PHYSIOLOGY OF CARDIAC HYPERTROPHY IN SEVERELY IRON DEFICIENT RATS USING PRESSURE-VOLUME LOOPS

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Enlargement of the heart

- Can either be adaptive or pathological
  - Adaptive hypertrophy is seen in aerobic athletes
  - Pathological hypertrophy is seen in diseases of the heart such as congestive heart failure
Adaptive hypertrophy
- Increased cardiac output
- Increased heart chamber size
- Healthy heart wall muscle

Pathological Hypertrophy
- Decreased cardiac output
- No increase in heart chamber size
- Fibrotic heart wall
  - Due to increase in collagen
PROLONGED IRON DEFICIENCY CAUSES CARDIAC HYPERTROPHY

Iron is at the center of Heme, to which oxygen binds

Iron Deficiency causes hypoxia

Hypoxia causes activation of the sympathetic nervous system

Constant stimulation of SNS results in hypertrophy

Hypertrophy may result in a short term adaptation

Increased Cardiac Output

Over time, hypertrophy may result in a failing heart

Decreased cardiac output
CURRENT UNDERSTANDING OF CARDIAC HYPERTROPHY FROM IRON DEFICIENCY

- 12 weeks of iron deficiency
- Morphological indications of failure
- Apoptosis stimulated
- Cardiac function of this hypertrophy is poorly understood

Ref: Dong et al., 2007.
We hypothesized that four weeks of iron deficiency would result in failing cardiac function and decreased sympathetic neurotransmitter stores.
Two groups Sprague-Dawley Rats

- Four rats fed iron deficient diet (AIN-93G without iron)
- Four rats fed control diet (AIN-93G)

- Four weeks of the respective dietary intervention
- Cardiac pressure-volume loop protocol
- Plasma and hearts frozen for HPLC analysis
PV LOOP PROTOCOL: SURGERY

- 2 femoral vein catheters for drug infusion
- 1 jugular vein catheter for saline calibration
- 1 carotid artery exposure for PV loop transducer
  - Inserted into the carotid artery and passed into the left ventricle
Aortic pressure measurements and baseline cardiac function data

Inferior Vena Cava occlusion for measure of contractility

Saline calibration for parallel conductance subtraction

Dopamine infusion

Atenolol infusion

Second baseline data

Heparinized rat to prevent blood clotting

Cuvette calibration for measure of true blood volume

Collect microhematocrit samples

Centrifuge remaining blood for plasma

Freeze plasma and hearts for HPLC analysis
RESULTS: IRON DEFICIENCY

**Hematocrit**

- **Control** vs. **Iron Deficient**
- Statistical significance: *p* < 0.05

**Body Mass**

- **Control** vs. **Iron Deficient**
- Statistical significance: *p* < 0.05
RESULTS: CARDIAC HYPERTROPHY

Iron Deficient

Control

Heart • Body Mass\(^{-1}\) Ratio

*\(p<0.05\)
Cardiac output = (SV)(HR)

End Systolic PV relationship (ESPVR)

Isovolumic Relaxation

Stroke Volume

Ejection

End Diastolic Volume

Isovolumic Contraction

Heart Rate

Filling
RESULTS: PRESSURE-VOLUME LOOPS

- Control
- Iron Deficient-Adaptive
- Iron Deficient-Failing
RESULTS: PRESSURE-VOLUME LOOPS

Cardiac Output

*\( p < 0.05 \)

\[ \text{CO} = \text{HR} \times \text{SV} \]
RESULTS: PRESSURE VOLUME LOOPS

Heart Rate

<table>
<thead>
<tr>
<th>Group</th>
<th>Heart Rate (bpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>250</td>
</tr>
<tr>
<td>Iron Deficient</td>
<td>200</td>
</tr>
</tbody>
</table>

Stroke Volume

<table>
<thead>
<tr>
<th>Group</th>
<th>Stroke Volume (uL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>300</td>
</tr>
<tr>
<td>Iron Deficient</td>
<td>100</td>
</tr>
</tbody>
</table>

*p<0.05
Stroke volume is affected by three factors:
(1) Preload
   ▪ End diastolic volume

RESULTS: PRESSURE VOLUME LOOPS

* p<0.05
(2) Contractility

- Sympathetic nervous system
- Ejection fraction
- Frank-Starling Law of the Heart

![Ejection Fraction Graph]

*P<0.05
ESPVR AS A MEASURE OF CONTRACTILITY

- Control rat ejection fraction averaged 55%
- Iron deficient rat ejection fraction averaged 93%
## RESULTS: PRESSURE-VOLUME LOOPS

<table>
<thead>
<tr>
<th></th>
<th>Control Group</th>
<th>Iron Deficient Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>dp • dt⁻¹ Max (mmHg s⁻¹)</td>
<td>6500 ± 500</td>
<td>5000 ± 400</td>
</tr>
</tbody>
</table>
(3) Afterload
- Aortic diastolic pressure
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HPLC is a technique used to separate and quantify chemical compounds in a liquid medium.

Used to determine concentration of norepinephrine in extracted plasma.
RESULTS: HPLC

Plasma Norepinephrine Concentration

- Control Group
- Iron Deficient Group

NE (μg·ml⁻¹)
CONCLUSION: 3 ADAPTIVE ID HEARTS, 1 FAILING ID HEART

Cardiac Output Increased → Heart Rate → Unchanged

Increase in Preload

Increase in Stroke Volume → Increase in End Diastolic Volume → Frank-Starling Law of the Heart

Uncertain changes in Contractility

ejection fraction 93% in ID rats

ESPVR can't be used as a measure of contractility

Possible decrease in afterload

Aortic diastolic pressure not significantly different

Trend

More experiments may show a significant difference
ACKNOWLEDGMENTS

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