Brain Activity in Farmworkers Occupationally Exposed to Pesticides in Costa Rica

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Pesticides and human health

Occupational exposure to pesticides and respiratory health

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Pesticide exposure and risk of Parkinson's disease: Dose-response meta-analysis of observational studies

Dandan Yan\textsuperscript{a}, Yunjian Zhang\textsuperscript{b}, Liegang Liu\textsuperscript{a}, Nian Shi\textsuperscript{a}, Hong Yan\textsuperscript{a,4}

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Review

Association between Exposure to \(p,p'\)-DDT and Its Metabolite \(p,p'\)-DDE with Obesity: Integrated Systematic Review and Meta-Analysis

German Cano-Sanchez, Andrew G. Salmon, and Michele A. La Merrill

Exposure to non-persistent pesticides and thyroid function: A systematic review of epidemiological evidence

Elida Campos\textsuperscript{a}, Carmen Freire\textsuperscript{a,b}

* Correspondence to: https://orcid.org/0000-0003-2208-2540
# Pesticides and neurotoxicity

<table>
<thead>
<tr>
<th>Pesticide type/class</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organophosphates (OPs) and carbamates</td>
<td>Behavioral problems, and poorer working memory, executive function, and motor skills</td>
</tr>
<tr>
<td>Ethylene bisdithiocarbamates</td>
<td>Poorer verbal learning skills and cognitive function, attention problems, behavioral disinhibition, impaired motor function</td>
</tr>
<tr>
<td>Pyrethroids</td>
<td>Poorer perceptual reasoning, attention deficit hyperactivity disorder (ADHD), slower processing speed</td>
</tr>
<tr>
<td>Glyphosate</td>
<td>Decreased locomotor activity, impaired recognition memory, and depressive-like behavior (animal studies)</td>
</tr>
</tbody>
</table>

Pesticides and neurotoxicity

*Epidemiological evidence comes from studies that have used neuropsychological testing*

*Lack of information on the brain structures or neural functions targeted by pesticides*
Pesticides and structural neuroimaging

- Brain volume measured using magnetic resonance imaging (MRI)
- Farmworkers with high (n=10) and low/no (n=10) pesticide exposure, South Africa
  - Farmworkers exposed to herbicides had smaller white matter volumes
- Latino tobacco farmworkers (n=48) vs. non-farmworkers (n=26), North Carolina
  - Farmworkers had greater gray matter signal in putamen and cerebellum, and lower gray matter signal in frontal and temporal lobes

Laurienti et al. 2016; Holtman et al. in prep.
Pesticides and functional neuroimaging

- Latino tobacco farmworkers (n=48) vs. non-farmworkers (n=26), North Carolina
- Brain network connectivity patterns
  - Functional interactions among brain areas
  - Measured using resting-state functional magnetic resonance imaging (rs-fMRI)
Pesticides and functional neuroimaging

- Latino tobacco farmworkers (n=48) vs. non-farmworkers (n=26), North Carolina
- Brain network connectivity patterns
  - Functional interactions among brain areas
  - Measured using resting-state functional magnetic resonance imaging (rs-fMRI)
- Brain networks in farmworkers had more clustered and modular structures
  - More segregated neural processing and less sharing of information between brain regions

Bahrami et al. 2017
Pesticides and functional neuroimaging

No published studies of pesticide exposure have used functional neuroimaging while administering cognitive tasks

Need to elucidate how pesticides affect neural dynamics underlying cognitive function and localize pesticide-related effects on the brain
Pesticides and cortical brain activity

Fuhrimann et al. submitted
Pesticides and cortical brain activity

• Cross-sectional pilot study in Zarcero County, Costa Rica (July-August 2016)
• Convenience sample from PESTROP study (n=48)
  • 23 workers from conventional farms and 25 from organic farms
• Eligibility criteria
  • ≥18 years old
  • No psychiatric disorder or medications
Pesticides and cortical brain activity: data collection

- Interview
- Functional near-infrared spectroscopy (fNIRS)
- Urinary pesticide metabolites
  - Mancozeb (ETU)
  - Chlorpyrifos (TCPy)
  - Pyrethroids (3-PBA, DCCA, CFCA)
  - Tebuconazole (TEB-OH)
  - Glyphosate (GLY, AMPA)
Pesticides and cortical brain activity: fNIRS

• Noninvasive optical brain imaging technology
• Measures localized changes in blood flow related to brain activity during a task
• Benefits over fMRI for population-based studies
  • Low cost
  • Portable
  • Greater tolerance to movement artifacts
• Correlates highly with fMRI across a variety of cognitive tasks

Baker et al. 2017; Cui et al. 2011
Pesticides and cortical brain activity: fNIRS

- Source and detector optodes are held in contact with a participant's scalp by a headpiece.
- Source optodes emit near-infrared light that penetrates the skull and outer 3-4 cm of the underlying cortex.
- Detector optodes arranged near a source optode quantify unabsorbed light.
Pesticides and cortical brain activity: fNIRS optode configuration

- Optodes configured over the dorsolateral prefront
- 18 channels
- 8 regions of interest

Baker et al. 2017
Pesticides and cortical brain activity: neuropsychological tasks

Baker et al. 2017
Pesticides and cortical brain activity: neuropsychological tasks
Pesticides and cortical brain activity: fNIRS data preprocessing

• Cleaning and conversion of optical density data into time series of oxygenated (HbO) and deoxygenated (HbR) hemoglobin concentrations

• Generalized linear modeling (GLM) used to estimate a metric (beta coefficient) that describes the change in HbO and HbR concentrations during each component of the task

Pesticides and cortical brain activity: fNIRS data preprocessing

• Contrast between each $\beta$ coefficient and its corresponding control for each task
  • Encoding vs. Recall
  • Matching vs. Control
  • Go vs. No-Go

• Identification of the single channel within each region of interest that showed the greatest response for each contrast

Characteristics of farmworkers

31.0  years old (median)
96%  male
71%  born in Costa Rica
65%  ≤ 6th grade
73%  living above poverty level
19.0  years worked in agriculture (median)
Distribution of urinary metabolite (specific gravity-adjusted) concentrations
Preliminary results: pesticide exposure and working memory-related brain activity

- Decreased activation in the prefrontal cortex of the left hemisphere
- Exposure has altered the overall neural response, including the ability of a region or network to marshal a typical response to a task
- Models adjusted for age and educational level
Preliminary results: pesticide exposure and working memory-related brain activity

Mora et al. in prep.
Preliminary results: pesticide exposure and executive function-related brain activity

Mora et al. in prep.
Preliminary results: pesticide exposure and brain activity

- Null associations with task of attention and response inhibition (Go/No-Go)
- Null associations with ETU, PTU, TEB-OH, and glyphosate
Future steps

• Examine associations of pesticide exposure with HbR and functional connectivity

• Examine exposure-task performance and task performance-brain activation associations

• Investigate impacts of pesticide exposure during critical windows of brain development on cortical brain activity and functional connectivity
  • 600 Mexican American young adults from the CHAMACOS study
Collaborators

Joseph M. Baker
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Brenda Eskenazi
Sharon Sagiv
Christian L. Lindh
Funding sources
Questions welcome
Additional slides
Pesticides and agriculture

25 million lbs of pesticide active ingredients per year
1.2 million harvested acres

United States (2012):
800 million lbs of pesticide active ingredients
315 million harvested acres
## Distribution of urinary metabolite specific gravity-adjusted concentrations (ng/mL)

<table>
<thead>
<tr>
<th>Urinary metabolites</th>
<th>LOD</th>
<th>% &gt;LOD</th>
<th>Average of two measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1st sample</td>
<td>2nd sample</td>
</tr>
<tr>
<td></td>
<td></td>
<td>GM (GSD)</td>
<td>P25</td>
</tr>
<tr>
<td>ETU</td>
<td>0.08</td>
<td>98.0</td>
<td>95.7</td>
</tr>
<tr>
<td>TCP</td>
<td>0.05</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>3-PBA</td>
<td>0.03</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>DCCA</td>
<td>0.04</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>CFCA</td>
<td>0.10</td>
<td>61.2</td>
<td>63.0</td>
</tr>
<tr>
<td>TEB-OH</td>
<td>0.10</td>
<td>83.7</td>
<td>91.3</td>
</tr>
<tr>
<td>GLY</td>
<td>0.20</td>
<td>69.4</td>
<td>69.6</td>
</tr>
<tr>
<td>AMPA</td>
<td>0.20</td>
<td>55.1</td>
<td>73.9</td>
</tr>
</tbody>
</table>
Differences in metabolite concentrations specific gravity-adjusted by farm type