

# Pharmacodynamics of Psychoactive Drugs in the Elderly

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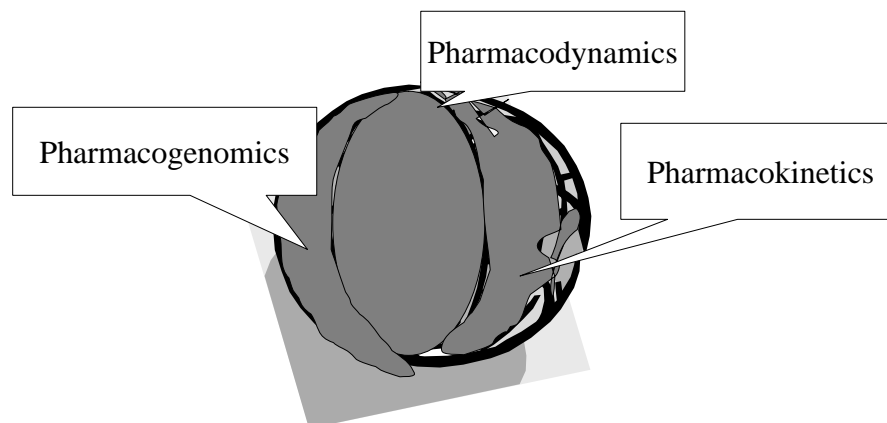
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Albertinen Haus, Hamburg

EAMA Jan. 2008 Sion, CH, Student's state of the art lecture

Pharmacologia est omnis divisa in partes  
tres ...

The World of Pharmacology



## Pharmacodynamics: „What the drug does to the body“

- The study of
  - biochemical and physiological effects of drugs
  - mechanisms of drug action
  - relationship between drug concentration and effect.

## What I am NOT speaking about...

- Basic problems of pharmacological research
  - Research with animal models
  - Research with healthy male (!) volunteers
- Most psychotropic drugs are not tested and not investigated for elderly patients
  - Exception: Paroxetine is effective for the frail, very old, depressed patient  
(Burrows 2002)



The focus is  
laid on ...

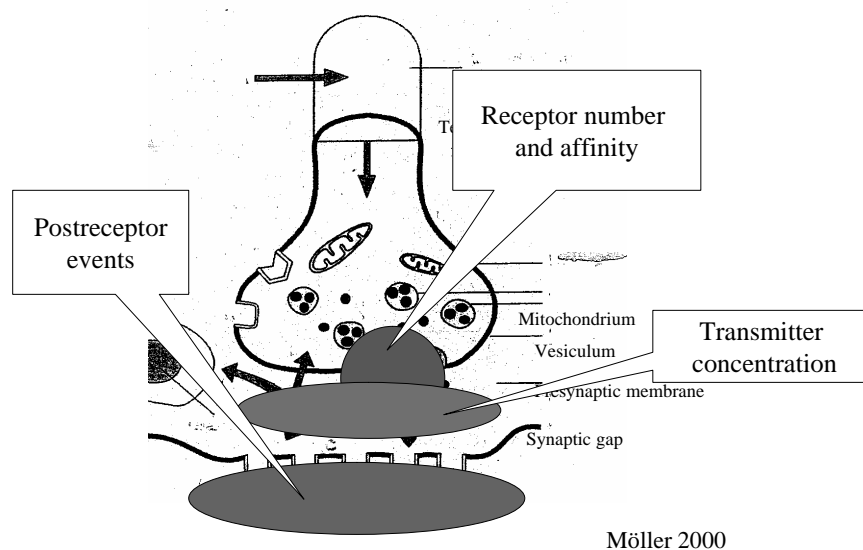
... Factors, influencing the  
pharmacodynamics of

- Antidepressives
  - Neuroleptics
  - Benzodiazepines
- in the elderly

## Factors, Influencing Pharmacodynamics of Psychoactive Drugs in the Elderly

- The normal aging process
- Pathological changes in mentally and physically ill patients
- Interactions with other drugs

## Neurotransmitter system of the brain



## Factor: Normal Aging Process

- Intracerebral neurotransmitter concentration ↑
  - Noradrenaline & metabolites (Sunderland 2004)
- Number of receptors ↓
  - Several dopamine receptors
- Binding affinity ↓ ↑
  - GABAergic system ↑ (Klotz 1998)
- Intracellular second messenger pathways ↓
  - Proteinkinase A and C
- Homeostatic reserve ↓
  - striatal dopamine D2-receptors (Swift 1990)

Factor: Normal Aging Process  
Clinical Conclusion: Example of  
Anticholinergic Adverse Effect

Dry mouth → Dentures fit poorly  
→ More pain → Less appetite, more  
constipation → More Depression

## Factor: Normal Aging Process

- Increase in SIADH
  - Syndrome of inappropriate antidiuretic hormone → Hyponatremia with SSRIs (Fabian 2004)
- SSRI-effect on platelets and/or warfarin metabolism
  - Gastrointestinal bleeding (Caird 1973)
- Blockade of alpha1-adrenergic receptors
  - Orthostatic hypotension → falls (Lotrich 2005)

## Factor: Pathological changes in mentally and physically ill patients

- Dementia
    - Regional cerebral blood flow ↓
  - Depression
    - Decrease of 5HT2A-Receptor level in the C/C genotype for 5HT2A-Receptors → higher drop-out due to adverse side effects
- (Lotrich 2005)

## Factor: Interactions with other drugs

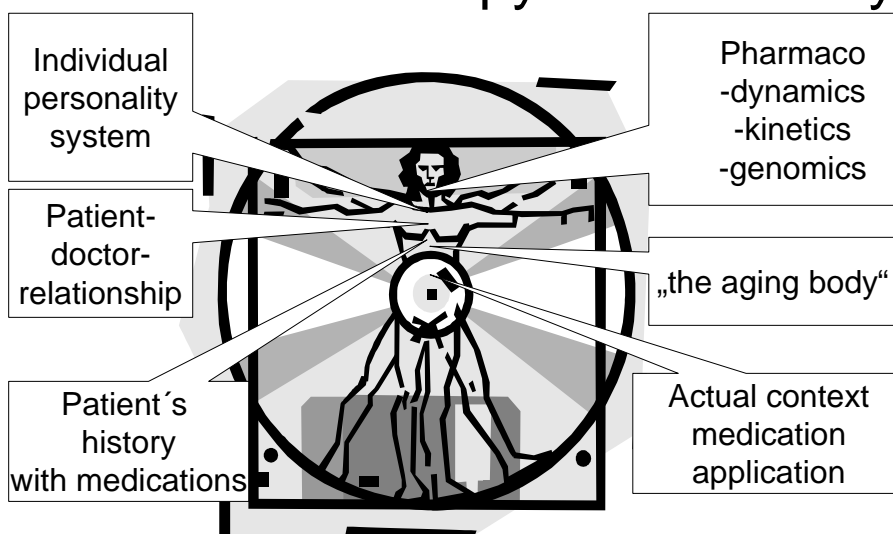
- Tricyclic antidepressants and classical neuroleptics
  - TCA plasma level ↑
- Anticonvulsives, sedatives and neuroleptics
  - Sedation, delirium
- Anticoagulation and neuroleptics
  - Anticoagulation ↑
- Cimetidin and neuroleptics
  - Neuroleptics plasma level ↓

(Schmauß 2006)

~~Pharmacodynamics ...~~ ●

# Psychodynamics ... of pharmacotherapy in the elderly

## Psychodynamics of Pharmacotherapy in the Elderly



Lindner 2003

## Take Home Message

- More beneficial and adverse effects even with less medication dosage
- Do not give too less
- Know your patient
- Think of non-pharmacological treatment possibilities of psychiatric diseases

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