HRV 2006

Time Domain Measures: From Variance to pNNx

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Outline

- Background concepts
- Basic time and frequency domain measures
  - Definitions
  - Representative values
  - Correlations between measures
- Confounding factors
  - False/missed normal beat detections
  - Fiducial point misalignment
  - Supraventricular ectopy/conduction disorders
- The pNNx family of statistics

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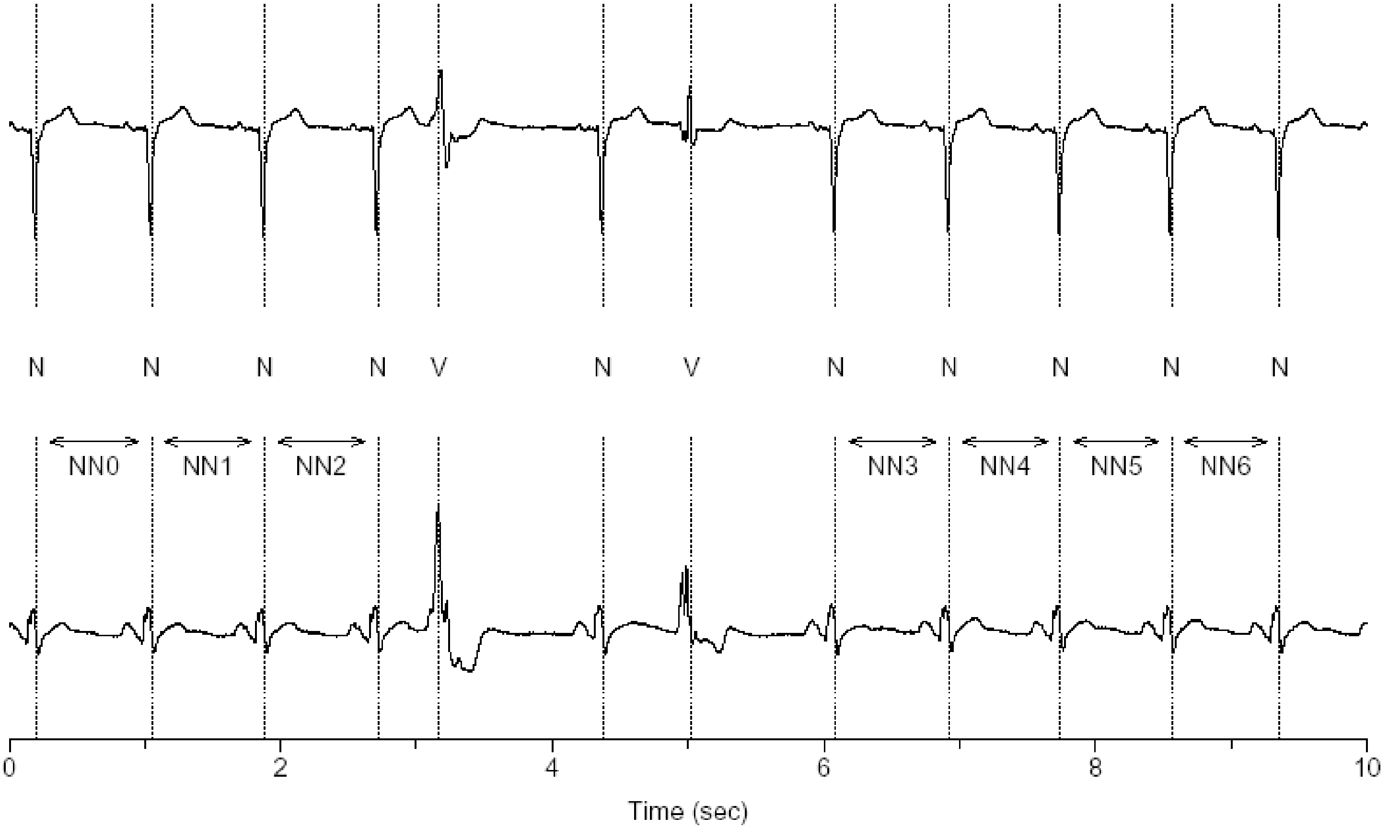
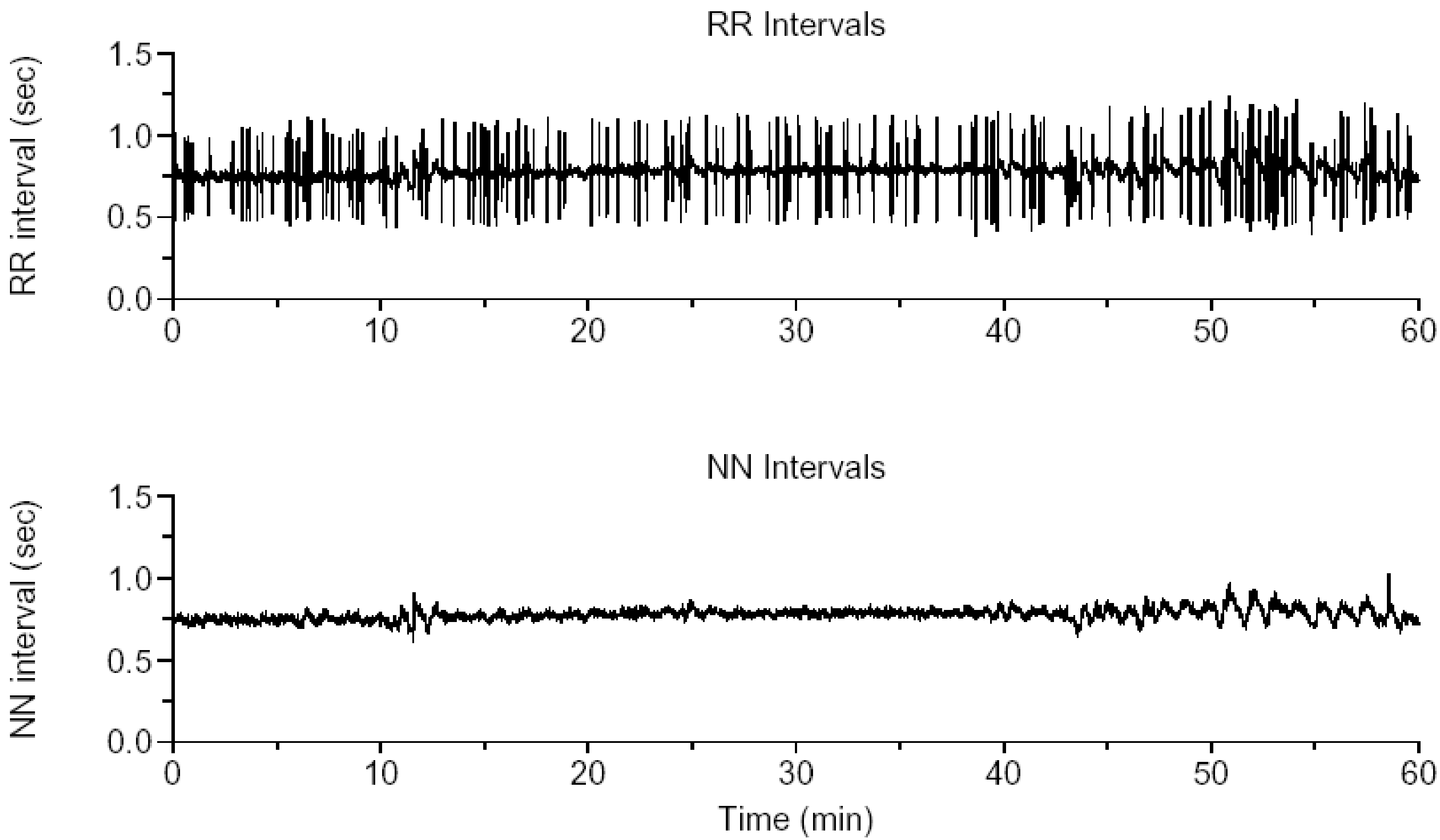
HRV and Cardiac Autonomic Tone Modulation

- HRV analysis attempts to assess cardiac autonomic regulation through quantification of sinus rhythm variability
  - Fast variations reflect parasympathetic (vagal) modulation
  - Slower variations reflect a combination of both parasympathetic and sympathetic modulation and non-autonomic factors

Sinus rhythm time series is derived from the RR interval sequence by extracting only normal sinus to normal sinus (NN) interbeat intervals



Underlying sinus rhythm time series in the presence of frequent PVCs



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Classification of HRV Measures

- Time domain measures
  - Treat the NN interval sequence as an unordered set of intervals (or pairs of intervals) and employ different techniques to express the variance of such data

- Frequency domain measures
  - Power spectral density analysis provides information on how the power (variance) of the ordered NN intervals distributes as a function of frequency

- Complexity/Non-linear measures
  - Analysis also based on the time-dependent ordering of the NN interval sequence

Commonly Used Time Domain Measures

- AVNN : Average of all NN intervals
- SDNN : Standard deviation of all NN intervals
- SDANN : Standard deviation of the average of NN intervals in all 5-minute segments of a **24-h recording**
- SDNNIDX (ASDNN) : Mean of the standard deviation in all 5-minute segments of a **24-h recording**
- rMSSD : Square root of the mean of the squares of the differences between adjacent NN intervals
- pNN50 : Percentage of differences between adjacent NN intervals that are >50 msec; this is one member of the larger pNNx family

Commonly Used Frequency Domain Measures

- Total power : Total NN interval spectral power up to 0.4 Hz.
- ULF (Ultralow frequency) power : Total NN interval spectral power up to 0.003 Hz. of a **24-h recording**
- VLF (Very Low Frequency) power : Total NN interval spectral power between 0.003 and 0.04 Hz.
- LF (Low Frequency) power : Total NN interval spectral power between 0.04 and 0.15 Hz
- HF (High Frequency) power : Total NN interval spectral power between 0.15 and 0.4 Hz.
- LF/HF ratio : Ratio of low to high frequency power

Representative values of HRV measurements in a 24 hour data set of ostensibly healthy subjects*

(35 males, 37 females, ages 20-76, mean 55)

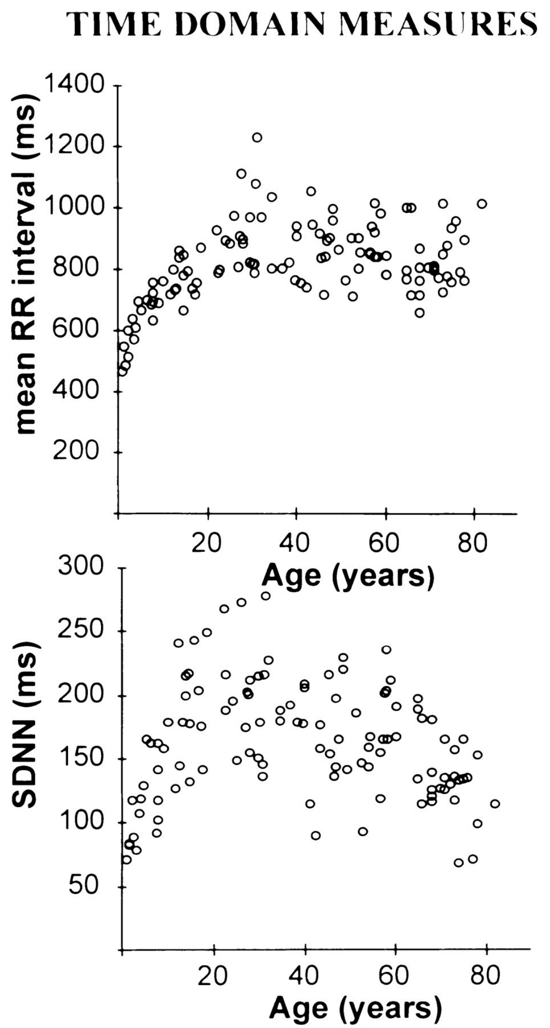
Measurement	Average Value
AVNN (msec)	787.7 ± 79.2
SDNN (msec)	136.5 ± 33.4
SDANN (msec)	126.9 ± 35.7
SDNNIDX (msec)	51.3 ± 14.2
rMSSD (msec)	27.9 ± 12.3
pNN20 (%)	34.2 ± 13.7
pNN50 (%)	7.5 ± 7.6
TOTPWR ($msec^2$)	21470 ± 11566
ULF PWR ($msec^2$)	18128 ± 10109
VLF PWR ($msec^2$)	1900 ± 1056
LF PWR ($msec^2$)	960 ± 721
HF PWR ($msec^2$)	483 ± 840
LH/HF ratio	2.9 ± 1.4

* Data from http://www.physionet.org/physiotools/pNNx

Values of HRV measurements are dependent on:

- Data length
- Age
- Physical conditioning
- Activity
- Sleep/wake cycle
- Disease
- Drug effects
- Gender

Time Domain Measures Change with Age

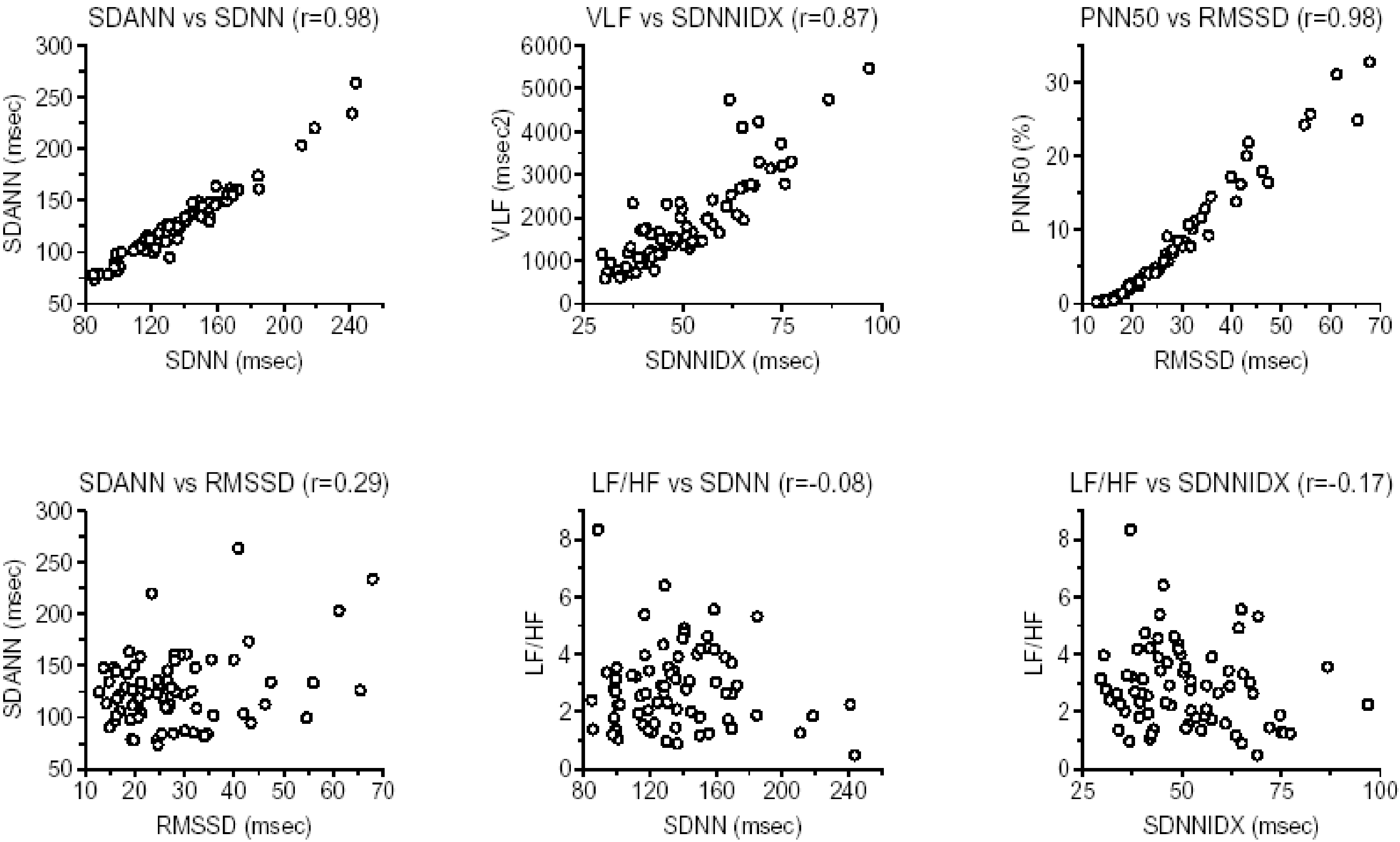


From: Pikkujamsa, et al. Circulation 1999;100:393-399

Correlations between HRV Measures

- Highly correlated measures
  - SDNN, SDANN, total power and ULF power
  - SDNNIDX, VLF power and LF power
  - rMSSD, pNN50 and HF power
- LF/HF ratio does not strongly correlate with any other HRV measures

Examples of strong and weak HRV correlations



* Normal data from http://www.physionet.org/physiotools/pNNx

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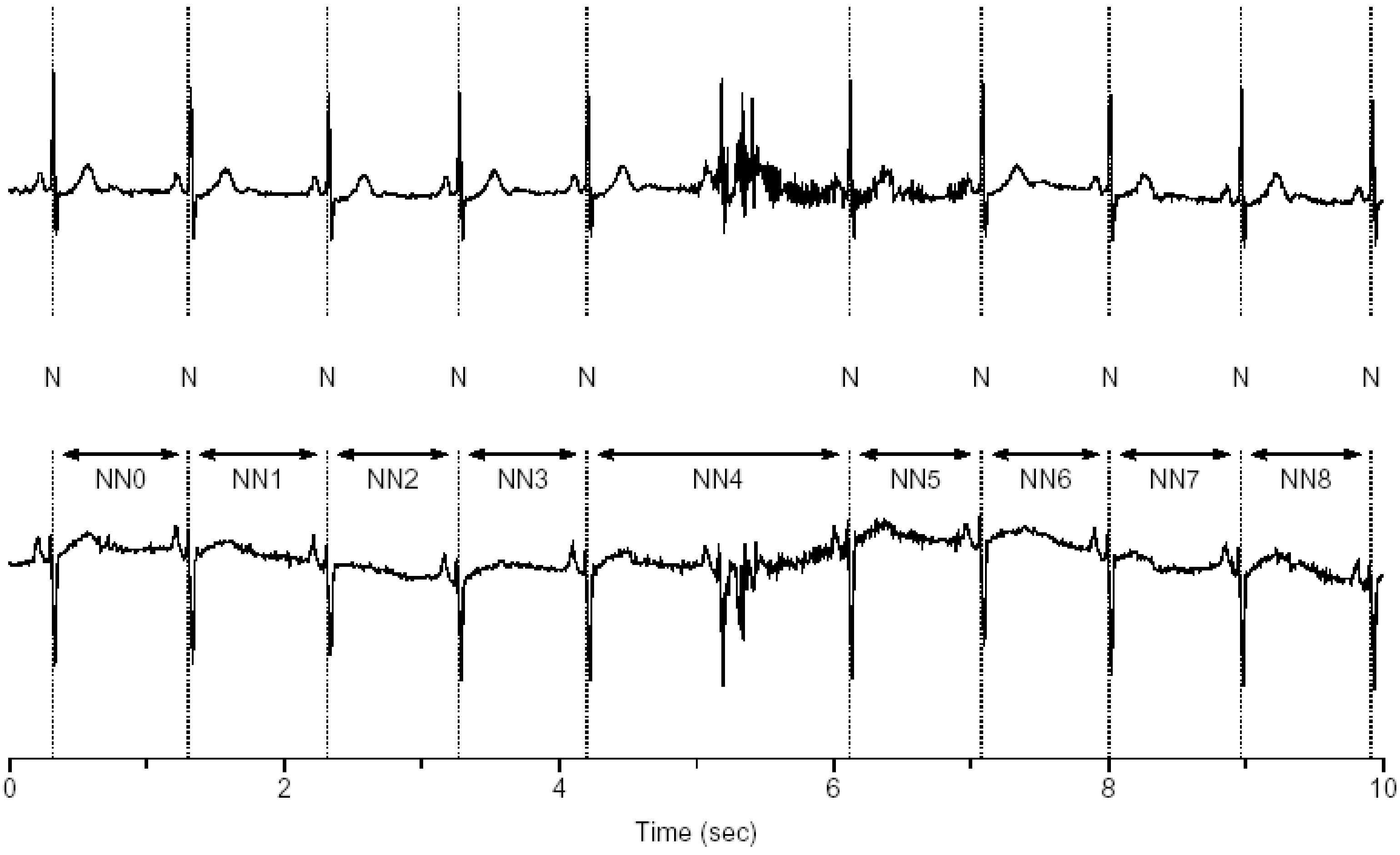
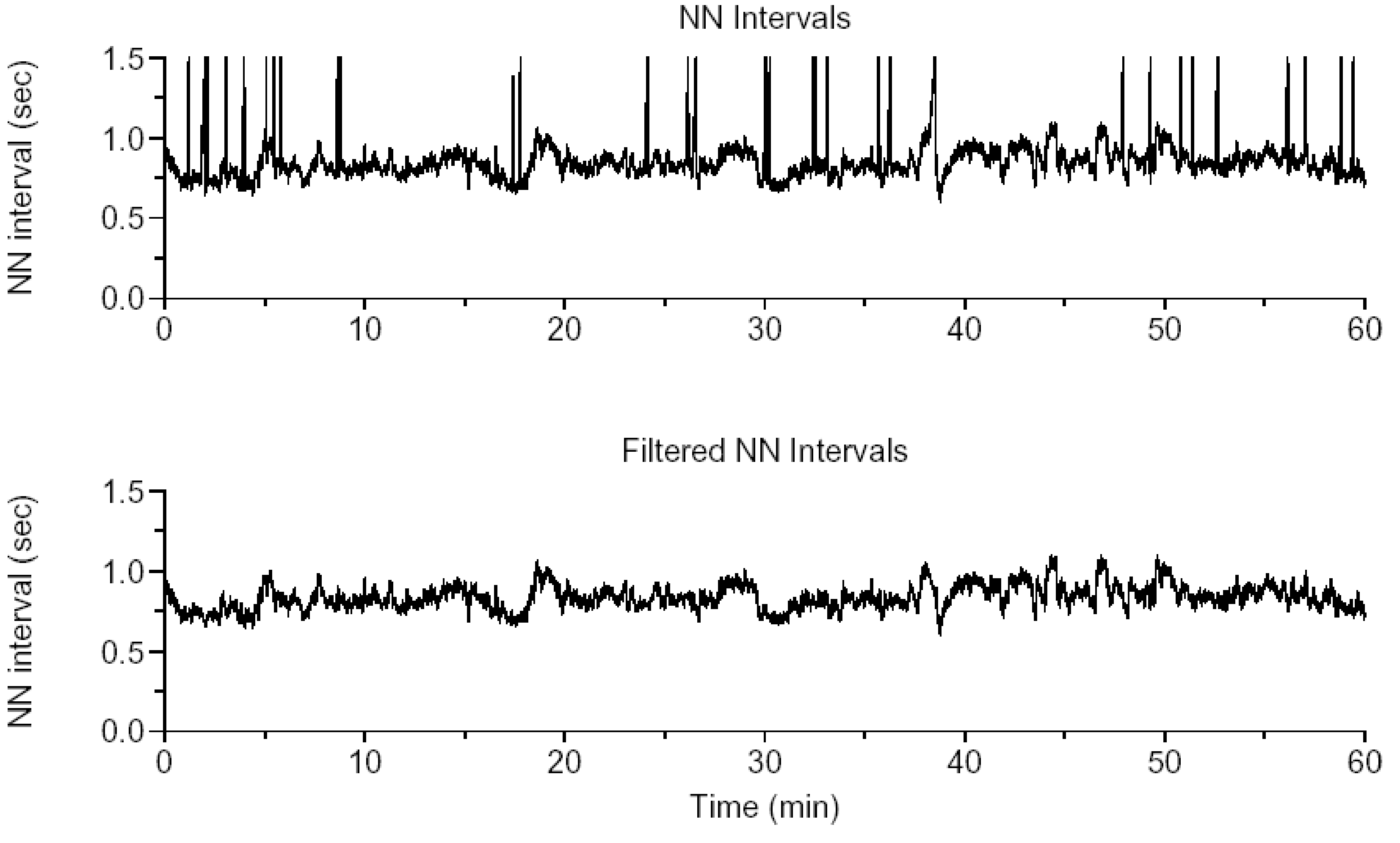
Missed Normal Sinus Beat Detection



Outliers due to missed normal beat detections



Sliding Window Average Filter

- Delete non-physiologic intervals (e.g., <0.4 or >2.0 sec)
- Select a window size of 2N+1 (e.g. 41) data points
- Average the N data points on either side of the central point
- Exclude central point if it lies some fixed fraction (e.g. 20%) outside of window average
- Advance to next data point
- Variations
  - Use window median rather than mean
  - Calculate the standard deviation of data in window and reject central point if it lies outside 3 standard deviations

Effect of Outliers on HRV Measurements in One 24-Hour Data Set

Measurement	Filtered	Unfiltered	%Change
AVNN (msec)	920.9	961.7	4%
SDNN (msec)	134.6	1090.1	710%
SDANN (msec)	119.1	241.6	103%
SDNNIDX (msec)	61.7	503.7	716%
rMSSD (msec)	25.6	1539.8	5907%
pNN20 (%)	39.2	40.3	3%
pNN50 (%)	5.0	6.7	35%
TOTPWR ($msec^2$)	22430.4	916873.0	3988%
ULF PWR ($msec^2$)	14989.5	16255.8	8%
VLF PWR ($msec^2$)	4740.5	84665.3	1686%
LF PWR ($msec^2$)	2092.3	249524.0	11826%
HF PWR ($msec^2$)	608.0	566427.0	93058%
LH/HF ratio	3.4	0.4	-87%

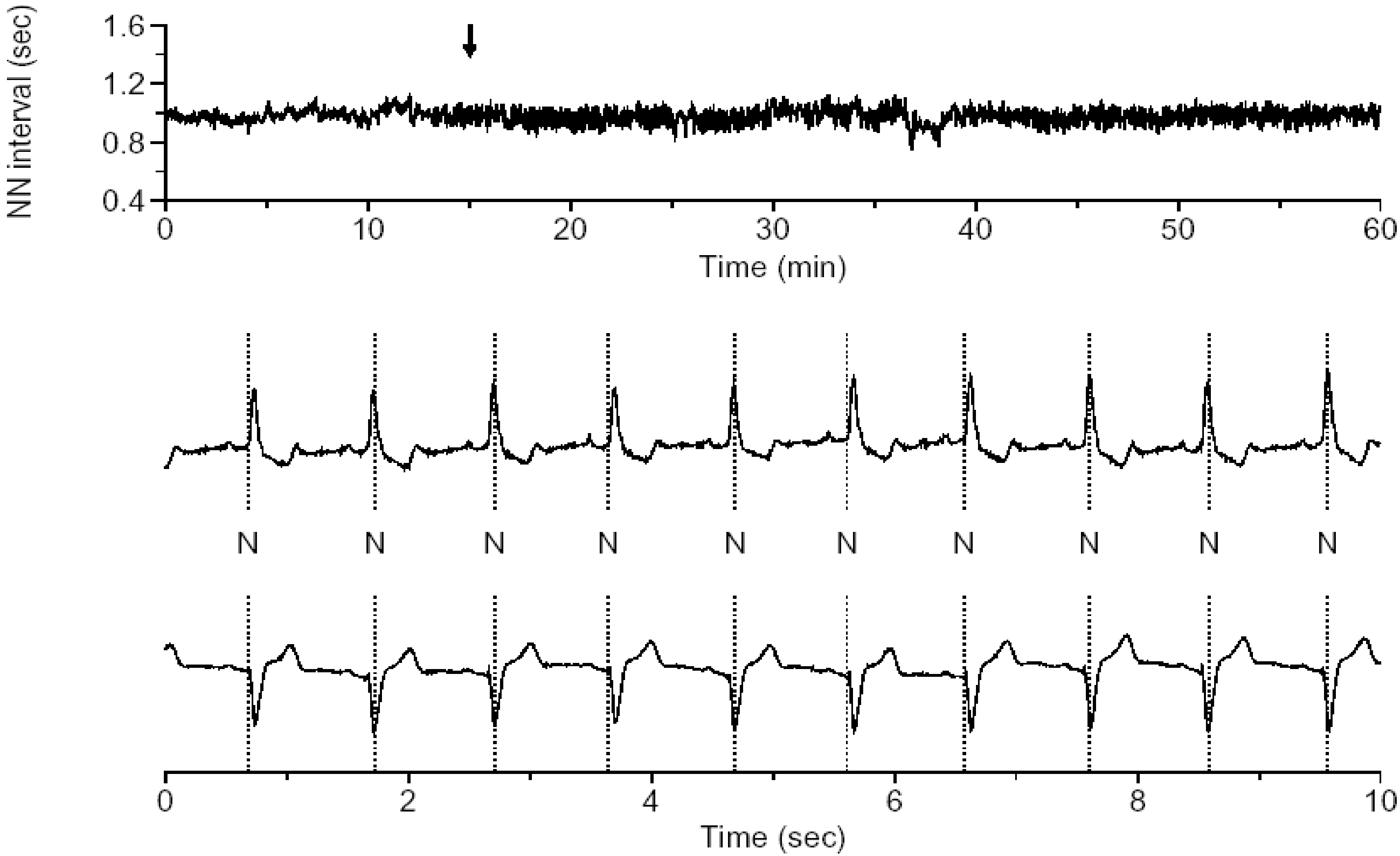
Effect of Outliers on HRV Measurements

- Most frequency domain measures are especially susceptible to outliers particularly LF and HF power, can be >1000% error

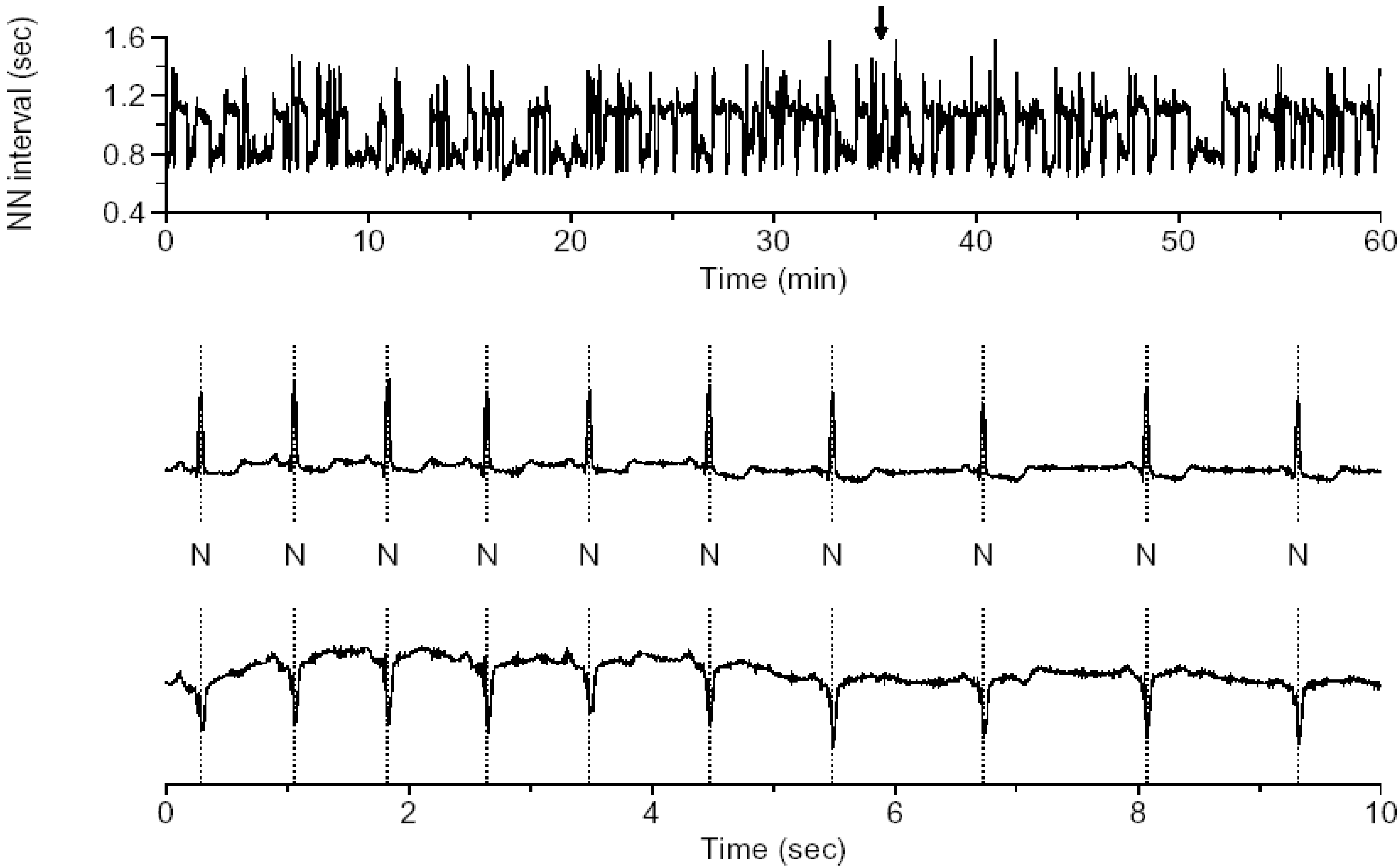
- Most time domain measures are less affected but still give erroneous results, can be >100% error

- AVNN, pNN20 and ULF power are least affected generally <10% error

Artifactual variability due to fiducial point misalignment



Erratic supraventricular rhythm: wandering atrial pacemaker vs SA node dysrhythmia



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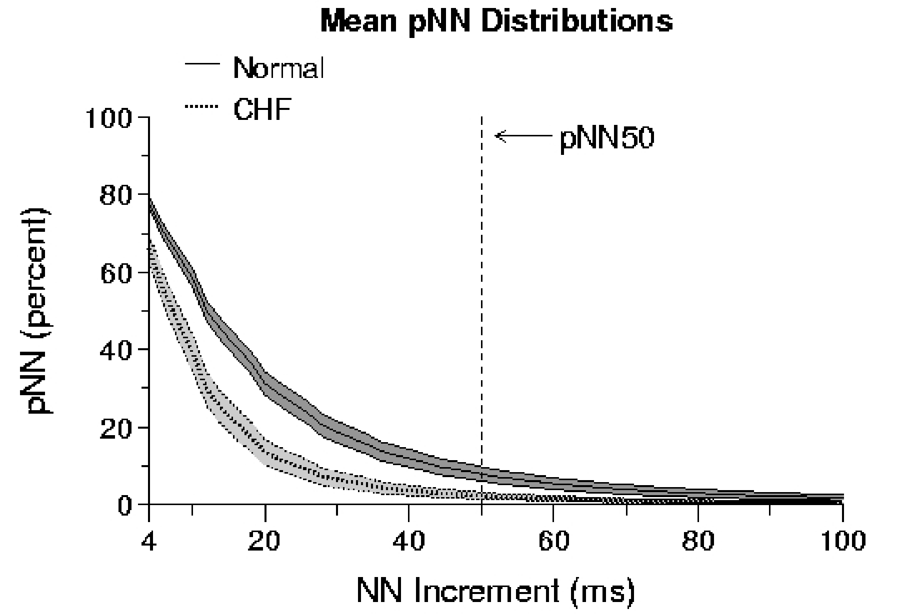
- **The pNNx family of statistics**

The pNNx Family of HRV Statistics: a measure of cardiac vagal tone modulation

- 1984: Ewing et al. introduced the NN50 count
  - Defined as the mean number of times per hour in which the change in successive NN intervals exceeds 50 msec
- 1988: Bigger et al. introduced the pNN50 statistic
  - Defined as the NN50 count / total NN count
- 2002: Mietus et al. introduced the pNNx family of statistics
  - Defined as the NNx count / total NN count for values of $x \geq 0$
  - Finding pNNx for $x < 50$ msec provided more robust discrimination between groups

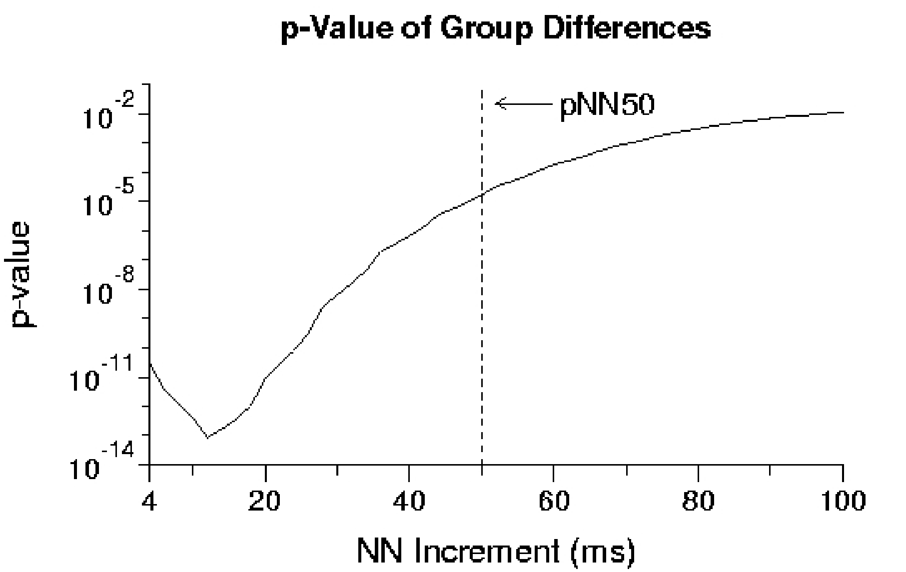
pNN distributions for Healthy subjects (n=72) and Congestive Heart Failure subjects (n=43)



p-values for the separation of groups (t-test)

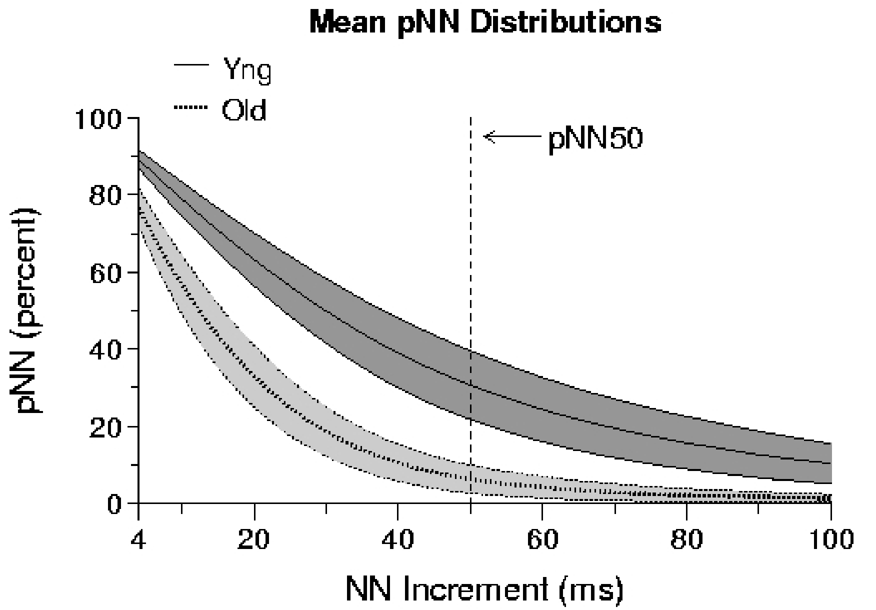
pNN50 : $p<10^{-4}$

pNN12 : $p<10^{-13}$



Data from http://www.physionet.org/physiotools/pNNx

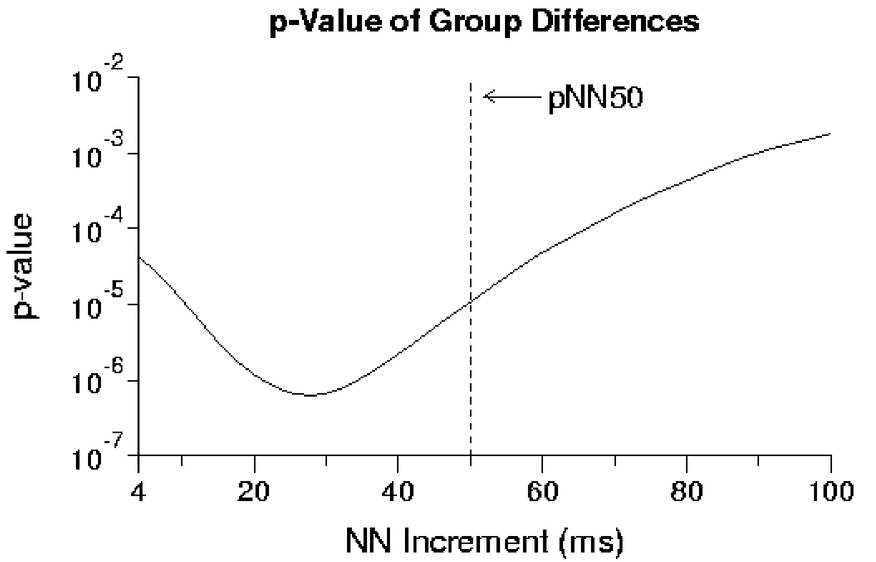
pNN distributions for Young subjects (n=20, ages 21-34) and Old subjects (n=20, ages 68-85)



p-values for the separation of groups (t-test)

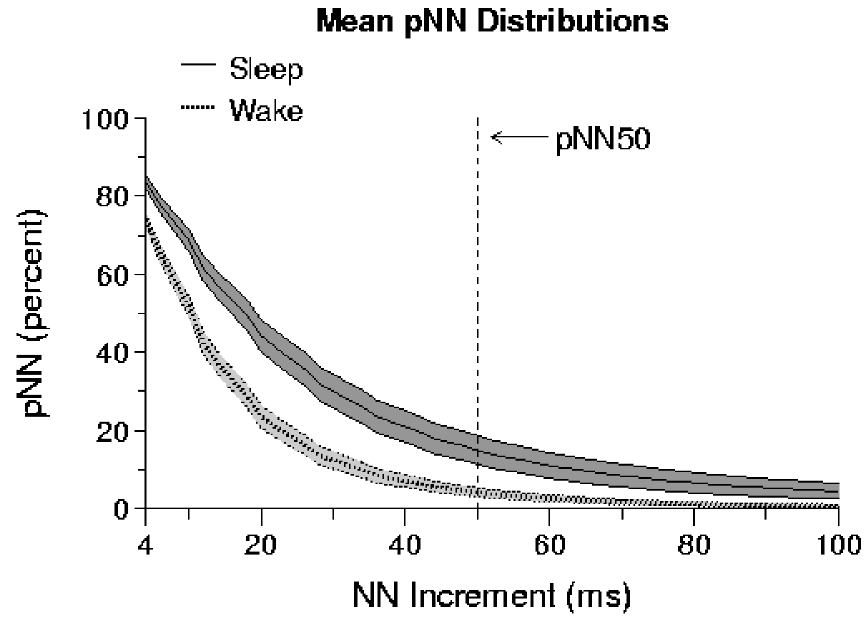
pNN50 : $p<10^{-4}$

pNN28 : $p<10^{-6}$



Data from http://www.physionet.org/physiotools/pNNx

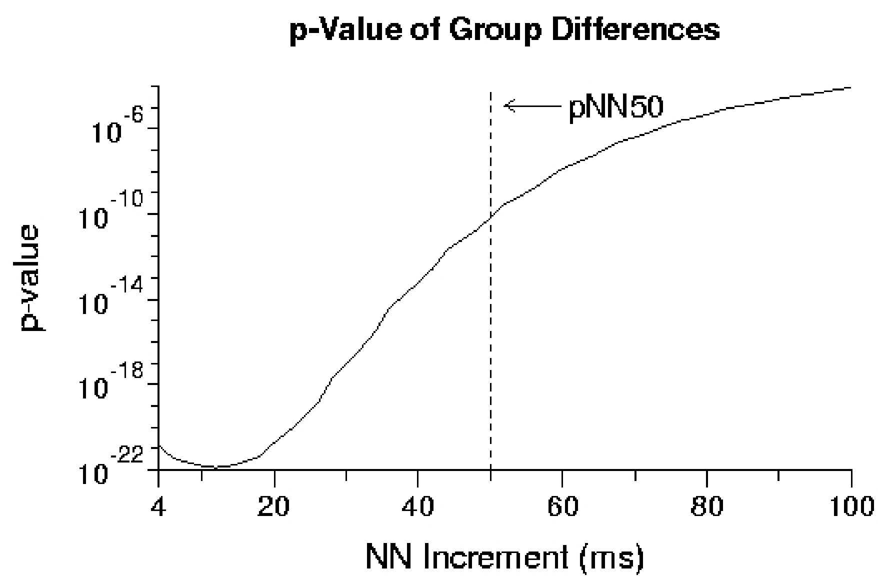
pNN distributions for Normal subjects (n=72) during 6 hours of Sleep and Wake



p-values for the separation of groups (paired t-test)

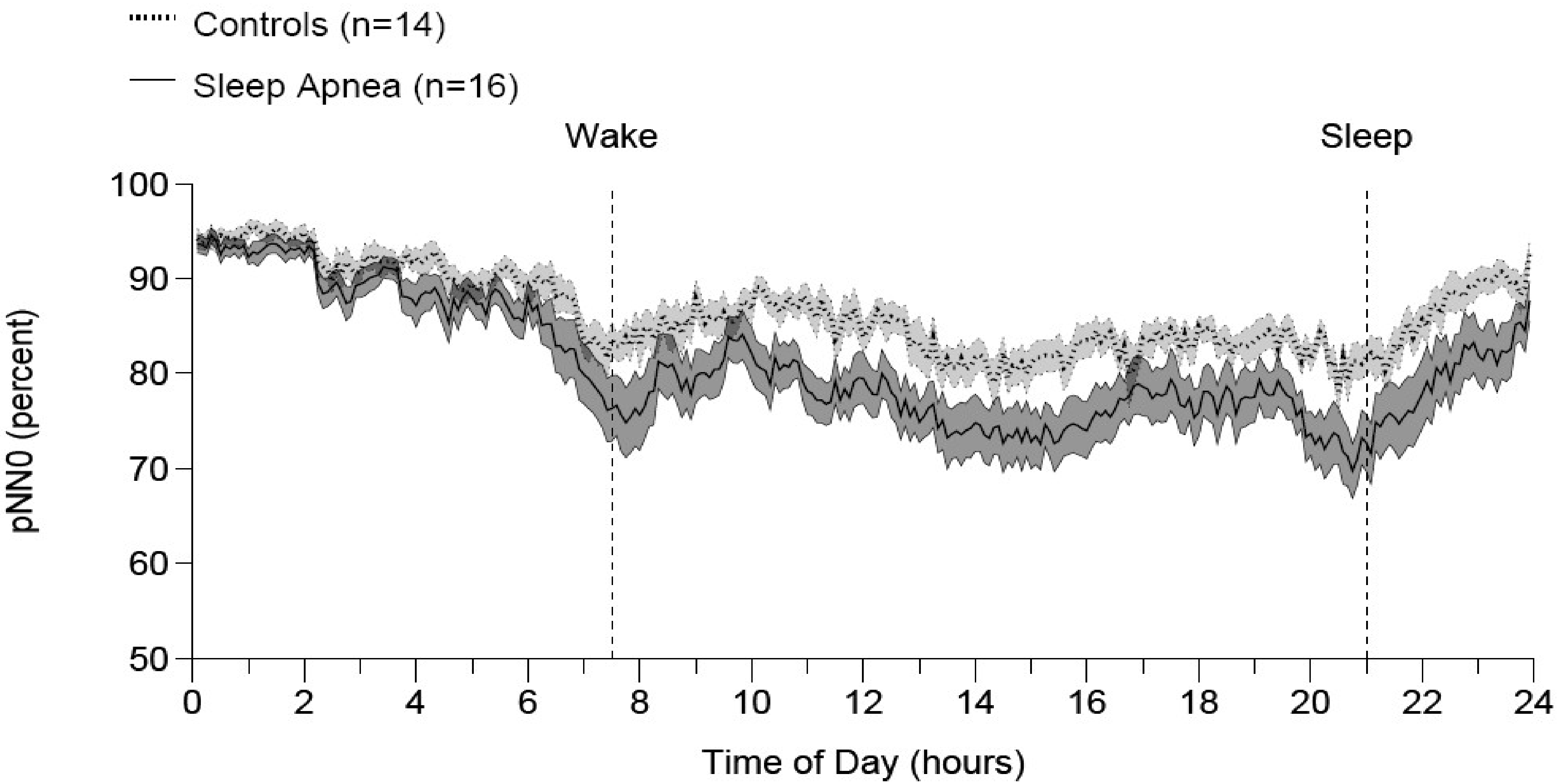
pNN50 : $p<10^{-10}$

pNN12 : $p<10^{-21}$



Data from http://www.physionet.org/physiotools/pNNx

Loss of daytime cardiac vagal modulation in sleep apnea hypopnea syndrome



Unpublished data courtesy of Steven Shea and Michael Hilton, Brigham and Women's Hospital

The pNNx Heart Rate Variability Metric: A Generalization of pNN50 (`pnnlist`)

JE Mietus,[1] C-K Peng,[1] I Henry,[1] RL Goldsmith,[2] AL Goldberger[1]

[1]Margret and H.A. Rey Institute for Nonlinear Dynamics in Physiology and Medicine, Cardiovascular Division, Harvard Medical School/Beth Israel Deaconess Medical Center, Boston, MA

[2]Division of Circulatory Physiology, Columbia-Presbyterian Medical Center, New York, NY

A detailed description of an application of the `pNNx` algorithm can be found in:

Mietus JE, Peng C-K, Henry I, Goldsmith RL, Goldberger AL. The pNNx files: re-examining a widely used heart rate variability measure. *Heart* **88**:378-380; 2002.

Please cite this publication when referencing this material, and also include the standard citation for PhysioNet:

Goldberger AL, Amaral LAN, Glass L, Hausdorff JM, Ivanov PCh, Mark RG, Mietus JE, Moody GB, Peng C-K, Stanley HE. PhysioBank, PhysioToolkit, and PhysioNet: Components of a New Research Resource for Complex Physiologic Signals. *Circulation* **101**(23):e215-e220 [Circulation Electronic Pages; http://circ.ahajournals.org/cgi/content/full/101/23/e215]; 2000 (June 13).

http://www.physionet.org/physiotools/pNNx

Source code freely available

Conclusions

- Most time and frequency domain measures are sensitive to outliers
- Always visually inspect data and filter outliers if necessary
- pNNx for values of x<50 msec may provide more robust estimates of cardiac vagal tone modulation even in the presence of outliers

References

- Bigger JT Jr, Kleiger RE, Fleiss JL, et al. Components of heart rate variability measured during healing of acute myocardial infarction. Am J Cardiol 1988;61:208-215
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