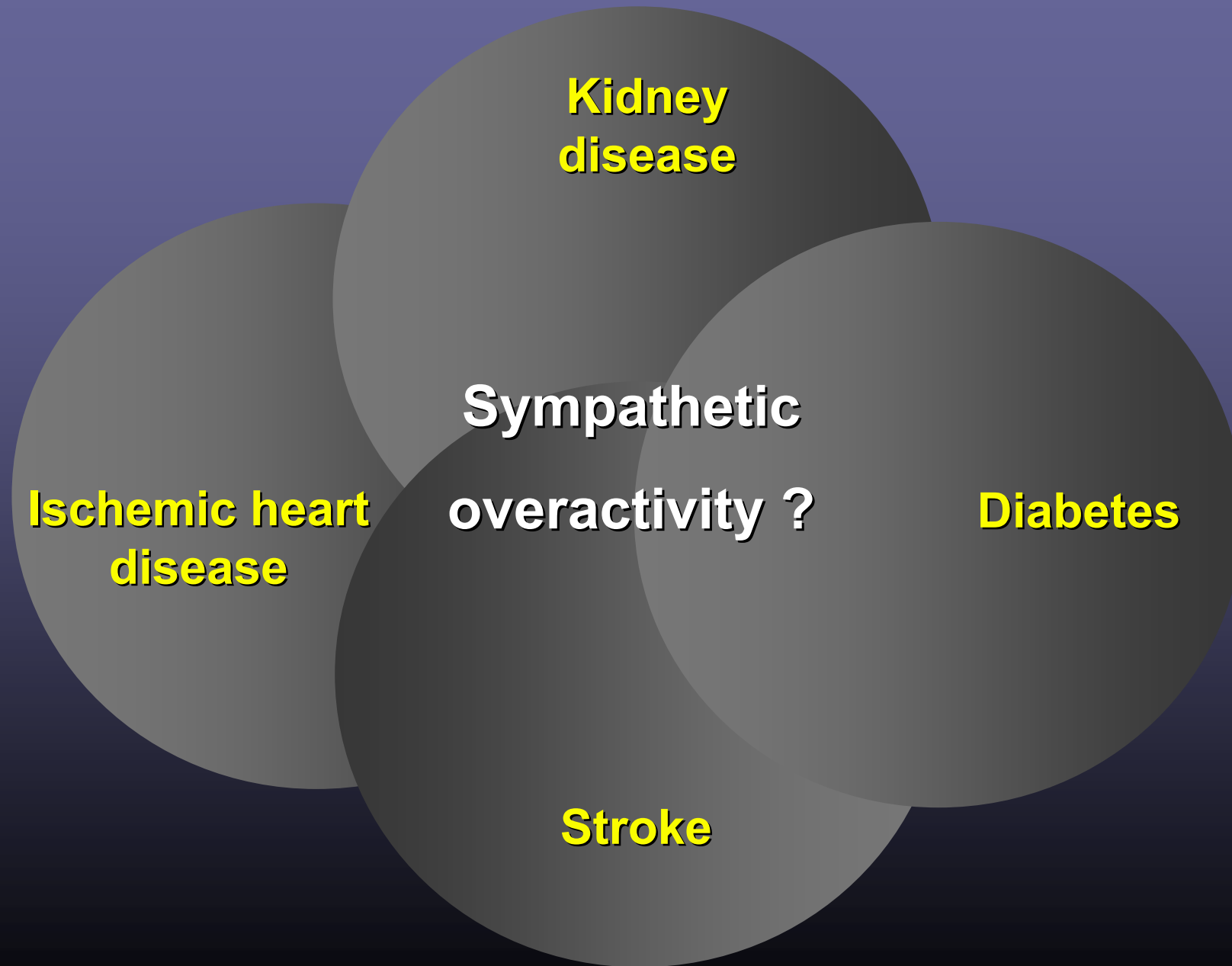
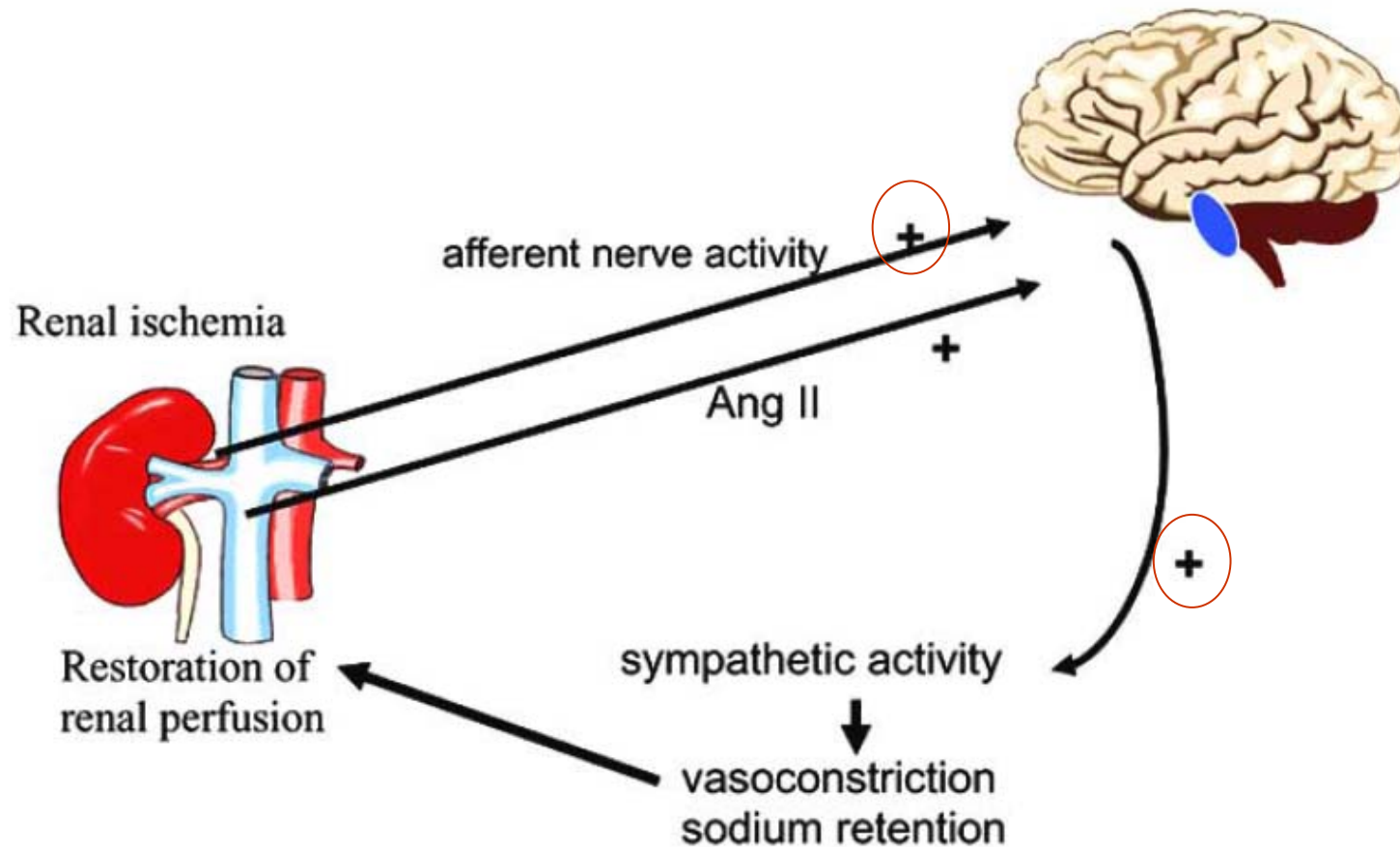


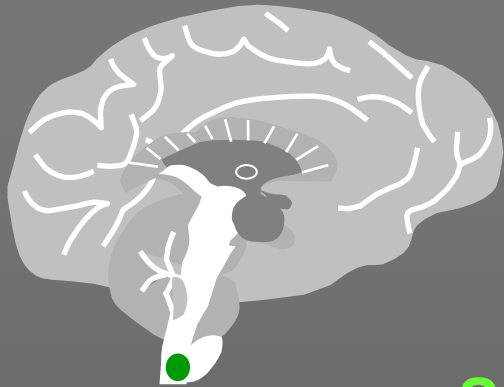
Pathophysiological links?





Already minimal kidney damage, not necessarily affecting kidney function, results in area(s) of ischemia. Increased plasma levels of Ang II and/or increased afferent renal nerve activity stimulates the central nervous system to increase central sympathetic outflow, which results in sodium retention and vasoconstriction which are meant to restore kidney perfusion.

SNS overactivity: From wire to pill



Sympatholytic (moxonidine)



Sympathetic denervation



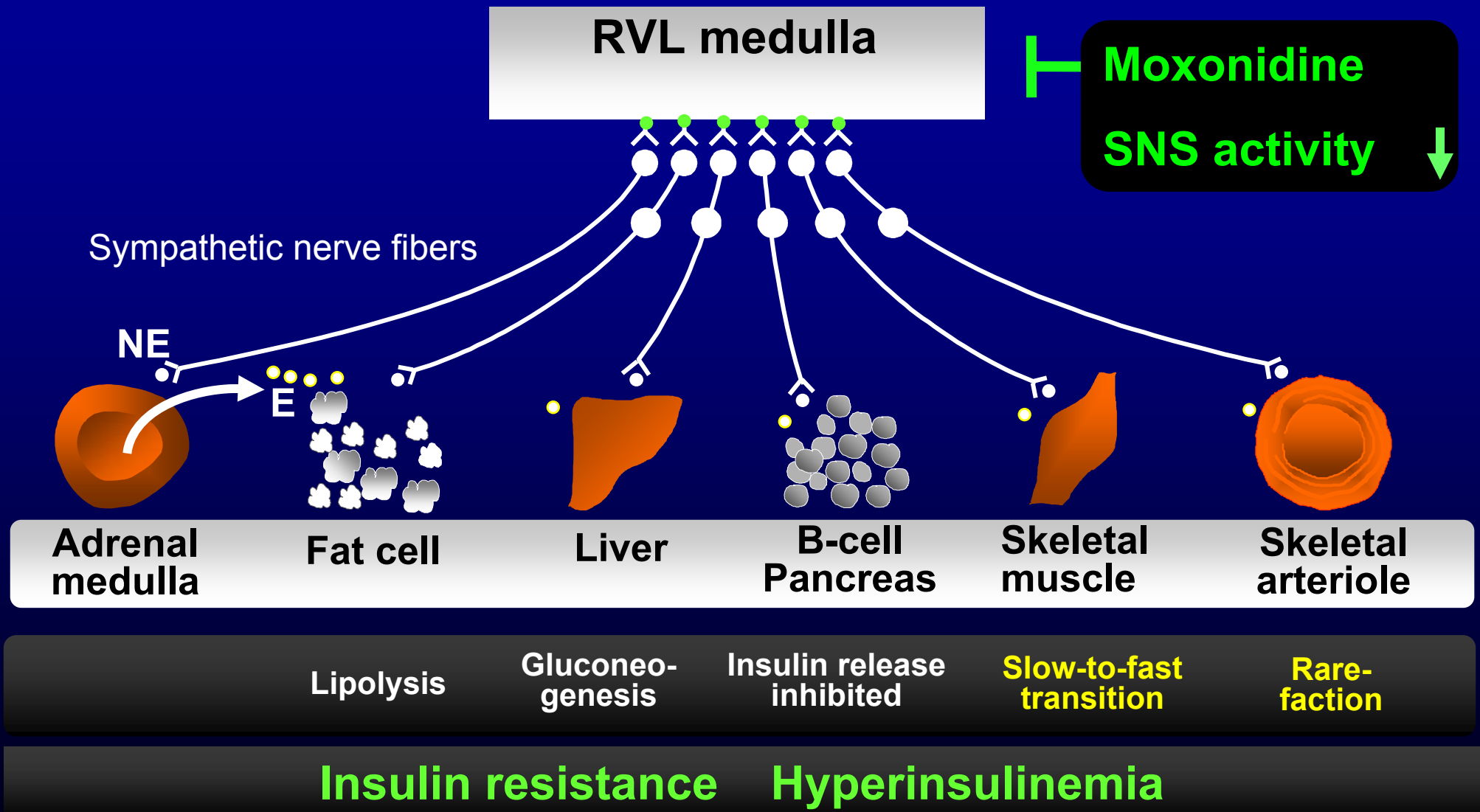
**Renin
increased**



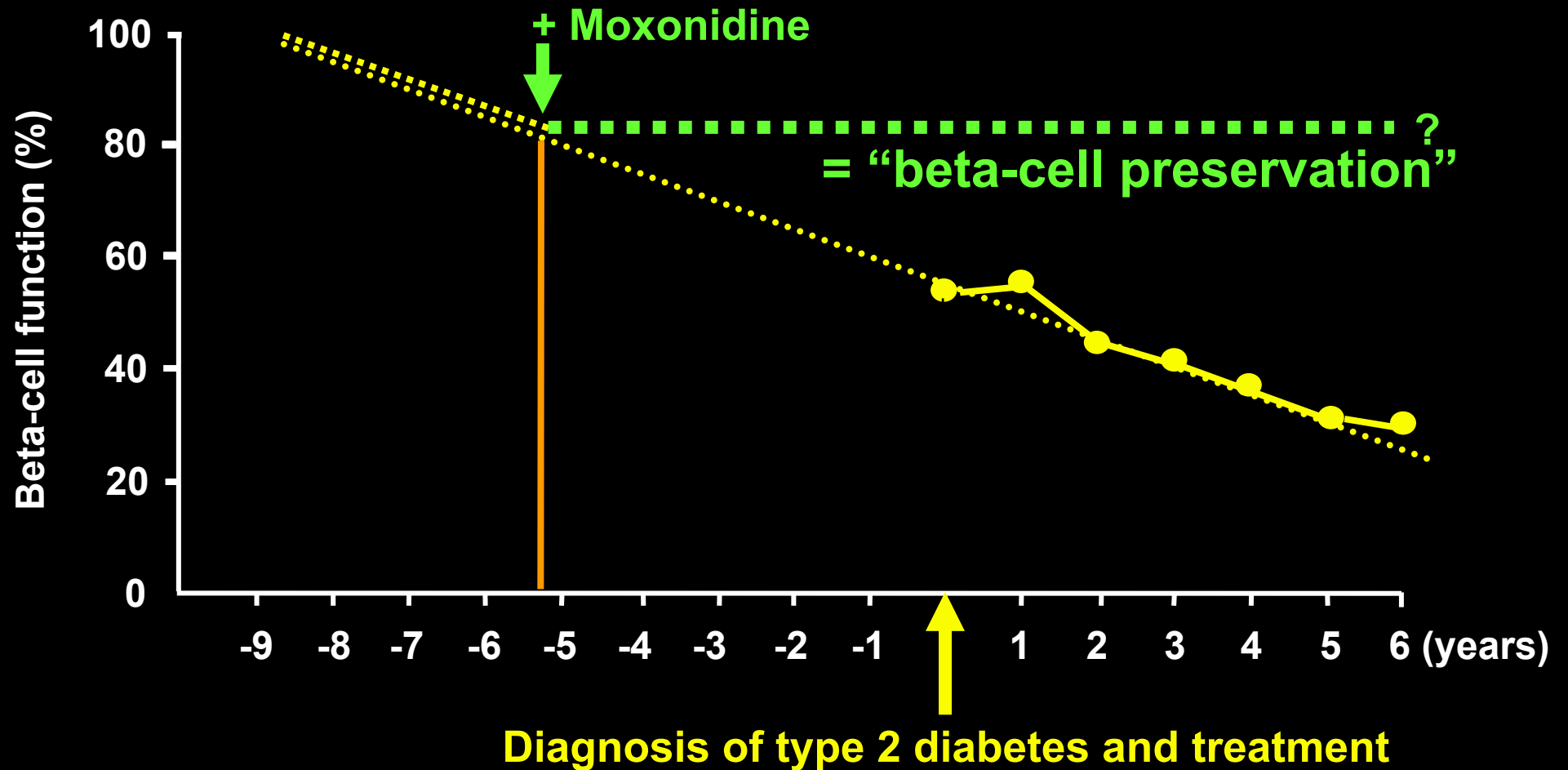
Hypertension

**CHD
Kidney disease
Stroke**

Chronic SNS Overactivity: Insulin Resistance and Hyperinsulinemia

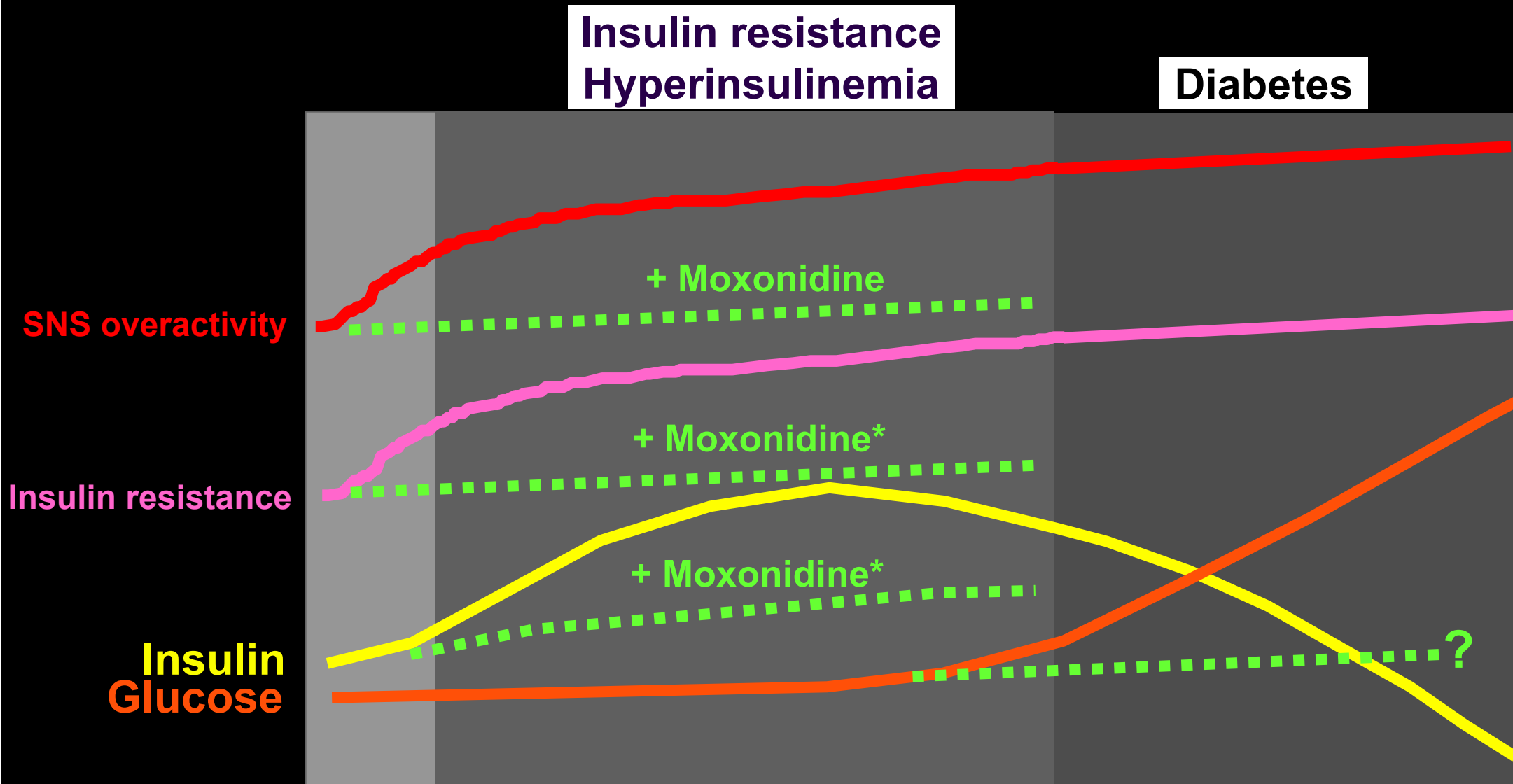


Beta-cell Preservation by Enhancing the Insulin Sensitivity



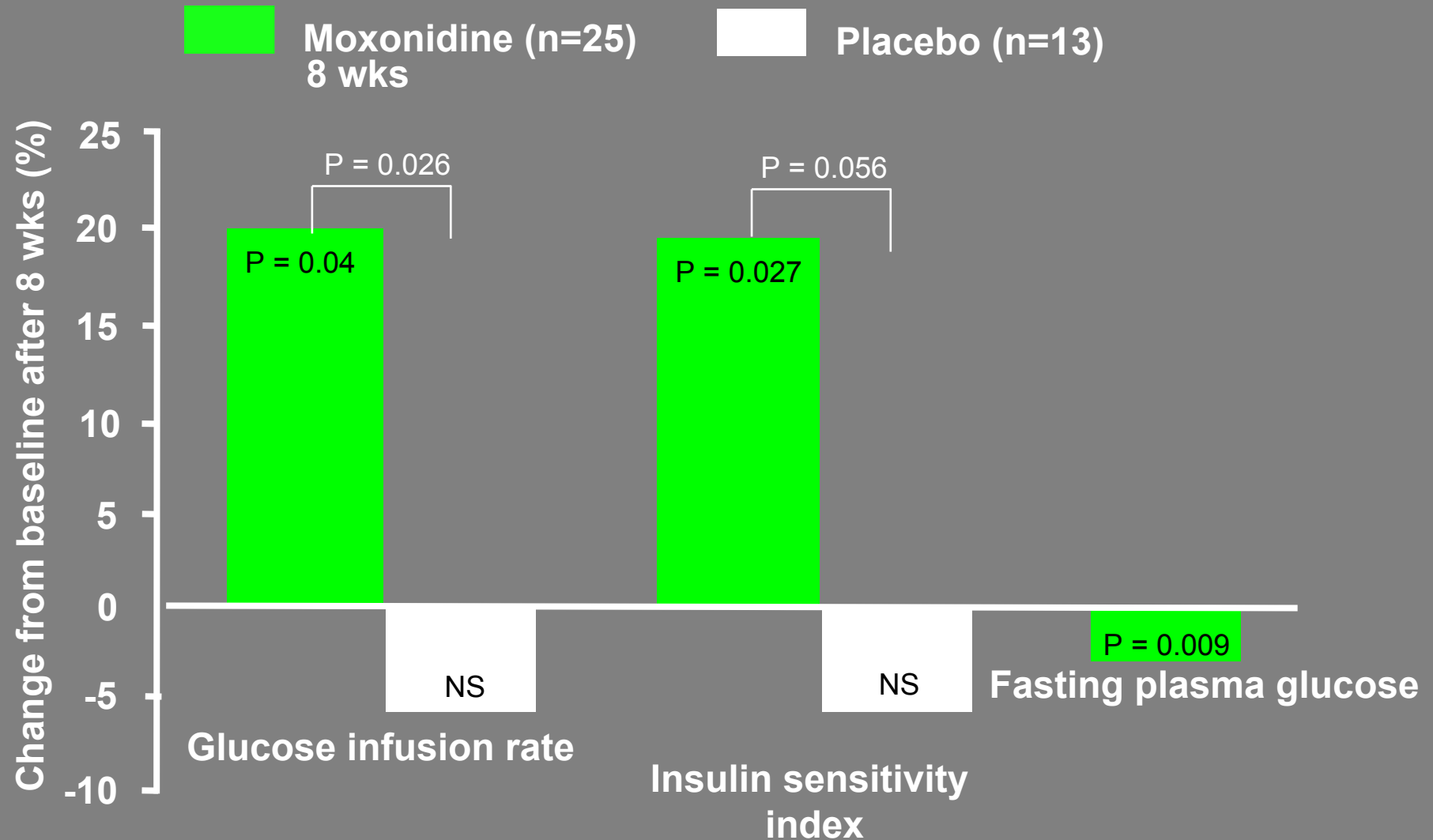
Glucose Intolerance is a Continuum

From Early Endocrine Disturbances (Pre-diabetes) through Clinical Diabetes Stage to Development of Diabetic Complications

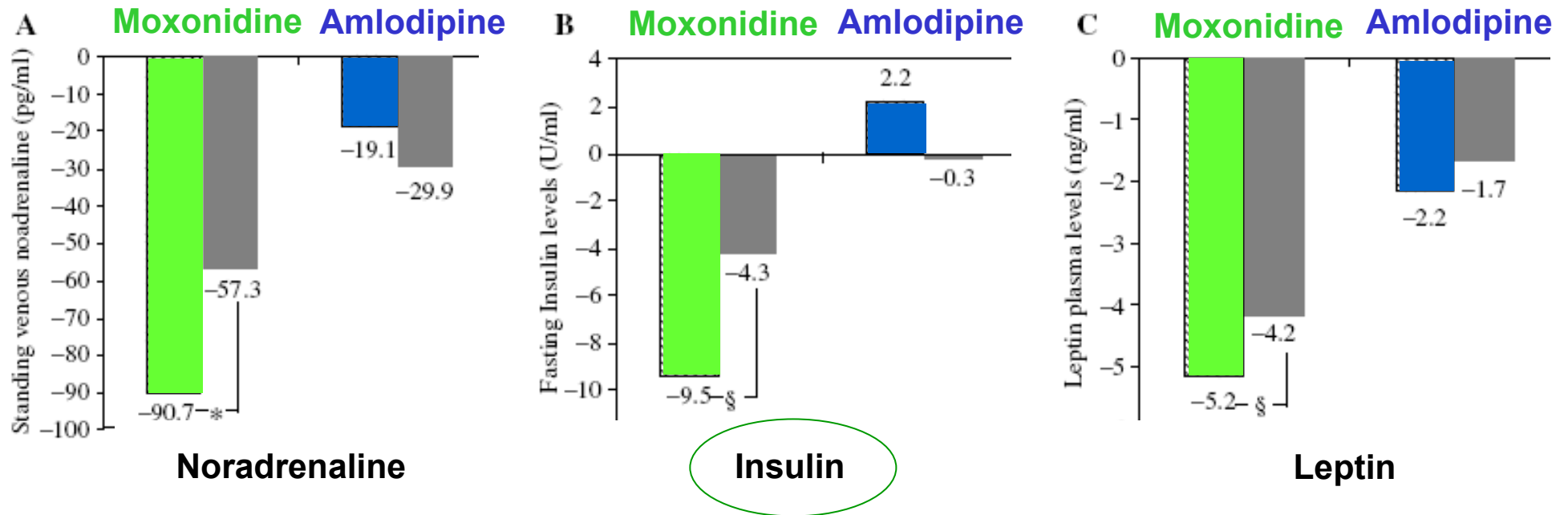


*based on Haenni A & Lithell H. J Hypertens Suppl 1997;17:S29-35

Increased Insulin Sensitivity after Moxonidine Treatment Overweight Insulin-resistant Hypertensives Euglycemic Hyperinsulinemic Clamp



Norepinephrine and Insulin Obese Hypertensives before and after Moxonidine and Amlodipine



Moxonidine responders: <140 and <90 mmHg
Amlodipine responders: <140 and <90 mmHg

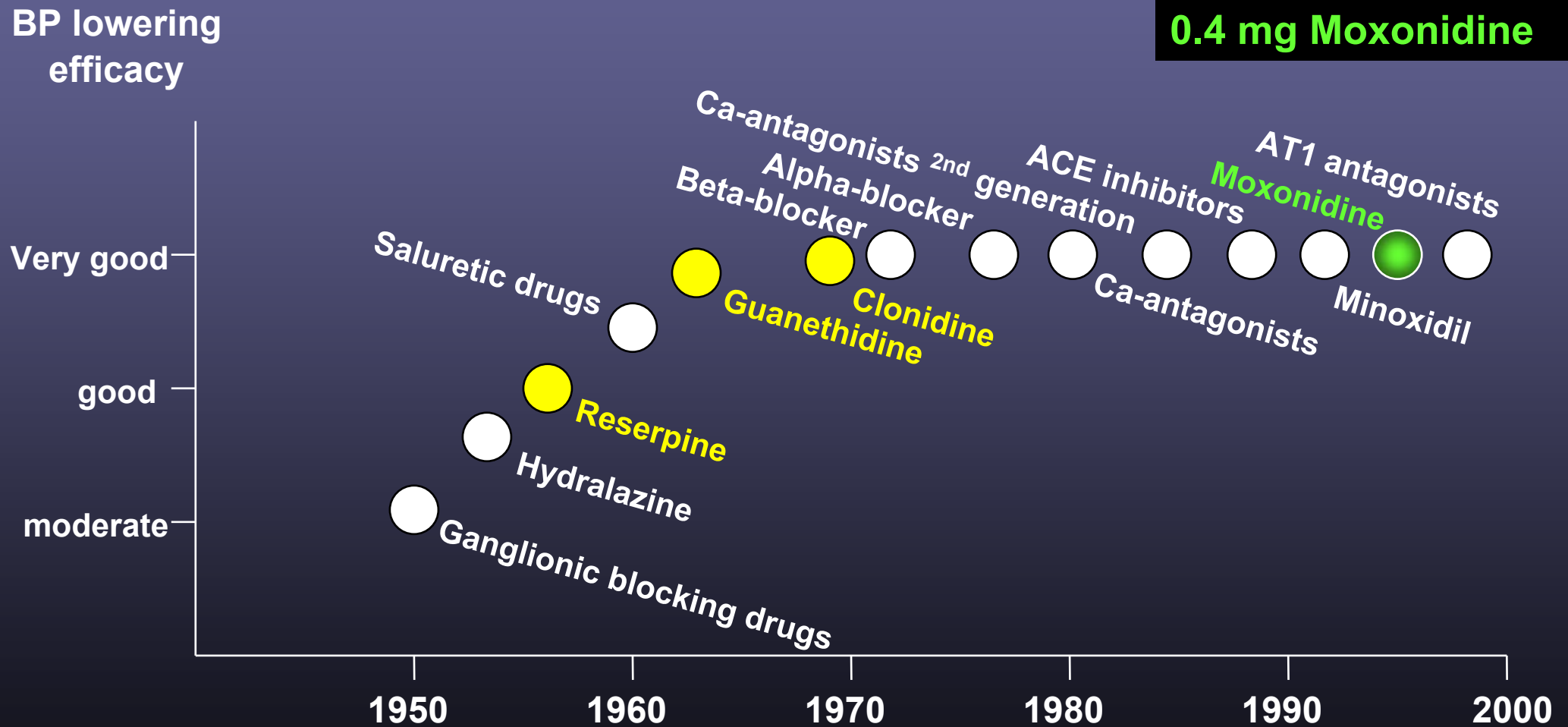
Moxonidine (but not CCBs) interferes with the time-course of diabetes

Glucose: 99 mg/dl
BMI: 35

ESH - Hypertension Management: Beneficial Combinations (selection)

Drugs	Potential use
Diuretics + ACE-inhibitors	Hypertension + congestive heart failure (CHF)
Diuretics + AT1-blockers	Isolated systolic hypertension (ISH) + CHF Possibly: ISH
Diuretics + imidazoline (I1)-receptor agonists	To be used when an α-blocker (contra-indications) cannot be added to a diuretic
Diuretics + calcium-antagonists (dihydropyridines)	ISH (usually elderly patients)
α -blockers + ACE-inhibitors	Hypertensives: post MI (sec. prevention) CHD, CHF
Ca-antagonist + α -blockers	Hypertension + CHD
Ca-antagonist + ACE-inhibitors	Hypertension + nephropathy, CHD or atherosclerosis
Ca-antagonists + AT1-blockers	Hypertension + nephropathy, CHD or atherosclerosis (?)
ACE-inhibitors + AT1-blockers	Hypertension + nephropathy
ACE-inhibitors + imidazoline (I1)-receptor agonists	Patients with activated RAAS and SNS
Diuretics + calcium antagonists + ACE-I	Accelerated hypertension ISH, hypertension + diabetes mellitus
Diuretics + calcium antag.+ AT1-antagonists	Ibid.
ACE-I + α1-blockers + imidazoline (I1)-receptor agonists	Hypertension + diabetes mellitus. Metabolic syndrome

Modern Antihypertensive Drugs with Similar Efficacy



modified after F Gross

High caloric intake
Psychosocial stress
Kidney ischemia



Hypertension



CV & renal disease

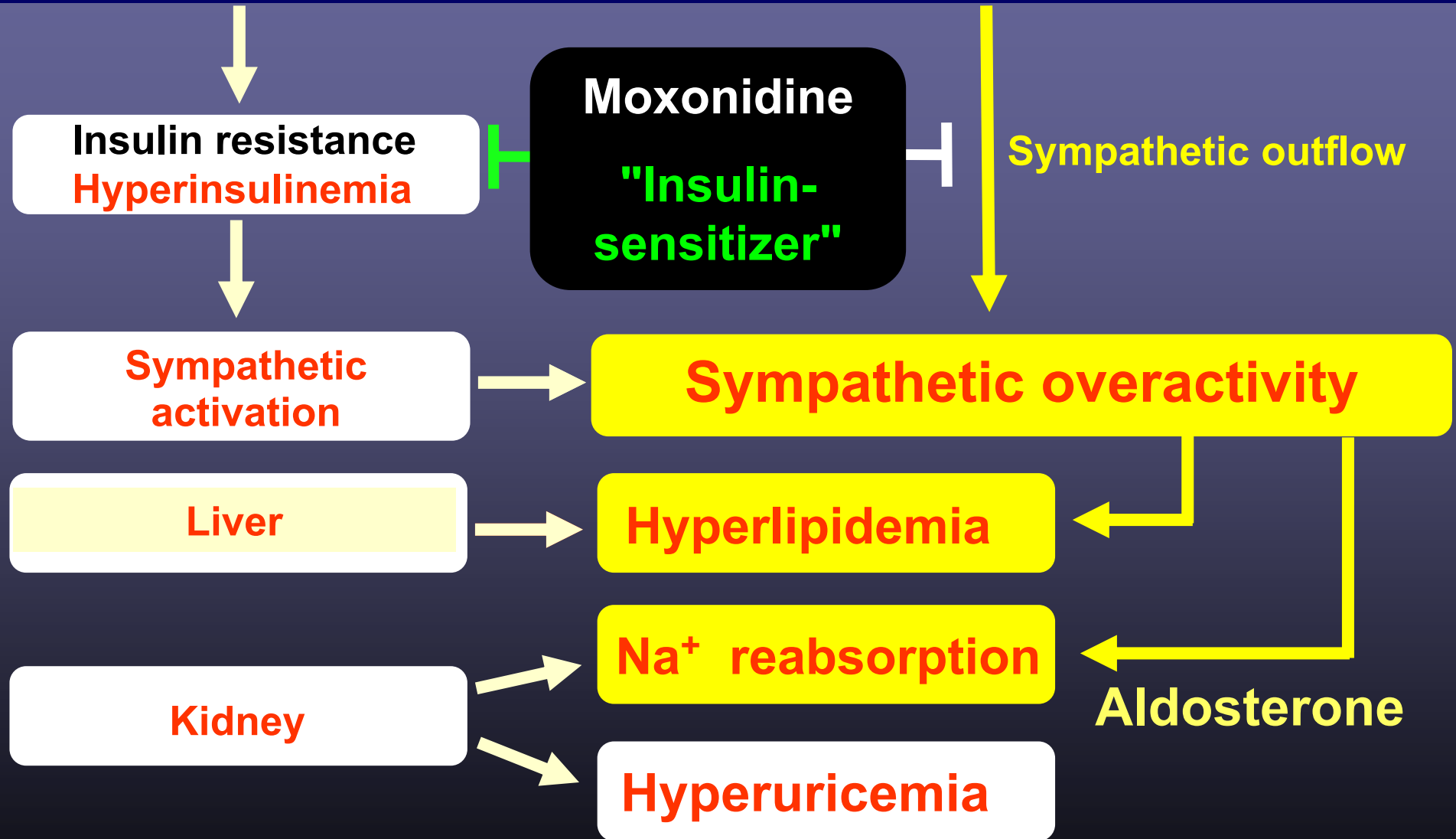
Insulin resistance



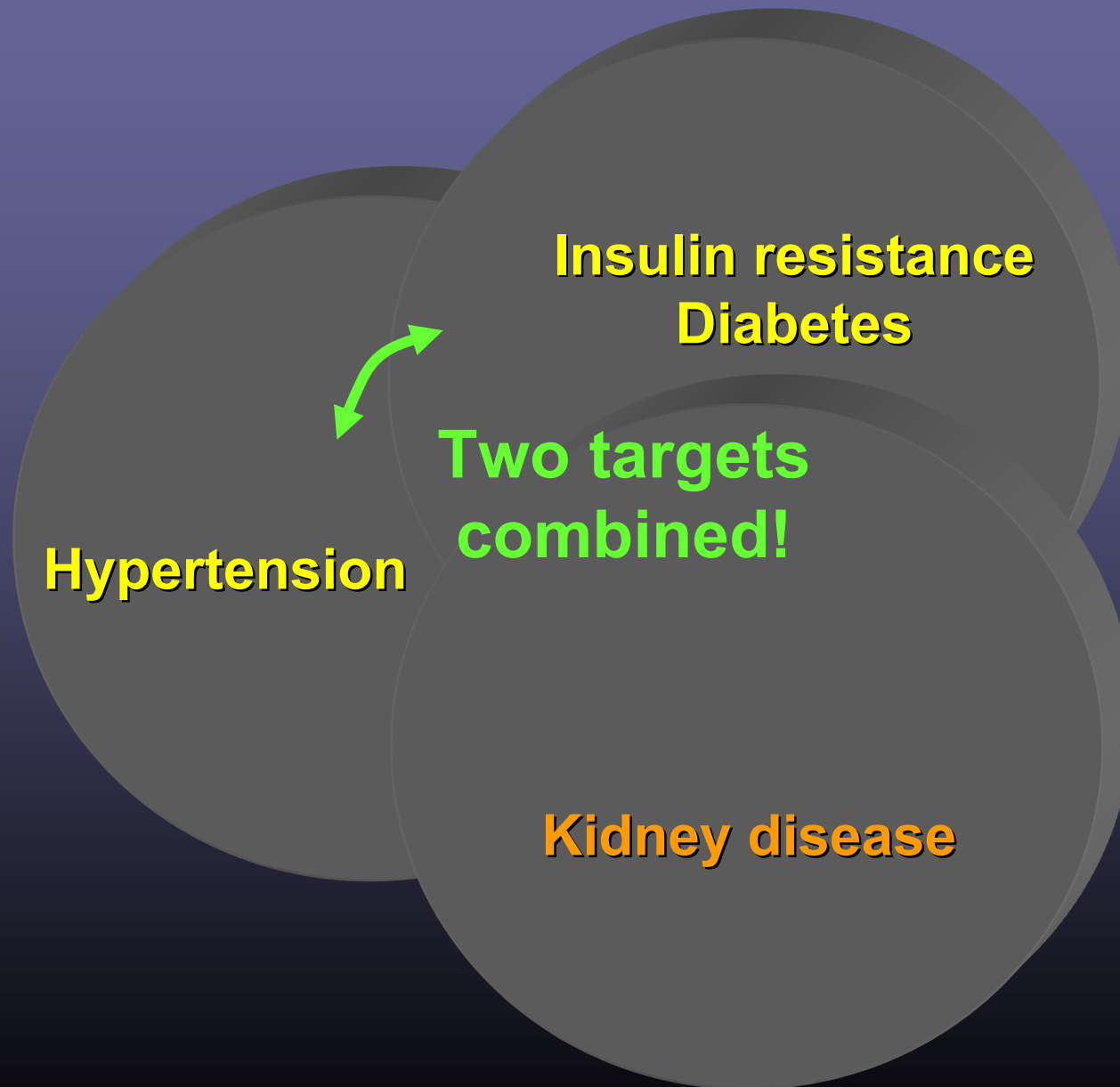
DM-2

ACE-I / ARB
Moxonidine

Sedentary Lifestyle ... High Caloric Intake ... Psychosocial Imbalance ... Postmenopause



Treatment Targets of Moxonidine



Challenges for the Next Decade

Be Aware of Kidney Ischemia

Therapy for hypertension ?

Therapy for insulin resistance / type 2 diabetes !

- go for the symptoms ?

-go with which guidelines ?

- **go for the causes**

don't ignore SNS overactivity - „from wire to pill“