Inhibition of blood cholinesterase activity is a poor predictor of acetylcholinesterase inhibition in brain regions of guinea pigs exposed to repeated doses of low levels of soman.

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Inhibition of blood cholinesterase activity is a poor predictor of acetylcholinesterase inhibition in brain regions of guinea pigs exposed to repeated doses of low levels of soman.

The experiment:

Expose male guinea pigs to subclinical doses of soman (0.1, 0.2, and 0.4 LD50) daily (M-F) for two weeks.

Collect blood and brain regions on exposure Day 5 and exposure Day 12, and after 3 and 17 days of recovery (Day 15 and Day 29).

Characterize inhibition of cholinesterase activity in blood and several brain regions: frontal cortex, parietal cortex, Hippocampus, cerebellum, brain stem and thalamus.
There is great inhibition of AChE in red blood cells after 5 days of exposure to 0.1, 0.2, or 0.4 LD50 soman.

AChE inhibition in brain is significant but not as extreme as in red blood cells.
Soman inhibition of AChE in red blood cells is not greater on Day 12 than on Day 5.

Inhibition of brain AChE by soman is greater in Day 12 than Day 5.

Inhibition of AChE in red blood cells by 0.1 or 0.2 LD50 Soman is much greater than inhibition in brain.
Day 5

Day 12

AChE activity, as percent control

RBC, Hip, FCTX, PCTX, BS, CB, TH

0.1, 0.2, 0.4
Recovery of AChE activity is apparent 3 days after the last exposure to soman.
AChE activity, as percent control

Day 5

Day 12

Day 15
Seventeen days after exposure AChE activity is still less than control levels in red blood cells and several brain regions.
Amount of inhibition of AChE activity was highly correlated between whole blood, and red blood cells, and plasma.
RBC vs. Whole Blood AChE

RBC vs. Plasma AChE

RBC AChE Activity, as percent control

Whole Blood AChE Activity, as percent control

Plasma AChE Activity, as percent control

r = 0.962

r = 0.920
Amount of inhibition of AChE activity in frontal cortex is highly correlated with amount of inhibition in parietal cortex and in hippocampus.
FCTX vs. PCTX AChE

PCTX AChE Activity, as percent control

FCTX AChE Activity, as percent control

r = 0.986

FCTX vs. Hip AChE

Hip AChE Activity, as percent control

FCTX AChE Activity, as percent control

r = 0.947
Amount of inhibition of AChE activity in cerebellum
Is highly correlated with inhibition in brain stem and
Thalamus.
CB vs. BS AChE

CB vs. TH AChE

$\text{BS AChE Activity, as percent control}$ vs.
$\text{CB AChE Activity, as percent control}$

$r = 0.942$

$\text{TH AChE Activity, as percent control}$ vs.
$\text{CB AChE Activity, as percent control}$

$r = 0.920$
Amount of inhibition in brain stem, cerebellum, and thalamus is not as well correlated with inhibition in cortical regions or hippocampus.
FCTX vs. BS AChE

FCTX vs. CB AChE

FCTX vs. BS AChE
Correlations between inhibition of AChE in red blood cells amount of inhibition in brain was only modest.
RBC vs. FCTX AChE

RBC vs. CB AChE

FCTX AChE Activity, as percent control

RBC AChE Activity, as percent control

r = 0.875

CB AChE Activity, as percent control

RBC AChE Activity, as percent control

r = 0.742
<table>
<thead>
<tr>
<th>Brain Region</th>
<th>RBC AChE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontal Cortex AChE</td>
<td>0.875</td>
</tr>
<tr>
<td>Parietal Cortex AChE</td>
<td>0.871</td>
</tr>
<tr>
<td>Hippocampus AChE</td>
<td>0.776</td>
</tr>
<tr>
<td>Cerebellum AChE</td>
<td>0.742</td>
</tr>
<tr>
<td>Brainstem AChE</td>
<td>0.723</td>
</tr>
<tr>
<td>Thalamus AChE</td>
<td>0.788</td>
</tr>
</tbody>
</table>
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