is **caused by the effects of inflammatory insults to the brain**.
 - No correlation with physical disability.
 - No genetic loading.
 - Periods of immune activation correlate with increased depression and suicides.

Depression and Quality of Life

- Multiple studies have shown that depression is the **primary determining factor** in a patient's self reported **quality of life**, with greater impact than other variables investigated, including physical disability, fatigue, and cognitive impairment.
- Also, depression is the number 1 correlate of the **quality of life** of the patient's **caregiver**.

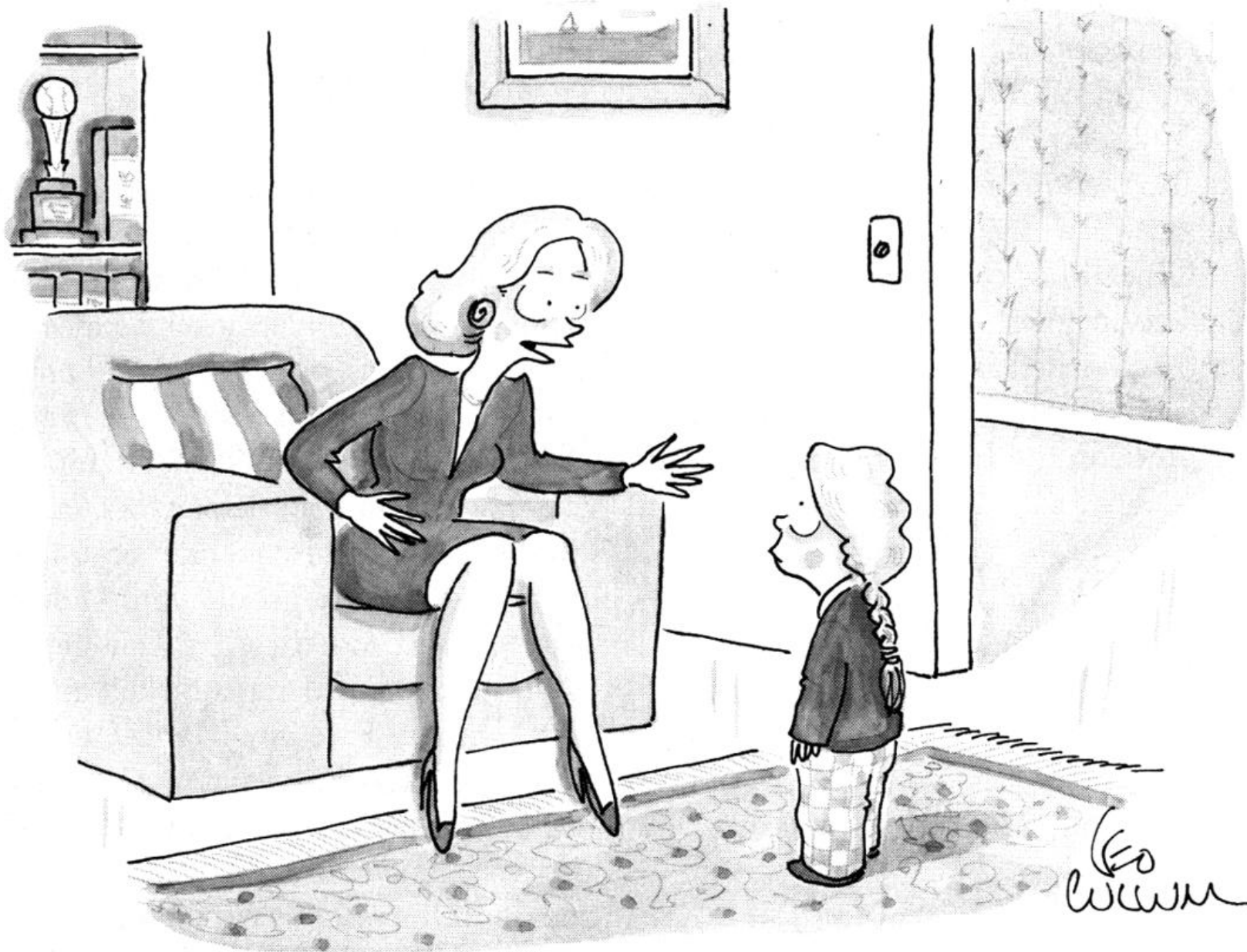
Are you getting enough oxygen?



MS Depression and Suicide: Epidemiology

- 30% lifetime incidence of suicidal intent in patients with MS.
- 6%–12% of patients with MS attempt suicide.
- Suicide in MS patients occurs at 7.5 times the rate of the general population.
- Suicide was the 3rd leading cause (15%) of death of 3000 outpatients in Canadian MS clinics from 1972–1988.
 - MS patients dying from suicide were younger and less disabled than patients dying from pneumonia (23%) and cancer (16%).¹

¹Sadovnick AD, Eisen K, Ebers GC, et al. Cause of death in patients attending multiple sclerosis clinics. *Neurology*. 1991;41:1193-1196.



***"Of course your daddy loves you.
He's on Prozac--he loves everybody."***

Treating Depression May Improve MS Disease Severity

- Patients with depression had biological evidence of worse MS disease severity.
- Treatment of depression in MS patients (with either medication or psychotherapy) correlated with improvement in their autoimmune disease status.
- Suggests that treatment of depression may be an important component in the management of patients with MS:
 - “Treatment of depression may provide a novel disease-modifying therapeutic strategy as well as a symptomatic treatment for patients with MS.”¹

¹Mohr et al. Treatment of depression is associated with suppression of nonspecific and antigen-specific T(H)1 responses in multiple sclerosis. *Arch Neurol.* 2001;58:1081-1086.

Effects of fluoxetine on disease activity in relapsing multiple sclerosis: a double-blind, placebo-controlled, exploratory study

J P Mostert,¹ F Admiraal-Behloul,² J M Hoogduin,³ J Luyendijk,² D J Heersema,¹ M A van Buchem,² J De Keyser¹

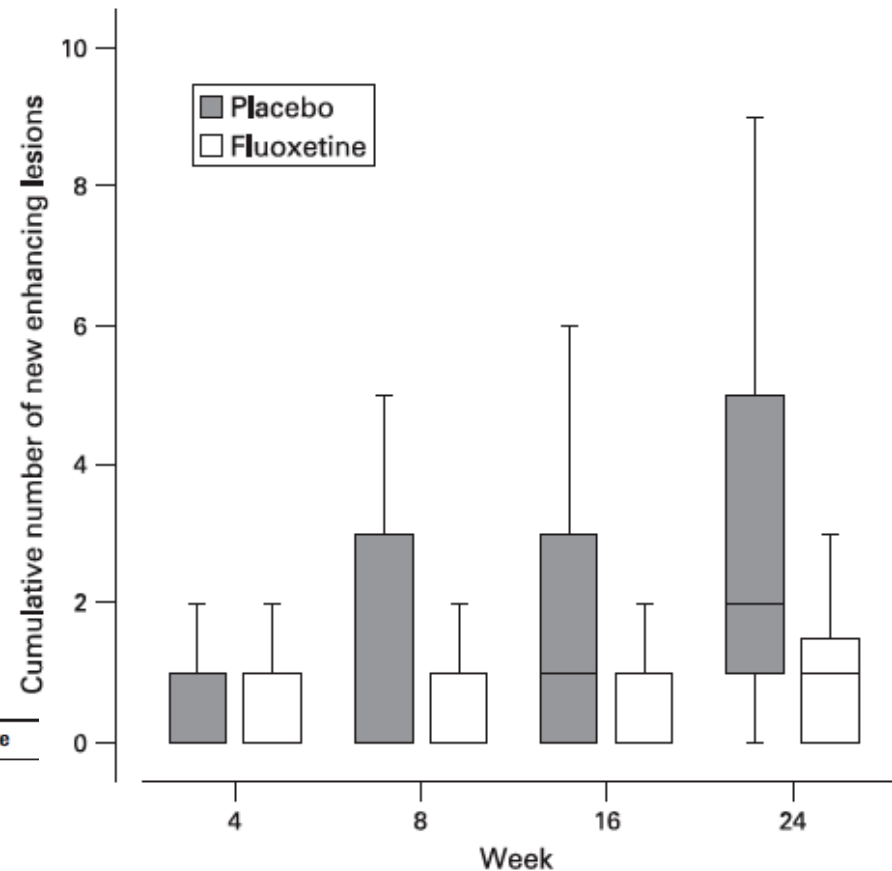
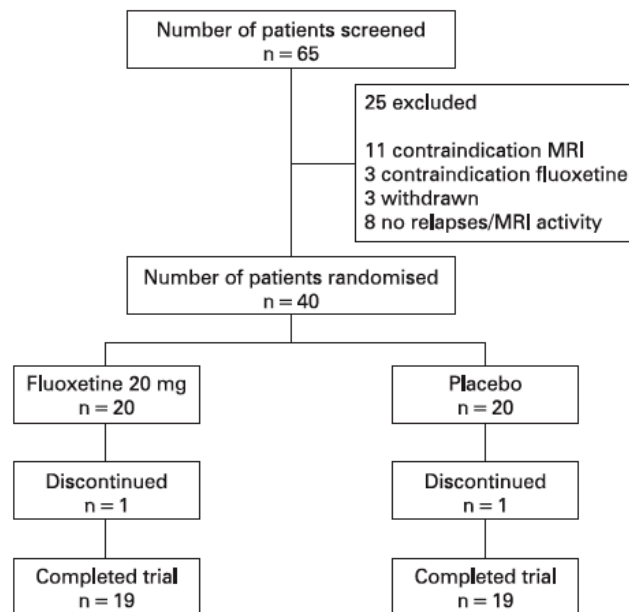
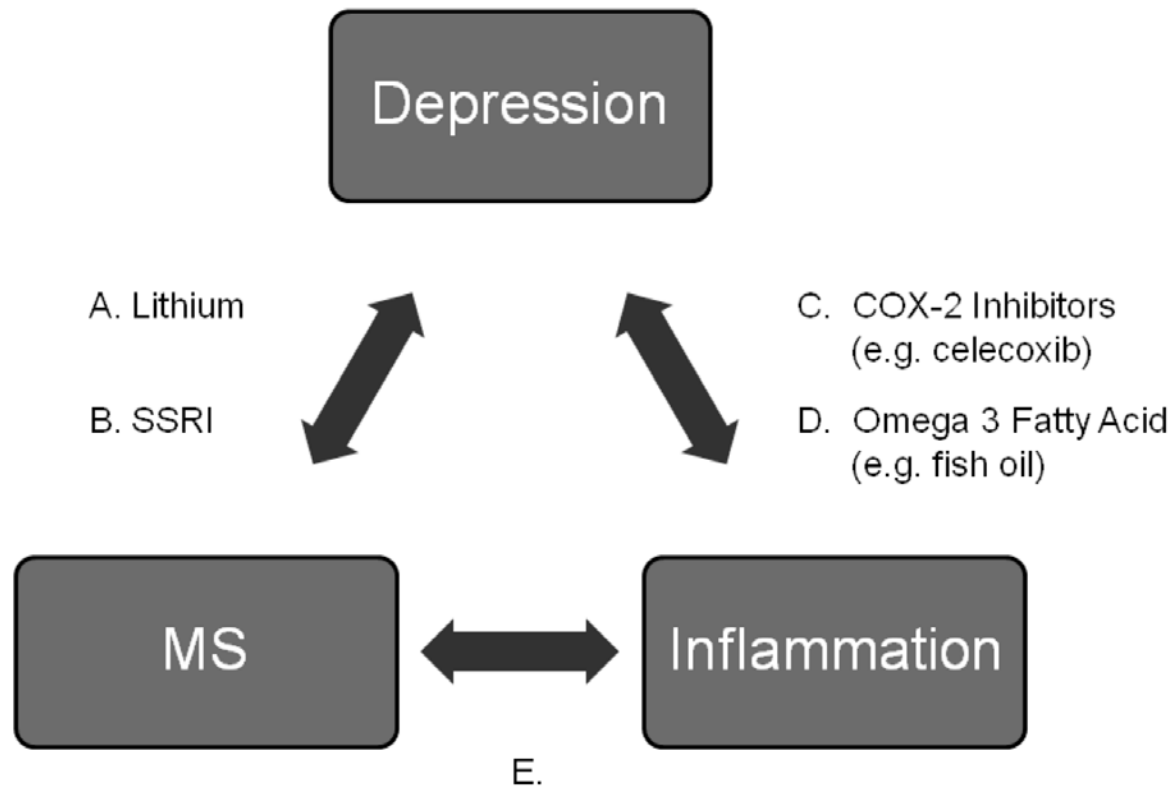


Table 3 MRI outcomes during the past 16 weeks.

	Fluoxetine (n = 19)	Placebo (n = 19)	p Value
Cumulative number of new enhancing lesions			0.05
Mean (SD)	1.21 (2.6)	3.16 (5.3)	
Median (range)	0 (0–11)	1 (0–22)	
Cumulative volume of new enhancing lesions (mm ³)			0.06
Mean (SD)	90 (231)	227 (485)	
Median (range)	0 (0–961)	35 (0–2095)	
Number of patients with no new enhancing lesions	12 (63%)	5 (26%)	0.02
Scans showing new enhancing lesions	9 (24%)	18 (47%)	0.03
Scans showing enhancing lesions	9 (24%)	18 (47%)	0.03

Depression-MS-Inflammation Triad



Relationship Between Depression & Autoimmune CNS Diseases

- Depression and MS: A Two-Way Street
 - MS causes depression.
 - Depression worsens MS.
 - Treating depression improves MS.
 - Treating MS improves depression.
 - Autoimmunity and depression are a two-way street.
- Depression is a lethal consequence of MS if left untreated.
- Depression is common and important, caused by the immune system in autoimmune diseases, and treatable.

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