

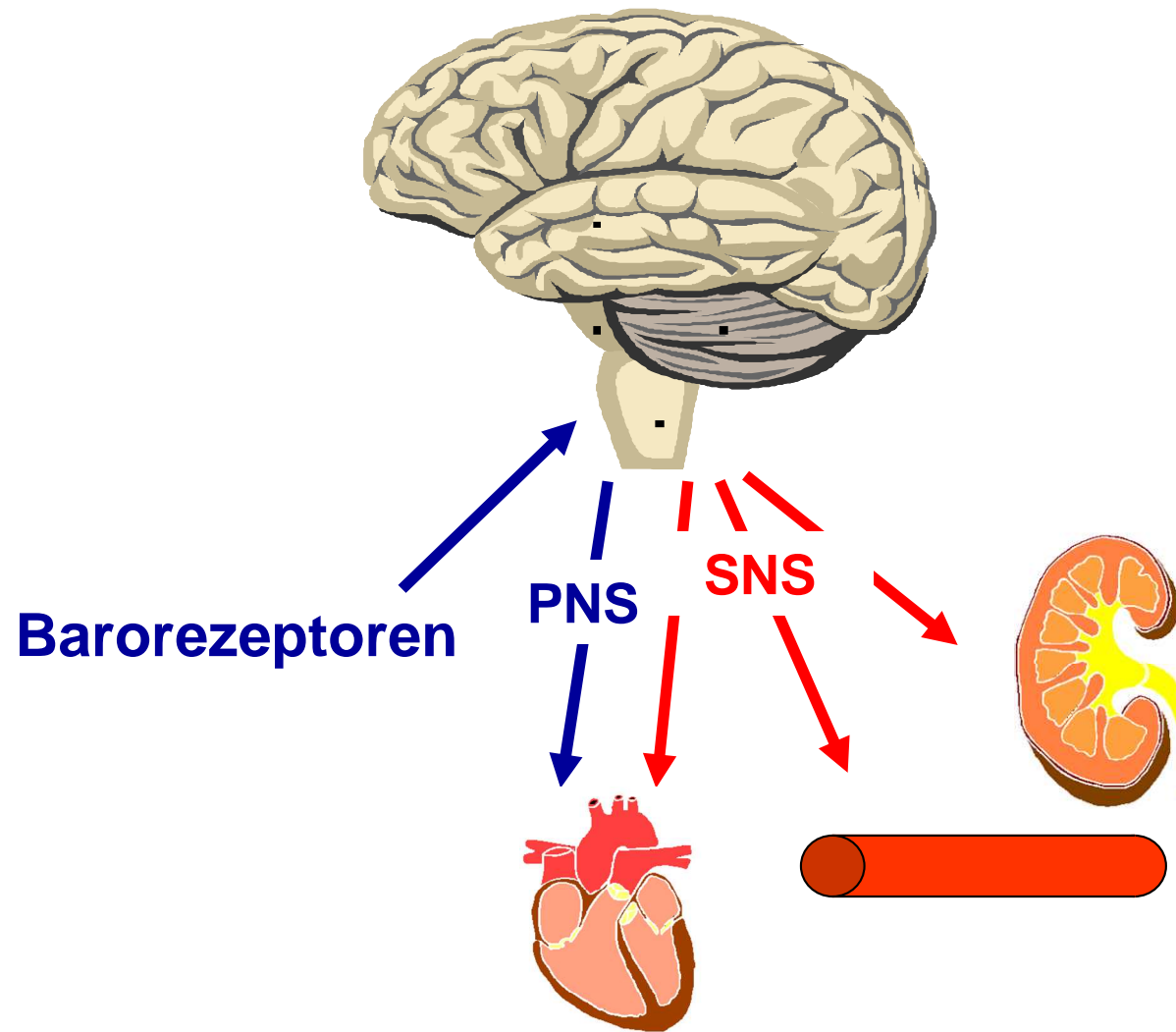
Wenn der Baroreflex streikt

Prof. Dr. med. Jens Jordan

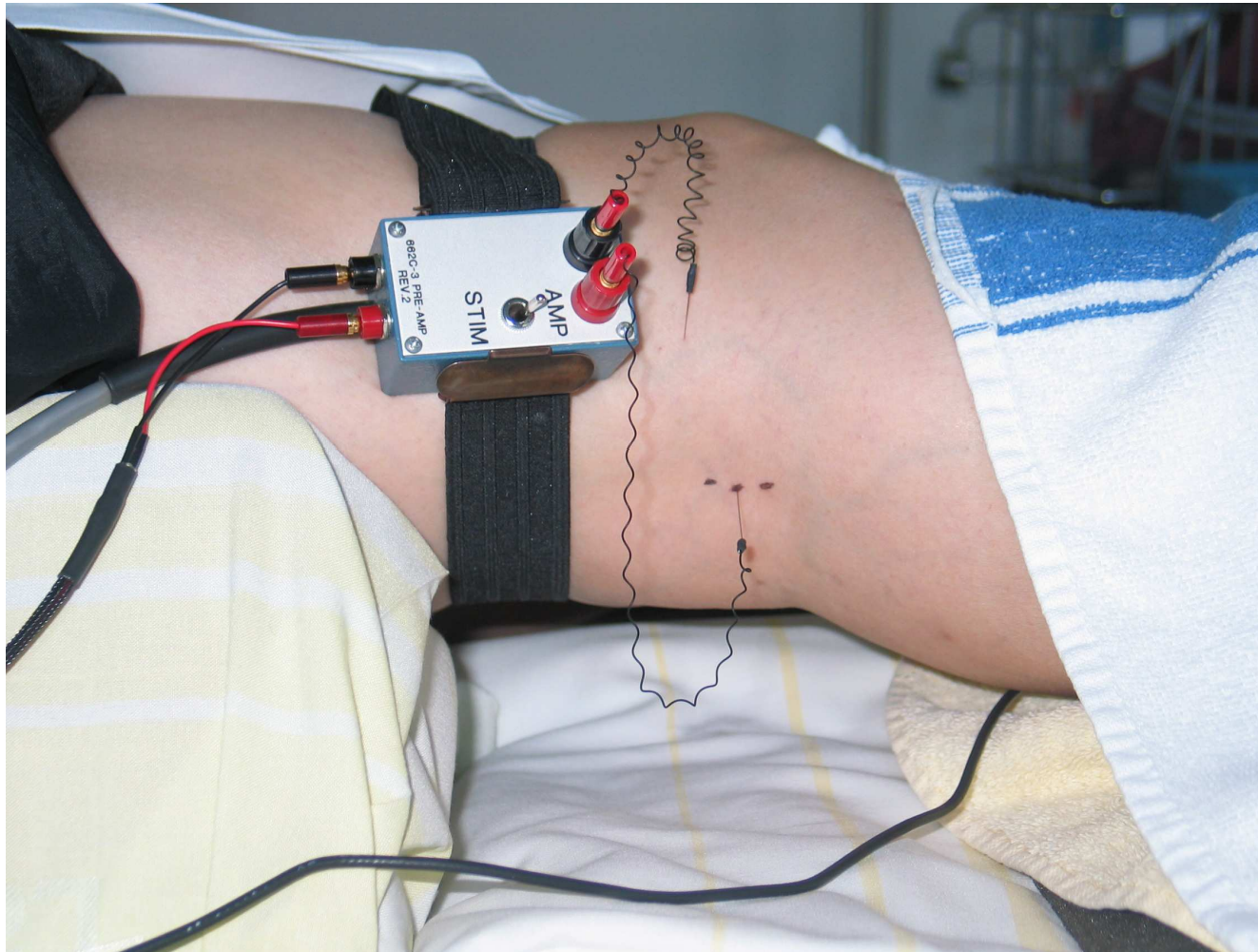


Medizinische Hochschule
Hannover

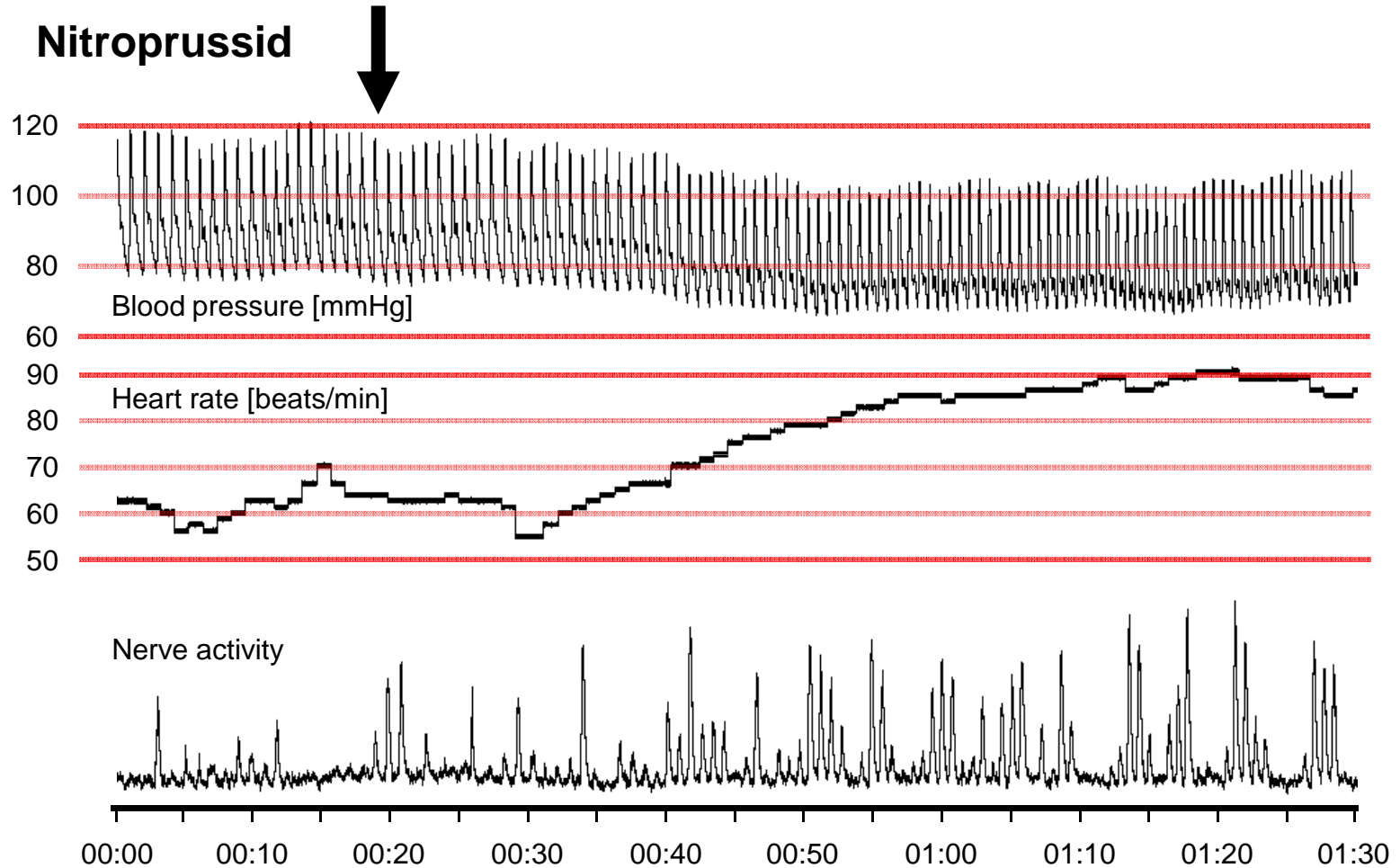
Baroreflexregulation



Was sagt der Baroreflex dem Blutgefäß?



Baroreflexregulation bei Gesunden



Störungen der Baroreflexregulation - Klinik

Diagnostik und Therapie:

- **Baroreflexversagen**
- **Autonomes Versagen**
 - **Zentral**
 - **Peripher**
- **Posturales Tachykardiesyndrom**
- **„Supramaximale“ vasovagale Synkopen**

Wenn der Baroreflex streikt

- **Wenn das Gehirn macht was es will**
- **Der Hexamethonium Mann**
- **Kann man den Baroreflex überlisten?**

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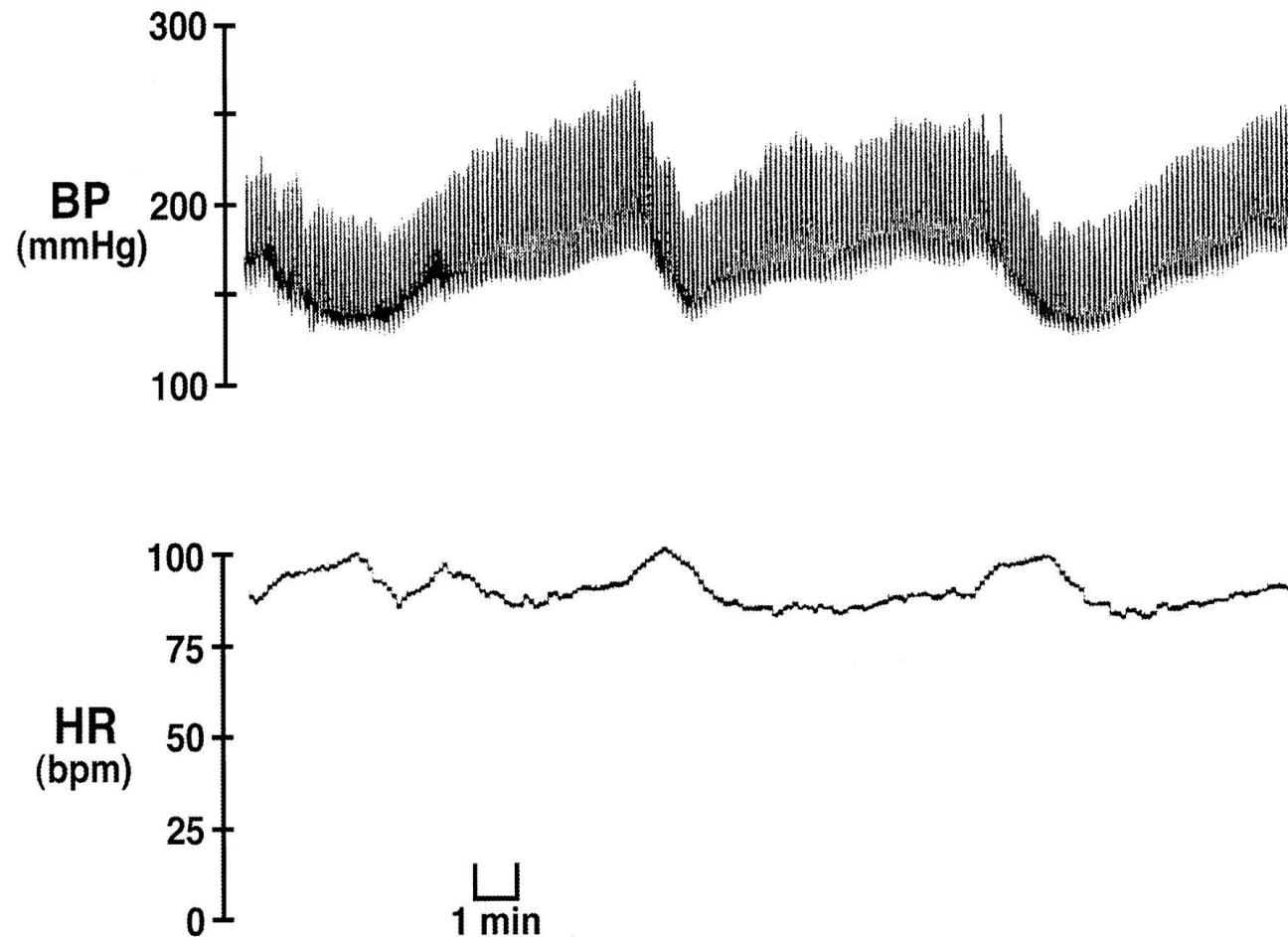
Fallbericht – Patientin 1

- **54-jährige Patientin**
- **In Vergangenheit normotensiv**
- **Trauma im Halsbereich:**
 - **OP: Fusion C4 / C5 and C5 / C6.**
 - **Autounfall, Op: Fusion C6 / C7**
- **Anschließend stark schwankende Blutdruckwerte**
 - **Hypertensive Phasen: 270/140 mm Hg, 120 / min**
 - **Hypotone Phasen: <50 mm Hg, Bradykardie**
 - **Keine orthostatische Hypotonie**

Fallbericht – Patientin 1

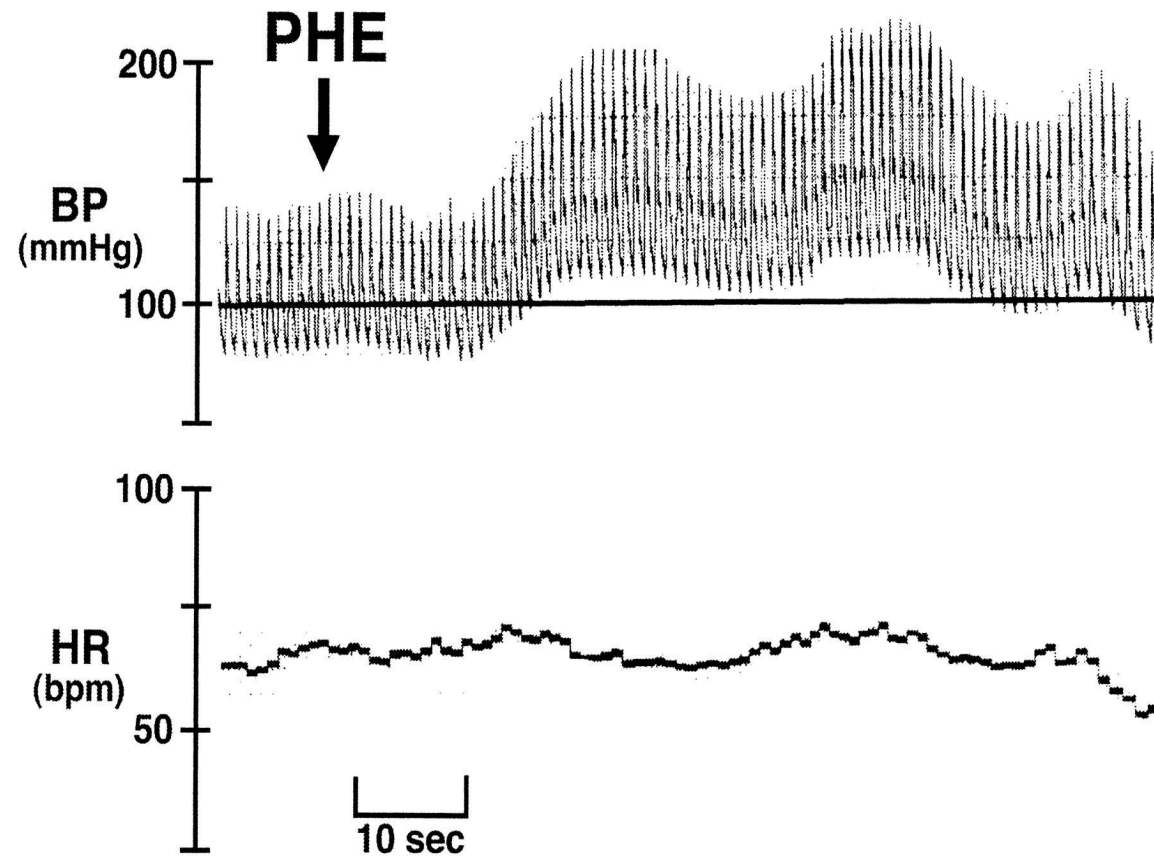
- **Hypersensitivität gegenüber Arzneimitteln:**
 - **Reanimation nach Gabe von Nitroprussid**
 - **Ausgeprägte Hypotonie nach Verwendung von NTG Spray**
 - **Starker Blutdruckabfall nach niedriger Dosis Clonidin**

„Ruheblutdruck“ im Liegen



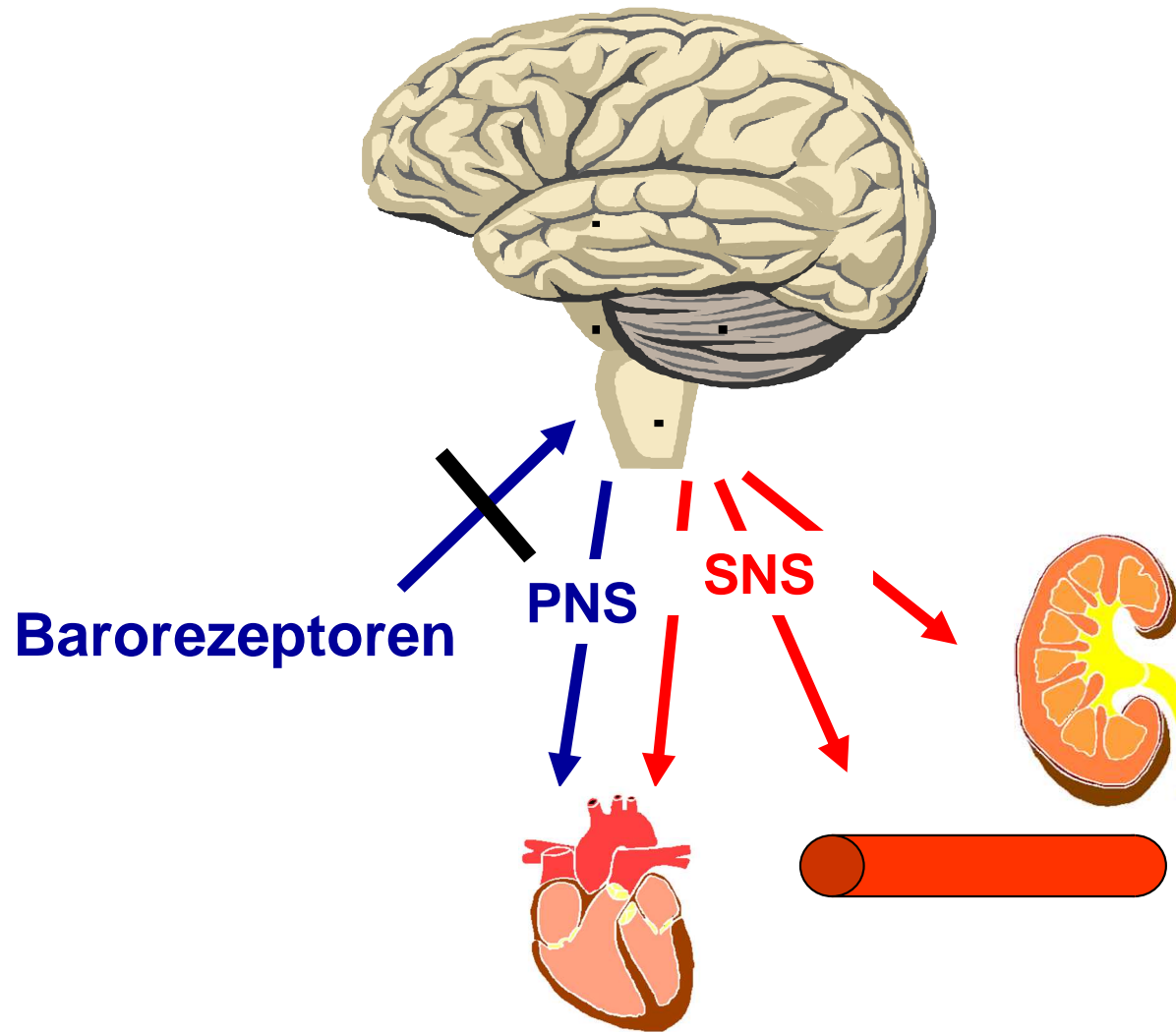
Jordan et al. Hypertension 1997

Phenylephrin Test

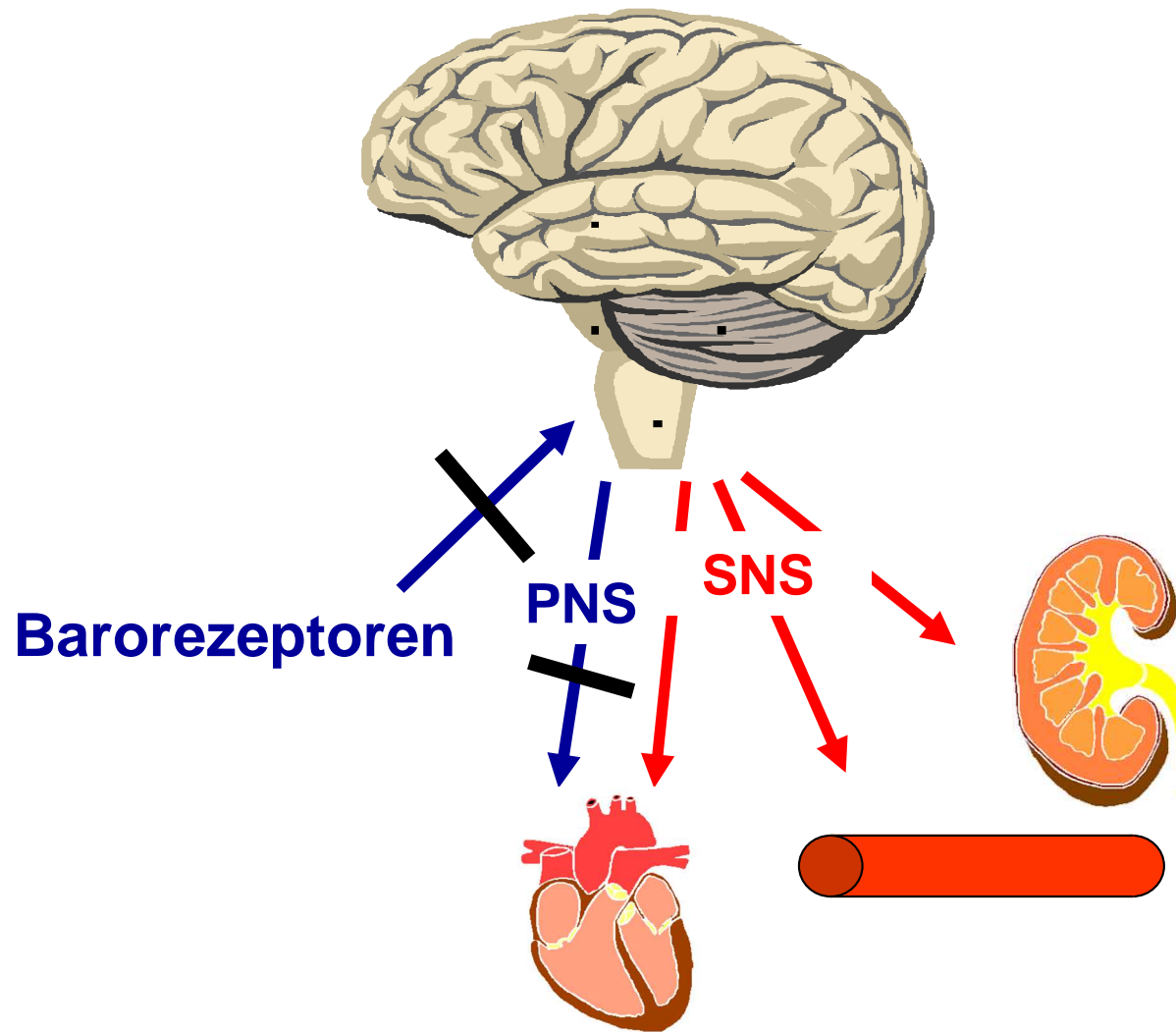


Jordan et al. Hypertension 1997

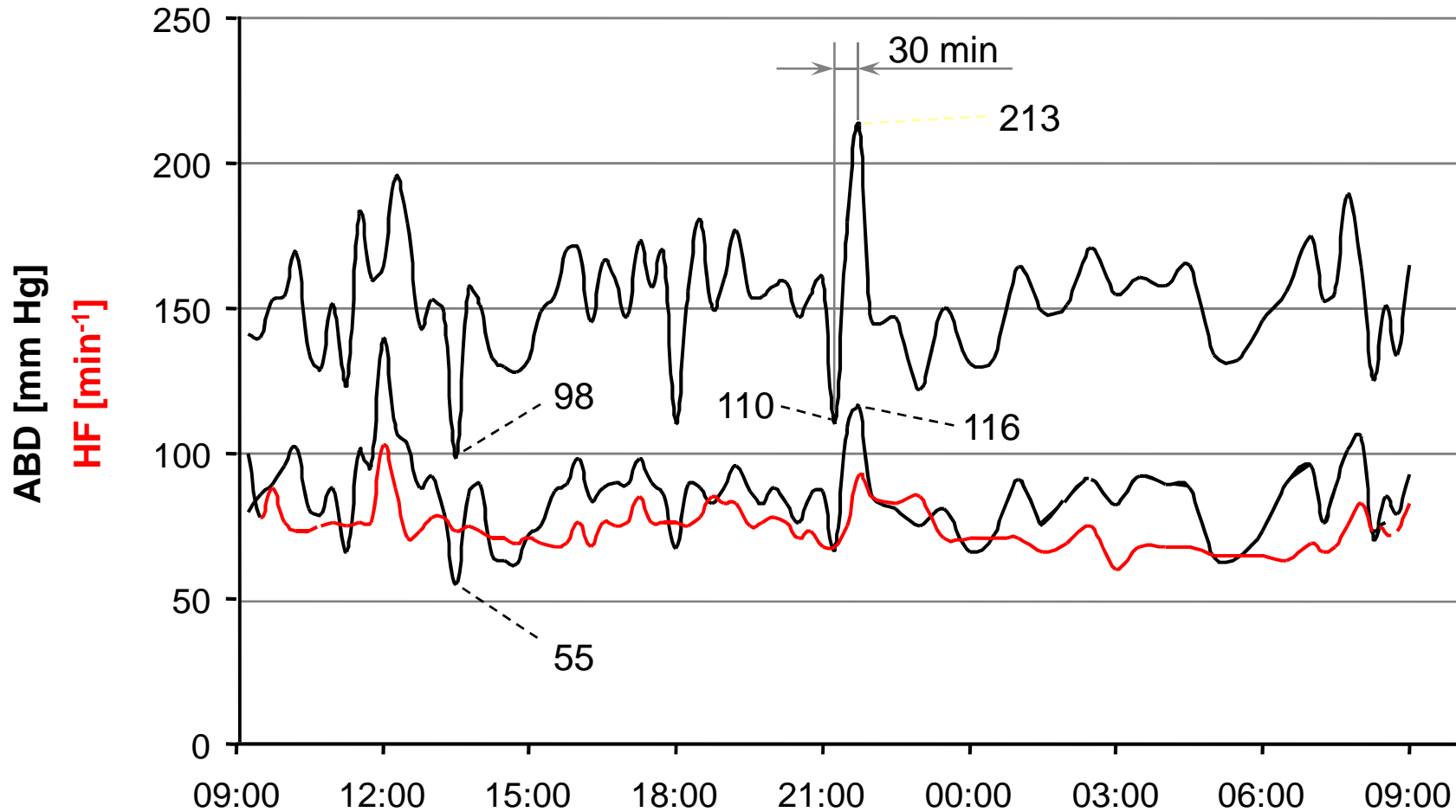
Selektives Baroreflexversagen



Nichtselektives Baroreflexversagen



Baroreflexversagen - 24-h Blutdruck



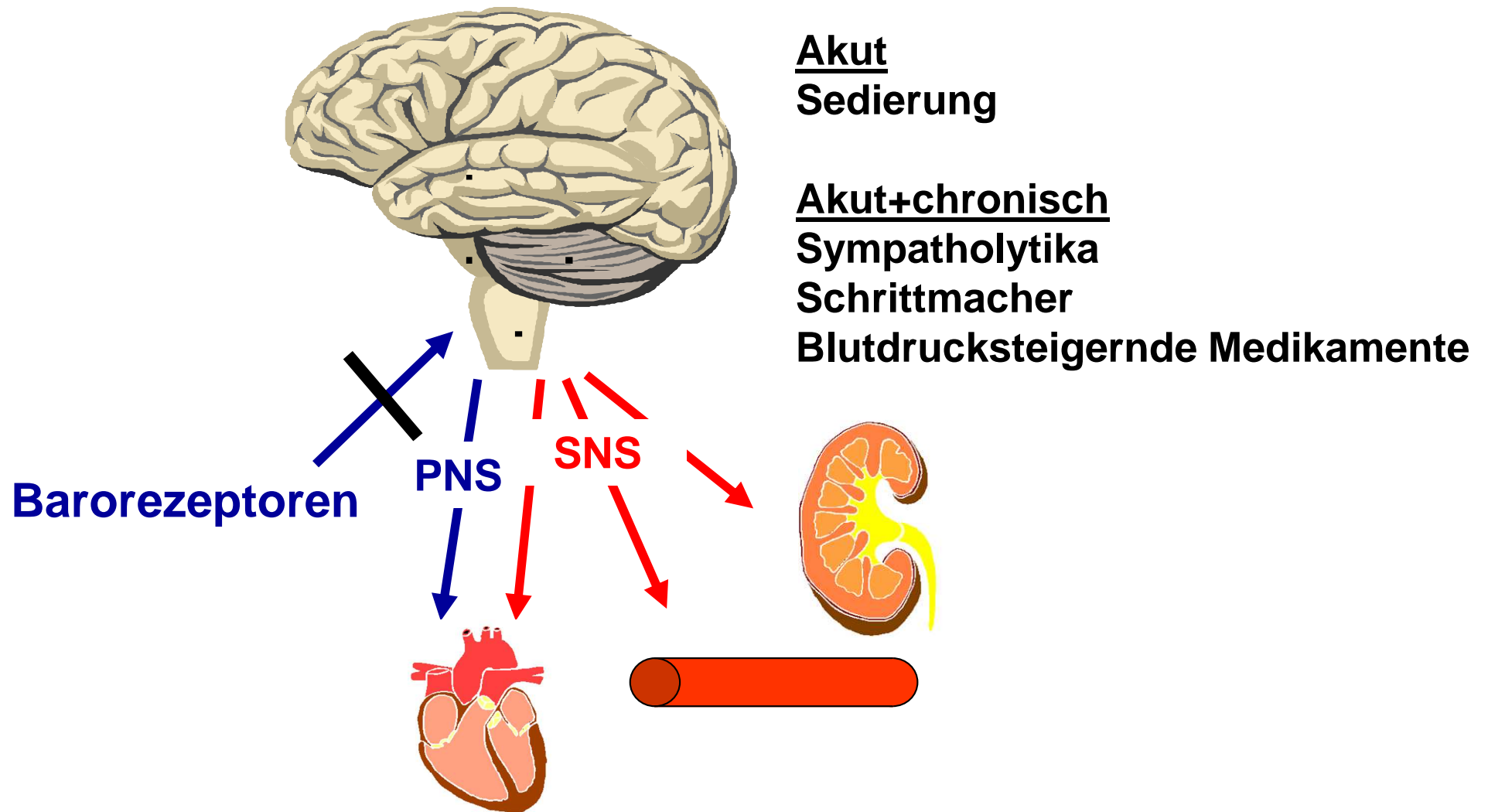
Ursachen von Baroreflexversagen

Halstrauma

- Operationen
- Unfälle
- Strahlentherapie

Neuropathie?

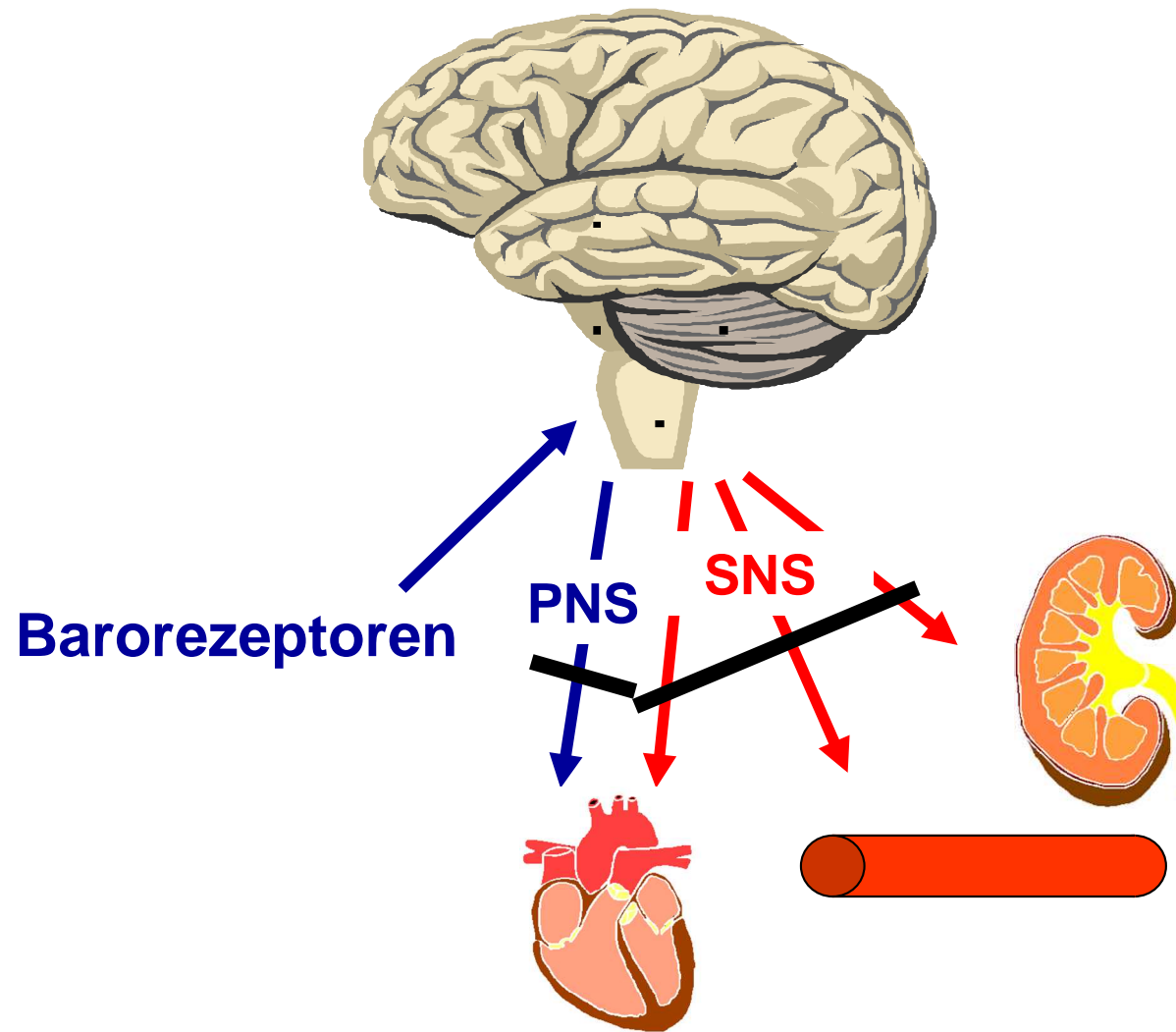
Baroreflexversagen - Therapie



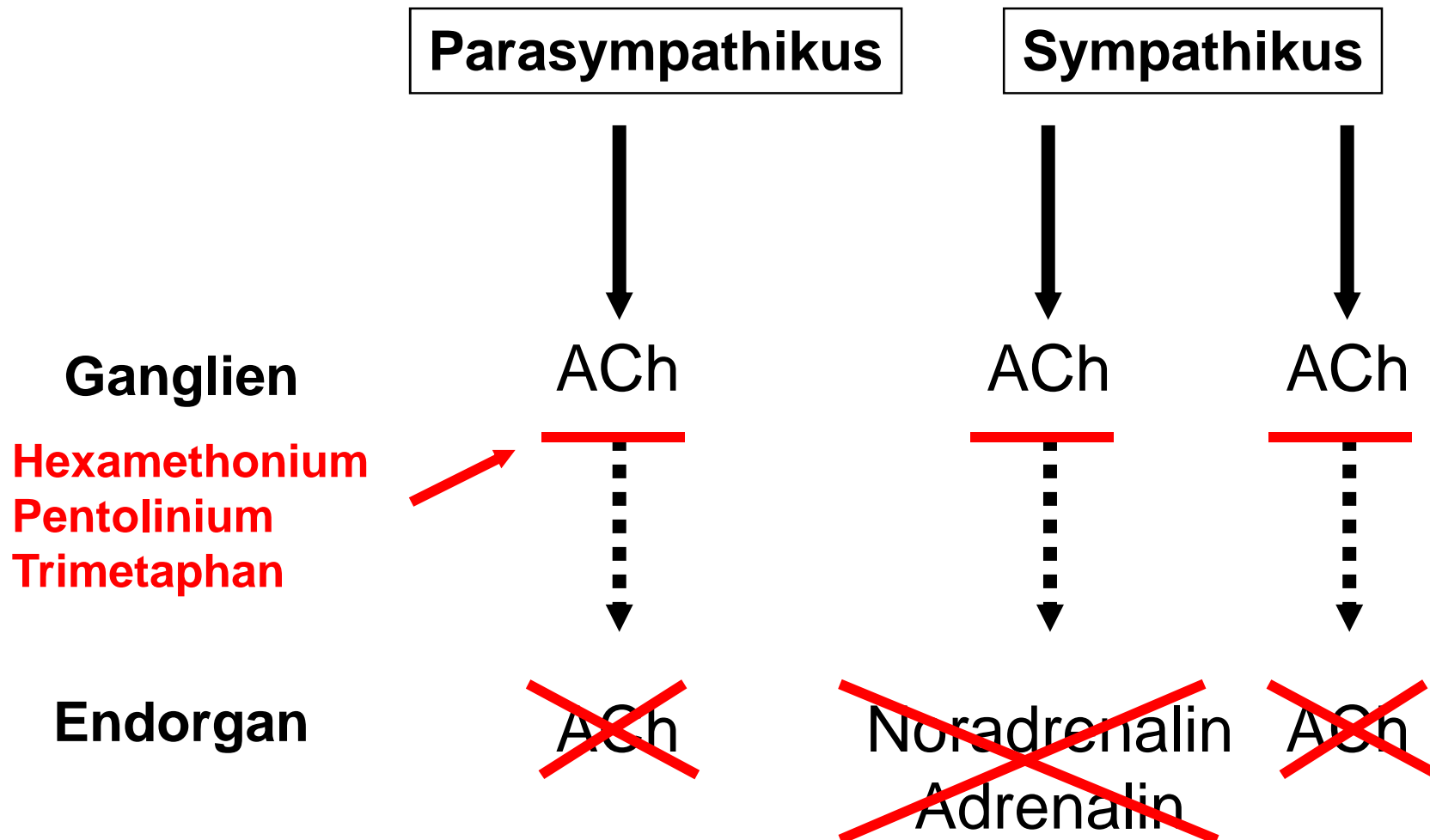
Wenn der Baroreflex streikt

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Autonomes Versagen



Pharmakologische Ganglienblockade

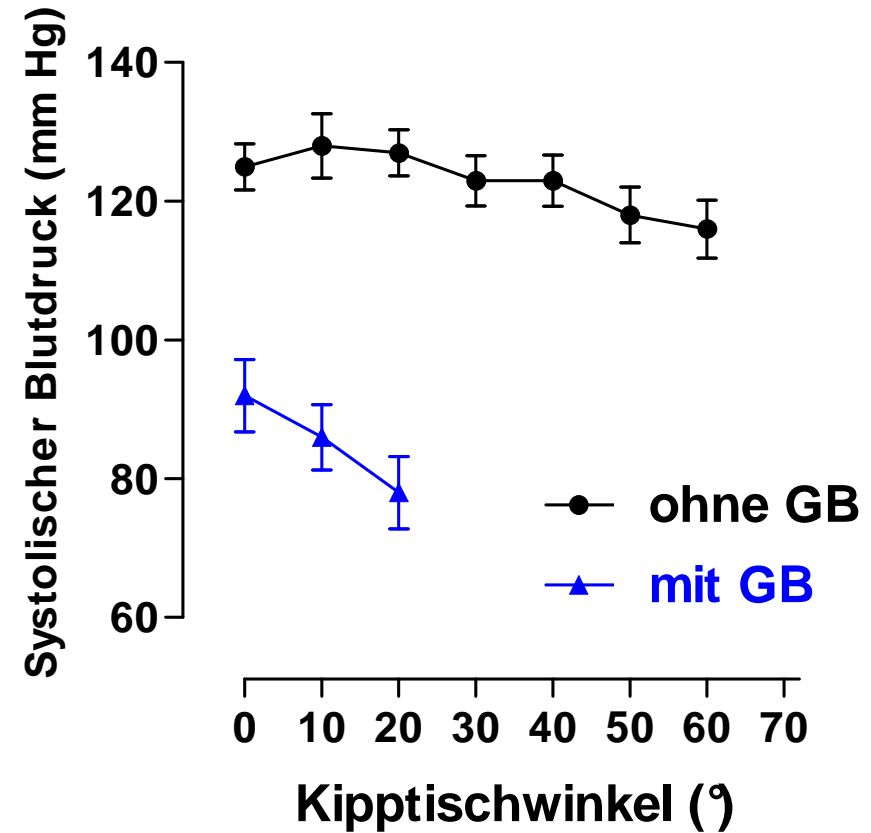


Paton's Hexamethonium Man (Auszug)

“He is a pink complexioned person, except when he has stood for a long time, when he may get pale and faint. His handshake is warm and dry. He is thin because his appetite is modest; he never feels hunger pains and his stomach never rumbles. As old age comes on he will suffer from retention of urine and impotence but frequency, precipitancy, and strangury will not worry him. One is uncertain how he will end, but perhaps if he is not careful, by eating less and less and getting colder and colder, he will sink into a symptomless, hypoglycemic coma and die, as was proposed for the universe, a sort of entropy death.”

Paton WDM. Pharmacol Rev. 1954;6:59-67

Ganglienblockade bei Gesunden



Jordan et al. Hypertension 1998

Der Hexamethonium-Mann

Anamnese:

43 jähriger Mann

Rezidivierende orthostatische Synkopen seit >20 Jahren

Anhidrose, Xerostomie, Völlegefühl, Obstipation

Körperliche Untersuchung:

Warme und trockene Haut

Konnte nicht stehen, orthostatische Hypotonie

Tonische Pupillen

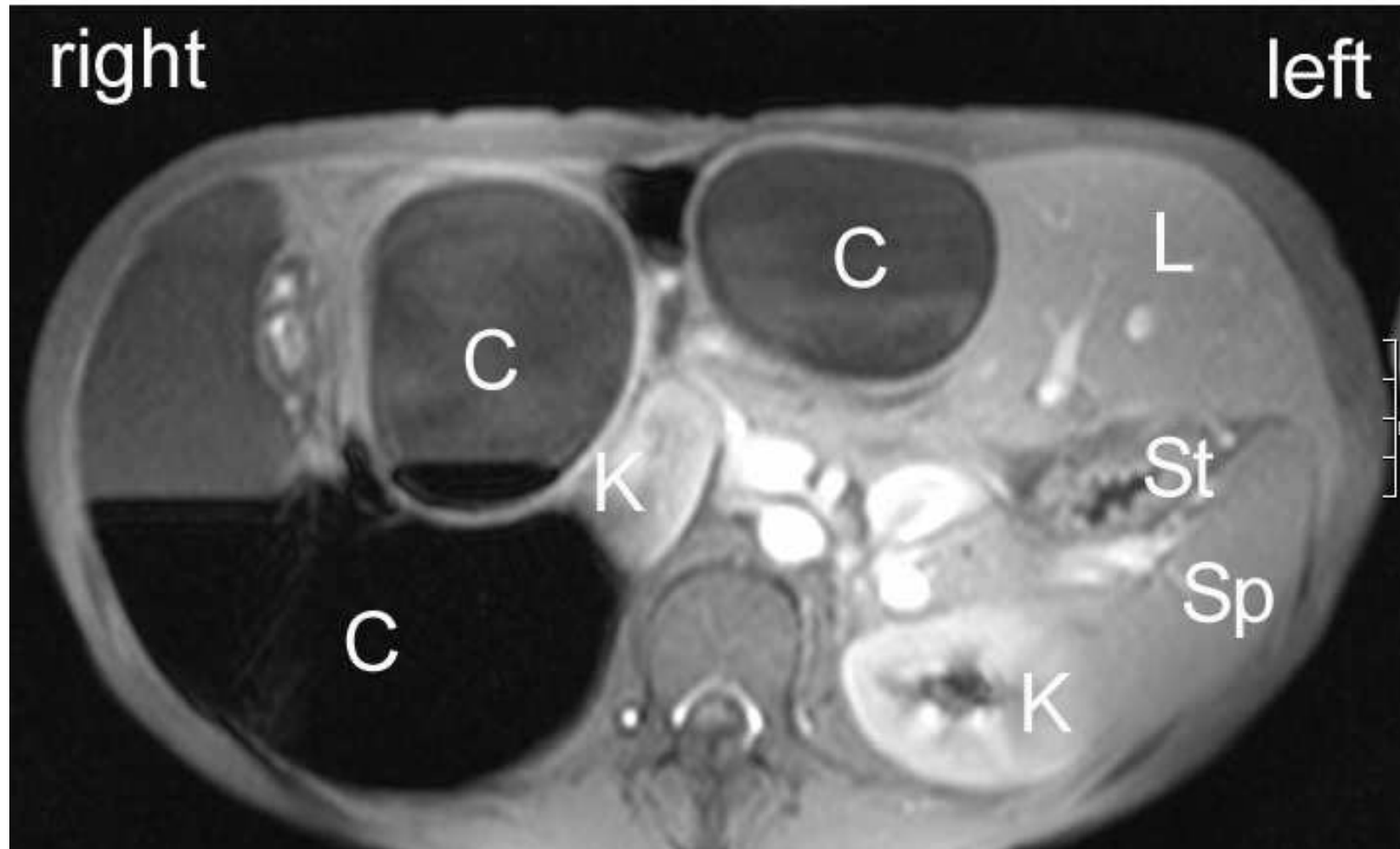
Weitergehende Untersuchungen:

Stark verlangsamte gastrointestinale Passage

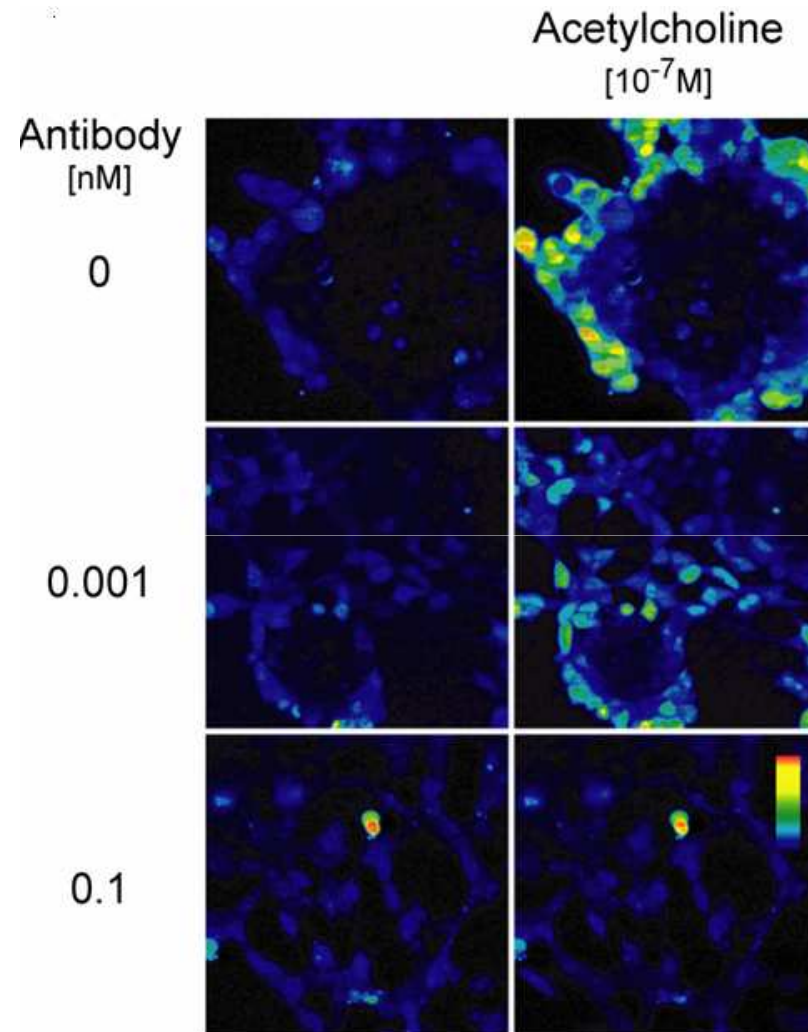
Flache Herzfrequenzkurve

Noradrenalin im Plasma stark reduziert

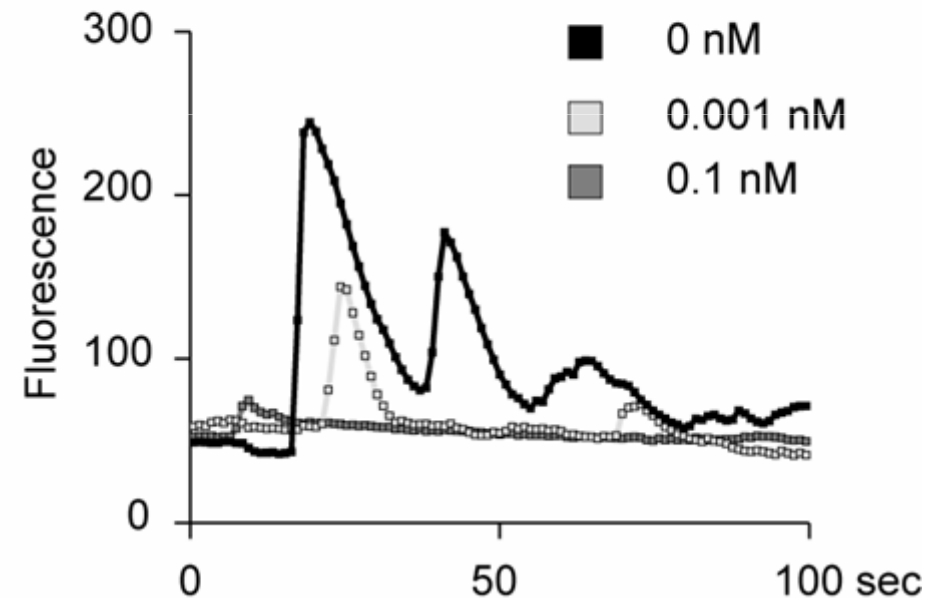
„...his stomach never rumbles”



Patientenantikörper blockieren ACh Wirkung



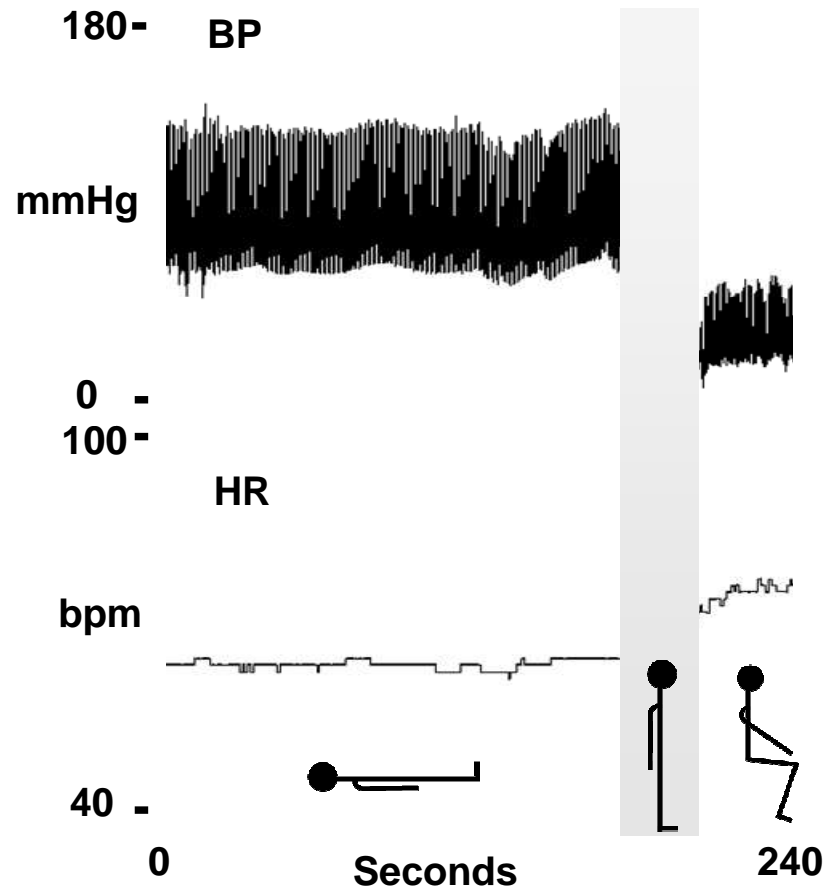
AK Konzentration beim Patienten: 0.54 nM



Schroeder et al. N Engl J Med 2005

Stehversuch

vorher

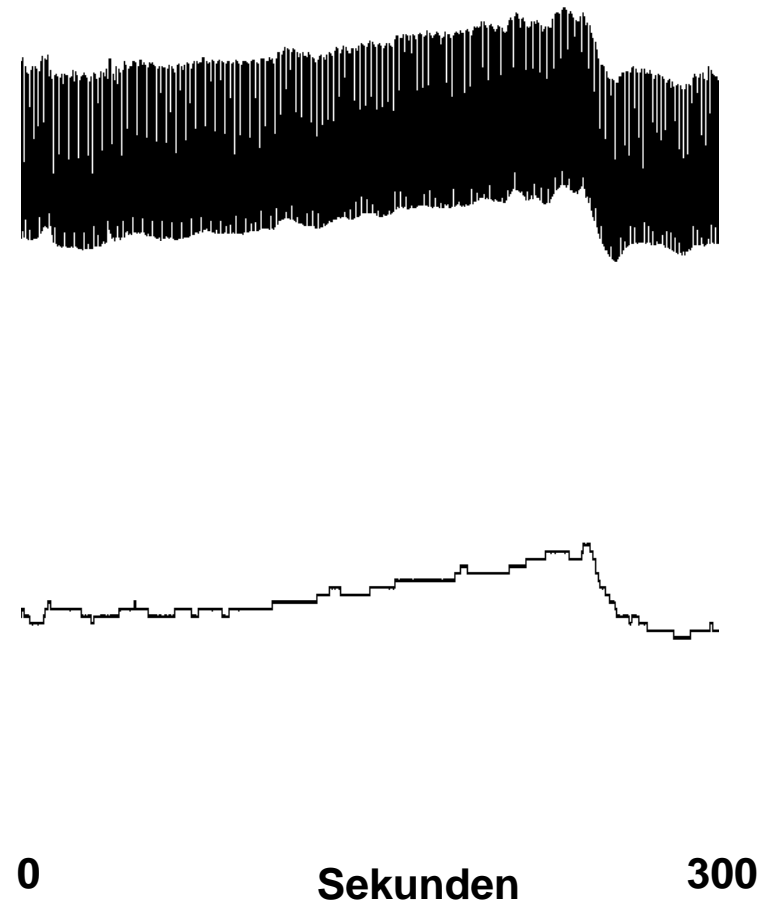
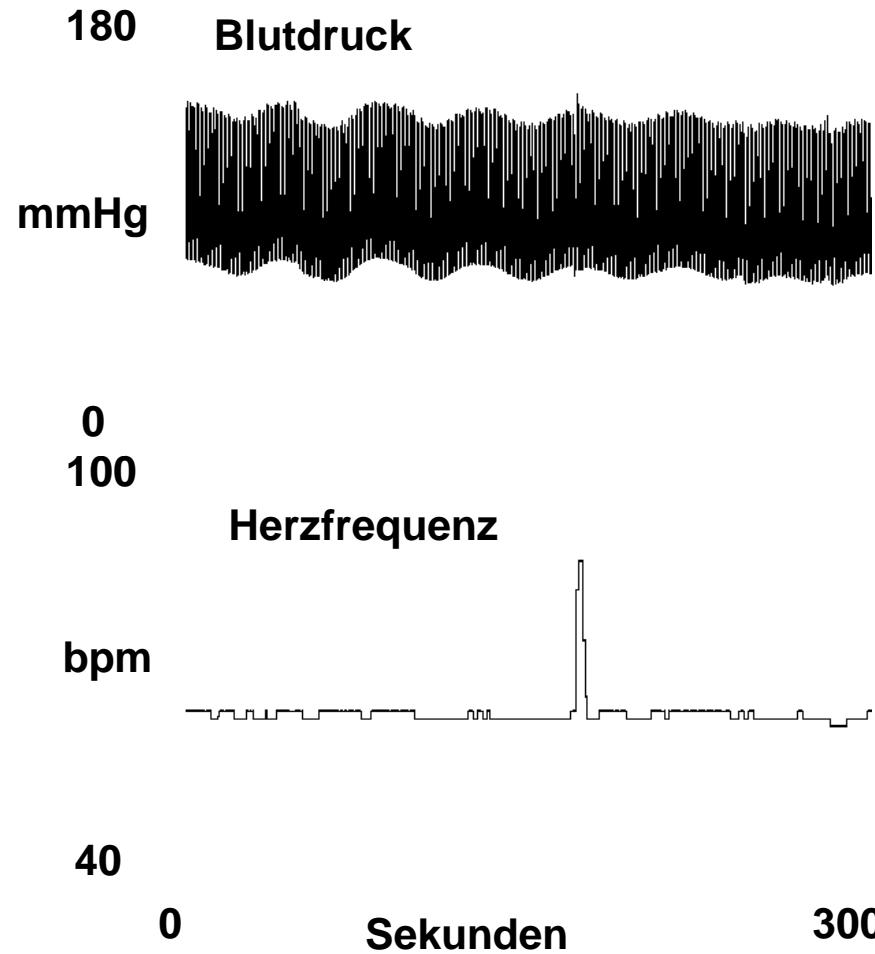


Schroeder et al. N Engl J Med 2005

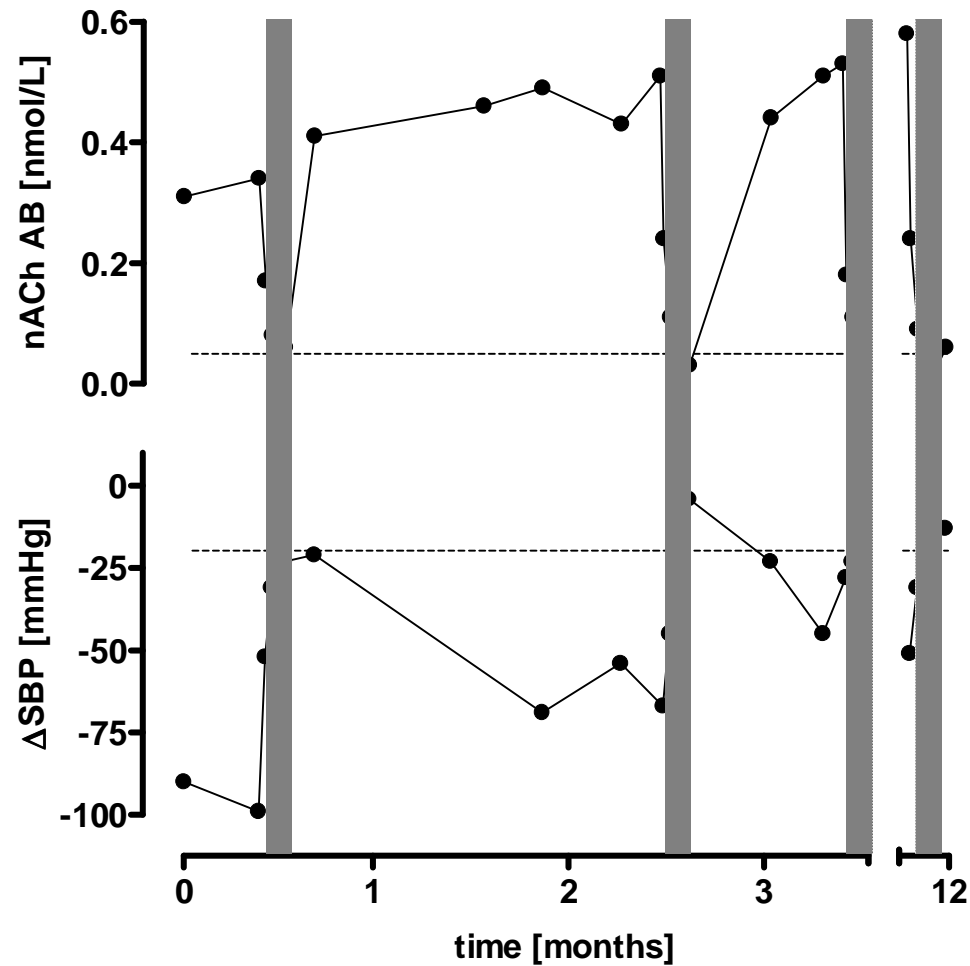
Handgrip Test

vorher

nachher



Orthostatische Hypotonie und Antikörper



Schroeder et al. N Engl J Med 2005

Differentialdiagnose

Sekundäre autonome Neuropathie?

- **Diabetes mellitus**
- **Paraneoplastisch**
- **Autoimmun**
- **Amyloidose**
- **Medikamente...**

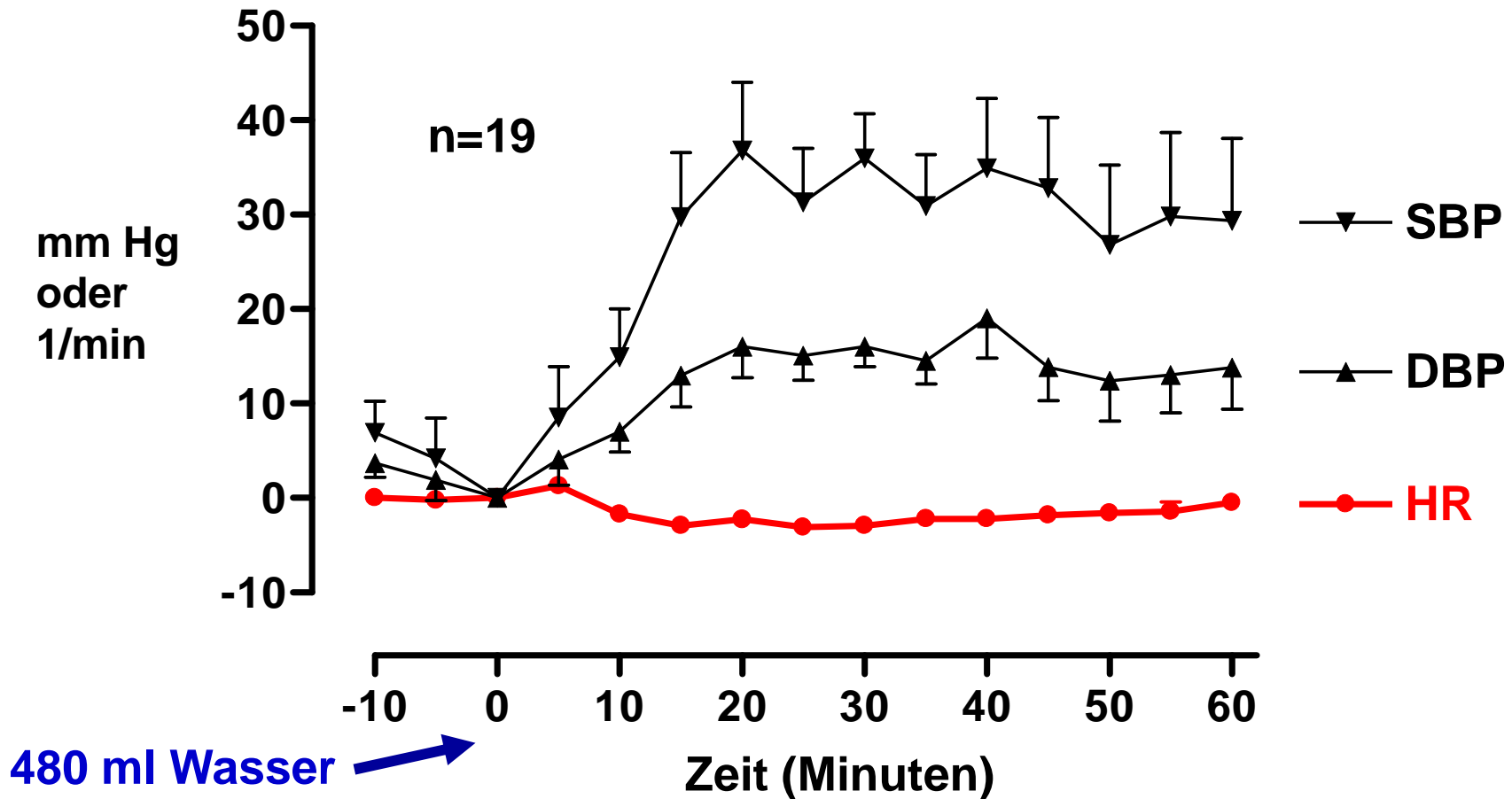
“Primäres” autonomes Versagen

- **Multisystematrophie**
- **Bradbury-Eggleston Syndrom (PAF)**
- **Genetische Erkrankungen (z.B. DBHD)**

Therapie

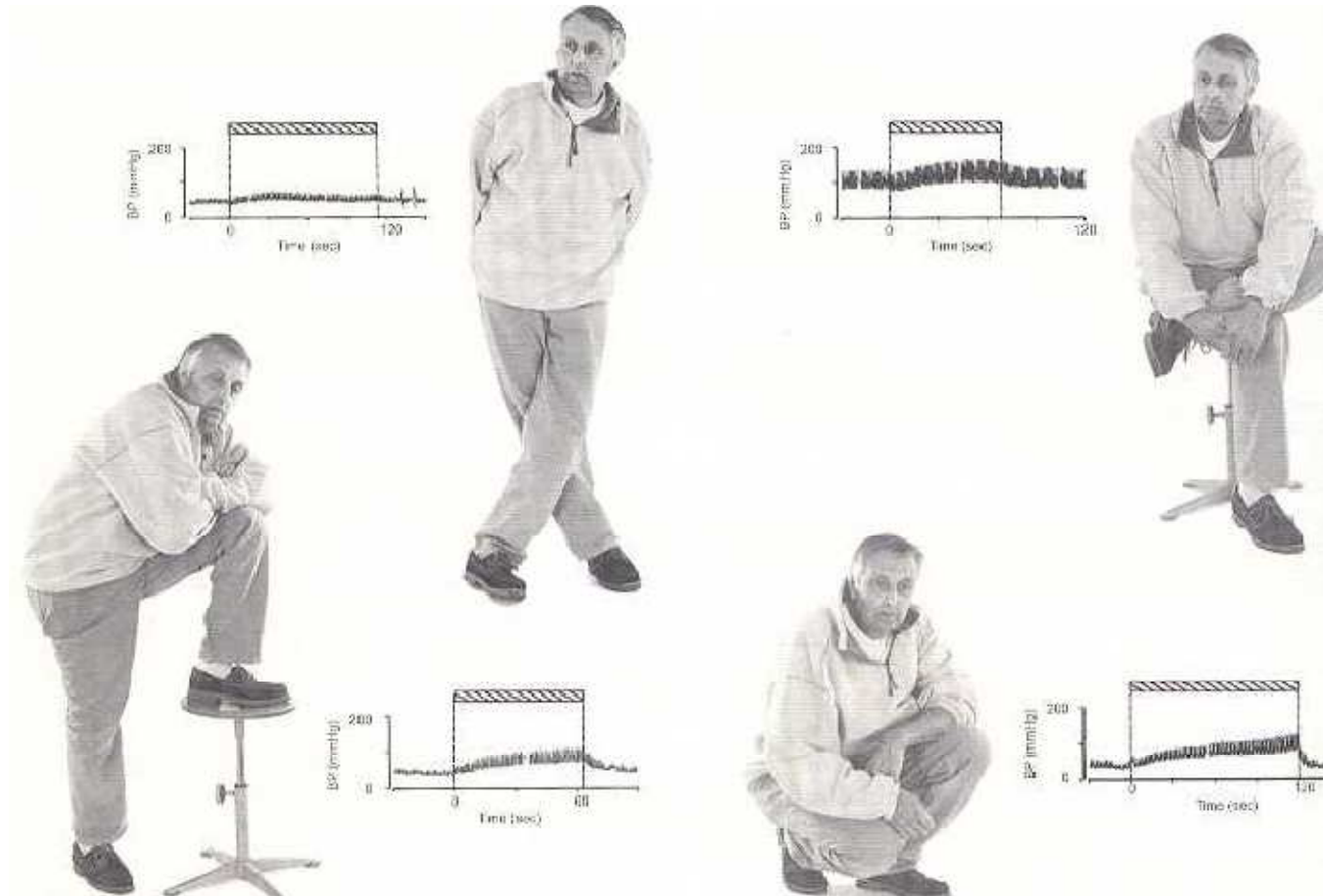
- In der Regel keine kausale Therapie bekannt
- Therapie der orthostatischen Hypotonie
- Therapie der nächtlichen Hypertonie
- Therapie anderer vegetativer Symptome

Wassertrinken – Peripheres Autonomes Versagen



Jordan et al. Lancet 1999, Circulation 2000

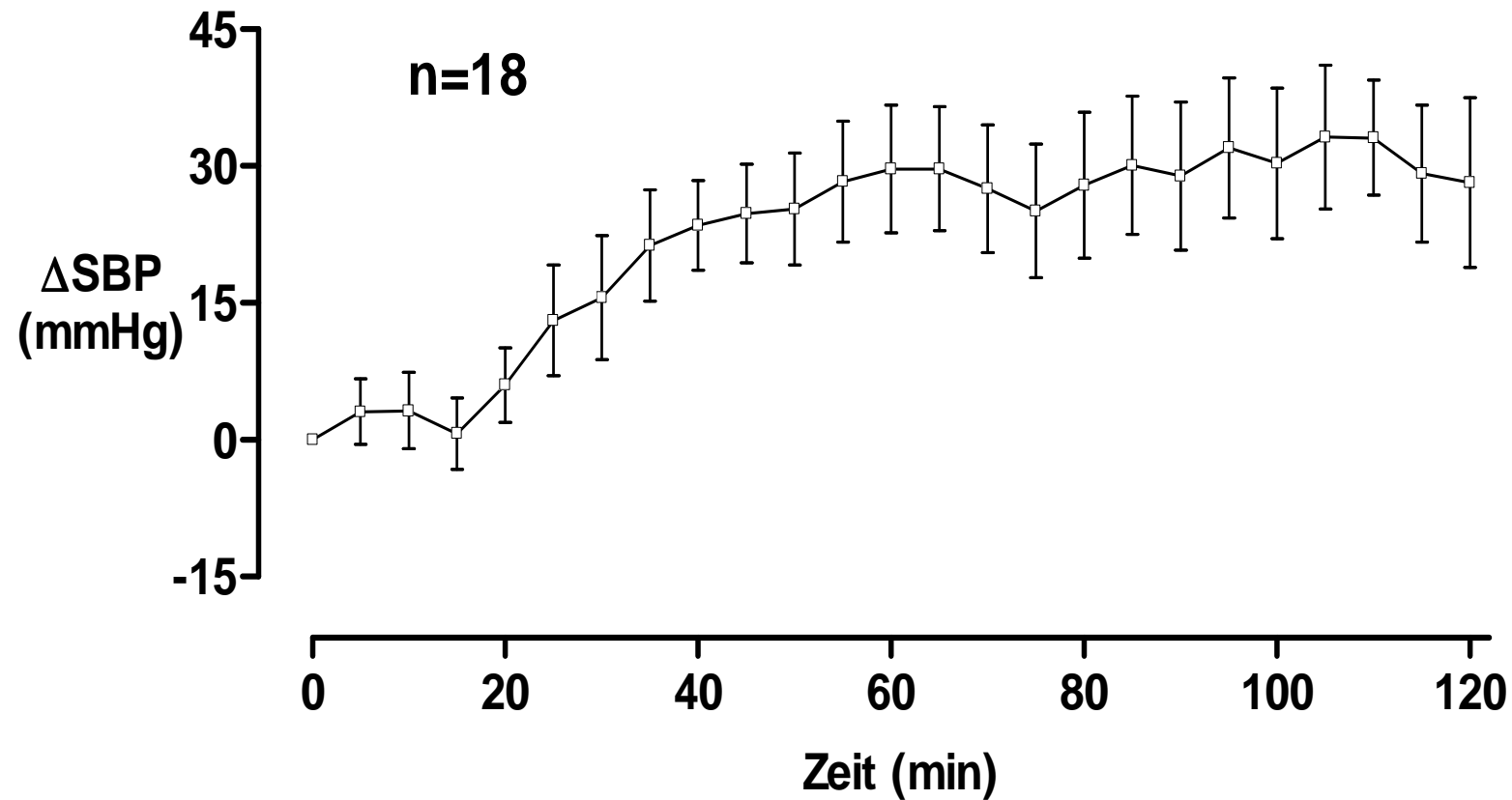
Manöver zur Blutdruckstabilisierung



Wieling W. et al. Nonpharmacological treatment of reflex syncope. CAR 2004 (14):I/62-I/70.

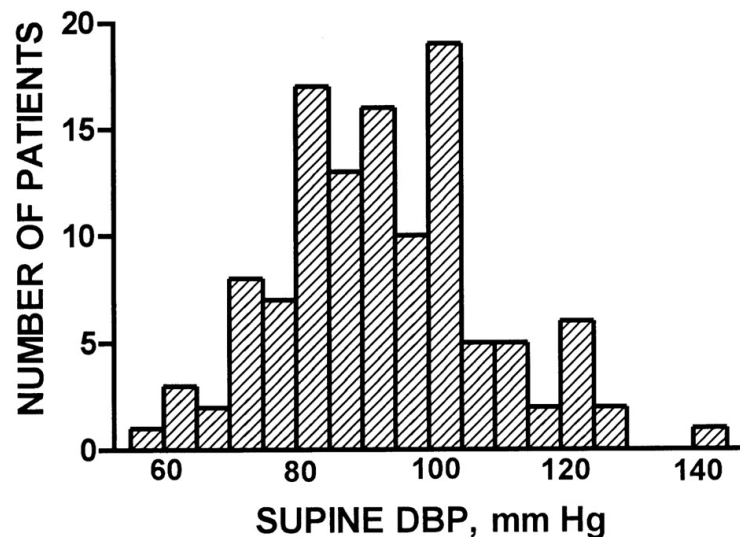
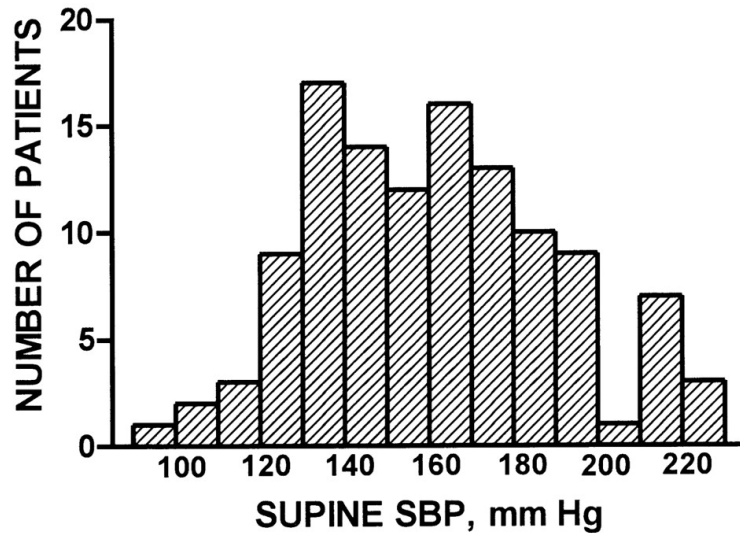
Blutdrucksteigernde Arzneimittel

Indomethacin 50mg



Jordan et al. Am J Med 1998

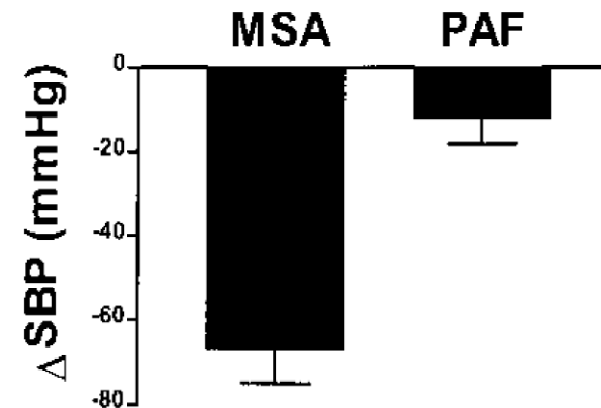
Autonomes Versagen - Hypertonie im Liegen



Blutdrucksenkung durch Ganglienblockade

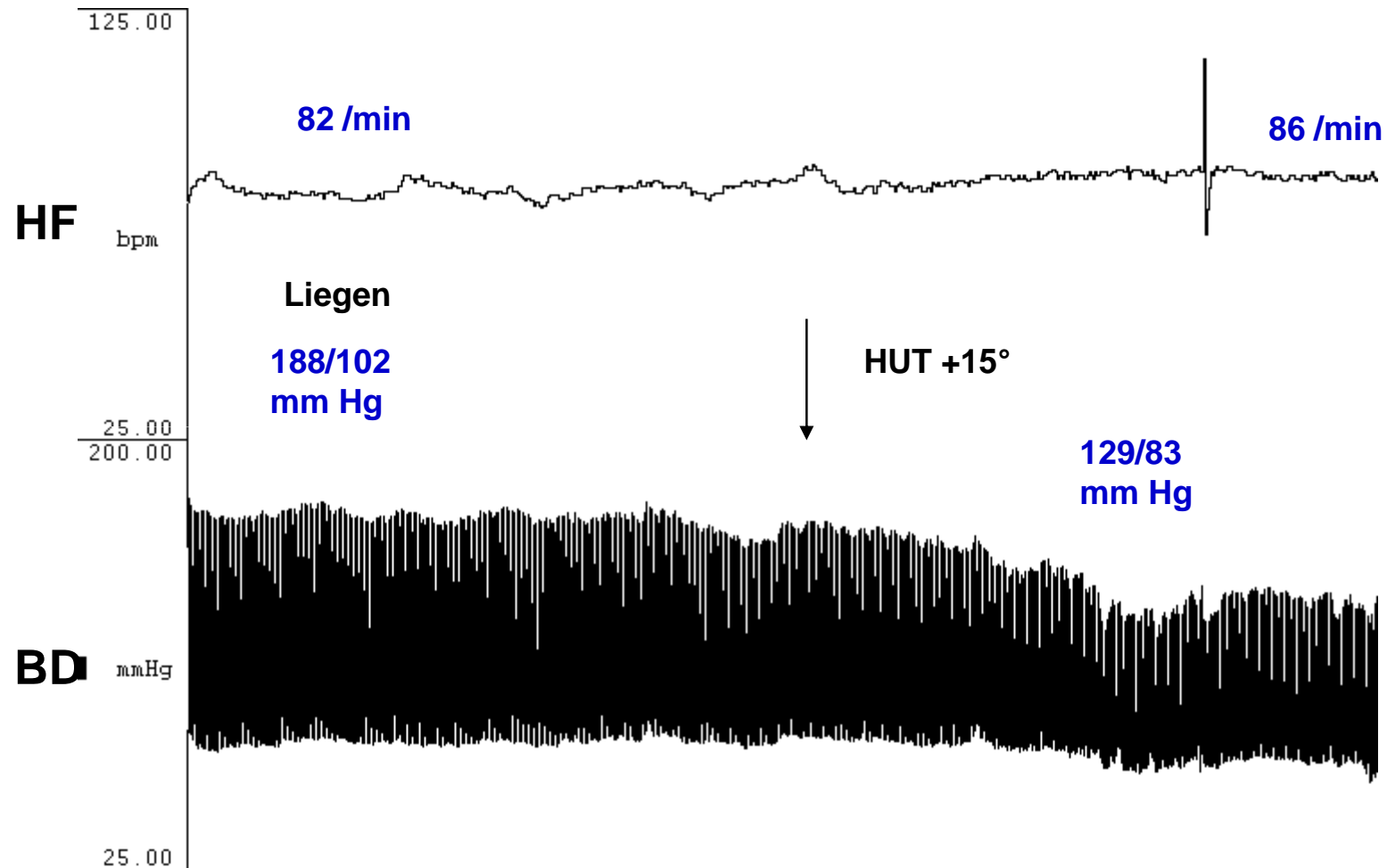
PAF = periphere Neuropathie

MSA = zentrale Neuropathie



Shannon JR et al. Hypertension 1997
Shannon JR et al. Circulation 2000

Ziegelstein unterm Bett oder Kipptisch...

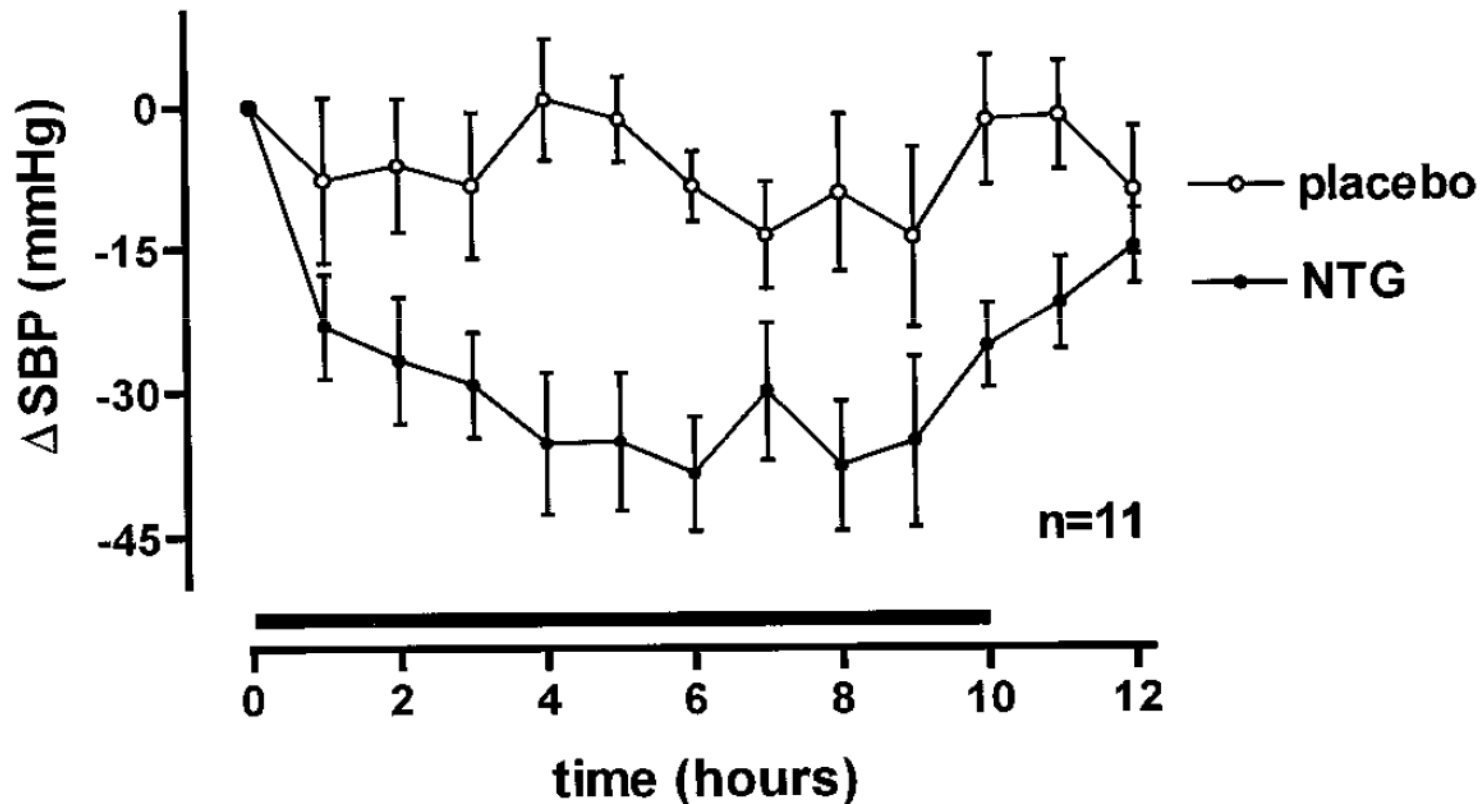


Ziegelstein unterm Bett oder Kipptisch...



Antihypertensiva bei Hypertonie im Liegen?

Nitroglycerinpflaster in niedriger Dosis

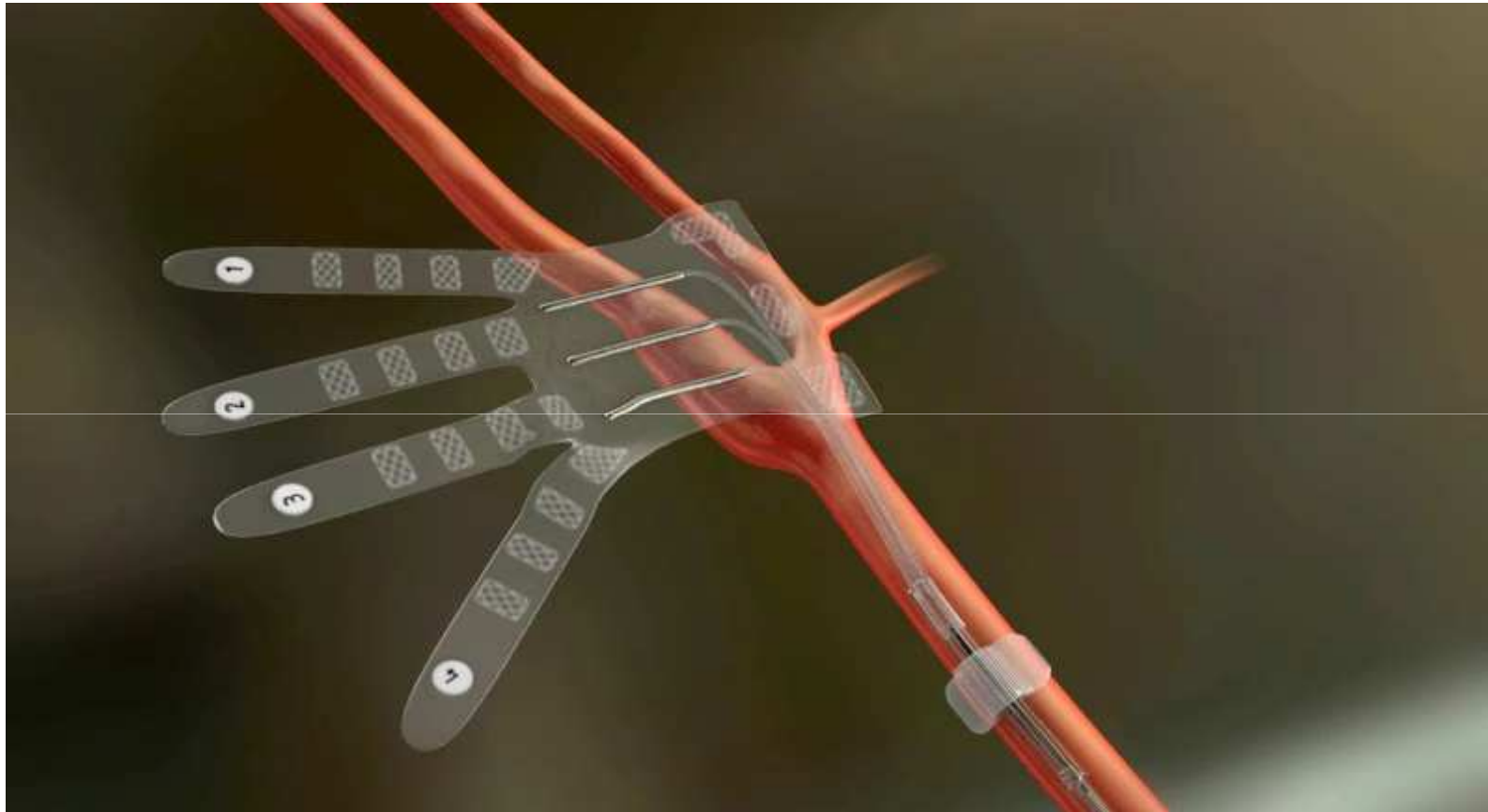


Jordan et al. JASN 1999

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Baroreflexschrittmacher

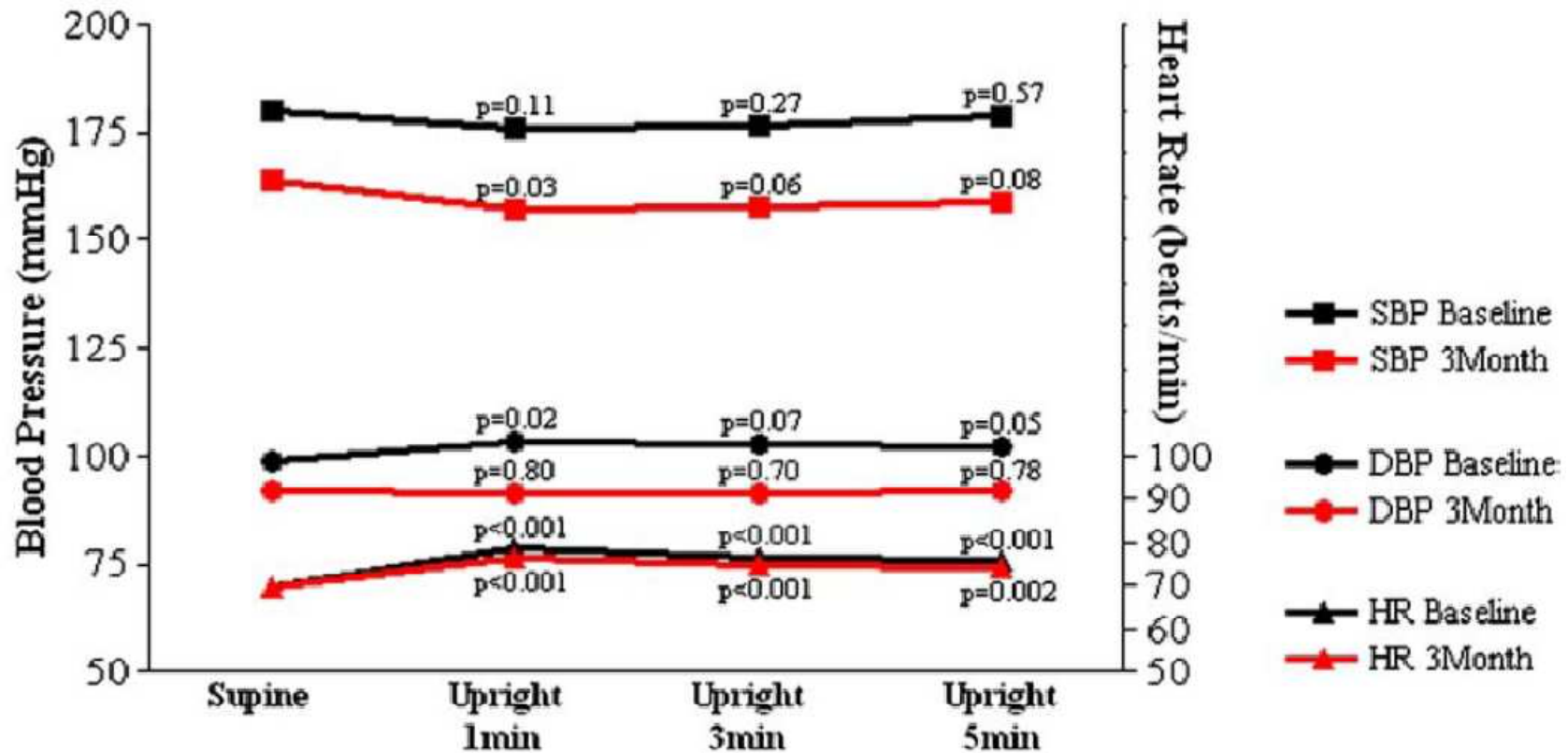


Baroreflexschrittmacher



DEBUT Ht Studie

- 45 Patienten mit therapierefraktärer Hypertonie
- Keine Kontrollgruppe



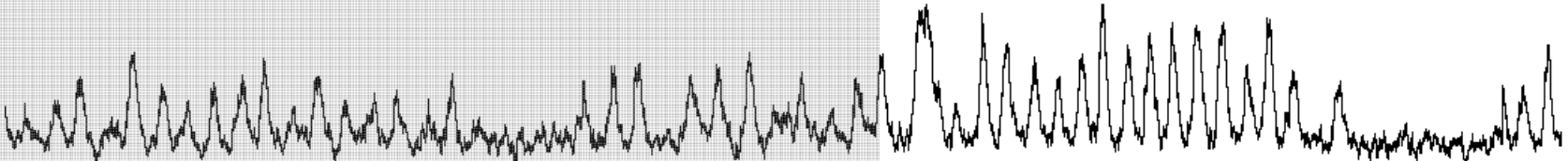
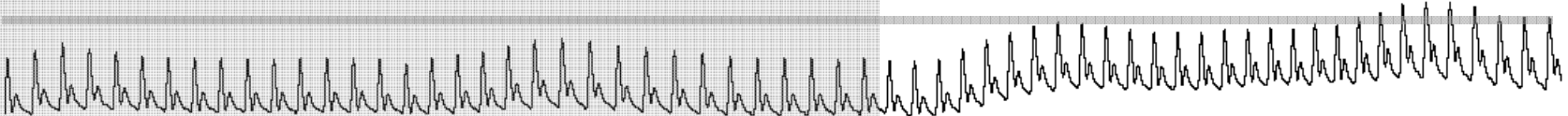
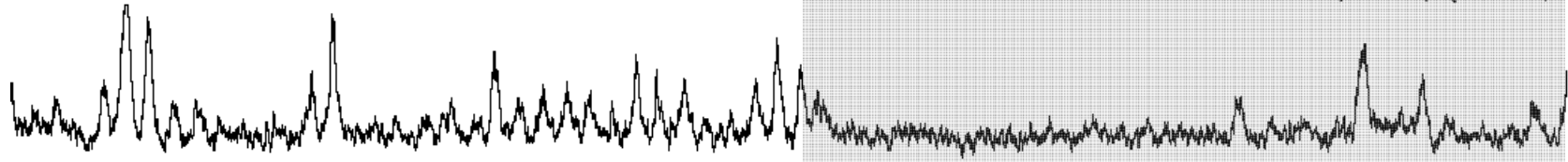
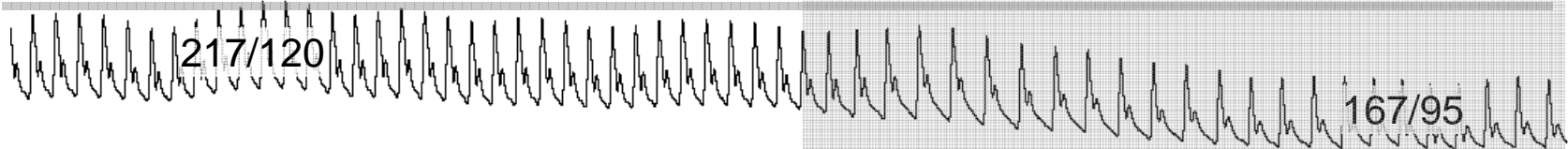
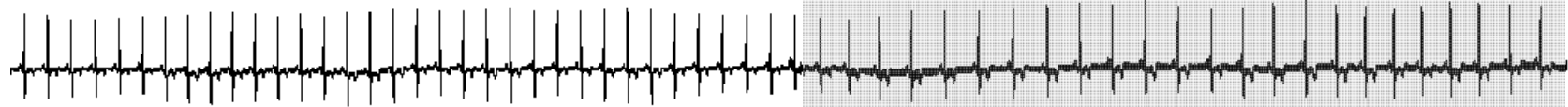
Scheffers IJ et al. *J Am Coll Cardiol* 2010

Substudie von DEBUT Ht

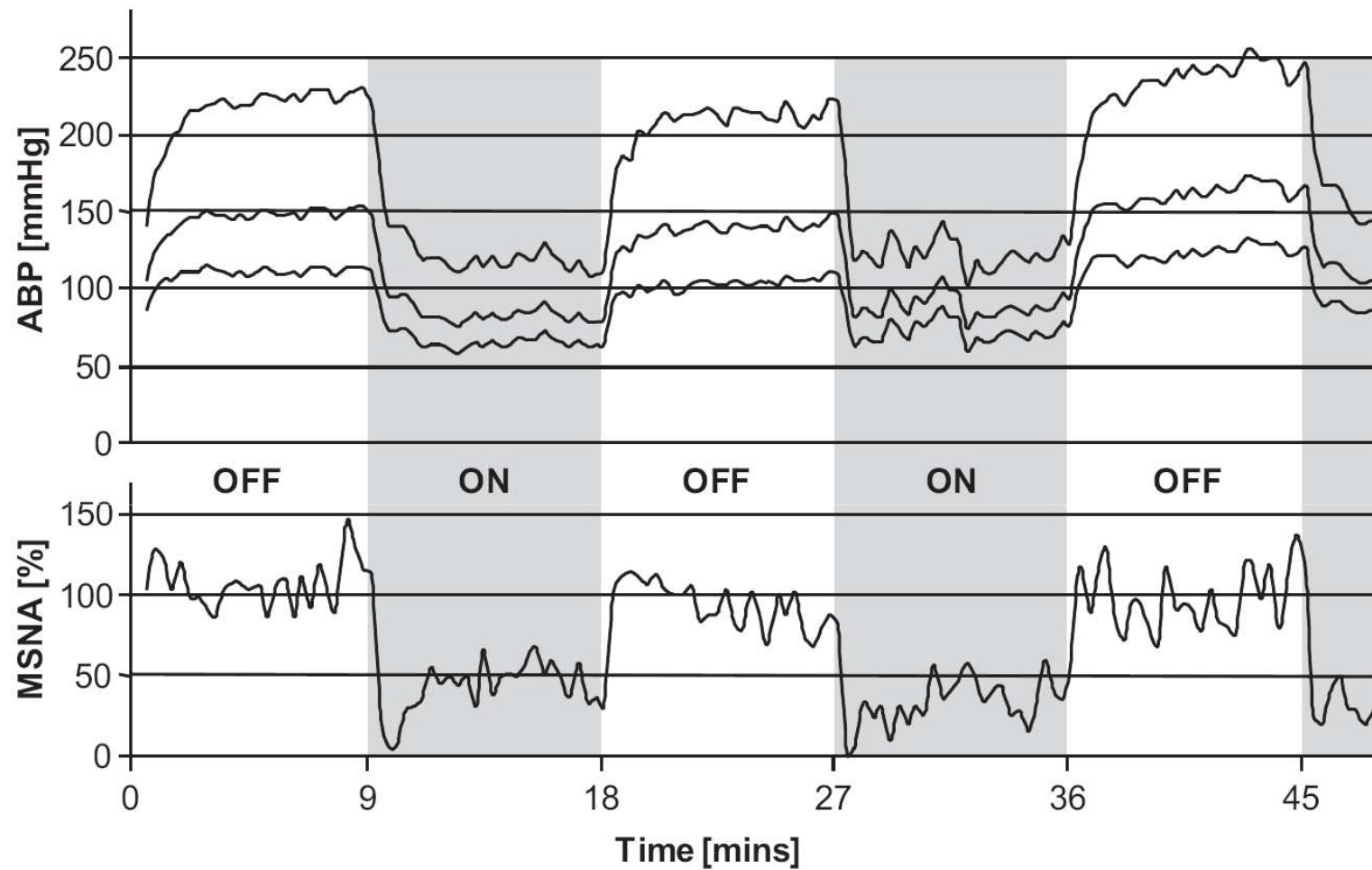
Identification No.	Age, y/Sex	BMI, kg/m	DM	CAD/MI	Stroke/TIA	Antihypertensive Medication																					
1	60/M	33			•	Metoprolol, valsartan, hydrochlorothiazide, amlodipine, urapidil																					
2	<table border="1"> <thead> <tr> <th></th> <th>mean±SEM</th> <th>range</th> </tr> </thead> <tbody> <tr> <td>Number/gender</td> <td>12 / 7 m 5 w</td> <td></td> </tr> <tr> <td>Age [years]</td> <td>58 ± 2.6</td> <td>43 - 70</td> </tr> <tr> <td>BMI [kg/m²]</td> <td>31 ± 2.1</td> <td>22 - 49</td> </tr> <tr> <td>SAP [mmHg]</td> <td>193 ± 8.7</td> <td>132 - 232</td> </tr> <tr> <td>DAP [mmHg]</td> <td>94 ± 5.1</td> <td>65 - 126</td> </tr> <tr> <td>HR [bpm]</td> <td>73 ± 3.9</td> <td>58 - 97</td> </tr> </tbody> </table>							mean±SEM	range	Number/gender	12 / 7 m 5 w		Age [years]	58 ± 2.6	43 - 70	BMI [kg/m ²]	31 ± 2.1	22 - 49	SAP [mmHg]	193 ± 8.7	132 - 232	DAP [mmHg]	94 ± 5.1	65 - 126	HR [bpm]	73 ± 3.9	58 - 97
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8						le,																					
9						,																					
10																											
11						amlodipine, doxazosin, moxonidine, urapidil																					
12*	68/F	28				Hydrochlorothiazide, losartan																					

BMI indicates body mass index; CAD, coronary artery disease; DM, diabetes mellitus; MI, myocardial infarction; TIA, transient ischemic attack; M, male; F, female.

*Patient experienced side effects with other hypertensive drugs.



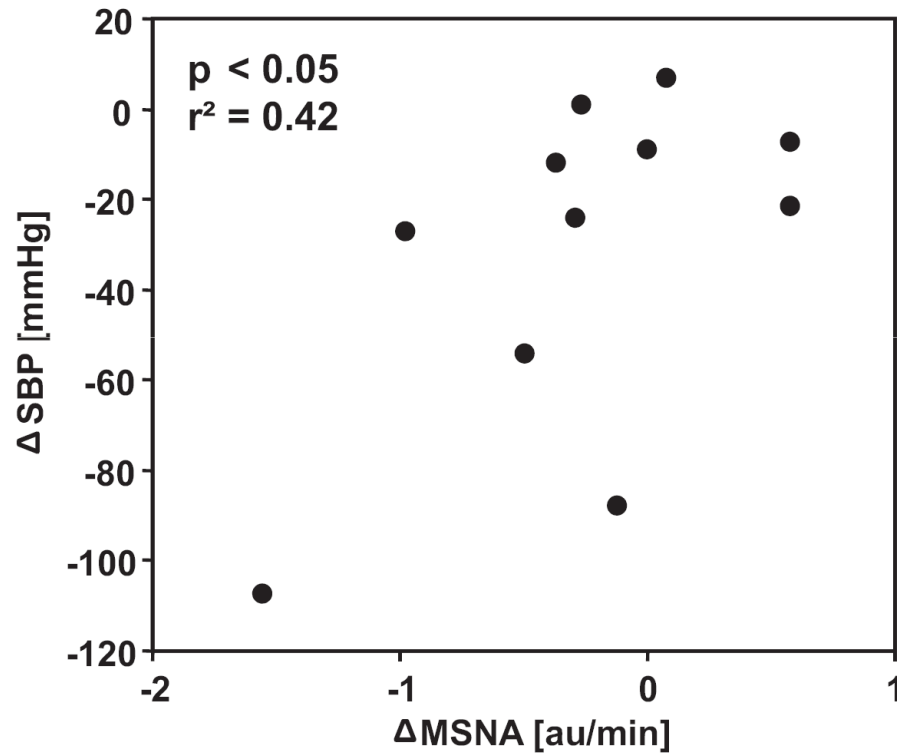
Heusser K et al. *Hypertension* 2010; 55:619-26



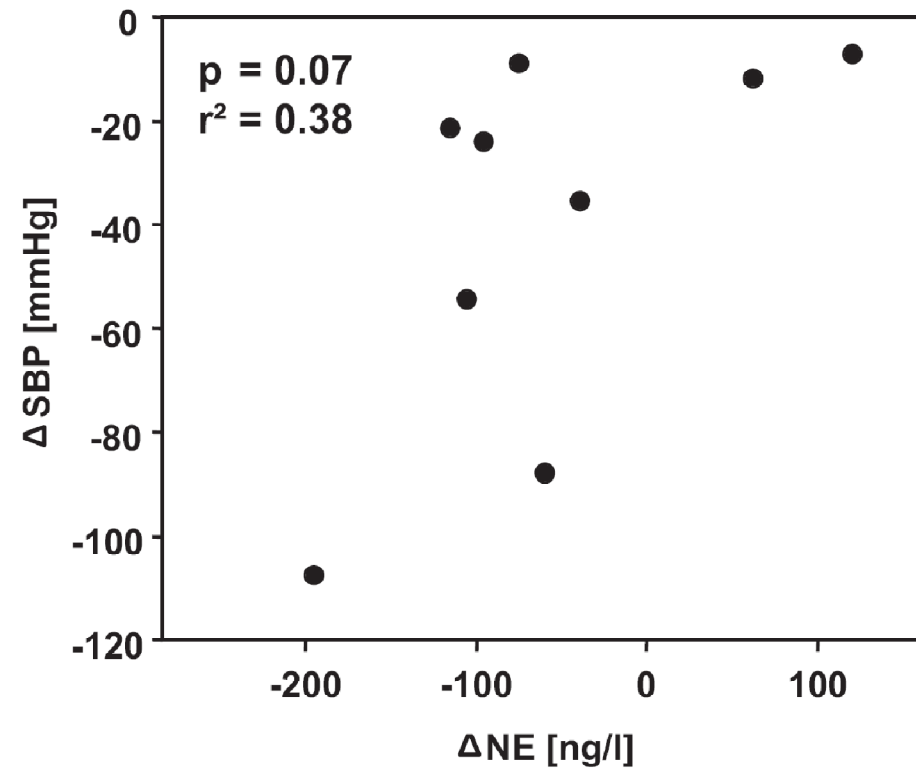
Heusser K et al. *Hypertension* 2010; 55:619-26

Sympatholytische Wirkung und Blutdrucksenkung

Sympathische Nervenaktivität



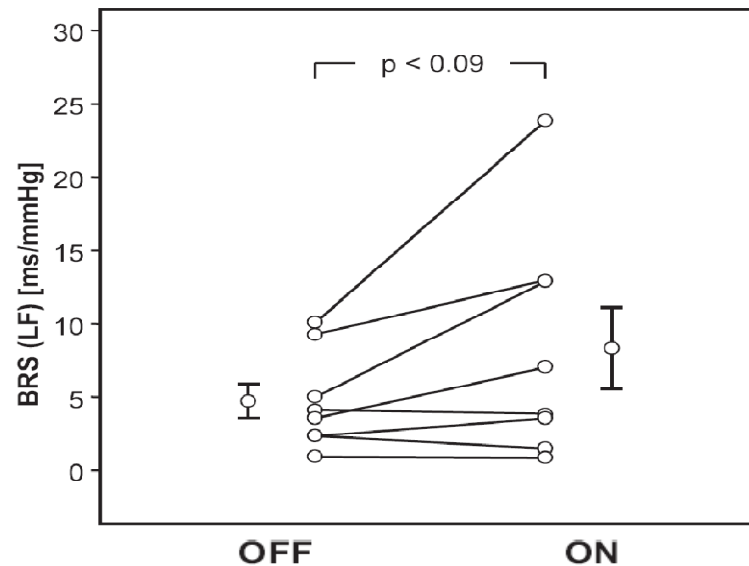
Plasma Noradrenalin



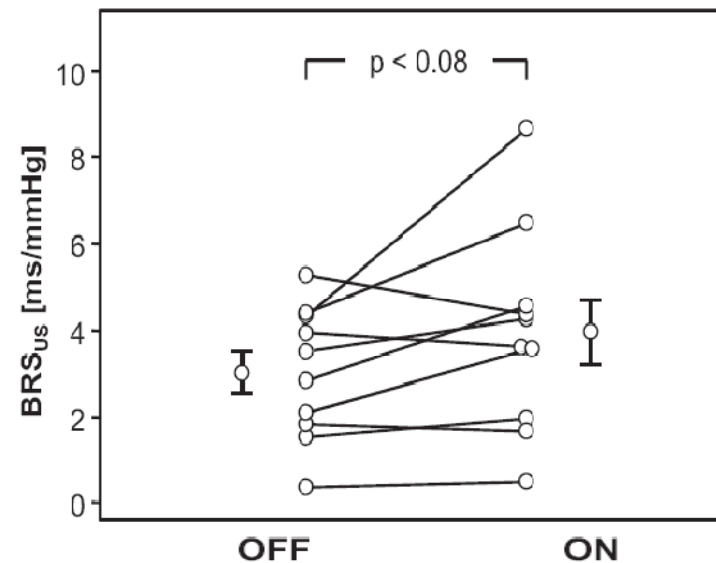
Heusser K et al. *Hypertension* 2010, 55:619-26

Ist physiologische Baroreflexfunktion intakt?

Cross spectral analysis



Sequence technique



Heusser K et al. *Hypertension* 2010, 55:619-26

Baroreflex und Hypertensiologie

