

Using Green Tea Extract to Modulate Neuroinflammation from Diesel Exhaust in a Murine Model of Chronic Cerebral Hypoperfusion

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Background

- Exposure to air pollution derived particulate matter (PM) is associated with increased risks of vascular dementia and Alzheimer's disease.
- Neuroinflammation is a hallmark of particulate matter response in the brain and is recognized as a driver of neurodegeneration, with white matter showing increased susceptibility.
- Prior research suggests that epigallocatechin-3-gallate (EGCG), a polyphenol present in green tea extract, is anti-inflammatory and has implications in pathways responsible for neuroregeneration.
- We aim to evaluate the efficacy of EGCG as a neuroprotectant against neuroinflammation resulting from a joint exposure of diesel exhaust particulate (DEP) and chronic cerebral hypoperfusion (CCH).

Methods

- C57BL/6J mice (n=4/sex/group) were exposed to 8 weeks (200h) of DEP (100mg/m³) or filtered air (FA) for 5h per day, 5 days a week.
- CCH was induced via bilateral carotid artery stenosis (BCAS) surgery 30 days prior to the end of DEP/FA exposure.
- Following surgeries, oral EGCG (20mg/kg) or control PBS was administered daily for 30 days.
- Human Equivalent Dose of mouse EGCG in this exposure was estimated to be 1.62mg/kg, which equals to an estimated 100mg in average human (60kg) or 1 cup of green tea a day.
- Following humane euthanasia, neuroinflammation was measured using immunofluorescence in the corpus callosum (CC) by fluorescent density of microglia activation (Ionized Calcium-Binding Adaptor Molecule 1 - Iba-1) and complement component activation (C5 and C5a) in eight groups: FA, DEP, FA+BCAS, DEP+BCAS, FA+EGCG, DEP+EGCG, FA+BCAS+EGCG, DEP+BCAS+EGCG (Figure 1,3).

Figure 1

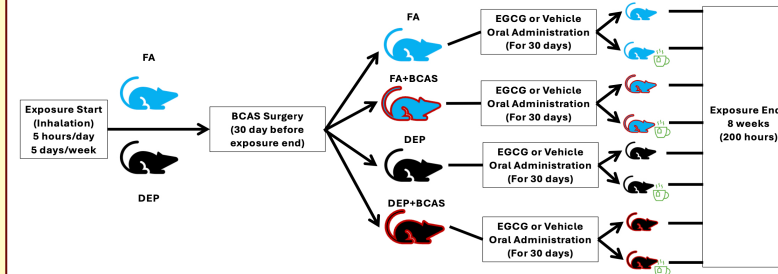


Figure 1. Experimental Model of DEP, BCAS, and EGCG Exposure. Note: FA, filtered air; DEP, diesel exhaust particulate; BCAS, bilateral carotid artery stenosis; EGCG, epigallocatechin-3-gallate.

Results

- There was a significant increase in Iba-1 (p=0.04), C5 (p=0.002), and C5a (p=0.006) in corpus callosum in a joint DEP and CCH exposure compared to FA control.
- Oral administration of green tea EGCG extract for 30 days markedly suppressed the inflammatory markers (Iba-1, C5, and C5a) elevated by combined DEP and CCH exposure (Figure 2).

Figure 2

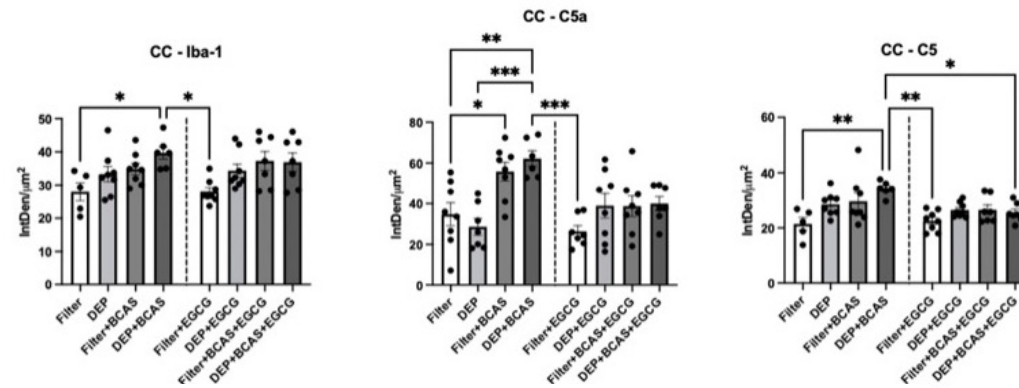


Figure 2. Immunofluorescent quantification of integrated density in corpus callosum for markers of Iba-1, C5, and C5a. Note: CC, corpus callosum; Iba-1, ionized calcium-binding adaptor molecule 1; C5, complement component 5; C5a, complement component 5a.

Figure 3

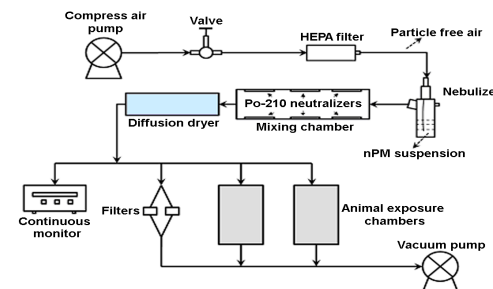


Figure 3. Graphical representation of DEP experiment set up

Conclusions

- Joint exposure to particulate matter and chronic cerebral hypoperfusion (CCH) results in significantly higher levels of neuroinflammation in white matter regions.
- Chronic EGCG therapy resulted in a reduced neuroinflammatory response. Regular consumption of green tea may be beneficial in mitigating neuroinflammation in a setting of air pollution exposure and vascular pathologies contributing to dementia.