生醫訊號於神經外科領域之應用

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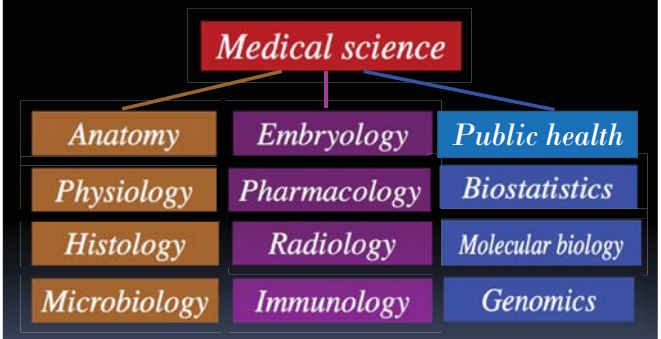
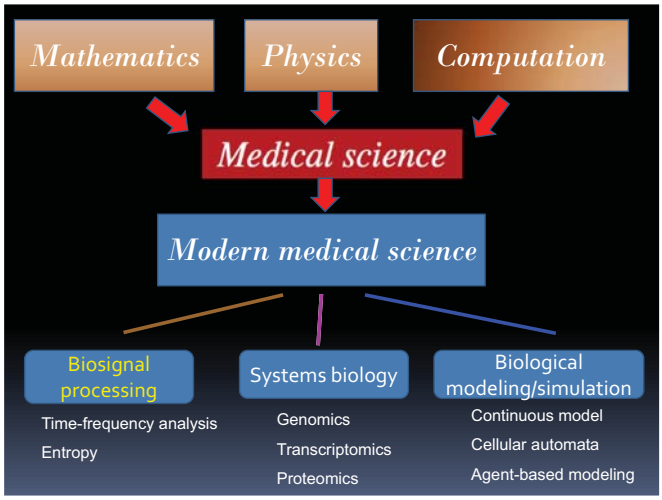
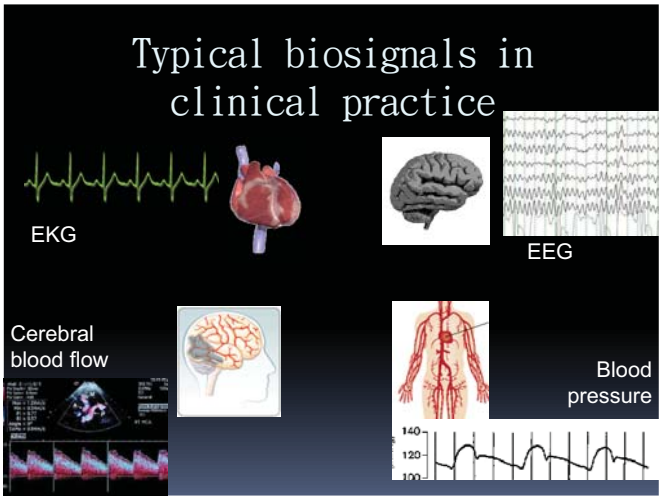
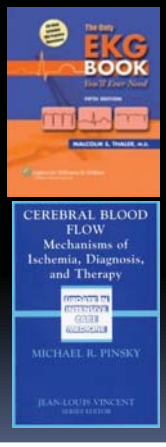
生物醫學的發展





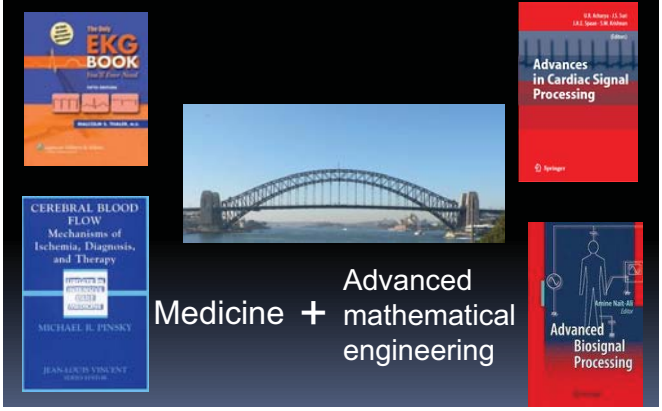
Typical biosignals in clinical practice





- 心電圖 (EKG): 心跳、心律不整
- 血壓 (BP): 收縮壓、舒張壓
- 腦血流 (Cerebral blood flow) : 腦血流速
- 腦波 (EEG)

Past　　Present



Medicine ＋ Advanced mathematical engineering

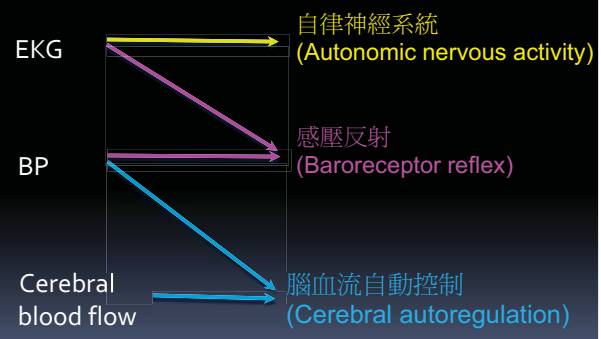
New era for biosignal applications

- Biological signals are no longer simple time-series data only
- When appropriately analyzed, advanced biosignal processing provide new information

New era for biosignal applications

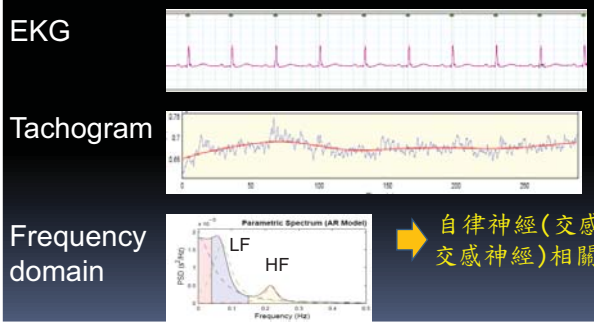
- Goals: Look for biological importance and clinical significance
- Pitfalls: mathematical games only
- Two major goals
  - Measurements of physiological parameters
  - Classification of disease severity

First goal: Physiological Parameters

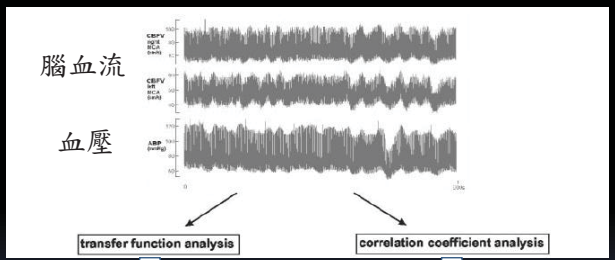


First goal: Physiological Parameters

Heart rate variability (HRV)



First goal: Physiological Parameters



腦血流自動控制指標

Stroke 2003;34:2138-44

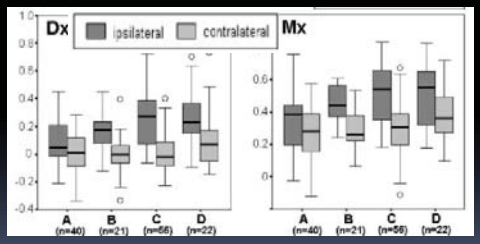
Second goal: Disease Classification

- 生理情形的分類
- 疾病嚴重度的分類

➔ 正確的分類是醫學上相當重要的課題

Second goal:
Disease Classification

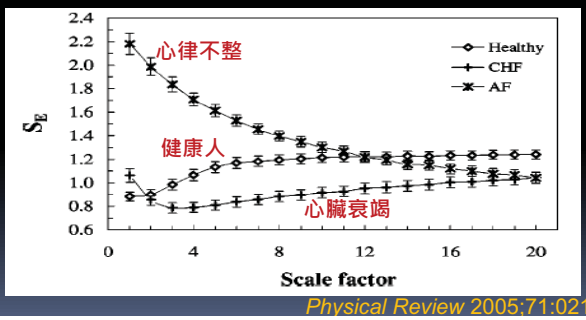
腦血流自動控制指標與不同程度腦血管阻塞之相關性



Stroke 2003;34:2138-44

Second goal:
Disease Classification

Multiscale entropy of HRV於心臟疾病之分類

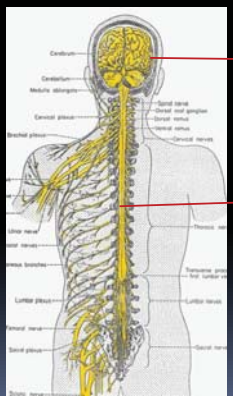


Physical Review 2005;71:021906

APPLICATIONS OF HRV IN NEUROSURGERY

Neuroanatomical evidence

Anatomy of central nervous system



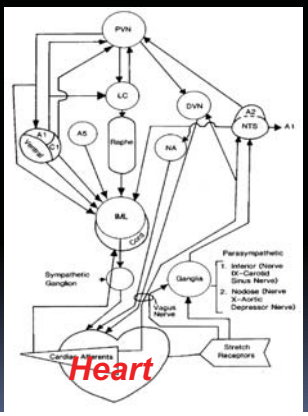
Anatomy of Cardiac Activity-regulating Circuitry

Hypothalamus下視丘

Brainstem 腦幹

Spinal cord 脊髓

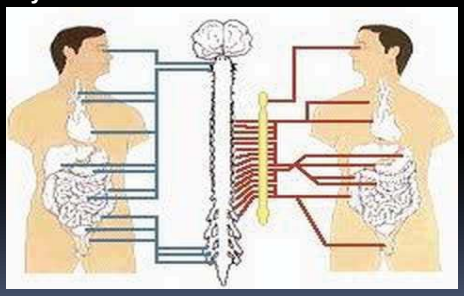
Heart 心臟



Anatomy of Cardiac Activity-regulating Circuitry

Parasympathetic system

Sympathetic system

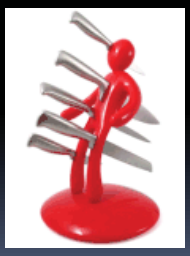


APPLICATIONS OF HRV IN NEUROSURGERY

Neurophysiological evidence

Brain-Heart connection

- Brain-heart connection
  - In 1942, Cannon made the first scientific description about *Voodoo Death*



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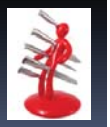
American Antropologist. 1942;44;169-181

Brain-Heart connection

- Brain-heart connection
  - In 1942, Cannon made the first scientific description about *Voodoo Death*
    - When subjected to spells or "black magic", men may be brought to death
    - The victim himself had no power to alter this curse



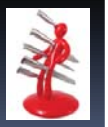
American Antropologist. 1942;44;169-181

Brain-Heart connection

- "....the death was caused by a lasting and intense action of sympatho-adrenal system...."
- Voodoo death in ancient people is a real phenomenon that provides an important clue to understand the phenomena of "sudden death" in modern world

Neurocardiology

Brain-heart connection



American Antropologist. 1942;44;169-181

Brain-Heart connection

- Clinical importance of brain-heart connection

" ...the brain's suprachiasmatic nucleus, higher nervous centres, depression, hostility and aggression appear to be important determinants of heart rate variability (HRV), which is, itself, an important risk factor of myocardial infarction, arrhythmias, sudden death & heart failure....."

Biomed Pharmacotherap 2002;56(S2):257-65

APPLICATIONS OF HRV IN NEUROSURGERY

Our experiences in clinical study

Subarachnoid hemorrhage
蜘蛛膜下腔出血

- **SAH: 1-7% of all strokes**
- **Up to half of all cases are fatal and 10-15% die before reaching a hospital**

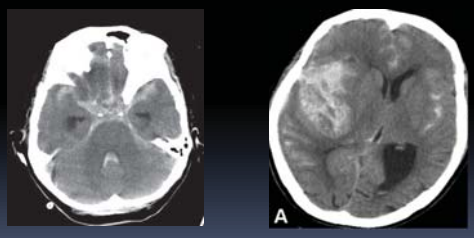
Subarachnoid hemorrhage
蜘蛛膜下腔出血

Clinical severity

Grade	Signs and symptoms	Survival
1	Asymptomatic or minimal headache	70%
2	Moderate to severe headache; no neurologic deficit except cranial nerve palsy	60%
3	Drowsy; minimal neurologic deficit	50%
4	Stuporous; possibly early decerebrate rigidity and vegetative disturbances	20%
5	Deep coma; decerebrate rigidity; moribund	10%

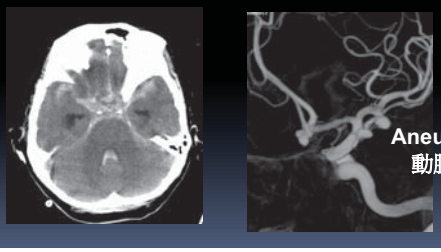
Subarachnoid hemorrhage
蜘蛛膜下腔出血

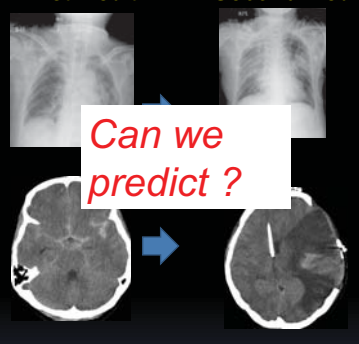
Typical example of brain-heart connection

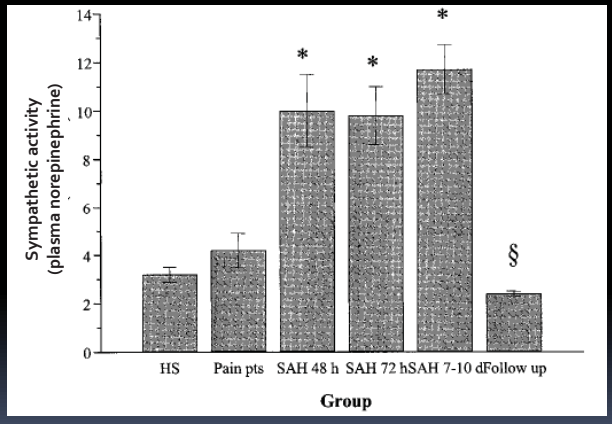


Subarachnoid hemorrhage
蜘蛛膜下腔出血

Typical example of brain-heart connection







Stroke 2003;31:901-6

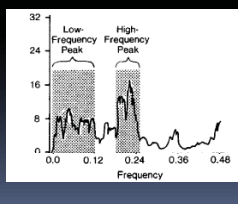
APPLICATION 1

HYPOTHESIS:

Can we predict early complications based on autonomic nervous activity?

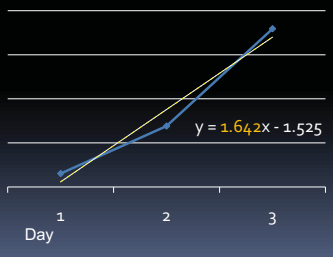
Can we predict early complications?

- Study design:
  - Observational prospective study
  - Retreive daily morning ECG from day 1 to day 3
- Biosignal processing
  - FFT analysis of of HRV
    - LF: sympathetic modulation
    - HF: vagal modulation
    - LF/HF: sympathovagal balance



Can we predict early complications?

- The trends of HRV changes from day 1 to day 3
  - LF slope
  - HF slope
  - LF/HF slope

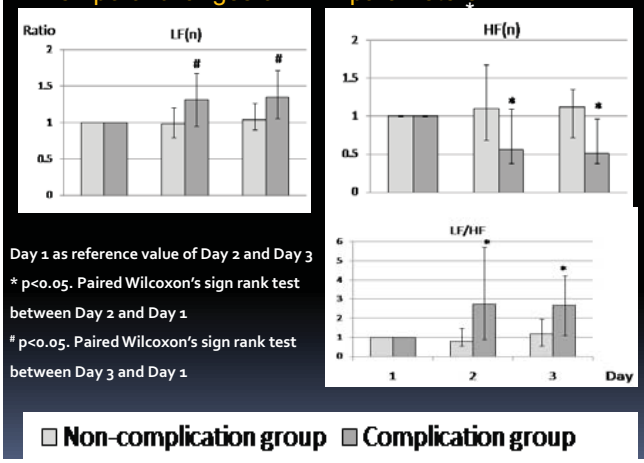


Can we predict early complications?

- Characteristics of the 30 patients in this study

	No.
Age	52 (26~68)
Sex(M:F)	11:19
Clinical severity	
Low(WFNS grade I~III)	15
High(WFNS grade IV~V)	15
Complications	16 (53%)
ICH	1
Symptomatic vasospasm	3
Infarction	6
Neurogenic edema	3
Early death	4

Temporal changes of HRV parameters



Day 1 as reference value of Day 2 and Day 3

* p<0.05. Paired Wilcoxon's sign rank test between Day 2 and Day 1

# p<0.05. Paired Wilcoxon's sign rank test between Day 3 and Day 1

Can we predict early complications?

Logistic regression

	Regression coefficient	Odds ratio*	P value
Age	0.003	1.00	0.96
Female gender	-1.52	0.22	0.19
Clinical severity	2.44	11.47	0.04
LF/HF increment	2.71	14.98	0.02

*Non-complication group as reference

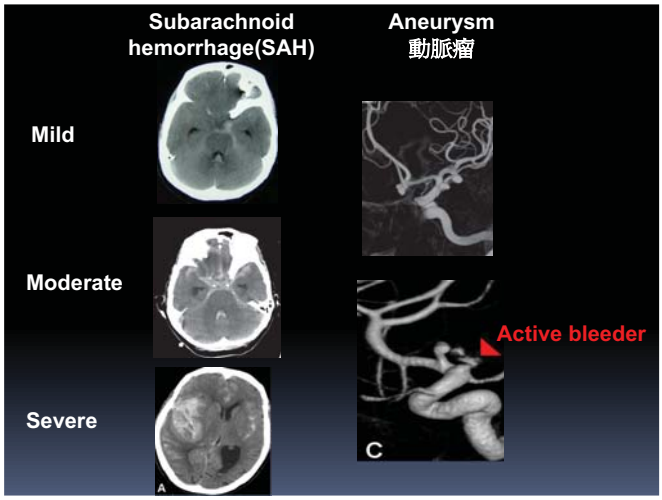
Conclusions

- *SAH patients who had early severe complications* exhibited an approximately 2~2.5-fold increase in sympathovagal ratio.
- Patients who had an increase of 1 unit of LF/HF slope in first three days are 15 times more likely to have severe complications in one week

Application 2

Poor grade SAH

Grade	Signs and symptoms	Survival
1	Asymptomatic or minimal headache	70%
2	Moderate to severe headache; no neurologic deficit except cranial nerve palsy	60%
3	Drowsy; minimal neurologic deficit	50%
4	Stuporous; possibly early decerebrate rigidity and vegetative disturbances	20%
5	Deep coma; decerebrate rigidity; moribund	10%



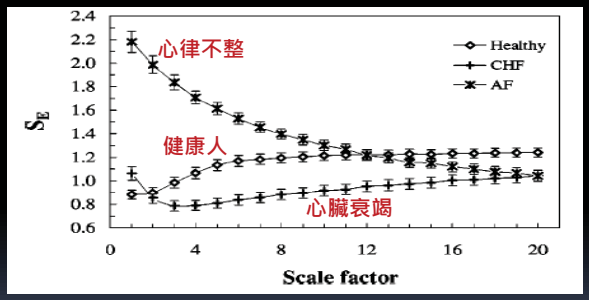
Poor grade SAH

- Management of good grade SAH is more straightforward, usually with favorable treatment outcomes
- Treatment outcomes of poor grade SAH is more variable
  - Good outcome: 40%
  - Poor outcome (vegetation or death): 60%
- ***Ethical issue***

Poor grade SAH

- The greatest issue is to find out a reliable way to early predict possible outcomes of the poor-grade patients after treatment

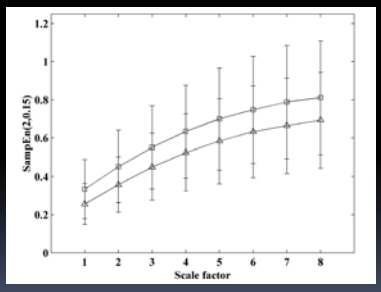
Examples of MSE in severity classification



Physical Review 2005;71:021906

Examples of MSE in severity classification

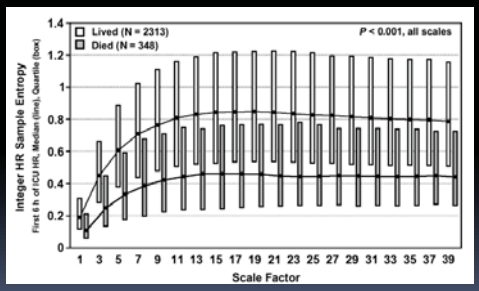
- Fetal heart beat
  - Normal birth fetus *VS* distressed fetus at birth



IEEE Trans Biomed Eng 53;1:119-124

Examples of MSE in severity classification

- Trauma pateints
  - Lived *VS* Died



J Crit Care 2008;23:399-405

Application 2

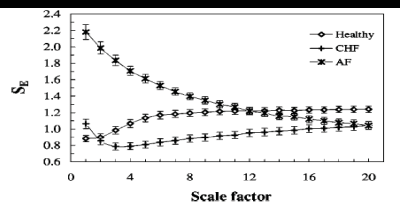
Hypothesis:

Can MSE analysis of HRV reflect the severity of brain damage and predict treatment outcomes?

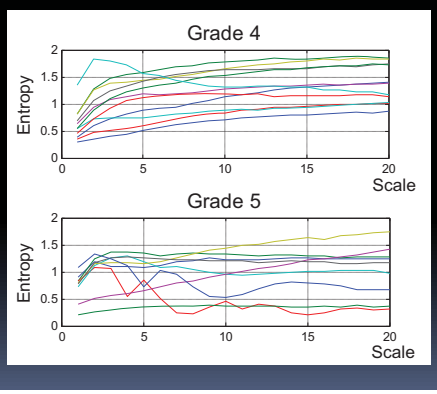
MSE analysis of HRV

- Two important parameters of MSE curve
  - Sample entropy(S_E) value: MSE value
  - Trends of S_E changes along the scales: MSE curve

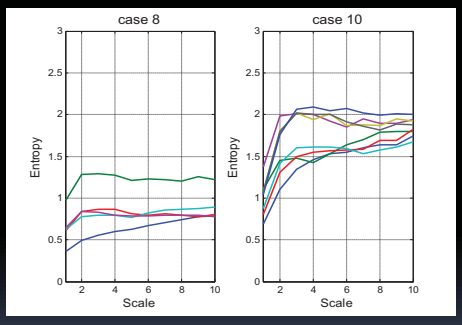
Indicators of complexity



MSE value

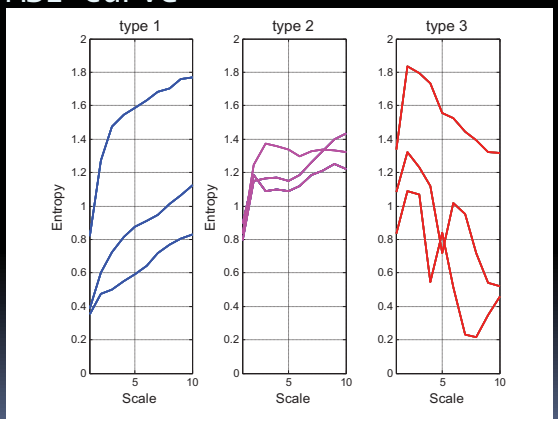


MSE value



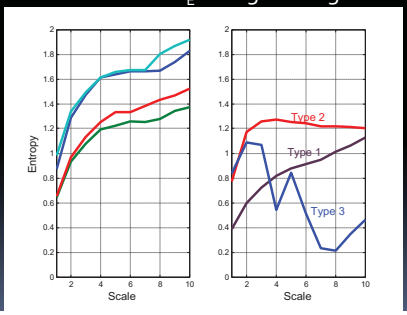
➔Area under curve (AUC) as the indicator of entropy value

MSE curve

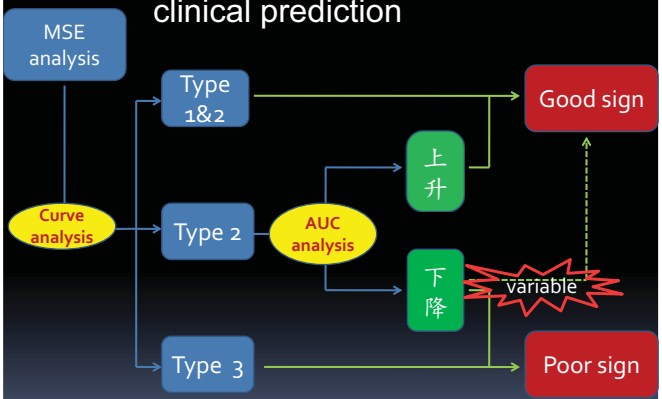


MSE analysis of HRV

- Indicators of complexity
  - AUC: comparable in the same subject only
  - MSE curve: trends of S_E changes along the scales



Proposed algorithm for clinical prediction

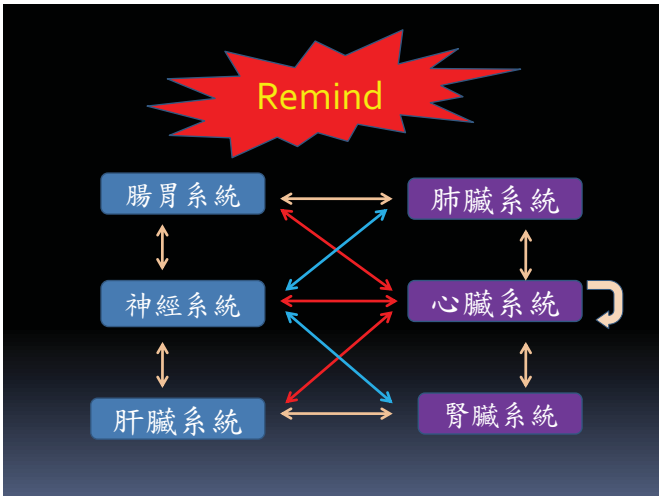


Conclusions

- In a certain degree, MSE analyses of HRV reflect the clinical course of the patients
- Can MSE results of HRV be regarded as another useful vital sign?
- How about MSE-based treatment monitoring & treatment plan design? Is it clinical relevant?
  - ➔ Further validation is mandatory

CLINICAL APPLICATIONS OF MODERN BIOSIGNAL PROCESSING

Personal opinion

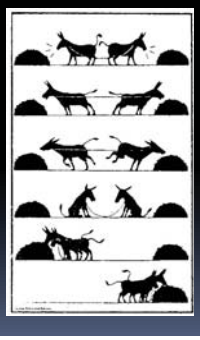


Clinical applications of modern biosignal processing

- 新一代的利器，提供傳統判讀無法分析出、甚至不曾得知的新思維。
  - 然而，甚麼是最適當的分析方法?
  - So what? Is it just a game?
- 最重要的課題依舊是賦予生理或病理意義，以及其臨床價值

Ultimate goal

訊號分析專家



生物醫學專家

Thanks for your attention