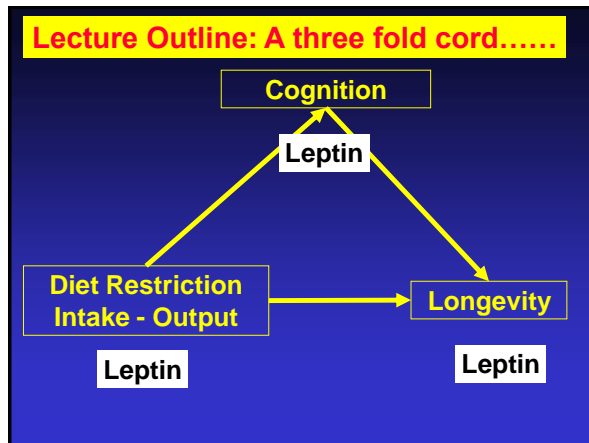


11<sup>th</sup> EUROPEAN NUTRITION CONFERENCE **madrid2011** Madrid Convention Centre, Paseo de la Castellana, 99, 28016 Madrid - Spain. [www.kennedy2011.com](http://www.kennedy2011.com)

Diversity vs Globalization: A Nutritional Challenge for a Changing Europe

**Leptin as a Survival Hormone: Diet Restriction, Cognition & Longevity: Relationship to Eating Disorders**

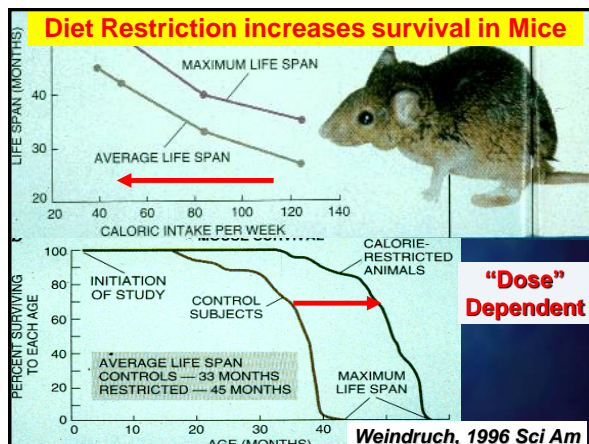
**Elliot M. Berry MD, FRCP**  
 Head, Dept of Human Metabolism & Nutrition, & WHO Collaborating Center in Public Health  
 Hebrew University-Hadassah Medical School  
 Jerusalem, Israel



**Different effects of Diet Restriction – Undernutrition vs Malnutrition**


	<u>Undernutrition</u>	<u>Malnutrition</u>
	Diet Restriction	
Quantity	Decreased	Decreased
Essential nutrients	NORMAL	Decreased
Longevity	Increased	Decreased
Cognitive Function	Increased	Decreased

*Use of Animal Models*




**Does anorexia occur in nature?**  
*Only short-term starvation.*  
*No animal will starve itself to death....*

**Hibernation**  Bears

**Migration**  Birds, Whales, Turtles

**Territorial Defense**  Seals

**Egg Incubation Care**  Penguins (1), Octopus (200,000)

**Clinical Cases of anorexia**  
**Similar Weights, Different Responses**

**Patient 1** Restrictive Anorexia, admitted at weight of 26 kg  
 ~ **Diet Restriction**

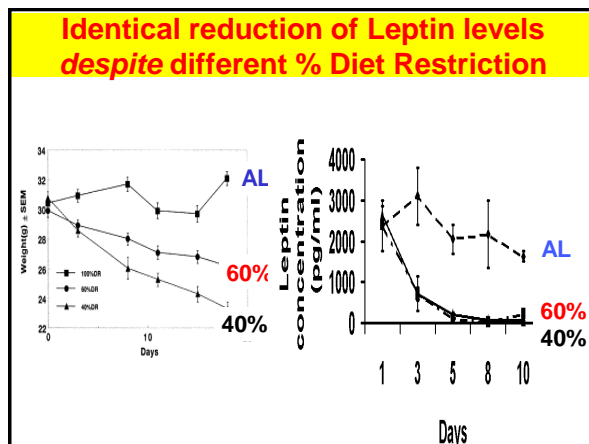
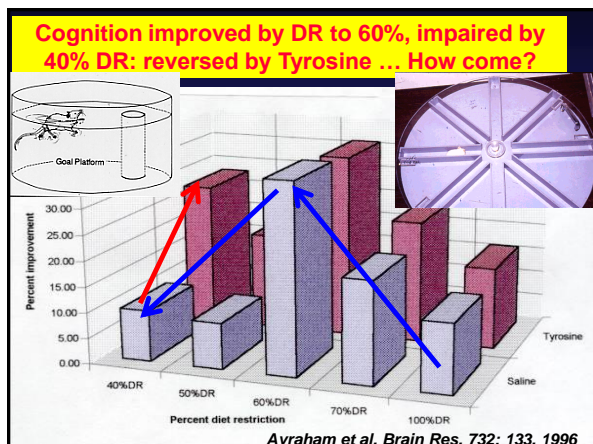
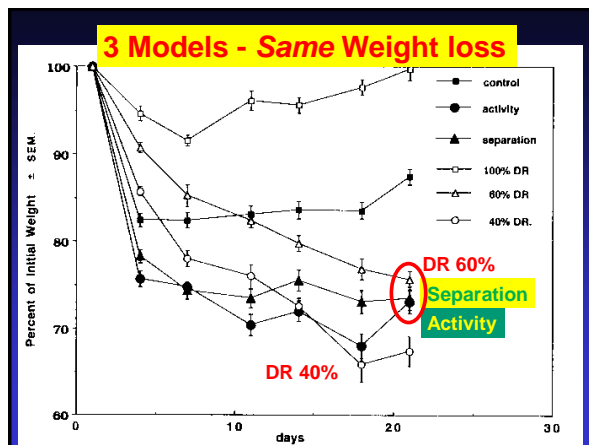
**Patient 2** Social isolation & Depression  
 No school parties for 2 years  
 ~ **Separation**

**Patient 3** Hospitalized, ate diet but did not gain weight.  
 No evidence of vomiting ???  
 ~ **Activity**

reduce your Separation anxiety

**Models for Anorexia:**  
Diet Restriction (DR)  
Separation (Sep)  
Activity (Act)

Avraham et al Brain Res. 1996; 732: 133.  
Van Leeuwen et al. Phys & Behav. 1997; 62:77



**DR to 60% (but not 40%) stimulates hippocampal OB-long receptor expression & signaling**

OBR's

relative mRNA level (percent)

control DR to 60% DR to 40%

Long

relative mRNA level (percent)

control DR to 60% DR to 40%

Short

Actin

**Leptin Receptor Isoforms**

Long OB-Rb  
Short OB-Ra  
Soluble OB-Rs

Extracellular  
Transmembrane  
Intracellular

Signaling

**OB receptor signal transduction**

OB-Ra  
OB-Rb  
Leptin  
STAT3  
STAT1

**Other "players" .....**

**Leptin reverses dose-dependent activation of Hippocampal AMPK (X6) following Diet Restriction**

AMPK phosphorylation (percent)

Days

Control 80% 60% 40% Diet Restriction

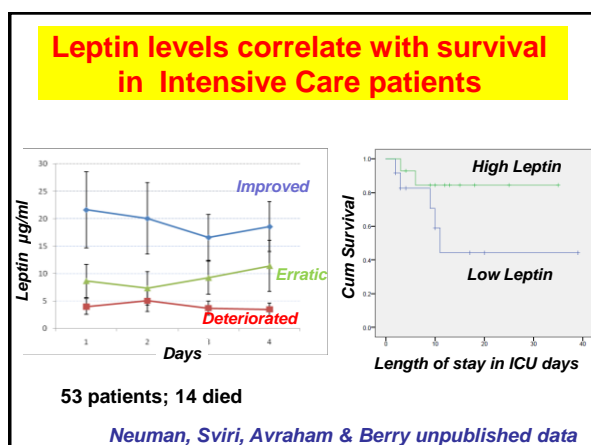
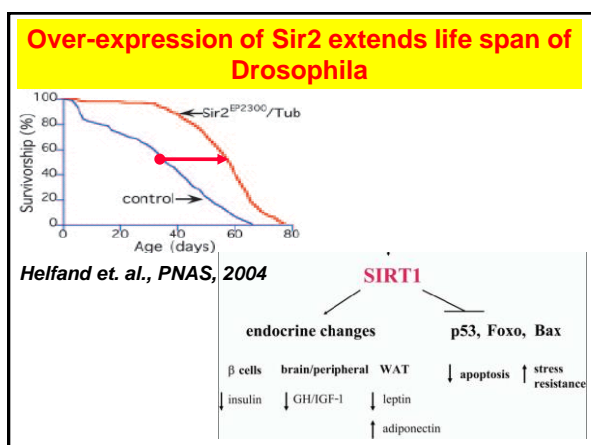
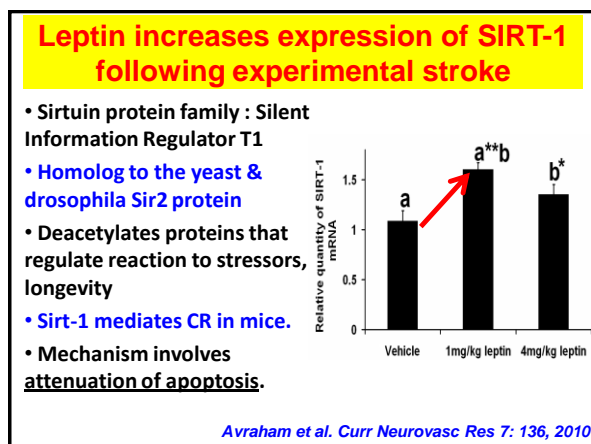
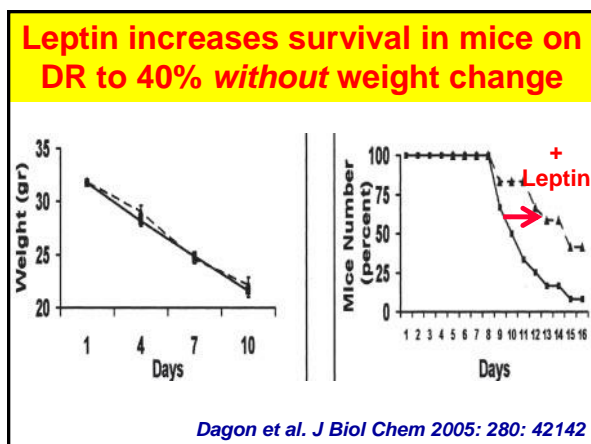
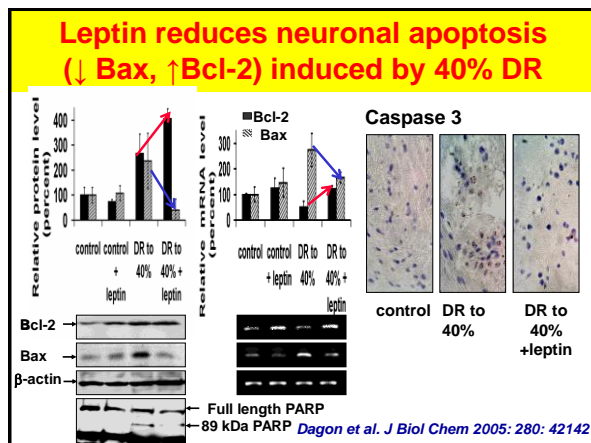
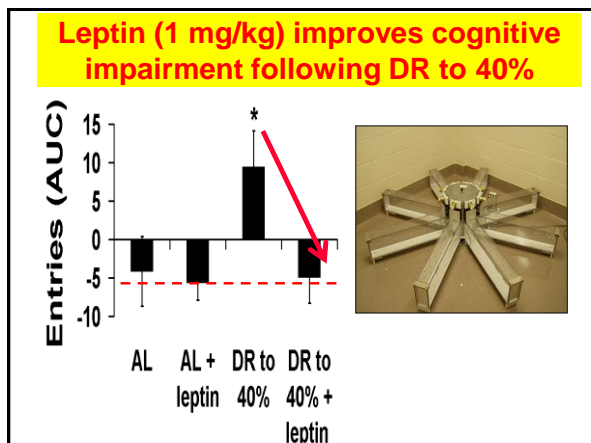
P-AMPK  
AMPK

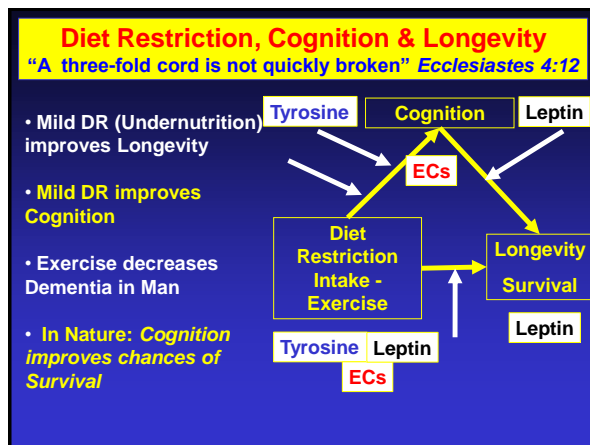
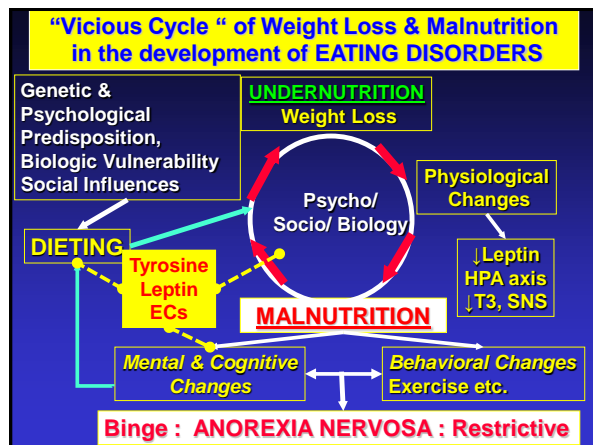
AMPK phosphorylation (percent)

control control DR to 40% DR to 40% + leptin + leptin

P-AMPK  
AMPK

Dagon et al. J Biol Chem 2005; 280: 42142





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Diversity vs Globalization:  
A Nutritional Challenge for a Changing Europe

**The Link between Caloric Restriction, Cognitive Function & Longevity**

- In states of negative energy balance (Under AND Malnutrition), Leptin improves Cognition (via AMPK, Neuroprotection) & Longevity (via Sirtuins)
- **LEPTIN acts as a SURVIVAL Hormone**

**Therapeutic implications for catabolic, weight loss states such as Cachexia, Cancer, HIV/AIDS, Malnutrition & Eating Disorders**

**Thanks to all the co-workers.....**

- Dr. Yosefa Avraham
- Dr Yossi Dagon
- Dr Ronen Lecker
- Prof Aron H. Lichtman
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