Distinct Brain Lipid Profiles in a 3xTg-Alzheimer's Disease Mouse Model with Subchronic Exposure to $PM_{2.5}$

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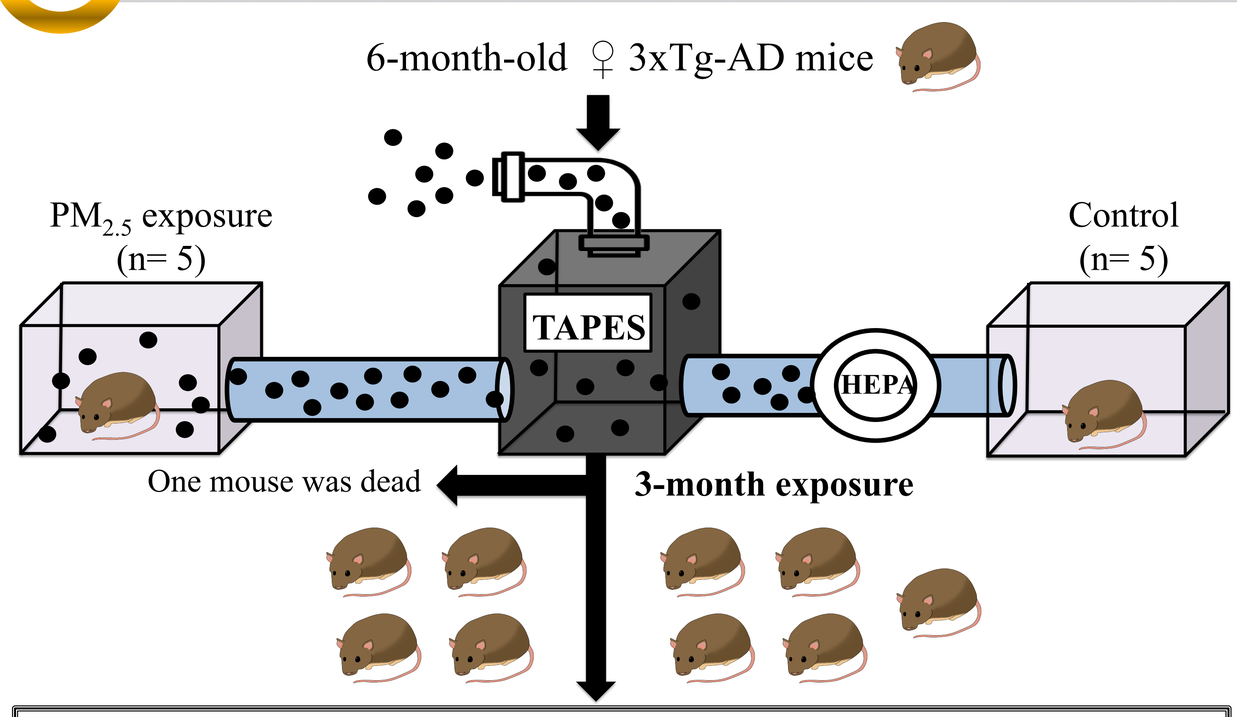
Introduction

Ambient fine particulate matter ($PM_{2.5}$) is an important risk factor for human health. Several epidemiological and animals studies revealed associations between $PM_{2.5}$ exposure and central nervous system (CNS) injury, including Alzheimer's disease (AD). However, the detailed mechanisms of low-level $PM_{2.5}$ exposure are still unknown. Since the brain is a lipid-rich organ, the lipid alterations in response to $PM_{2.5}$ exposure can help us to understand PM-induced neurotoxicity more clearly. Thus, we conducted a non-target lipid profiling system to study more $PM_{2.5}$-induced lipid changes in an AD transgenic mouse model. These molecular changes in each brain area may help us to yield more knowledge of PM-contributed CNS health in AD progression.

Materials and Methods



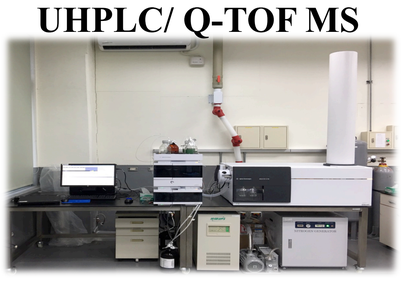
Non-target lipidomic analysis

Sample collection & preparation

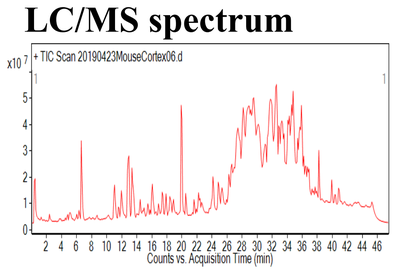
Cortex
Hippocampus
Olfactory bulb
Cerebellum

Instructmental analysis

UHPLC/ Q-TOF MS



LC/MS spectrum



Data preprocessing

Agilent MassHunter Qualitative Analysis

$CV_{pool\ QC}$< 20%

Data analysis & interpretation

Multivariate analysis
SIMCA
Partial least squares discriminant analysis (PLS-DA)

Univariate analysis
R
Mann-Whitney U test

All the animal experiments in the current study were performed in compliance with the Institutional Animal Care and Use Committee of the College of Medicine and the College of Public Health, National Taiwan University (Permit Number: 20160545)

Figure 1. Flow chart of experiments

Results

Mean mass concentration of $PM_{2.5}$: **11.15 μg/m³** (range: 6.14~17.39)

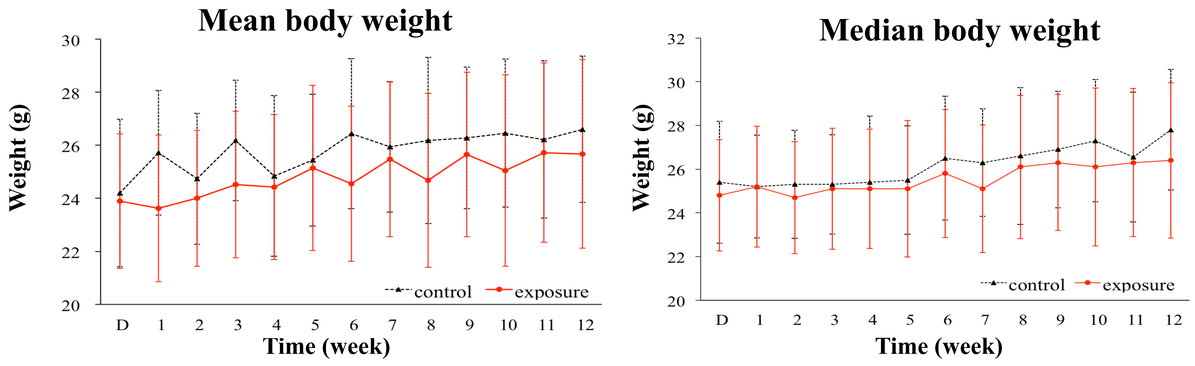


Figure 2. The mean and median body weight changes of AD mice around $PM_{2.5}$ exposure period

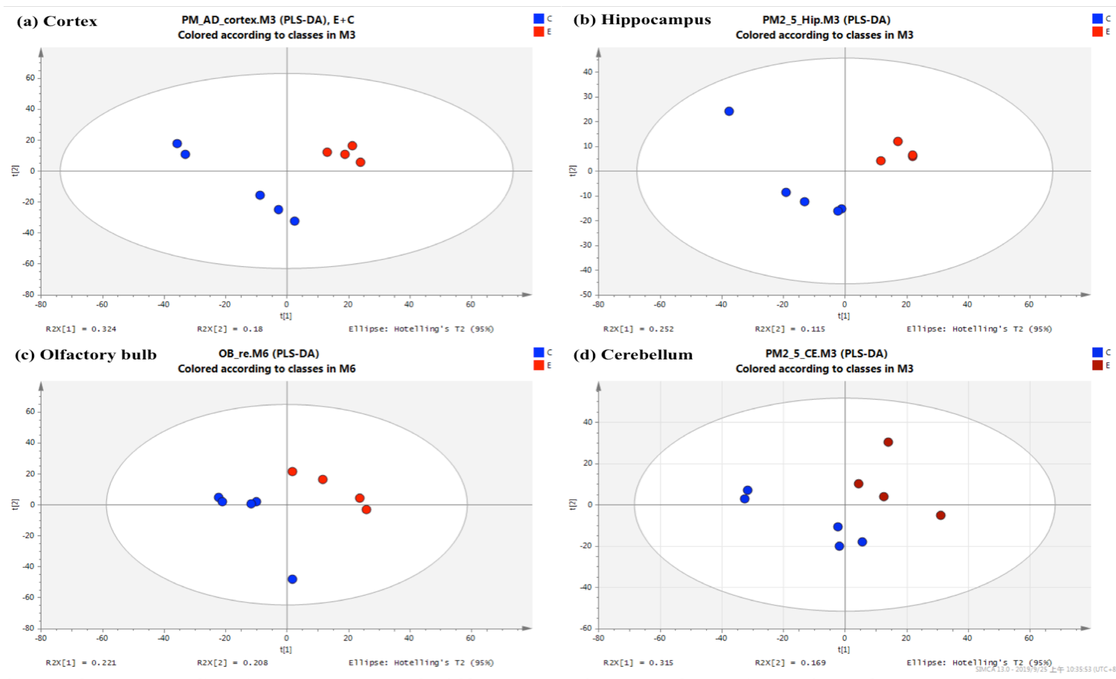


Figure 3. The PLS-DA score plots of different brain area from AD mice after $PM_{2.5}$ exposure: (a) cortex, (b) hippocampus, (c) olfactory bulb, (d) cerebellum

Table 1. The suggested numbers of significant changed lipid from different statistical criteria in each brain regions after subchronic exposure of $PM_{2.5}$

	#All lipids	#VIP> 1.5	#MWU test [a]	#VIP> 1.5 & #MWU test
Cortex	2083	262	130	121
Hip	1921	253	140	111
OB	2001	246	67	67
CE	1906	180	40	40

Hip: hippocampus; OB: olfactory bulb; CE: cerebellum; VIP: Variable importance in projection; MWU: Mann-Whitney U. #: numbers of lipids. [a]: p< 0.05

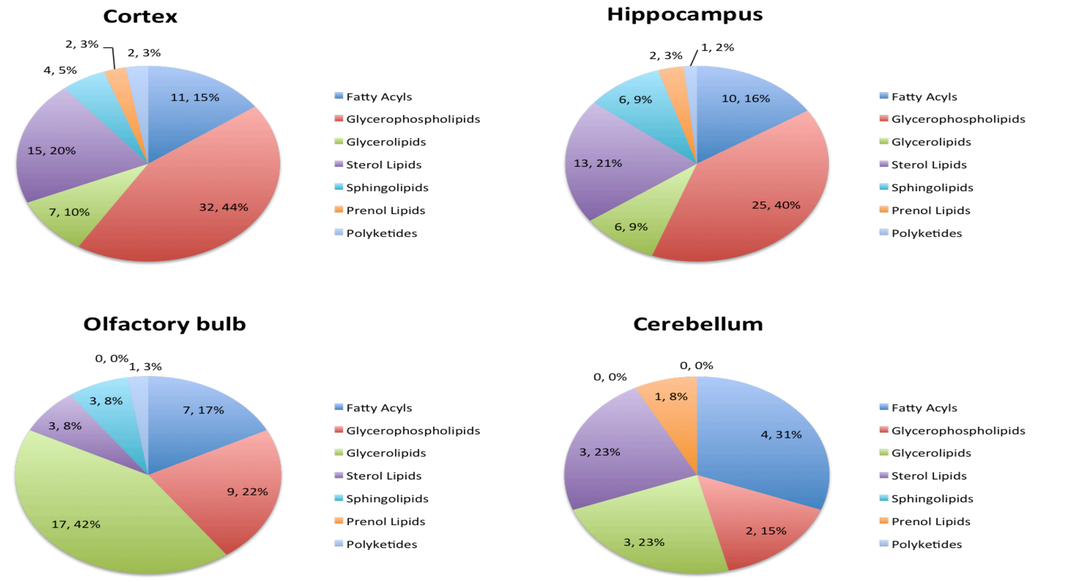


Figure 4. The numbers and ratios of identified lipid classes in each brain area

Discussion & Conclusion

Subchronic exposure to environmental levels of $PM_{2.5}$ did induce lipid perturbations in the 3xTg-AD mouse brains.

More lipid alterations in response to $PM_{2.5}$ were observed in the cortex and hippocampus than those in olfactory bulb and cerebellum.

Lipidomics is a powerful tool to study the subchronic effects of environmental-leveled of $PM_{2.5}$ for future researches.

Acknowledgements

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