Research Article

# The Relationship Between Pesticide Use and Cognitive Impairment in an Agricultural Community of Tomohon City, North Sulawesi

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Received 18 November 2024; Accepted 11 April 2025
https://doi.org/10.23886/ejki.13.961.42

***Abstract***

*This study investigates the cognitive effects of pesticide exposure on agricultural workers from a village in Tomohon City, North Sulawesi, Indonesia. Employing a cross-sectional design from July to September 2024. This study assessed the demographic characteristics, pesticide exposure patterns, and cognitive function of 97 participants aged ≥18 using the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA-INA). The findings reveal a clear association between direct and indirect pesticide exposure and cognitive impairment. Direct exposure was linked to slightly lower cognitive scores than indirect exposure, with both groups scoring below established thresholds for normal cognitive function, particularly in memory, attention, and executive functions. Inconsistent use of personal protective equipment was noted among participants, with common immediate symptoms including visual disturbances and memory deficits following pesticide application. These results suggest that minimal pesticide exposure may contribute to cognitive decline, potentially accelerating age-related impairments. The underlying neurotoxic mechanisms likely involve oxidative stress, mitochondrial dysfunction, and neuroinflammation, which disrupt neuronal integrity. These findings underscore the urgent need for enhanced occupational health policies, stricter safety measures, and further research to mitigate the cognitive risks of pesticide exposure in agricultural populations.*

***Keywords:*** *pesticides, cognitive impairment, MMSE, MoCA-INA.*

# Hubungan Penggunaan Pestisida dan Gangguan Kognitif pada Komunitas Pertanian di Kota Tomohon, Sulawesi Utara

***Abstrak***

*Studi ini mengkaji dampak pajanan pestisida terhadap fungsi kognitif pada pekerja pertanian di Kecamatan Tomohon Utara, Sulawesi Utara, Indonesia. Penelitian menggunakan desain potong lintang dan dilakukan pada bulan Juli hingga September 2024. Dilakukan evaluasi karakteristik demografis, pola pajanan pestisida, dan fungsi kognitif 97 subjek berusia ≥18 tahun menggunakan Mini-Mental State Examination (MMSE) dan Montreal Cognitive Assessment (MoCA-INA). Hasil penelitian menunjukkan hubungan antara pajanan pestisida, secara langsung dan tidak langsung, dengan gangguan kognitif. Pajanan langsung berkaitan dengan skor kognitif yang lebih rendah dibandingkan pajanan tidak langsung. Kedua kelompok menunjukkan skor di bawah batas normal, terutama aspek memori, perhatian, dan fungsi eksekutif. Terdapat penggunaan alat pelindung diri yang tidak konsisten dan ditemukan gejala umum seperti gangguan penglihatan dan penurunan memori setelah pajanan pestisida. Hasil ini menunjukkan bahwa pajanan pestisida yang rendah berkontribusi pada penurunan kognitif dan berpotensi mempercepat gangguan kognitif terkait usia. Kemungkinan mekanisme neurotoksik adalah stres oksidatif, disfungsi mitokondria, dan neuroinflamasi, yang dapat merusak fungsi neuronal. Penelitian ini menegaskan perlunya kebijakan kesehatan kerja yang lebih baik, penerapan langkah keselamatan yang lebih ketat, serta penelitian lanjutan untuk memitigasi risiko kognitif akibat pajanan pestisida pada pekerja pertanian.*

***Kata kunci:*** *pestisida, kognisi, MMSE, MoCA-INA.*

## Introduction

The global use of pesticides has grown significantly, reaching 3.70 million tonnes in 2022, marking a 4% increase from 2021 and a 13% increase over the past decade. Pesticides, such as insecticides, are essential for supporting the agro-economy due to the persistent presence of crop pests. However, emerging research has linked occupational pesticide exposure to chronic health issues, with agricultural workers facing heightened risks due to direct exposure to concentrated pesticide formulations. Their children may also be exposed to areas where pesticides are applied.[1–4]

Studies have shown that self-reported pesticide exposure is associated with poorer cognitive function, affecting various cognitive domains such as memory, attention, language, and executive functions. The underlying mechanisms involve disruptions to neurological processes, particularly affecting the cholinergic system, which is crucial for cognitive processes. Pesticide exposure has been associated with DNA damage, oxidative stress, mitochondrial dysfunction, and neuroinflammation, with synthetic pesticides, especially organophosphorus compounds, implicated as significant contributors to cognitive impairment and other neurological disorders.[5–9]

Tomohon City, situated 900 meters above sea level and known for its fertile soil, has a strong agricultural sector, with "W" Village as a key agricultural hub. Farmers in this region rely heavily on pesticides to enhance productivity. Despite this, there is currently no data on the impact of pesticide use on the cognitive health of local farmers. This study aims to fill that gap by analyzing farmers' demographic data, pesticide use patterns, and the potential cognitive effects of pesticide exposure in the village.

## Methods

### *Study Design and Ethical Approval*

This descriptive, observational study employed a cross-sectional design to assess the demographic characteristics, cognitive function, and pesticide usage patterns among residents, including farmers, of "W" Village, North Tomohon District, Tomohon City, North Sulawesi, Indonesia. from July to September 2024. Ethical approval was obtained from the RSUP Prof. Dr. R.D. Kandou Ethics Committee No.130/EC/KEPK-KANDOU/VII/2024.

### *Study Population and Sampling*

The study population comprised individuals aged 18 and older, selected through simple random sampling. The sample size is determined using this formula:

$$n = \frac{NZ^2_{1-\frac{\alpha}{2}}pq}{d^2(N-1) + NZ^2_{1-\frac{\alpha}{2}}pq}$$

Where N represents the total population size (1107), Z is the standard normal value (1.96 for a 95% confidence level), p is the estimated proportion (0.5), q is calculated as 1 - p, and d is the margin of error (0.1). Substituting these values into the formula, the initial sample size calculation resulted in n = 88.45. To account for potential non-response, an additional 10% was added, yielding a final adjusted sample size of 97 participants.

### *Variables and Measurements*

Independent variables were obtained from auto-anamnesis use included pesticide exposure (type of pesticides used and duration of exposure), socio-demographic factors (age, gender, education level, and occupation), personal protective equipment (PPE) usage, and medical history (difficulty breathing, blurred vision, and memory impairment). At the same time, dependent variables were blood pressure (measured using automatic blood pressure monitors) and cognitive function (measured and interpreted by trained and licensed medical doctors using the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment-Indonesian version (MoCA-INA), which also supervised by two licensed neurologists).

### *Statistical Analysis*

Descriptive statistics were employed to summarize demographic variables, including age and gender, with mean, median, standard deviation, and range values calculated for each exposure group (direct vs. indirect), stratified by gender. Fisher's exact test was used to compare education level distributions between exposure groups, addressing small subgroup sizes.

Spearman's rank correlation was used to assess the relationship between using PPE and discomfort symptoms following pesticide exposure. PPE usage was coded on a frequency scale (never = 1, occasionally = 2, almost every time = 3, every time = 4), while discomfort symptoms were inversely coded (never = 4, occasionally = 3, almost every time = 2, every time = 1).

Cognitive function was assessed using MMSE and MoCA-INA, with scores >27 and >26, respectively, indicating normal function. Mean scores for both cognitive assessments were calculated and compared between direct and indirect exposure groups to evaluate the impact of pesticide exposure on cognitive health. All statistical analyses were performed using R software, with significance at $p < 0.05$.

## Results

The data collection process resulted in a total of 109 responses. Following this, thorough data cleaning was conducted to remove duplicate respondents and incomplete or non-compliant responses. After this screening, a refined dataset of 97 valid responses—representing 88.99% of the total collected data—was prepared for further analysis.

### *Demography*

The respondents were categorized based on their pesticide exposure. Of the 97 participants, 53 reported direct exposure, having personally interacted with or used pesticides. The remaining 44 respondents were classified as having indirect exposure, as they did not directly handle pesticides but lived and carried out daily activities in agricultural areas where pesticides are regularly applied. The data reveals that male respondents predominate in the direct exposure group, likely because they primarily work as farmers. Specifically, 31 of 39 male respondents (79.49%) reported direct pesticide exposure. In contrast, 22 out of 58 female respondents (37.93%) experienced direct pesticide exposure.

In general, respondents ranged in age from 20 to 87 years. Table 1 displays the age distribution of respondents, categorized by gender and pesticide exposure levels. For the group with direct pesticide exposure, the mean age for male respondents was 59.87 years with a standard deviation of 13.76, while for female respondents, the mean age was 48.50 years with a standard deviation of 15.35. In the group without direct exposure, the mean age for males was 54.75 years with a standard deviation of 19.40, whereas for females, it was 66.17 years with a standard deviation of 10.34.

**Table 1. Age Range of Respondents, Grouped by Pesticide Exposure and Gender**

| Pesticide exposure | Gender | n | Min | Median | Mean | Q1 | Q3 | Max | Stdev |
|---|---|---|---|---|---|---|---|---|---|
| Direct | Male | 31 | 21 | 62 | 59.87 | 55.5 | 68.5 | 85 | 13.76 |
| Direct | Female | 22 | 20 | 60.5 | 57.45 | 48.5 | 68.5 | 82 | 15.35 |
| Indirect | Male | 8 | 20 | 60 | 54.75 | 42 | 68 | 78 | 19.4 |
| Indirect | Female | 36 | 34 | 68 | 66.17 | 62.75 | 71.25 | 87 | 10.34 |

n: total number of samples, Min: minimum, Q1: 1st quartile, Q3: 3rd quartile, Max: maximum, Stdev: standard deviation

### *Pesticide Application Practices*

Figure 1 shows the pattern of PPE use in relation to years of pesticide application experience. Respondents who are farmers with over 10 years of pesticide use tend to consistently use masks/ respirators, head coverings, and long-sleeved shirts or aprons. However, this group tends to use eye protection and gloves less consistently.

Figure 2 shows the immediate effects experienced by respondents after pesticide application. Vision disturbances are the most frequently reported symptom compared to other conditions. Memory impairment and blurred vision were reported by respondents who had been applying pesticides for a period ranging from 1 year to over 10 years. Difficulty breathing was experienced by all respondent groups, including farmers who had been using pesticides for less than 1 year and those with over 10 years of experience.

Correlation testing was conducted to explore the relationship between the variables of discomfort experienced immediately after pesticide use and the frequency of PPE usage. From Figure 3, it can be observed that respondents tend to experience multiple symptoms simultaneously after pesticide exposure. Visual and memory impairments are the most commonly reported, with a correlation coefficient of 0.56. On the other hand, PPE such as masks, protective glasses, and gloves are commonly used together. The correlation between the use of PPE and the symptoms experienced is generally low.


**Figure 1. PPE Use in Relation to Years of Pesticide Application Experience**

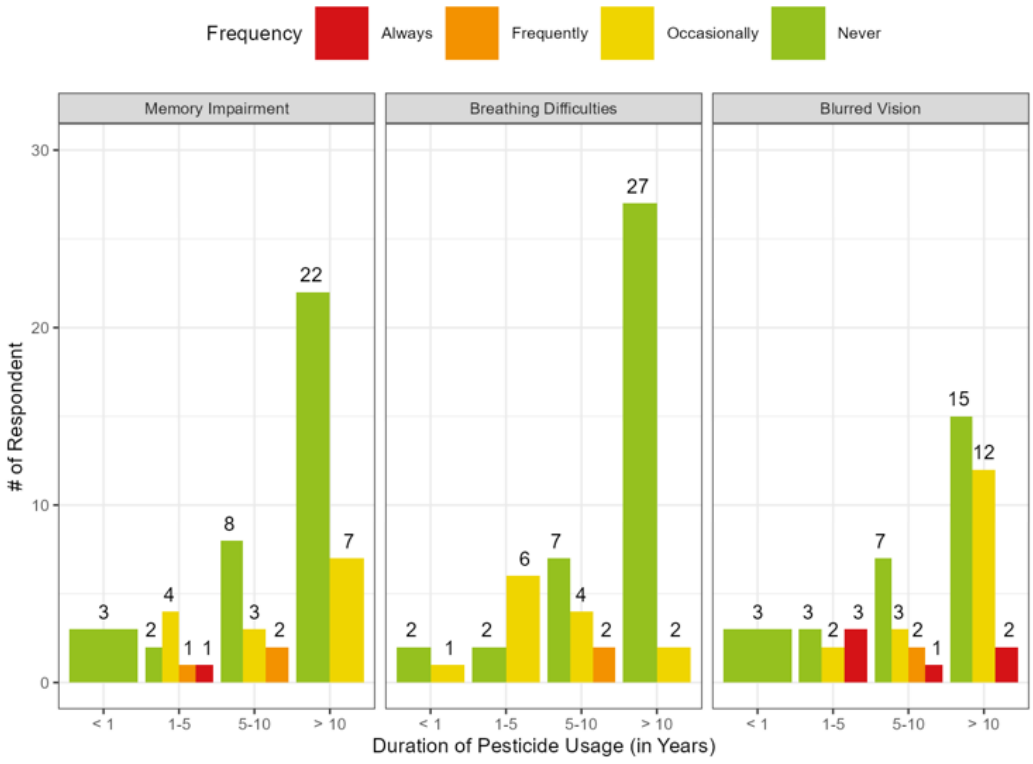


**Figure 2. Immediate Effects Experienced by Respondents after Pesticide Application**


**Figure 3. Correlation Coefficient and Significance from The Spearman Correlation Test**
***p<0,05, **p<0,01, ***p<0,001***

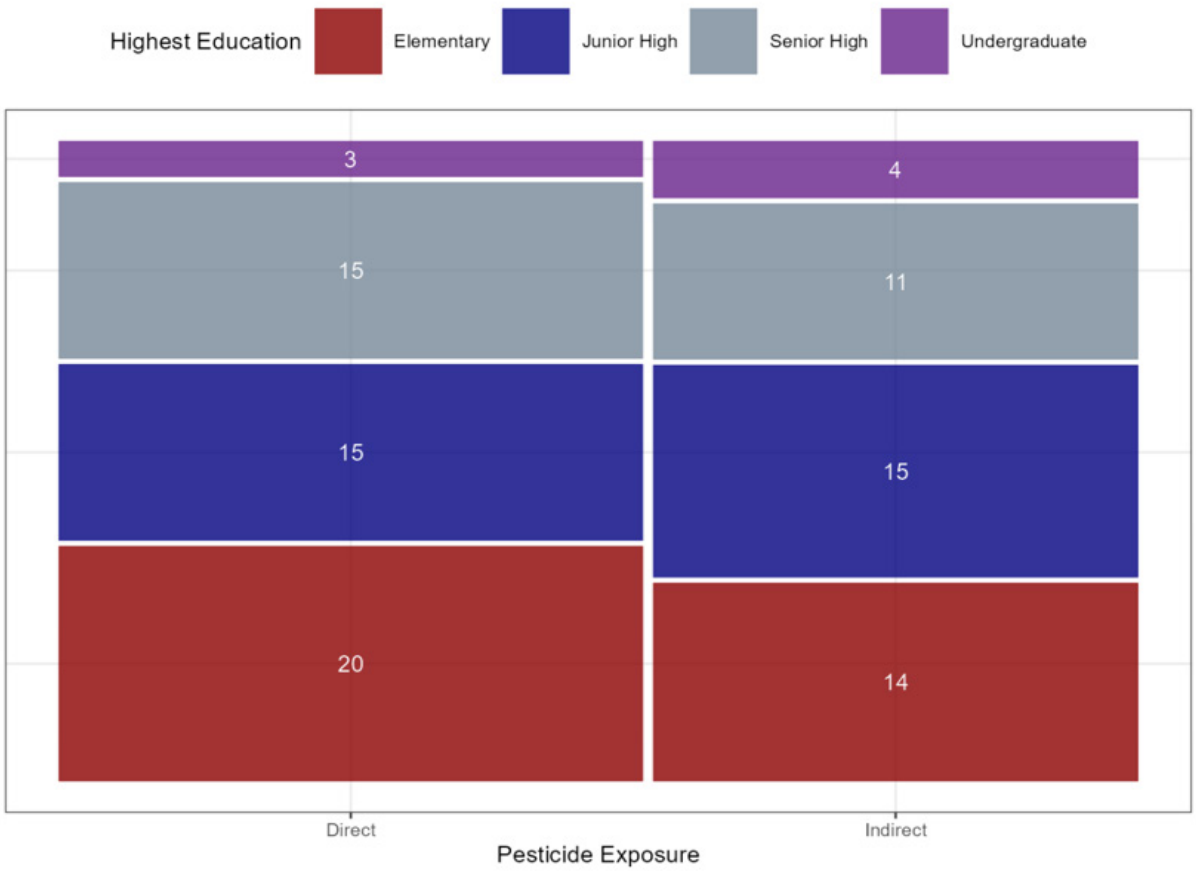


**Figure 4. Comparison of Education Levels Across Exposure Groups**

***Cognitive Function***

Figure 4 shows a comparison of education levels across exposure groups. Significant disparities in educational performance between those exposed to pesticides directly and indirectly are seen in the chart. With 20 participants, primary schooling was the most prevalent among those who were directly exposed. The distribution of the indirect group, on the other hand, was somewhat more even, with fewer people in the elementary school level (n=14) and slightly more people with college degrees (n=4, as opposed to 3 in the direct group). The direct group had somewhat more participants with senior high education (n=15) than the indirect group (n=11), but both groups were equally represented at the junior high level. According to these findings, those with less education are more likely to be directly exposed to pesticides.

In a sample of 97 observations, the relationship between two category variables was investigated using the Fisher's Exact Test. The two-sided analysis looked for differences in both directions. A p-value of 0.815 from the test indicated that the outcome was not statistically significant ($p>0.05$). This implies that any observed differences are probably the result of random chance and that there is no proof of a significant relationship between the variables.

MMSE scores above 27 indicate a normal function for cognitive assessment, while MoCA-Ina scores of 26 or above are similarly classified as usual. As shown in Figure 5, a higher proportion of respondents in both exposure groups exhibit cognitive impairment. Specifically, the 53 respondents with direct pesticide exposure hadan average MMSE score of 24.32, ranging from 11 to 30, and a standard deviation of 3.75. In contrast, the 44 respondents with indirect exposure reported an average MMSE score of 24.18, with a range of 13 to 30 and a standard deviation of 4.32. Regarding MoCA-Ina scores, the mean for the directly exposed group was 18.21, with scores ranging from 4 to 30 and a standard deviation of 5.09. The mean MoCA-Ina score for the indirectly exposed group was 18.00, ranging from 5 to 27, and a standard deviation of 5.62.

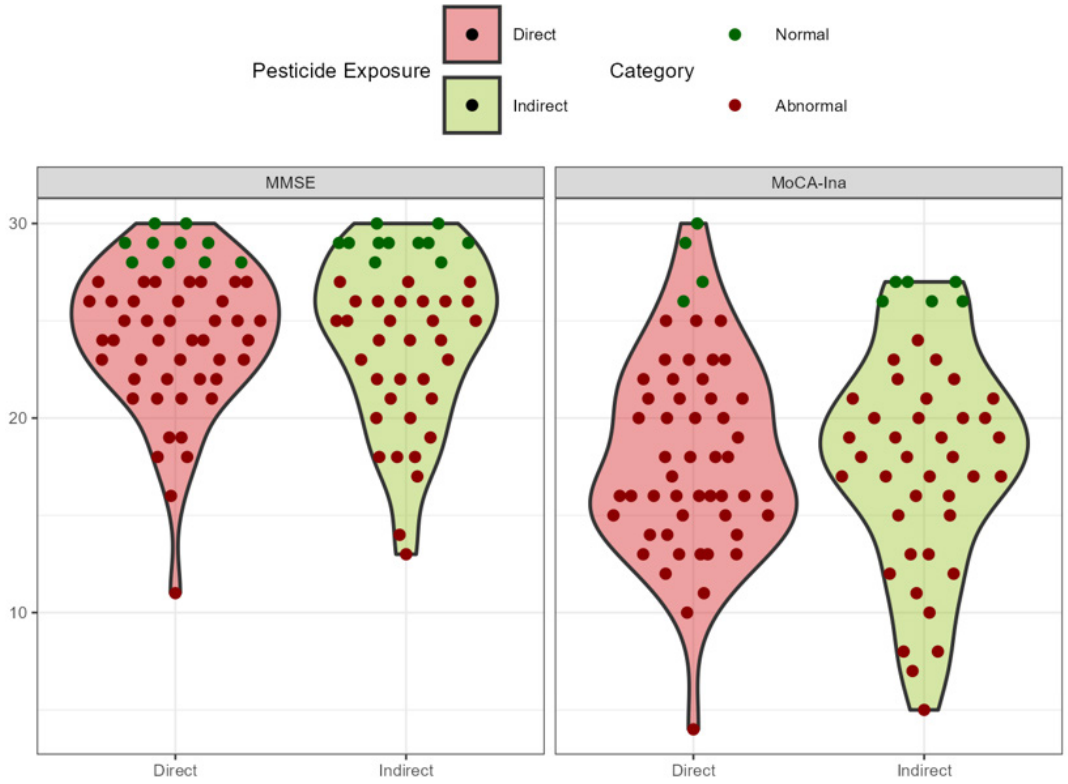


**Figure 5. Distribution of Cognitive Function Scores Categorized by Pesticide Exposure Levels.**

## Discussion

### *Cognitive Impairment in Exposed Groups*

Our research underscores the significant cognitive impact of direct and indirect pesticide exposure among agricultural workers. As assessed through the MMSE and the Indonesian version of the MoCA-Ina, analysis of cognitive performance reveals marked deficits across multiple cognitive domains. Participants who experienced direct pesticide exposure demonstrated slightly lower cognitive scores than those with indirect exposure. Nonetheless, both groups exhibited scores below the established normative thresholds indicative of healthy cognitive function.

These findings highlight a concerning trend: pesticide exposure, whether direct or indirect, compromises cognitive abilities and poses a substantial risk to neurological health. The marginal differences observed between the directly and indirectly exposed groups suggest that while the intensity of exposure may influence the degree of cognitive decline, any level of pesticide exposure is detrimental. The implications of these cognitive impairments are profound, affecting not only individual health and quality of life but also productivity and long-term occupational safety.

These findings align with a substantial body of contemporary research that associates chronic pesticide exposure with a range of cognitive impairments, including deficiencies in memory, attention, executive functioning, and visuospatial abilities.[10–17] Such cognitive deficits are vital indicators of neurotoxic effects, particularly in populations subjected to prolonged occupational exposure. Recent studies have reinforced the understanding that pesticide-related cognitive decline stems from mechanisms involving oxidative stress, mitochondrial dysfunction, and disruption of gut microbiota, which affects the gut-brain axis and neurotransmitter systems.[6,18–22]

The marginal differences observed between the directly and indirectly exposed groups suggest that while the degree of exposure impacts the severity of cognitive decline, any level of pesticide contact poses significant risks. This underlines the pressing need for enhanced safety measures and exposure mitigation strategies to safeguard the neurological health of agricultural workers. The broader implications are substantial, affecting personal well-being, workforce productivity, and public health. To mitigate these risks effectively, further research should delve into the specific pathways through which pesticides exert neurotoxic effects and investigate targeted interventions that could preserve cognitive function among vulnerable populations. Such initiatives are crucial for developing comprehensive strategies that protect against cognitive impairments linked to pesticide exposure.[6,8,22–25]

Pesticides, particularly organophosphates, are potent neurotoxins that primarily inhibit acetylcholinesterase (AChE), essential for cholinergic neurotransmission. By blocking AChE, pesticides cause acetylcholine to accumulate in synaptic clefts, leading to overstimulation of cholinergic receptors. Chronic overstimulation induces maladaptive neuroplasticity, altering synaptic architecture and receptor density, which impairs cognitive functions.[26,27] The persistent cholinergic disruption from pesticide exposure can trigger neurodegenerative changes, correlating with the cognitive deficits observed in our study.

Pesticide exposure exerts neurotoxic effects through diverse mechanisms beyond cholinergic disruption. For instance, certain insecticides can inhibit chitin synthesis and interfere with neural signaling.[22] Despite these varied modes of action, oxidative stress is a common and critical pathway underlying pesticide-induced neurotoxicity. Many pesticides stimulate the production of reactive oxygen species (ROS), which damage cellular macromolecules such as lipids, proteins, and DNA, ultimately impairing cellular function. Due to their high metabolic demand and limited antioxidant capacity, neurons are especially vulnerable to ROS-induced damage. Oxidative stress in neuronal cells can disrupt signaling pathways and trigger apoptosis, leading to deficits in memory, attention, and executive function.[7,18,20–22] Our findings align with this mechanistic framework, underscoring oxidative stress as a significant factor contributing to cognitive impairments observed in individuals exposed to pesticides.

In addition to oxidative stress, mitochondrial dysfunction and neuroinflammation are emerging as key mechanisms underlying pesticide-induced neurotoxicity. Pesticides can impair mitochondrial function, critical for neuronal energy metabolism, leading to energy deficits that exacerbate oxidative stress. This disruption in mitochondrial function affects calcium homeostasis and cellular metabolism, impairing synaptic plasticity, which is vital for learning and memory. Chronic pesticide exposure also triggers glial cell activation, promoting a pro-inflammatory state within the central nervous system. Persistent neuroinflammation disrupts synaptic transmission and plasticity,

contributing to cognitive decline and potentially accelerating neurodegenerative processes. The interaction between mitochondrial dysfunction and neuroinflammation may be a crucial biomarker for assessing cognitive impairment in pesticide-exposed populations.[21,28]

***Cognitive Impairment Due to Pesticide Exposure Versus Normal Aging***

The cognitive impairments observed in pesticide-exposed groups may reflect an accelerated aging trajectory, in which pesticide exposure exacerbates the natural decline in cognitive function associated with aging. Normal aging is characterized by a gradual deterioration in cognitive abilities, often driven by physiological alterations such as reduced cerebral perfusion, neuronal loss, and the accumulation of oxidative stress. These age-related changes are known to compromise memory, processing speed, and executive function.[29] However, pesticide exposure appears to amplify these effects, potentially precipitating earlier and more severe cognitive deficits than would be anticipated solely from the aging process.

Pesticide exposure may act as a catalyst for accelerated aging within the central nervous system (CNS), primarily through the enhancement of oxidative stress, induction of neuroinflammation, and disruption of mitochondrial function. While cognitive aging is typically a gradual process, pesticide-induced neurotoxic insults can hasten neuronal degeneration and impair synaptic plasticity, resulting in a more rapid depletion of cognitive reserve.[9] In this regard, the term “worsened aging” aptly characterizes the synergistic effects of pesticide exposure and the natural aging process, where cognitive decline manifests more swiftly and with greater severity than aging populations without such exposure.

The cognitive domains most prominently affected in our study—memory, attention, and executive function—are also those most susceptible to age-related decline. Pesticide exposure, however, seems to exacerbate deficits in these areas, likely through its impact on brain regions critical for these functions. Specifically, memory impairment may be attributed to hippocampal dysfunction, as the hippocampus is particularly vulnerable to oxidative stress and neuroinflammation, both intensified by pesticide exposure. Likewise, deficits in attention and executive function may be linked to disruptions in the prefrontal cortex, a region prone to oxidative damage and cholinergic dysregulationresulting from pesticide toxicity. These findings highlight a pattern of selective vulnerability within specific cognitive domains in which pesticide exposure potentially accelerates age-related neurodegenerative processes.

***Public Health and Occupational Health Implications***

A significant occupational danger for agricultural workers exposed to pesticides for an extended period is cognitive impairment. In contrast to physical symptoms, these cognitive impairments frequently appear gradually and have long-term effects on productivity, safety at work, and quality of life. Although seasoned farmers often follow the guidelines for wearing PPE, there are still discrepancies, especially regarding gloves and eye protection, according to correlation testing. Symptoms including blurred vision, breathing difficulty, and memory problems continue even after wearing PPE, which may indicate that the present precautions are inadequate or not being utilized correctly. Cognitive decline may also make it harder to be aware of and follow PPE guidelines, which raises exposure risks and exacerbates memory, attention, and executive function issues.

Advanced computational models, remote sensing, and GIS provide precise, efficient tools for assessing pesticide exposure in air, soil, and water.[30] These methodologies facilitate comprehensive risk assessments and yield valuable insights to mitigate pesticide-related health and environmental impacts. Utilizing these tools can help researchers and policymakers devise strategies to protect cognitive health and enhance the well-being of agricultural communities.

The potential pesticide exposure to accelerate cognitive aging further underscores broader public health concerns. Mitigating exposure risks in agricultural communities can benefit cognitive health, mental well-being, and aging processes. These findings highlight the urgent need for policy measures that safeguard cognitive health and improve the welfare of rural populations.

While this study illuminates the cognitive impairments associated with pesticide exposure, certain limitations should be acknowledged. The absence of a control group of individuals from non-agricultural areas limits the ability to make definitive comparisons between exposed and unexposed populations. This constraint complicates the attribution of cognitive impairment solely to pesticide exposure versus other environmental or occupational factors inherent to agricultural settings. Future research should include

non-agricultural control groups to delineate better the specific impact of pesticide exposure on cognitive function.

Additionally, the study's participant pool, with an average age of approximately 60 years, falls within an age range where age-related cognitive decline is typical. This raises the possibility that observed impairments may partially reflect pre-existing age-related changes independent of pesticide exposure. Although the cognitive deficits reported are consistent with pesticide-induced neurotoxicity, the interaction between aging and pesticide exposure remains complex and merits further investigation. Comparative analyses of cognitive outcomes in similarly aged pesticide-exposed and non-exposed groups would help clarify whether the observed impairments stem from pesticide exposure, accelerated aging, or a combination of both.

## Conclusion

In conclusion, this research emphasizes the significant neurocognitive risks associated with pesticide exposure among agricultural workers, highlighting the pervasive impact on cognitive function in direct and indirect exposure scenarios. The observed deficits in memory, attention, and executive function may result from the neurotoxic effects of pesticides. Chronic exposure may accelerate age-related cognitive decline and increase susceptibility to neurodegenerative processes.

## Conflict of Interest

There are no conflicts of interest associated with this publication.

## Acknowledgement

This research was funded by the Riset Dasar/ Terapan Umum Unggulan UNSRAT (RDTU3) grant from Universitas Sam Ratulangi (Contract No. 109/UN12.27/LT/2024). Additionally, the neurology residents at the Faculty of Medicine, Universitas Sam Ratulangi, provided invaluable assistance with the MMSE and MoCA-INA examinations.

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