Cognitive Performance and Exposures to Different Rescue Activities at The World Trade Center Following the Terrorist Attacks of 9/11/2001

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Background

1. World Trade Center (WTC) Responders
   - On September 11, 2001, terrorists hijacked four planes, attacking the World Trade Center, the Pentagon, and a Pennsylvania field.
   - Over 90,000 WTC responders after the 9/11 event

2. Impaired Cognition in WTC Responders
   - Worse Cognition
   - Unique Brain Pathology

3. Particulate Matter (PM) & Cognition
   - PM Exposure Correlated with Lower Cognition
   - PM: Preventable Risk Factor

4. WTC Dust
   - Neurotoxic (PM, Polycyclic Aromatic Hydrocarbons, Metals)
   - Direct Enter the Brain
   - Indirect Enter the Brain through Lung
   - Indirect Affect the Brain through Immune System

5. Existed Variables Associated with Cognition
   - Time Duration on the Site
   - Dust-Cloud

Gap & Innovation & Objective

1. Gap
   - Quantity
     - Few studies in the WTC cohort have explored the link between air pollutants and cognition, despite numerous efforts investigating the relationship between PTSD and cognition.
   - Quality
     - There is no validated measure for indirect PM exposure.
     - Only has Exposure Assessment Questionnaire at the initial monitoring, lacks precision in capturing inhalation differences based on activity type and protective equipment used.

2. Innovation
   - Potential Information from Text
     - Unexamined information is embedded in freeform textual descriptions of individuals’ experiences and activities during the response efforts.
   - Activity Variable
     - We created and validated a new rescue activity variable combining all the WTC inhale particulate exposure-related variables.

3. Objective
   1) Cognition
      - Assess the relationship between WTC rescue activity and cognition.
   2) Neurofilament light (NFL)
      - Assess the relationship between WTC rescue activity with plasma neurodegenerative biomarker-NFL.

Methods

1. Population & Variables
   - Population
     - Of the 12,000 responders from Long Island, NY, those with missing data were excluded; final sample sizes are in the results table.

   - Human-Derived PM Sources
     - Transportation: Derived from brake dust, interactions between train/subway wheelsets and rails, tire and pavement contact, and fuel combustion.
     - Construction: Emissions from grinding, resurfacing roads, metalwork, welding, excavation, and construction equipment combustion fumes.
     - Household: use of cleaning products, burning candles and fires, and smoking
     - Rescue-Activity
       - Hypothesized high PM2.5 exposure activity: 1) transportation, 2) steel, 3) debris removal, 4) construction, 5) enclosed, 6) heavy equipment, 7) clean, 8) excavation 9) search
       - Hypothesized low PM2.5 exposure activity: 10) cable, 11) inspection, 12) morgue, 13) repair, 14) safety, 15) security, 16) supervision, 17) support, 18) utility
   - Cognition
     - Montreal Cognitive Assessment (MoCA), which was administered by trained staff.

   - Amyloid ratio 40:42 , p-Tau, GFAP, NFL, Aβ, p-Tau, NFL, GRAP were quantified from blood sample assays collected at 2019 screening visit.
   - Covariates
     - Personal Protective Equipment (PPE)
       - If participants had worn the PPE consistently, the activity variables were recoded to 0.
     - Demographic and comorbidity
       - age, gender, race, education, hypertension, diabetes, cholesterol, stroke, smoke, alcohol, police occupation, working hours, working location, exhaust exposure, dust exposure
     - Statistical Analysis
       - 1) Cognition: Poisson regression or negative binomial regression
       - 2) p-Tau, GRAP, NFL: Log gamma regression
       - 3) Amyloid ratio 40-42: Linear regression

   - Regression Formula: MoCA ~ MainPredictor(one of the 18 activities/ all 18 activities) + covariates
     - Biomarkers ~ MainPredictor(one of the 18 activities) + covariates

Limitations

1. Our exposure data were from recalled data which may have recall bias.
2. Some activities share great overlap and similar coefficients which means either they are indeed has similar effect on later life health or we do not have accurate enough data to explore. Future study, we will combine some activities.
3. People can have multiple activity during the rescue time, we did not examine the combination effect of the activities

Acknowledgement

I am deeply grateful to my mentor, Dr. Sean Clouston, for funding this research and providing invaluable guidance on both the research direction and the statistical methods.

Results

1. Cognition
   - 1) Interpretation of the Coeff: Compared to other possible activities, participant performing telecommunication activity is associated with multiplicatively 10% decrease in global mental status score.
   - 2) Protective Activity: Telecommunications, Enclosed working environment, Supervision.

2. Biomarkers
   - 1) Interpretation : Coefficients from log-gamma regression depict the multiplicative change in outcomes, while those from linear regression convey the additive change in outcomes. E.g. Participants carry out the debris removal rescue activity will have multiplicatively 21% decrease in plasma NFL compared to participants attending other activities.

3. Conclusion: Results suggest that specific activities undertaken at the WTC sites are associated with cognitive outcomes, including overall and domain-specific deficits. Supervision is protective for both cognition scores and plasma Aβ ratio.

Table 1. Demographics Description and Missing Value Analyses

<table>
<thead>
<tr>
<th>Age</th>
<th>Missing (N=1360)</th>
<th>Excluded (N=372)</th>
<th>P</th>
<th>Missing (N=1064)</th>
<th>Excluded (N=11253)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>58.6 (8.9)</td>
<td>60.0 (8.8)</td>
<td>0.01</td>
<td>59.1 (7.5)</td>
<td>59.2 (8.4)</td>
<td>0.54</td>
</tr>
<tr>
<td>Median (Min, Max)</td>
<td>58.2 (37.3, 96.6)</td>
<td>59.2 (36.5, 96.6)</td>
<td>0.43</td>
<td>59.0 (40.2, 84.2)</td>
<td>59.5 (36.9, 96.6)</td>
<td>0.03</td>
</tr>
<tr>
<td>Gender</td>
<td>Female</td>
<td>70.5%</td>
<td>59%</td>
<td>0.01</td>
<td>1004 (92.6%)</td>
<td>1016 (90.6%)</td>
</tr>
<tr>
<td>Race</td>
<td>White</td>
<td>75.8%</td>
<td>73.5%</td>
<td>0.01</td>
<td>997 (90.2%)</td>
<td>969 (79.9%)</td>
</tr>
</tbody>
</table>

Table 2. Multivariable-Adjusted Regression Analyses Illustrating Associations Between Activity Types and Baseline Cognitive Performance, as well as 2019 Plasma Biomarkers, in World Trade Center Responders

Figure 1. Multivariable-Adjusted Regression Analyses Illustrating Associations Between Activity Types and Baseline Cognitive Performance, as well as 2019 Plasma Biomarkers, in World Trade Center Responders