Long Term Cardiotoxic Effects of Sarin

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ACKNOWLEDGEMENTS

• Swapnil Shewale
• Mike Horenziak
• James Lucot
• Brent Izu
• Mary Key
• Mark Anstadt
• Vera Farah
• Teresa Garrett
HISTORICAL PERSPECTIVE
THE USE OF SARIN
GULF WAR 1991

Demolition of bunkers at Khamisiyah, 4 March 1991.
CIA, 1997; http://www.fas.org/irp/gulf/cia/970409/cia_wp.html

HISTORICAL PERSPECTIVE
USE OF SARIN
GULF WAR 1991


Quantitative magnetic resonance brain imaging in US army veterans of the 1991 Gulf War potentially exposed to sarin and cyclosarin
Kristin J. Heaton, Carole L. Palumbo, Susan P. Proctor, Ronald J. Killiany, Deborah A. Yurgelun-Todd, Roberta F. White
Neurotoxicology 28: 2007
- Reduced white matter
- Enlarged left cerebral ventricle
- Persistent CNS pathologies
Case Report: Long term cognitive sequelae of sarin exposure

Loh et al., Neurotoxicology, 2010

- Recent exposure Army captain
- Munition disposal
- Sustained neurocognitive deficits

OBJECTIVE 1:
Autonomic Cardiovascular Effects of Low Dose Sarin

- Radiotelemetry
- Sarin sc 0.4 LD$_{50}$
- Spectral analysis - autoregressive method
- Blood and brain AChE
Spectral Analysis for Characterization of Autonomic Balance

Statistical method for characterization of variability. Spectra of variability are composed of 2 oscillatory components; low frequency 0.1-1 Hz) and high frequency (1-5.0 Hz). Spectra are associated with autonomic balance, sympathetic and parasympathetic.
Low Dose Sarin
Blood Pressure and Heart Rate

Mean Arterial Pressure

<table>
<thead>
<tr>
<th></th>
<th>Basal</th>
<th>1</th>
<th>7</th>
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</thead>
<tbody>
<tr>
<td>mmHg</td>
<td></td>
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</tr>
<tr>
<td>Basal</td>
<td>40</td>
<td>80</td>
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<tr>
<td>1</td>
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<td>7</td>
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Heart Rate

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Variance                  Low Freq                 High Freq

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<thead>
<tr>
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<th>Control</th>
<th>Sarin</th>
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<tbody>
<tr>
<td>mmHg</td>
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<tr>
<td>Control</td>
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<tr>
<td>Sarin</td>
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Effect of Sarin on Heart Rate Variance and Frequency Domains

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<thead>
<tr>
<th></th>
<th>Variance</th>
<th>Low Freq</th>
<th>High Freq</th>
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<tbody>
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<td>ms²</td>
<td>40</td>
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</table>

Farah et al., Autonomic Neuroscience:
Clinical and Basic, 2007
CLINICAL IMPLICATIONS OF LOW HR VARIABILITY

LaRovere et al. 2003

Low Dose Sarin on Brainstem Catecholamine Systems

Sarin

Control
OBJECTIVE 2:

To identify the long term effects of low dose sarin on cardiac structure and function in mice
**TIME COURSE PROTOCOL**

- **SARIN (0.4 LD50) 8 WEEKS AGE**
- **CV DATA 10, 12, 18 WEEKS AGE**
- **SACRIFICE 18 WEEKS AGE**

**ECHOCARDIOGRAPHY (ECHO)**

**ELECTROCARDIOGRAM (ECG)**

**CV STRESS TEST**

**CARDIAC MARKERS**

**HEART AND CELL SIZE**

**METHODS PROTOCOL**

- 2D and M mode ECHO were used to measure left ventricular structure and performance at baseline and after dobutamine stress test at 2, 4, and 10 wks after sarin.
- ECG tracings were recorded at the 10 week point, baseline and after dobutamine.
- Histological and immunochemical parameters (i.e., natriuretic peptides) were measured upon sacrifice.
Echocardiography

- Piezoelectric crystals convert electrical current into sound waves
- Tissues of varying impedance create reflected sound waves
- Reflected sound waves produce electrical currents that are processed into images
Parasternal Long Axis (PLAX) 2-D ECHO

- Septal Wall
- Left Ventricle
- Papillary Muscle
- Right Atrium