

Plasma Fibrinogen Correlates with A β Clearance of monocytes and AD Biomarkers in Cognitively Normal Individuals

Sihan Chen

Beijing Anzhen Nanchong Hospital of Capital Medical University & Nanchong Central Hospital, North Sichuan Medical University

Min Wang

Beijing Anzhen Nanchong Hospital of Capital Medical University & Nanchong Central Hospital, North Sichuan Medical University

Yifei Ji

`jiyifei_2003@163.com`

Beijing Anzhen Nanchong Hospital of Capital Medical University & Nanchong Central Hospital, North Sichuan Medical University

Research Article

Keywords: Alzheimer's disease, Fibrinogen, A β , Monocytes, Peripheral clearance

Posted Date: September 8th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10658330/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Impaired peripheral clearance of amyloid- β (A β) contributes to Alzheimer's disease (AD) pathogenesis. Monocytes play a key role in this process, but their function declines with aging, is further impaired in AD. Fibrinogen, an acute-phase protein elevated in aging and AD, can bind monocyte integrin receptors and potentially alter their function. However, whether fibrinogen correlates with A β clearance of monocytes and plasma AD biomarkers in cognitively normal adults remains unknown. To investigate the association between plasma fibrinogen levels, monocyte counts, uptake of A β 42 by monocytes, and plasma AD-related biomarkers (A β 42, A β 40, T-tau) in cognitively normal older individuals. In this cross-sectional pilot study, 25 cognitively normal participants were enrolled. Plasma AD biomarkers were measured using SIMOA. Peripheral blood mononuclear cells were isolated, and monocytic uptake of FITC-labeled A β 42 was assessed by flow cytometry. Partial correlation analyses were performed, adjusting for age, sex, vascular risk factors, and APOE ϵ 4 genotype. After adjusting for confounders, plasma fibrinogen levels were significantly positively correlated with A β 42 (γ = 0.616, P = 0.005), the A β 42/A β 40 ratio (γ = 0.478, P = 0.038), and T-tau (γ = 0.544, P = 0.016), and negatively correlated with monocyte count (γ = -0.479, P = 0.038) and uptake of A β 42 by monocytes (γ = -0.569, P = 0.011).

In cognitively normal individuals, higher plasma fibrinogen is associated with impaired A β clearance of monocytes and elevated plasma AD biomarkers, suggesting that fibrinogen-related monocyte dysfunction may represent an early peripheral event in the AD continuum.

Introduction

Alzheimer's disease (AD) is the most common neurodegenerative disorder, with its pathogenesis not yet fully elucidated and effective therapeutic interventions remain limited. According to the widely accepted amyloid- β (A β) cascade hypothesis, the abnormal accumulation of A β in the brain, resulting from an imbalance between its production and clearance, is considered one of the core mechanisms in AD pathogenesis [1, 2].

Notably, the clearance of brain-derived A β depends not only on local degradation within the central nervous system but also on peripheral clearance systems. Approximately 40–60% of brain A β can be transported to the peripheral circulation via cerebrospinal fluid and interstitial fluid drainage through lymphatic pathways and the blood-brain barrier [3, 4]. In this process, peripheral blood monocytes, as key components of the innate immune system, play an indispensable role in maintaining A β metabolic homeostasis by phagocytosing and degrading circulating A β [5–7]. However, with aging and AD progression, phagocytic function of monocytes declines significantly, leading to reduced peripheral A β clearance efficiency. The underlying molecular mechanisms remain incompletely understood [8].

Recent evidence has demonstrated that plasma fibrinogen—an acute-phase protein—is significantly elevated in aging and AD patients, and its levels are positively correlated with the degree of brain atrophy, cognitive decline, and AD risk [9]. Beyond its classical role in coagulation, fibrinogen also functions as a key inflammatory mediator. It can bind to integrin receptors on the monocyte surface (such as Mac-

1/CD11b-CD18), activating downstream pro-inflammatory signaling pathways and thereby altering monocyte functional phenotypes and activity states [10–12]. These findings suggest that fibrinogen may participate in AD pathology by modulating immune cell function. However, whether it affects monocyte-mediated peripheral A β clearance remains unclear.

Based on this evidence, we hypothesized that fibrinogen may regulate the functional status of monocytes by influencing their capacity for peripheral A β clearance. To test this hypothesis, the present study aimed to investigate the associations between plasma fibrinogen levels, plasma AD-related biomarkers, monocyte counts, and uptake of A β by monocytes in a cohort of cognitively normal individuals, with the goal of providing preliminary clinical evidence for the potential involvement of the fibrinogen-monocyte axis in the preclinical stage of AD.

Materials and Methods

Study subjects

This study enrolled 25 cognitively normal participants recruited at the Army Medical Center between August 2019 and September 2019. Cognitive function was assessed using standardized scales. Exclusion criteria included: (1) presence of acute infection or inflammation; (2) severe hepatic, cardiac, renal disease, pulmonary, or malignancy; (3) hematological disorders including acute monocytic leukemia, myelodysplastic syndrome, or recovery phase of agranulocytosis; (4) immune system diseases such as rheumatoid arthritis or systemic lupus erythematosus; (5) epilepsy, acute cerebrovascular disease, or neurodegenerative diseases; (6) endocrine disorders; (7) other neurodegenerative conditions; (8) refusal to participate. The study was approved by the Ethics Committee of the Army Medical Center (Approval No. 2019-58), and all participants provided written informed consent.

Data Collection

Demographic information including gender, age, and education level was collected. Medical history regarding cardiovascular and cerebrovascular diseases, chronic hepatic/renal dysfunction, prior trauma and surgical history, neurodegenerative diseases, psychiatric disorders, and relevant medication use was documented. Laboratory and auxiliary examination results (electrocardiogram, blood pressure, blood glucose, lipid profile, routine blood tests, hepatic and renal function, and cranial CT or MRI) were also collected.

Blood Sample Collection and Processing

Fasting venous blood samples were obtained between 07:00 and 09:00. A portion of each sample was sent to the hospital laboratory for routine testing (lipid profile, blood glucose, complete blood count,

coagulation function, hepatic/renal function, thyroid hormones, and plasma fibrinogen levels). The remaining sample was used for PBMC isolation within 2 hours of blood collection as previously described [13]. Plasma was separated by centrifugation at $1,500 \times g$ for 15 minutes and stored at -80°C for subsequent biomarker analyses.

A β uptake assay

Isolated PBMCs were seeded in 24-well plates and incubated with FITC-labeled A β 42 (final concentration $2 \mu\text{g/mL}$, GL, Shanghai, China, 724354) in RPMI-1640 medium containing 10% fetal bovine serum overnight at 37°C in a 5% CO_2 humidified incubator. After incubation, cells were harvested, washed twice with FACS buffer, and stained with APC-conjugated mouse anti-human CD14 antibody (BD, USA, 561708) or corresponding APC-conjugated mouse IgG2a isotype control at 4°C for 30 minutes in the dark. After washing twice with FACS buffer, cells were fixed with 4% paraformaldehyde for 15 minutes at room temperature, washed again, and resuspended in FACS buffer for flow cytometric analysis.

Flow cytometric acquisition was performed using a Novocyte flow cytometer (Acea Biosciences, CA, USA). Monocytes were first gated based on forward scatter height (FSC-H) and side scatter height (SSC-H) to select the PBMC population (Fig. 1A). Doublets were excluded using FSC-H versus forward scatter area (FSC-A) (Fig. 1B). Monocytes were then identified as CD14-positive cells, and intracellular FITC-A β 42 mean fluorescence intensity (MFI) was measured to evaluate monocytic A β 42 uptake capacity (Fig. 1C). Data analysis was performed using NovoExpress software.

Measurement of Plasma AD Biomarker

Plasma A β 42, A β 40, and T-tau levels were measured using a SIMOA HD-1 Analyzer (Quanterix, USA) with the ultra-sensitive Single Molecule Array (SIMOA) technology. Plasma samples were transferred to individual tubes, mixed, and centrifuged at $10,000 g$ for 5 minutes. The SIMOA technology captures target proteins on magnetic beads, followed by addition of enzyme-labeled detection antibodies and precise digital quantification.

APOE Genotyping

Genomic DNA was extracted from peripheral venous blood using the standard phenol-chloroform method. Specific primers targeting human APOE polymorphic sites were designed and synthesized. Real-time quantitative PCR was performed with the following program: 95°C for 15 minutes, followed by 45 cycles of 94°C for 30 seconds, 55°C for 2 minutes, and 65°C for 45 seconds. PCR products were denatured at 99°C for 5 minutes and cooled on ice for 5 minutes, then hybridized with gene chip probes covering the target sites. Genotypes ($\epsilon 2/\epsilon 3/\epsilon 4$) were determined by chip scanning.

Statistical analysis

Statistical analyses were performed using SPSS version 19.0. Continuous variables are presented as mean $\pm$ standard deviation (SD), and categorical variables as n (%). Partial correlation analysis was used to examine the independent associations between fibrinogen and plasma AD biomarkers, monocyte counts, and A β 42 uptake capacity, after adjusting for age, sex, vascular risk factors, and APOE ϵ 4 genotype. A P-value < 0.05 was considered statistically significant. During the preparation of this work, the authors used DeepSeek, an AI language model, to assist with language polishing for improved readability and grammar; after using this tool, the authors reviewed and edited the content as needed and take full responsibility for the final content.

Results

Baseline Characteristics

A total of 25 cognitively normal participants were enrolled, with a mean age of 61.6 ± 17.7 years. Of these, 22 (88.0%) were male. The mean education duration was 11.4 ± 2.5 years. APOE ϵ 4 carriers accounted for 6 (24.0%) of participants. Hypertension was present in 5 (20.0%) and diabetes in 3 (12.0%) participants. No cases of hyperlipidemia were reported. The mean MMSE, ADL, and CDR scores were 26.0 ± 2.0 , 20.8 ± 1.2 , and 0, respectively. Baseline characteristics are summarized in Table 1.

Table 1
Baseline demographic and clinical characteristics (n = 17).

Baseline characteristics	Cognitive normal group(n = 25)
Age, y [mean (SD)]	61.6(17.7)
Male, n (%)	22(88.0)
Years of education, mean (SD)	11.4(2.5)
APOE ϵ 4 carriers, n (%)	6(24.0)
MMSE, mean (SD)	26.0(2.0)
CDR, mean (SD)	0.0
ADL, mean (SD)	20.8(1.2)
Comorbidities	
Hypertension, n (%)	5(20.0)
Diabetes mellitus, n (%)	3(12.0)
Hyperlipidemia, n (%)	0.0
Fibrinogen level(g/L)	3.5(1.1)
Plasma A β 42 level(pg/ml)	12.5(3.5)
Plasma A β 40 level(pg/ml)	221.6(53.1)
Plasma A β 42/40	0.1(0.0)
Plasma T-tauDI)	3.4(1.4)
Uptake of A β 42 by MONO($\times 10^5$)	1.2(0.86)
Number of blood MONO ($\times 10^9$ /L)	0.4(0.1)
Values are presented as mean (SD), number (%), or as specified. MMSE, Mini-Mental State Examination; CDR, Clinical Dementia Rating; ADL, Activities of Daily Living; APOE ϵ 4, apolipoprotein E ϵ 4 allele; A β , β -amyloid; T-tau, total tau; MONO, monocytes.	

Correlation between Fibrinogen and AD-Related Biomarkers

After adjusting for age, sex, vascular risk factors, and APOE ϵ 4 genotype, partial correlation analyses revealed that plasma fibrinogen levels were positively correlated with plasma A β 42 ($\gamma = 0.616$, $P = 0.005$), A β 40 ($\gamma = 0.431$, $P = 0.066$), the A β 42/A β 40 ratio ($\gamma = 0.478$, $P = 0.038$), and T-tau levels ($\gamma = 0.544$, $P = 0.016$) (Fig. 2A-D).

Correlation between Fibrinogen and Monocyte Counts and A β 42 Uptake Capacity

To further explore whether the associations between fibrinogen and plasma AD biomarkers could be linked to monocyte-related parameters, we examined the correlations between fibrinogen levels and monocyte count as well as A β 42 uptake capacity. We found that fibrinogen levels were significantly negatively correlated with both monocyte count ($\gamma = -0.479$, $P = 0.038$) and monocytic A β 42 uptake capacity ($\gamma = -0.569$, $P = 0.011$) (Fig. 3A, B).

Discussion

In this pilot study, we demonstrated for the first time that elevated plasma fibrinogen levels are significantly associated with increased plasma AD-related biomarkers (A β 42, A β 42/A β 40 ratio, and T-tau) and decreased monocyte count and A β phagocytic capacity of monocytes in cognitively normal individuals. These findings provide preliminary evidence supporting the hypothesis that fibrinogen may contribute to early AD pathophysiology by impairing monocyte-mediated peripheral A β clearance, potentially linking peripheral inflammation and immune dysfunction to central AD pathology.

Peripheral monocytes play a key role in clearing circulating A β [5–7], and their phagocytic function declines with aging and in AD [8], making them a potential link between peripheral inflammation and AD pathology. In this context, we examined whether fibrinogen—an inflammatory protein elevated in aging and AD—correlates with A β clearance of monocytes in cognitively normal individuals. Our observation that plasma A β 42 and T-tau levels were positively correlated with fibrinogen levels in cognitively normal individuals extends this understanding by suggesting that fibrinogen may be an upstream regulator of peripheral A β metabolism even before clinical symptoms manifest.

Our findings align with and extend previous research on fibrinogen in AD. Epidemiological studies have shown that elevated fibrinogen is an independent risk factor for AD and vascular dementia [9, 14]. Fibrinogen levels have also been associated with cognitive decline and brain atrophy in elderly populations [9]. Mechanistically, fibrinogen has been shown to bind to the Mac-1 (CD11b/CD18) receptor on myeloid cells, triggering pro-inflammatory signaling pathways and altering cellular functions [10, 15]. Our results provide human in vivo evidence supporting the translational relevance of these mechanistic insights: the negative correlation between fibrinogen levels and monocytic A β uptake capacity suggests that fibrinogen may directly impair the ability of monocytes to clear A β , potentially through Mac-1-mediated signaling. This is consistent with recent findings demonstrating that fibrinogen can induce inflammatory responses in monocytes through integrin-mediated pathways [11, 12]. Whether this effect is mediated through direct competition with A β for Mac-1 binding or through fibrinogen-induced inflammatory reprogramming of monocytes remains to be determined.

Notably, the fibrinogen-Mac-1 axis has recently emerged as a promising therapeutic target in AD. Preclinical studies have demonstrated that targeting the fibrinogen inflammatory binding site with

monoclonal antibodies can reduce neuroinflammation and cognitive decline in animal models [16]. Our findings extend this therapeutic concept to the peripheral compartment, suggesting that modulating fibrinogen-Mac-1 interactions may not only reduce central inflammation but also restore peripheral A β clearance capacity. This aligns with the concept that AD is a systemic disorder involving both central and peripheral pathophysiological processes.

The inverse relationship between fibrinogen levels and monocyte count is another notable finding. While the mechanism underlying this association cannot be determined from our correlational data, several possibilities warrant consideration. Chronic inflammation induced by elevated fibrinogen may promote monocyte apoptosis or impair their production and release from the bone marrow [17]. Alternatively, fibrinogen may enhance monocyte adhesion to the vascular endothelium, leading to reduced circulating monocyte numbers [15]. Future studies are needed to distinguish between these possibilities.

The associations we observed between fibrinogen and AD biomarkers are consistent with recent large-scale proteomic studies. A recent meta-analysis demonstrated that inflammatory proteins, including fibrinogen and other acute-phase reactants, are associated with cognitive decline and AD risk [18]. Our results provide supporting evidence that peripheral fibrinogen levels correlate with core AD pathological markers even in cognitively normal individuals, suggesting that systemic inflammation may influence AD pathology at a very early stage. This finding extends the current understanding of the temporal relationship between peripheral inflammation and AD pathology.

Interestingly, the positive correlation between fibrinogen and T-tau levels, although less robust than the A β correlations, suggests that fibrinogen may also be associated with neurodegenerative changes. This is consistent with prior studies showing that inflammatory markers correlate with tau pathology [19]. However, the relatively weak strength of this association compared to the A β correlations may reflect the fact that tau pathology typically emerges later than A β pathology in the AD continuum.

Limitations

This study has several limitations that should be acknowledged. First, given the exploratory and cross-sectional design, the observed associations should be interpreted as hypothesis-generating rather than causal. Second, the sample size is relatively small ($n = 25$), and the study population was predominantly male (88%), limiting the generalizability of our findings. Third, all participants were cognitively normal, and we did not include a comparison group of MCI or AD patients; thus, the dynamic changes of these associations across the AD spectrum remain unknown. Fourth, we measured plasma rather than CSF biomarkers; plasma A β and tau levels are influenced by peripheral metabolism and renal clearance and may not fully reflect brain pathology. Nevertheless, the SIMOA technology used in this study has been validated for sensitive and accurate detection of plasma AD biomarkers. Fifth, the mechanistic interpretation regarding fibrinogen-Mac-1 interactions is speculative and requires validation through functional studies, including cell culture experiments and animal models. Despite these limitations, the

consistency of our findings with existing mechanistic and epidemiological evidence supports the biological plausibility of the proposed fibrinogen-monocyte-A β axis.

Conclusions

In this pilot study, we observed significant associations between elevated plasma fibrinogen levels, increased plasma AD-related biomarkers, and impaired monocyte-mediated A β clearance in a small cohort of cognitively normal individuals. These findings suggest that fibrinogen-driven monocyte dysfunction may represent an early peripheral event in the AD pathological process, preceding clinical symptoms. From a translational perspective, the fibrinogen-monocyte axis warrants further investigation as a potential target for both early risk identification and intervention strategies in AD. Future studies combining functional experiments and large-scale prospective cohorts are needed to validate whether targeting this axis can restore peripheral A β clearance capacity and ultimately delay AD progression.

Declarations

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding

This study was supported by the Sichuan Provincial Medical Science Youth Innovation Project (Q2024098).

Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

C.S.H. contributed to conceptualization, review, and editing. C.S.H. and W.M. contributed to the investigation, the formal analysis, and the original draft. J.Y.F. contributed to the investigation, original draft and supervision. The authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics approval

This study was approved by the Ethics Committee of the Army Medical Center (Approval No. 2019-58). All participants provided written informed consent.

References

1. Wang J, Gu BJ, Masters CL, Wang YJ (2017) A systemic view of Alzheimer disease - insights from amyloid- β metabolism beyond the brain. *Nat Rev Neurol* 13(11):703. 10.1038/nrneurol.2017.147
2. Viola KL, Klein WL (2015) Amyloid β oligomers in Alzheimer's disease pathogenesis, treatment, and diagnosis. *Acta Neuropathol* 129(2):183–206. 10.1007/s00401-015-1386-3
3. Cheng Y, Tian DY, Wang YJ (2020) Peripheral clearance of brain-derived A β in Alzheimer's disease: pathophysiology and therapeutic perspectives. *Translational neurodegeneration* 9(1):16. 10.1186/s40035-020-00195-1
4. Simard AR, Soulet D, Gowing G, Julien J-P, Rivest S (2006) Bone marrow-derived microglia play a critical role in restricting senile plaque formation in Alzheimer's disease. *Neuron* 49(4):489–502. 10.1016/j.neuron.2006.01.022
5. Prokop S, Miller KR, Drost N, Handrick S, Mathur V, Luo J et al (2015) Impact of peripheral myeloid cells on amyloid- β pathology in Alzheimer's disease-like mice. *J Exp Med* 212(11):1811–1818. 10.1084/jem.20150479
6. Jansen IE, Savage JE, Watanabe K, Bryois J, Williams DM, Steinberg S et al (2019) Genome-wide meta-analysis identifies new loci and functional pathways influencing Alzheimer's disease risk. *Nat Genet* 51(3):404–413. 10.1038/s41588-018-0311-9
7. Butovsky O, Kunis G, Koronyo-Hamaoui M, Schwartz M (2007) Selective ablation of bone marrow-derived dendritic cells increases amyloid plaques in a mouse Alzheimer's disease model. *Eur J Neurosci* 26(2):413–416. 10.1111/j.1460-9568.2007.05652.x
8. Chen SH, Tian DY, Shen YY, Cheng Y, Fan DY, Sun HL et al (2020) Amyloid-beta uptake by blood monocytes is reduced with ageing and Alzheimer's disease. *Translational psychiatry* 10(1):423. 10.1038/s41398-020-01113-9
9. van Oijen M, Witteman JC, Hofman A, Koudstaal PJ, Breteler MM (2005) Fibrinogen is associated with an increased risk of Alzheimer disease and vascular dementia. *Stroke* 36(12):2637–2641. 10.1161/01.str.0000189721.31432.26
10. Deng ZJ, Liang M, Monteiro M, Toth I, Minchin RF (2011) Nanoparticle-induced unfolding of fibrinogen promotes Mac-1 receptor activation and inflammation. *Nat Nanotechnol* 6(1):39–44. 10.1038/nnano.2010.250
11. Strohmeyer R, Ramirez M, Cole GJ, Mueller K, Rogers J (2002) Association of factor H of the alternative pathway of complement with agrin and complement receptor 3 in the Alzheimer's disease brain. *J Neuroimmunol* 131(1–2):135–146. 10.1016/s0165-5728(02)00272-2
12. Zhang D, Hu X, Qian L, Chen SH, Zhou H, Wilson B et al (2011) Microglial MAC1 receptor and PI3K are essential in mediating β -amyloid peptide-induced microglial activation and subsequent neurotoxicity. *J Neuroinflamm* 8(1):3. 10.1186/1742-2094-8-3
13. Chen SH, He CY, Shen YY, Zeng GH, Tian DY, Cheng Y et al (2022) Polysaccharide Krestin Prevents Alzheimer's Disease-type Pathology and Cognitive Deficits by Enhancing Monocyte Amyloid- β

14. Xu G, Zhang H, Zhang S, Fan X, Liu X (2008) Plasma fibrinogen is associated with cognitive decline and risk for dementia in patients with mild cognitive impairment. *Int J Clin Pract* 62(7):1070–1075. 10.1111/j.1742-1241.2007.01268.x
15. Flick MJ, Du X, Witte DP, Jirousková M, Soloviev DA, Busuttill SJ et al (2004) Leukocyte engagement of fibrin(ogen) via the integrin receptor α M β 2/Mac-1 is critical for host inflammatory response in vivo. *J Clin Invest* 113(11):1596–1606. 10.1172/jci20741
16. Ryu JK, Rafalski VA, Meyer-Franke A, Adams RA, Poda SB, Rios Coronado PE et al (2018) Fibrin-targeting immunotherapy protects against neuroinflammation and neurodegeneration. *Nat Immunol* 19(11):1212–1223. 10.1038/s41590-018-0232-x
17. Hotamisligil GS (2017) Inflammation, metaflammation and immunometabolic disorders. *Nature* 542(7640):177–185. 10.1038/nature21363
18. Koyama A, O'Brien J, Weuve J, Blacker D, Metti AL, Yaffe K (2012) The Role of Peripheral Inflammatory Markers in Dementia and Alzheimer's Disease: A Meta-Analysis. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*. 68(4):433–440. 10.1093/gerona/gls187
19. Zhang Q, Yang G, Luo Y, Jiang L, Chi H, Tian G (2024) Neuroinflammation in Alzheimer's disease: insights from peripheral immune cells. *Immun Ageing* 21(1). 10.1186/s12979-024-00445-0

Figures

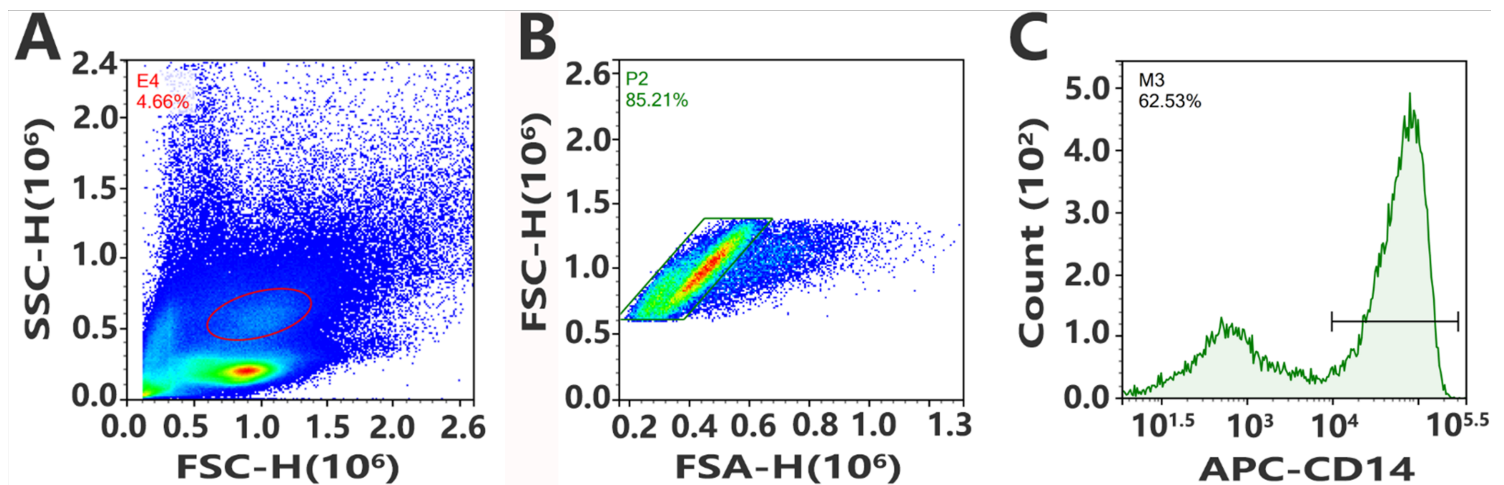


Figure 1

Flow cytometric analysis of uptake of A β 42 by monocytes. (A) PBMCs were gated based on FSC-H and SSC-H. (B) Doublets were excluded using FSC-H vs. FSC-A. (C) Monocytes were identified as CD14-positive cells, and intracellular FITC-A β 42 MFI was measured.

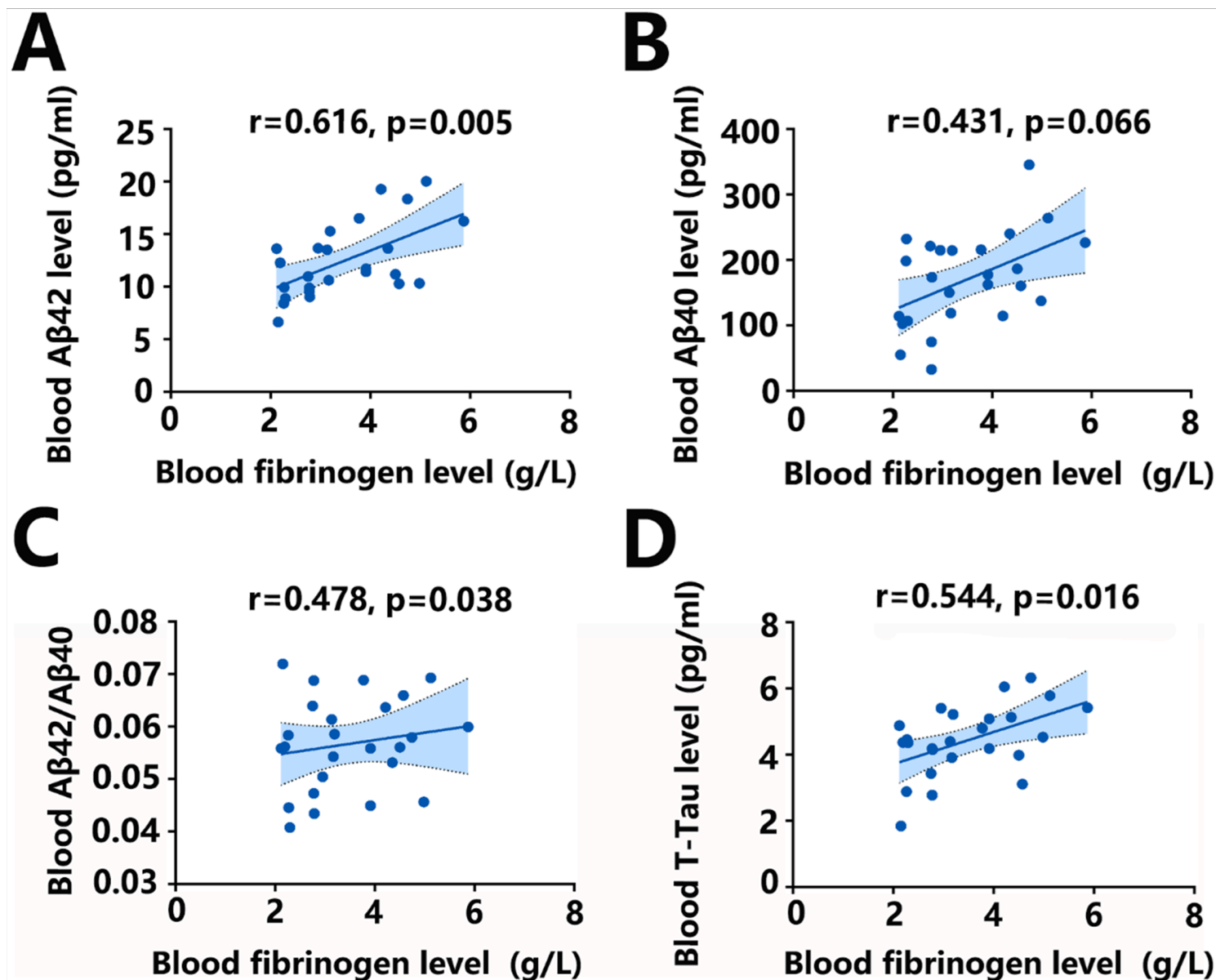


Figure 2

Associations between plasma fibrinogen levels and AD-related biomarkers. Partial correlation analysis was utilized to investigate the correlation between plasma fibrinogen levels and plasma A β 42 level (A), plasma A β 40 level (B), A β 42/A β 40 ratio (C) and plasma T-tau level (D).

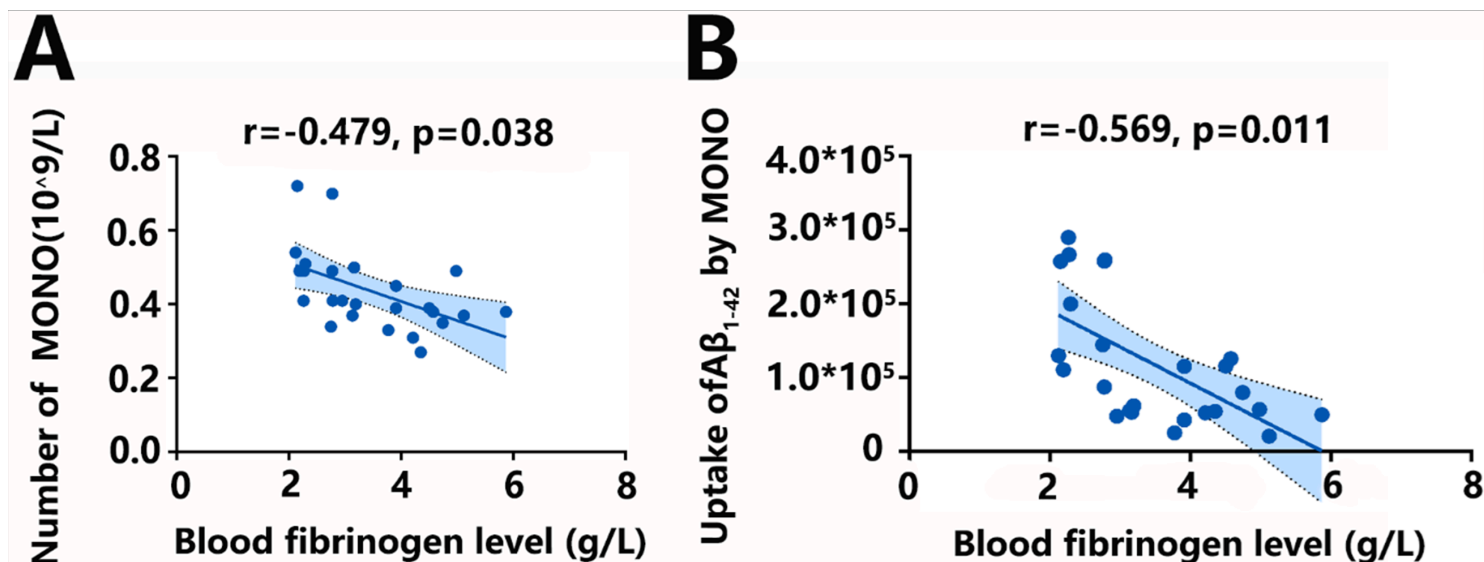


Figure 3

Associations between plasma fibrinogen levels and monocyte parameters. Partial correlation analysis was utilized to investigate the correlation between plasma fibrinogen levels and monocyte count (A), and uptake of $A\beta_{42}$ by monocytes (B).