

Potential Beneficial Effects of DHEA in Humans

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Potential Beneficial Effects of DHEA in Humans

- ❖ overview of DHEA metabolism
- ❖ effects of DHEA administration
 - ◆ animal models
 - ◆ young men
 - ◆ older women and men
- ❖ summary

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adrenals 95%

gonads 5%

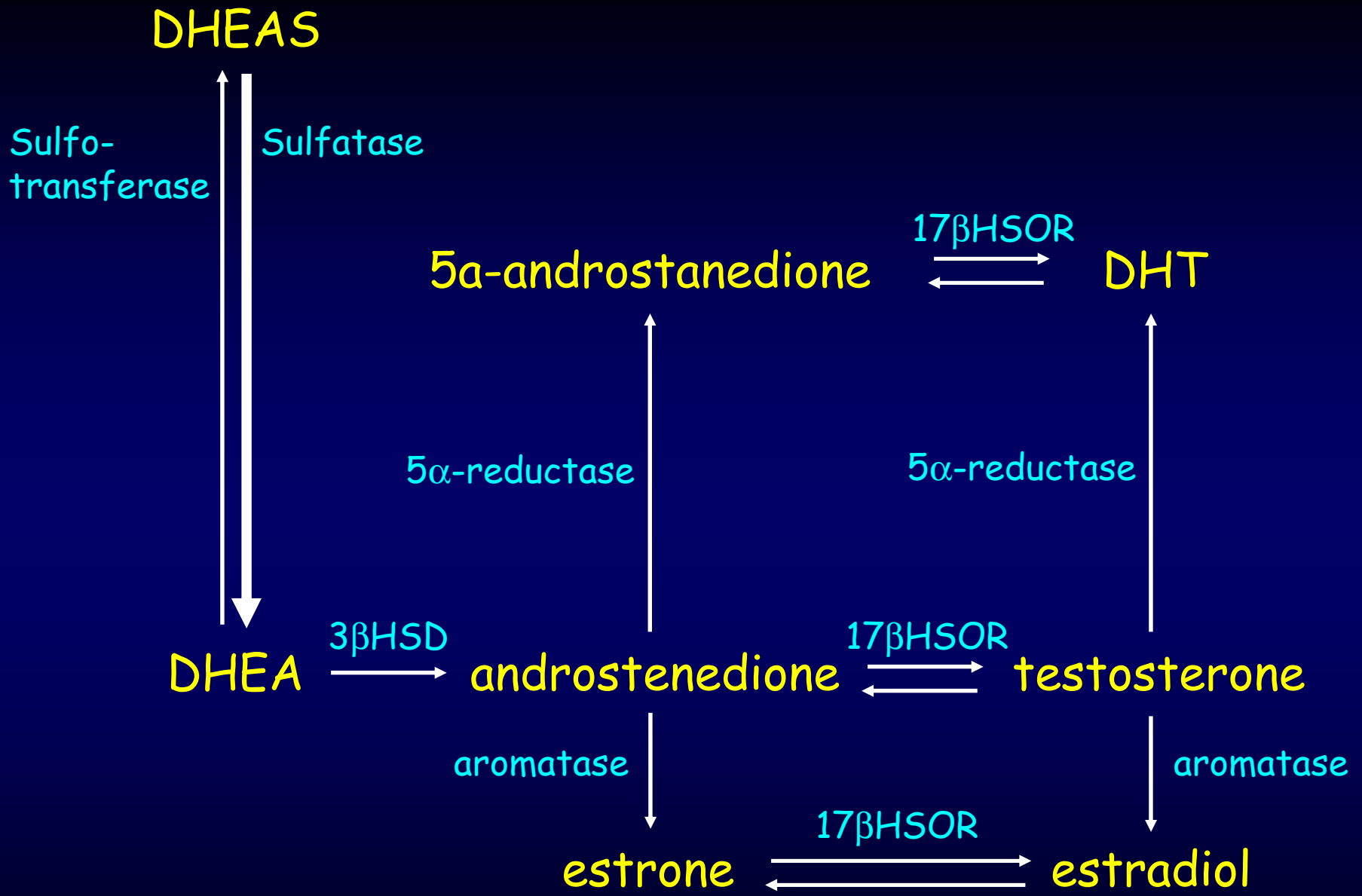
DHEA/DHEAS

androstenedione

testosterone

dht

estradiol



DHEAS

"The Mother Steroid"

DHEAS is an abundant hormone that serves as a precursor to:

- ❖ ~50% of androgens in adult men
- ❖ ~75% of active estrogens in premenopausal women
- ❖ nearly 100% of active estrogens in postmenopausal women

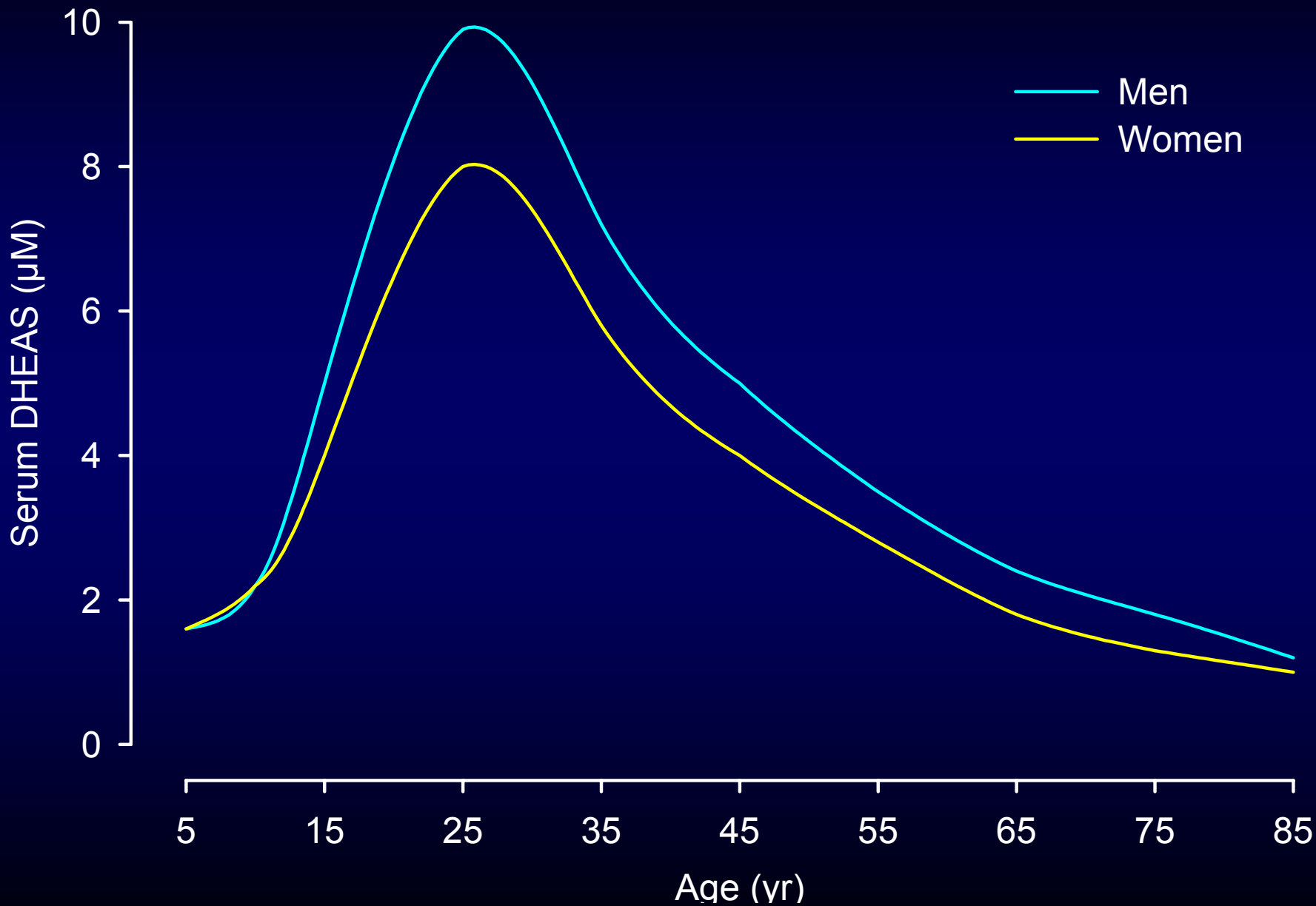
DHEA/DHEAS

- ❖ Most abundant steroid in human plasma
- ❖ Concentrations in humans are much higher than in animals
- ❖ Lack of an appropriate animal model has limited the understanding of the metabolism of DHEA(S) and its biological effects in humans
- ❖ DHEA is widely distributed in the body
brain > plasma > spleen > kidneys > liver

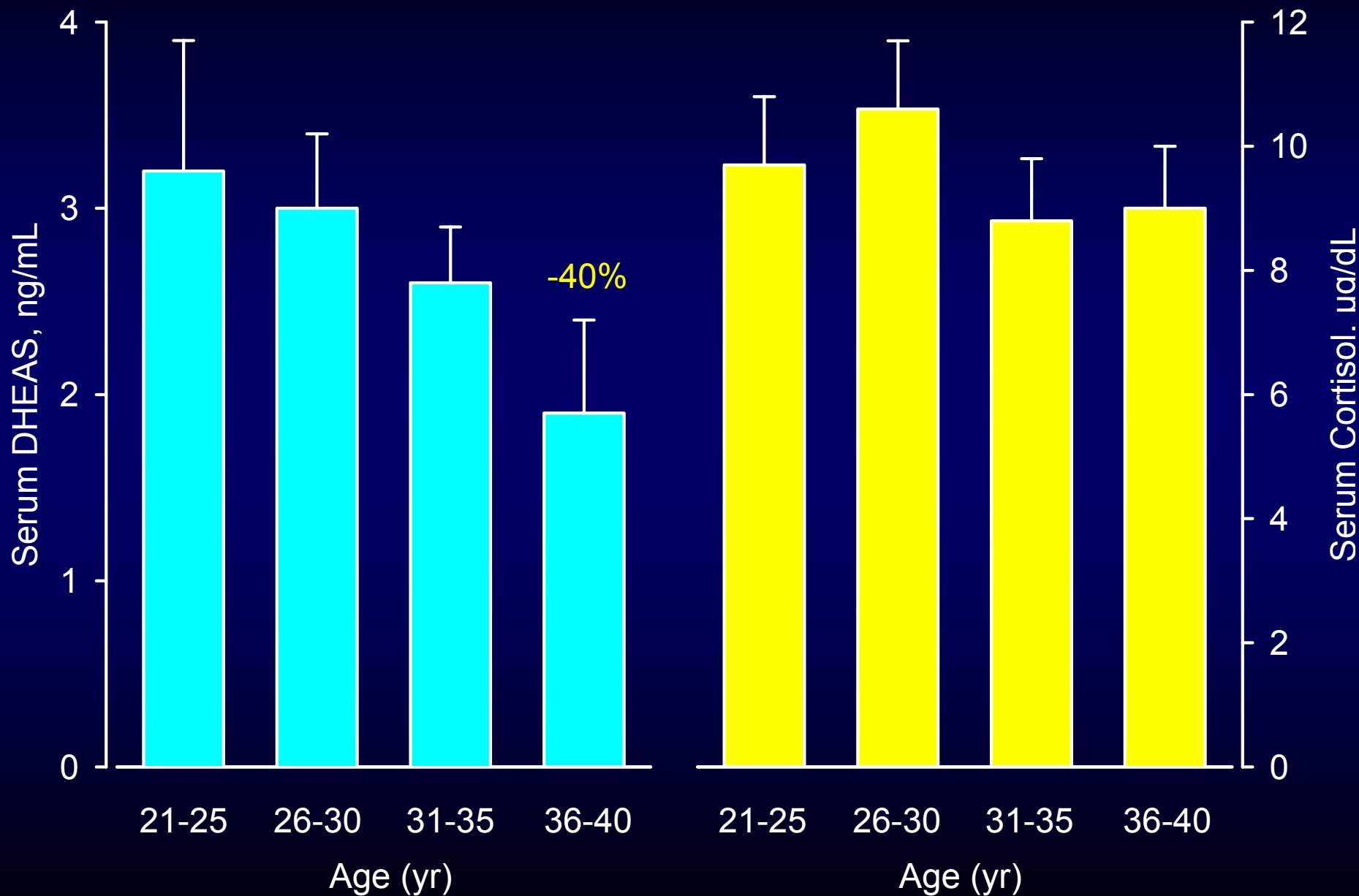
Abundance of DHEAS

Hormone	Women	Men
DHEAS	8,000 nM	10,000 nM
DHEA	32 nM	20 nM
T	3 nM	30 nM
E ₂	0.22 nM	0.15 nM

Serum DHEAS vs Age



Serum DHEAS and Cortisol Levels in Premenopausal Women



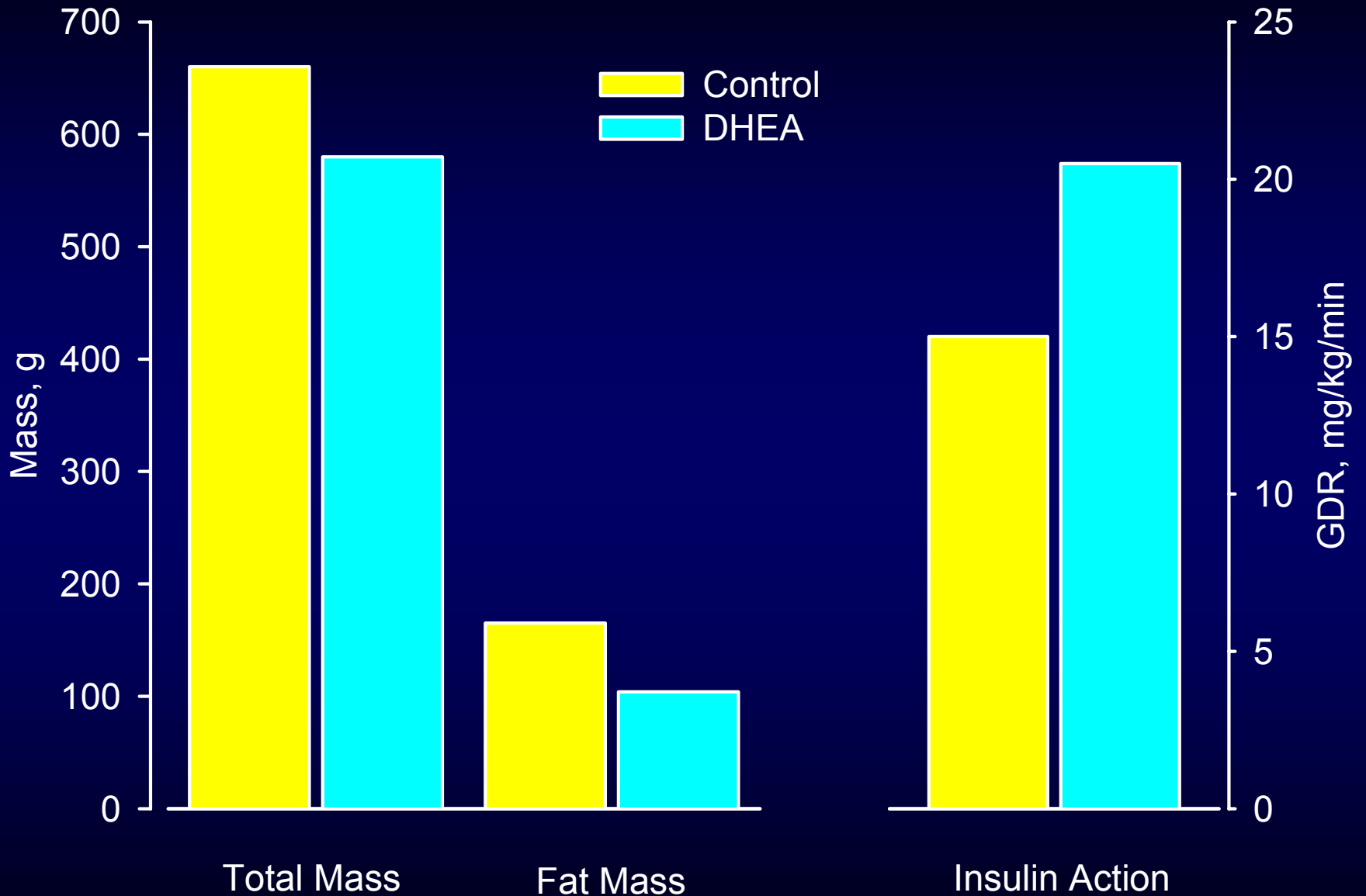
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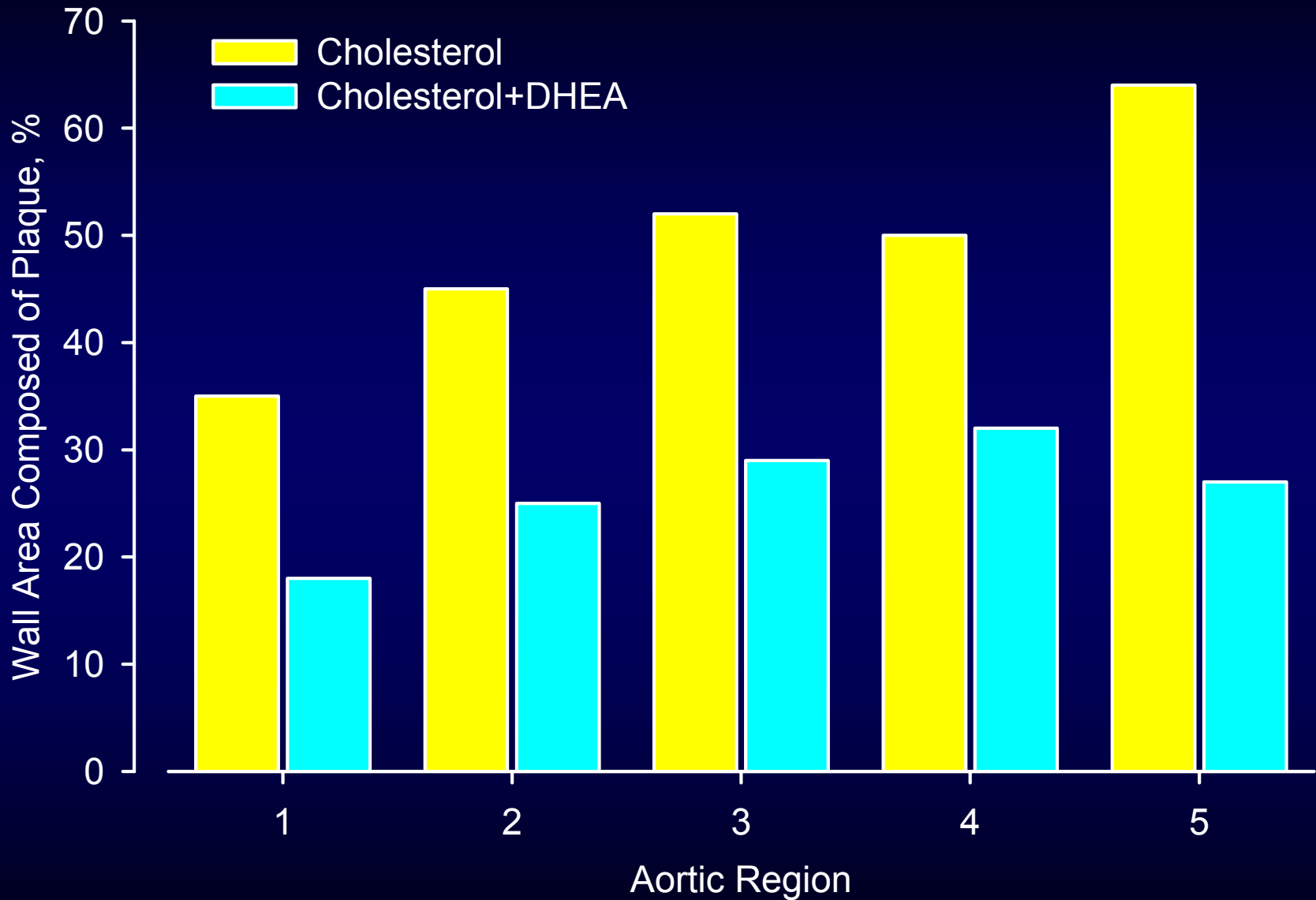
Effects of DHEA Supplementation in Rodents

- ❖ Anti-obesity
 - ❖ prevents fat gain in obesity-prone strains and reverses obesity
- ❖ Anti-diabetogenic
 - ❖ enhances insulin action
- ❖ Anti-atherogenic
 - ❖ diminishes atherosclerotic plaque

20 Months of DHEA Supplementation in Rats



Effects of a 12-wk Atherogenic Diet Plus DHEA on Aortic Plaque



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DHEA Reduces LDL Levels and Body Fat but does not Alter Insulin Sensitivity in Normal Men

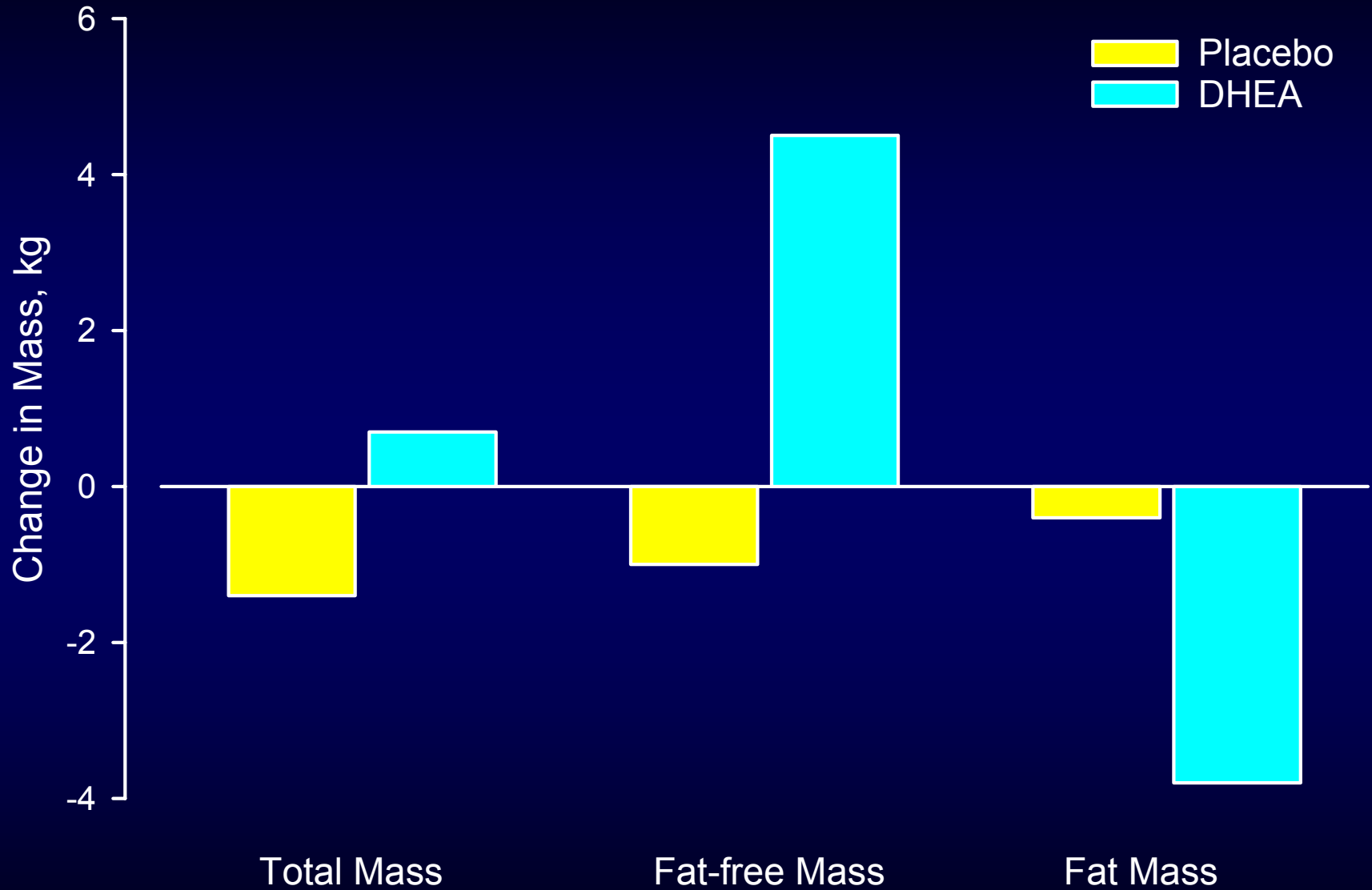
Nestler JE et al. *J Clin Endocrinol Metab* 66:57-61, 1988

- ❖ 10 men, aged 22-25 yr
- ❖ placebo or **DHEA, 1600 mg/d, 28 d**
- ❖ body composition - hydrodensitometry
- ❖ insulin action - euglycemic, hyperinsulinemic clamp
- ❖ no side effects noted in either group

	Placebo		DHEA	
	Baseline	Δ	Baseline	Δ
DHEAS, μM	9.9	-1.2	10.9	27.9*
Total T, nM	29.0	1.4	26.6	3.3
Free T, nM	12.9	-1.3	11.0	5.9
Andro, nM	5.5	0.3	4.3	4.3*
E ₂ , pM	117	-26	117	-14
E ₁ , pM	193	35	194	38
SHBG, nM	17.9	2.9	17.5	-3.6

Nestler JE et al. *J Clin Endocrinol Metab* 66:57-61, 1988

Effect of DHEA Supplementation on Body Composition



Nestler et al. *J Clin Endocrinol Metab* 66:57-61, 1988

Lack of an Effect of DHEA in Obese Men

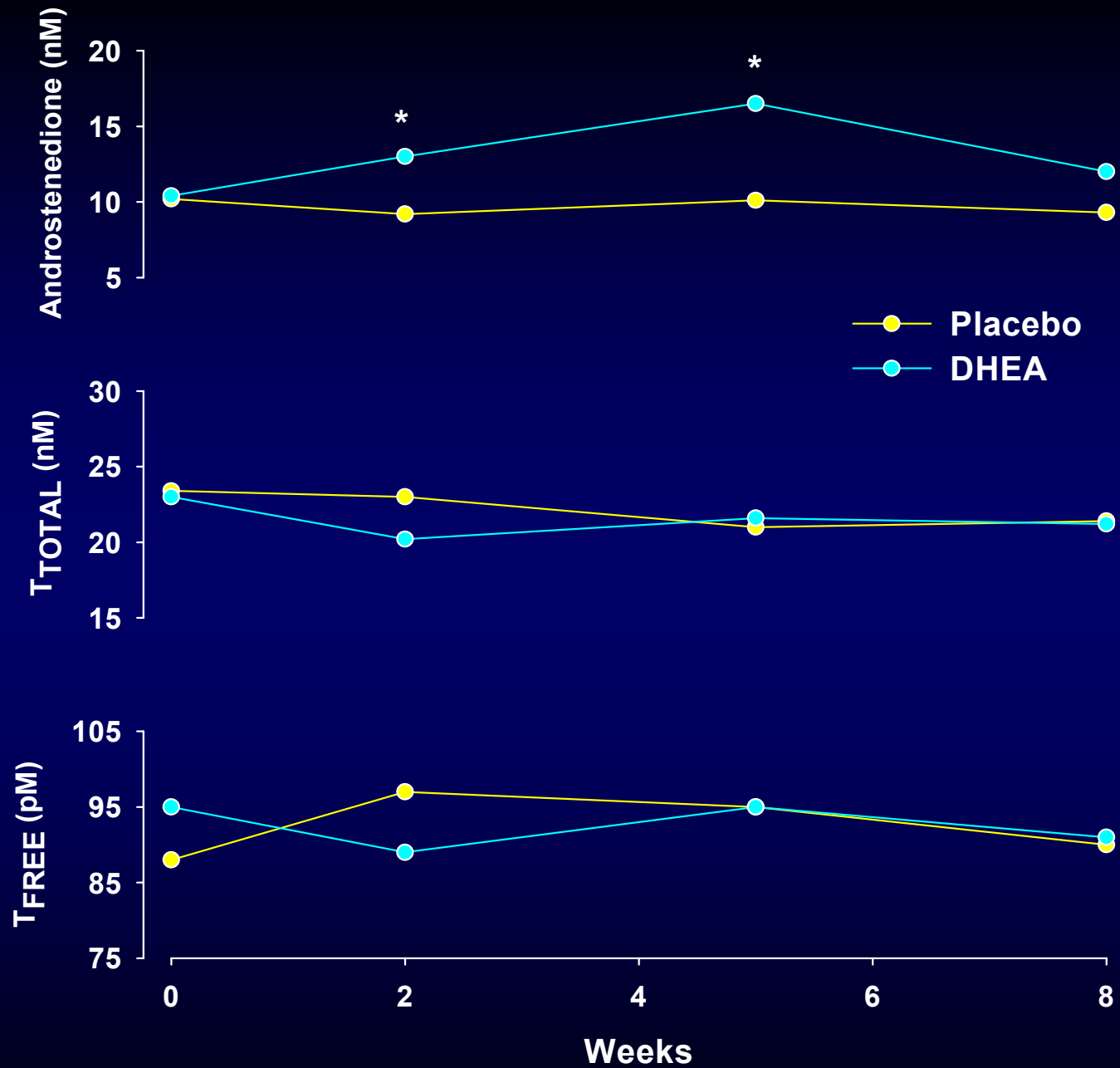
Usiskin KS et al. *Int J Obesity* 14:457-463, 1990

- ❖ 6 men, aged 21-37 yr, BMI 28-38 kg/m²
- ❖ DHEA, 1600 mg/d, 28 d
- ❖ body composition - hydrodensitometry, BIA, anthropometry
- ❖ no side effects of DHEA

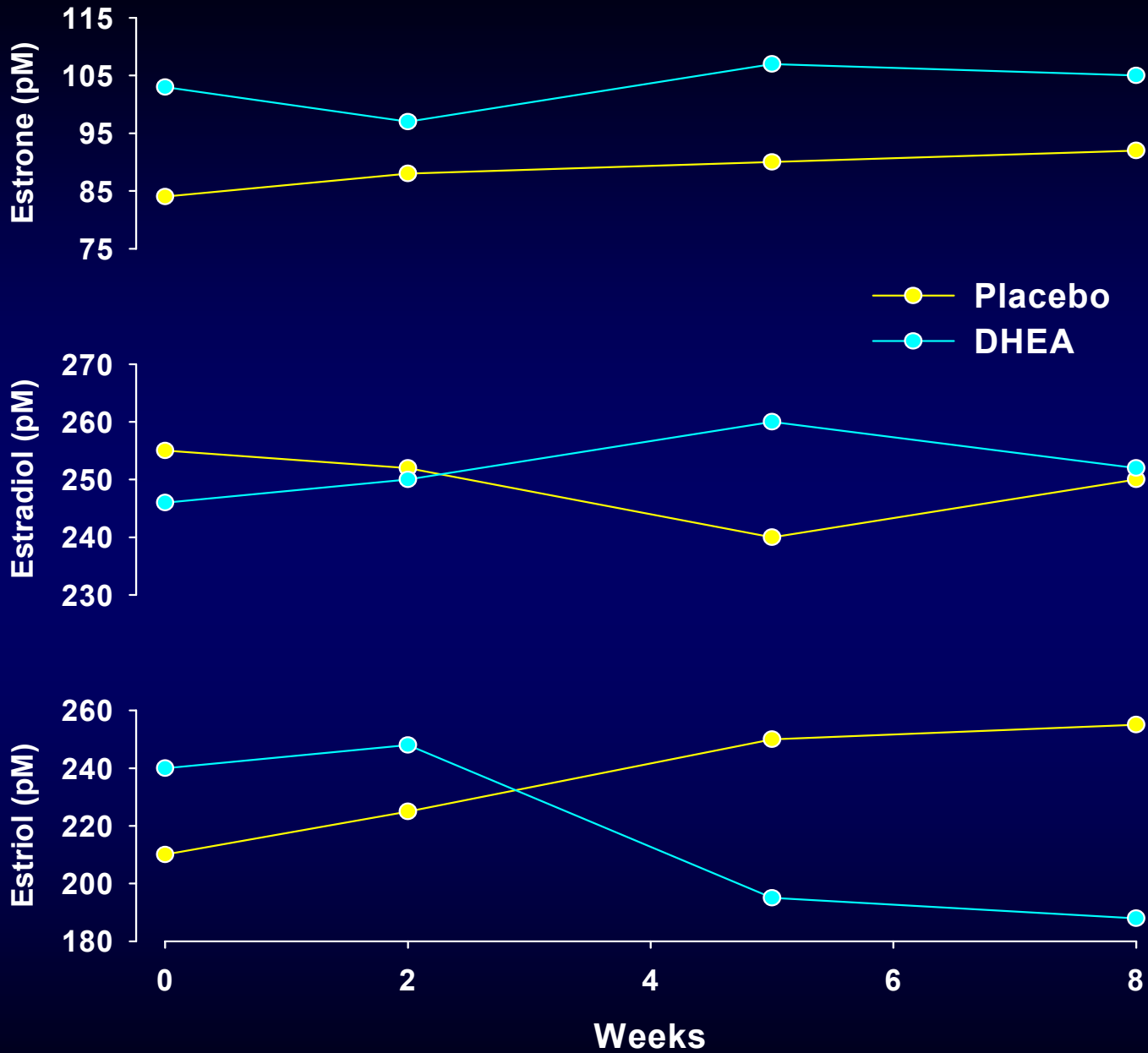
Effect of Oral DHEA on Serum Testosterone and Adaptations to Resistance Training in Young Men

Brown GA et al. *J Appl Physiol* 87:2274-2283, 1999

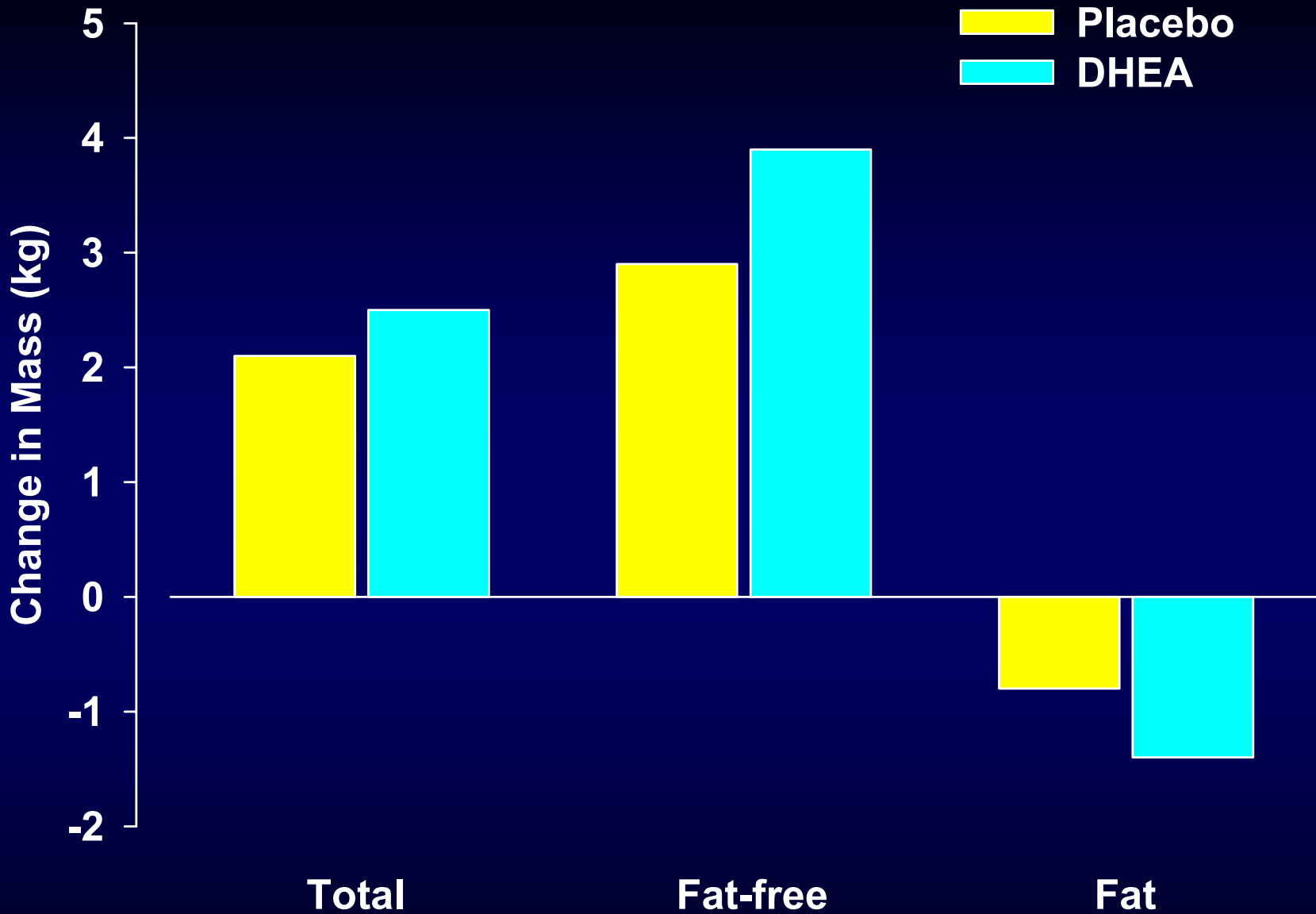
- ❖ 19 men, aged 19-29 yr
- ❖ placebo or **DHEA, 150 mg/d, wks 1,2,4,5,7,8**
- ❖ body composition - hydrodensitometry
- ❖ strength - 1 repetition maximums
- ❖ no side effects reported



Brown GA et al. *J Appl Physiol* 87:2274-2283, 1999



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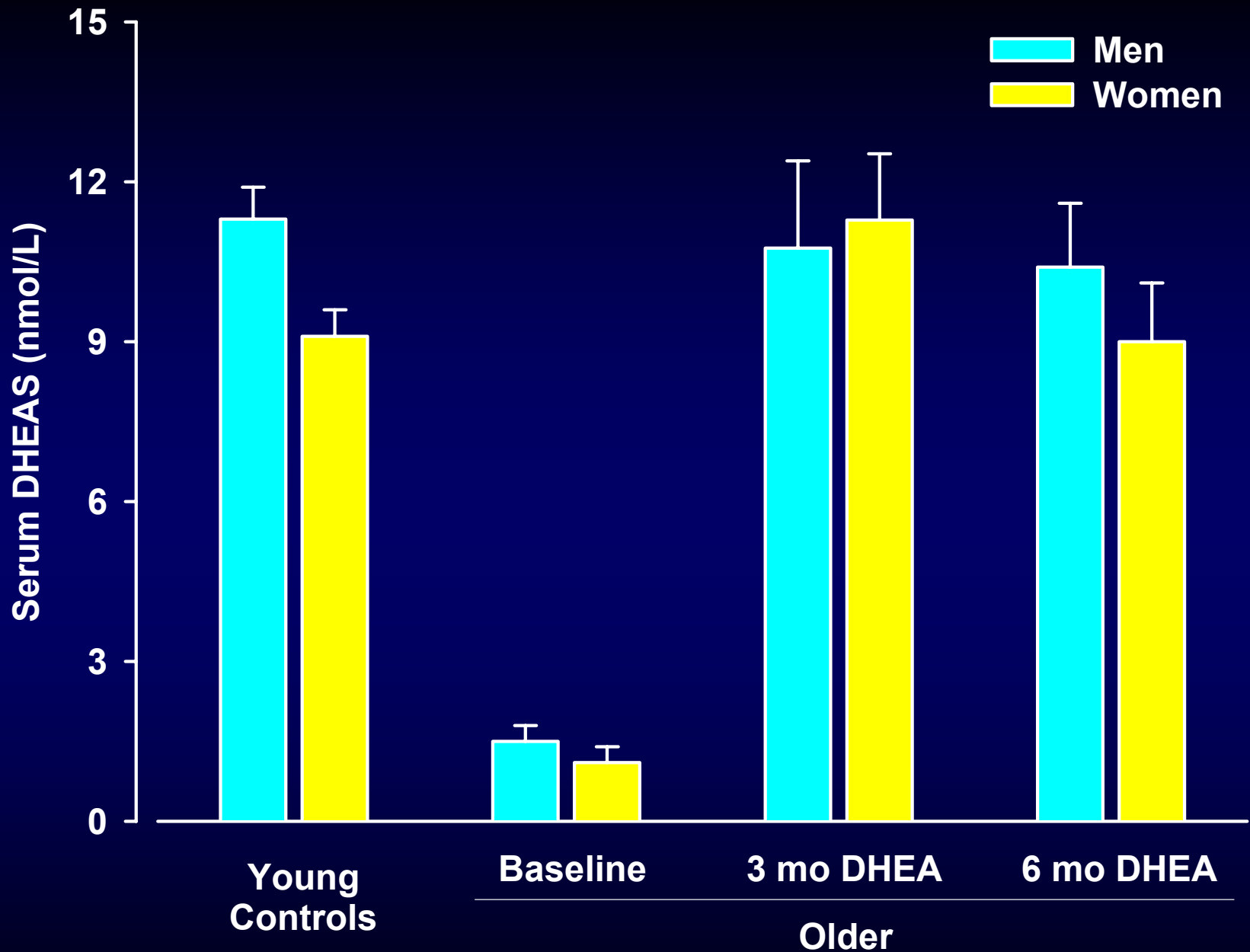
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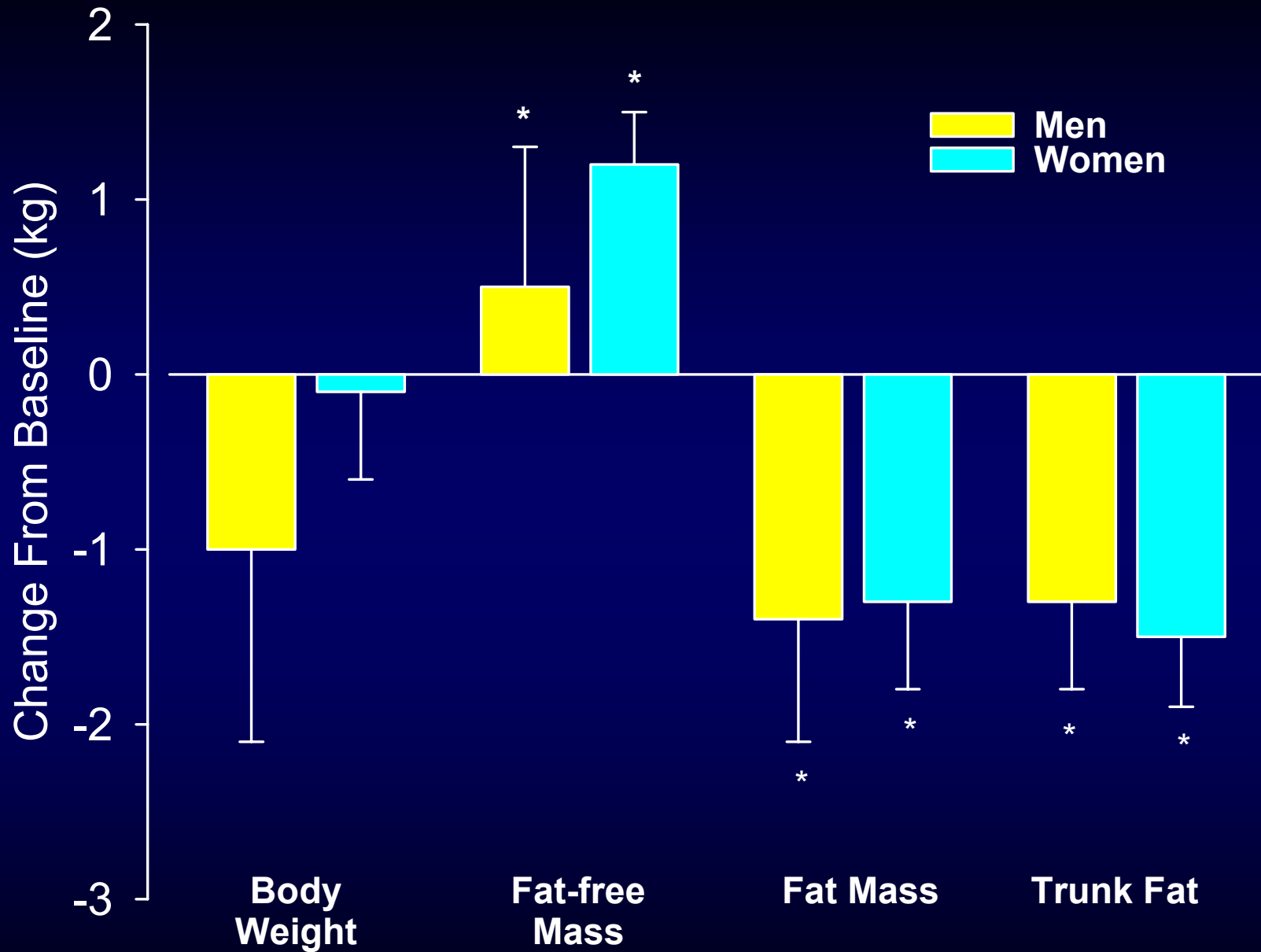
	M/W	Age	Treat	Results
Morales et al. (2 W, facial hair)	13/17*	40-70	3 mo 50 mg	↑ IGF-1 ↓ HDL-C (W) ↑ well-being
Morales et al. (no AE)	8/8*	50-65	6 mo 100 mg	↑ IGF-1 ↑ FFM ↓ FM (M)
Casson et al. (no AE)	0/13	>50	6 mo 25 mg	↑ IGF-1 ↓ HDL-C
Villareal et al. (1 W, acne)	16/20	64-82	6 mo 50 mg	↑ IGF-1 ↑ FFM, BMD ↓ FM
Baulieu et al. (no AE)	140/140	60-79	12 mo 50 mg	??

Effects of DHEA Replacement on Bone Mineral Density and Body Composition in Elderly Women and Men

Villareal DT et al. *Clin Endocrinol* 53:561-568, 2000

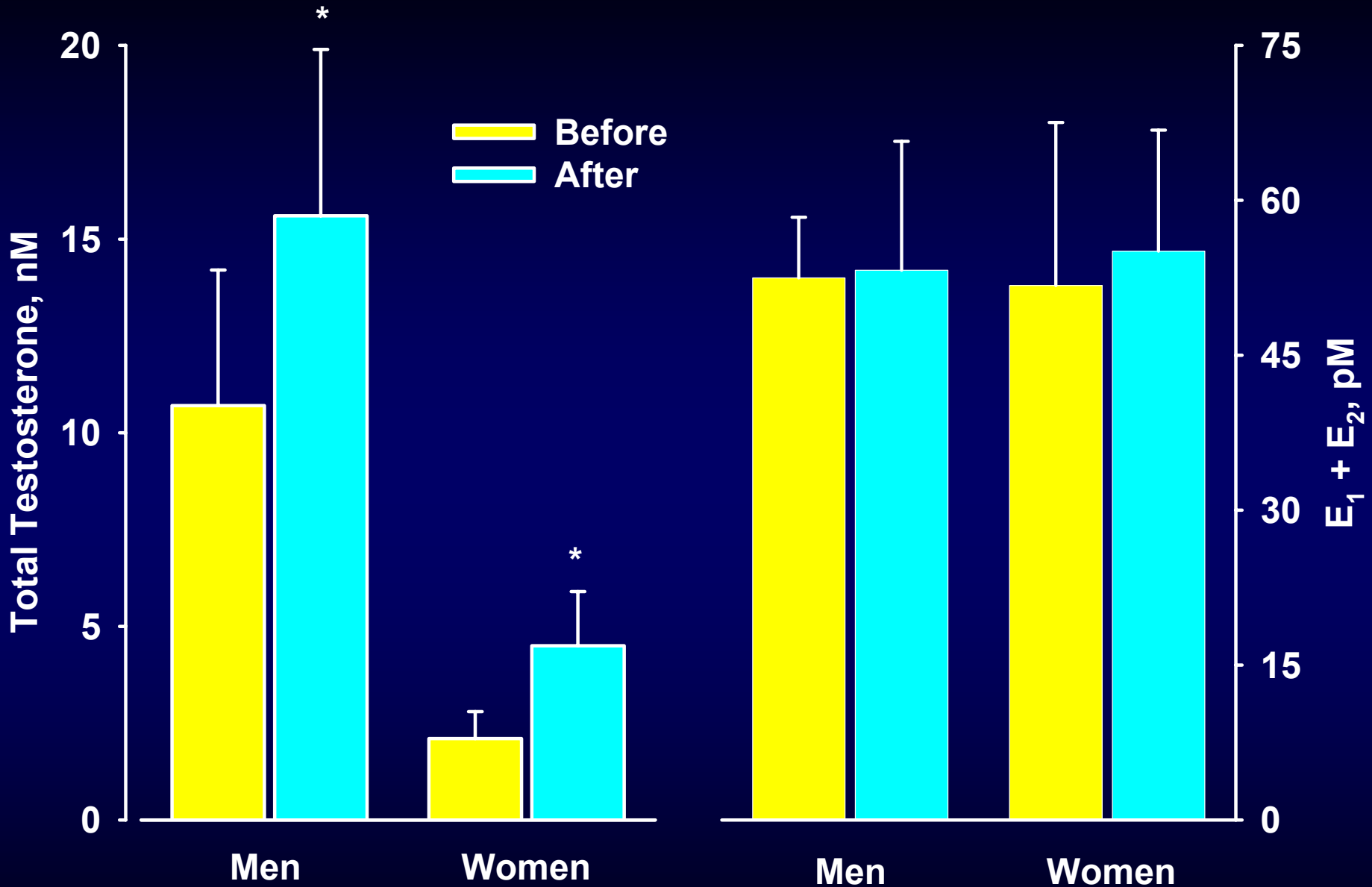
- ❖ open-label study of oral **DHEA replacement, 50 mg/d**
- ❖ 10 women, 8 men; aged 64 to 82 yr (18 sex- and age-matched convenience controls)
- ❖ serum DHEAS <20% of mean value in young subjects

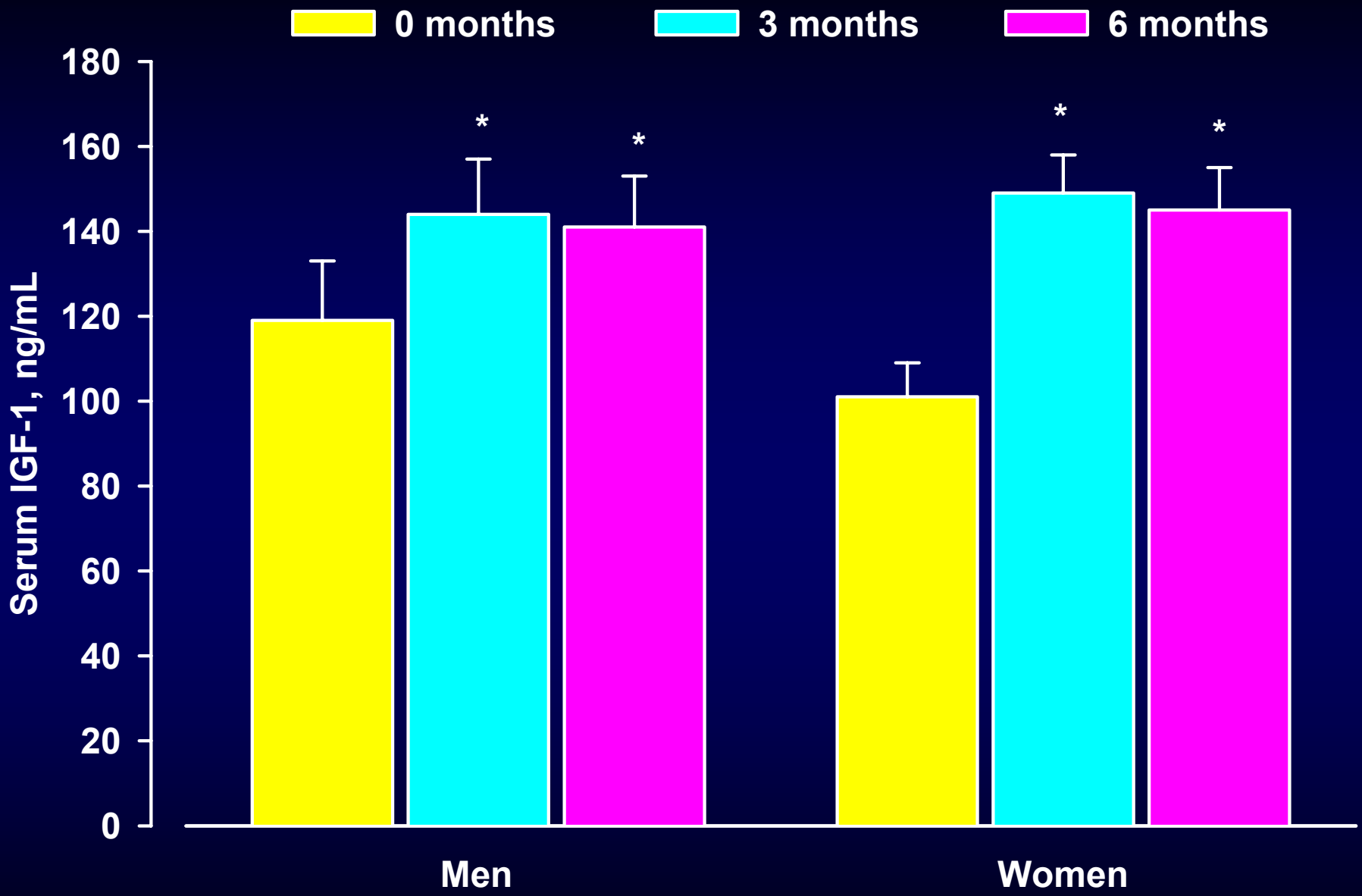






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Summary

- ❖ There have been few controlled trials of DHEA supplementation. Available data do not provide evidence that DHEA enhances performance.

Summary

- ❖ There are intriguing data that suggest that DHEA supplementation (replacement) can increase lean mass and decrease fat mass, but these findings are not uniform. Potential mechanisms include increases in androgens and/or growth factors in response to DHEA.

Future Research Directions

- ❖ In general, additional controlled trials are needed to better understand the sex- and age-specific responses to DHEA supplementation and the mechanisms of action.
- ❖ Preliminary studies should evaluate potential effects of DHEA supplementation in eugonadal and hypogonadal athletes.