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Deposited on: 10 March 2014
6.27 (95% CI 4.93–7.98). Dichotomizing the material according to CSF T-tau or P-tau did not change the ORs as compared with clinical diagnosis only (Figure 1). Even though the OR for the ratio P-tau/Aβ42 (6.50 (95% CI 5.07–8.35)) was slightly higher than for Aβ42 alone, the difference was not statistically significant.

We also compared patients, again disregarding the clinical diagnoses, who had a complete CSF biomarker signature indicative of AD, that is, low Aβ42 and both high T-tau and P-tau (n = 438, see Supplementary Material for a detailed description of the signature), with subjects with a negative CSF APOE AD. Second, clinical criteria that incorporate biomarker informed the association to diagnosis and a concordant complete biomarker profile in patients classified on the basis of biomarker data alone.

Finally, ORs were calculated on subjects having both a clinical diagnosis and a concordant complete biomarker profile (n(AD) = 324; n(control) = 155). This approach resulted in an even stronger association of APOE ε4 with AD (OR 10.4, 95% CI 6.65–16.3). Similar effects were seen when comparing non-carriers with ε4 heterozygotes and homozygotes across the different diagnostic groups (Figure 1, Supplementary Material).

These results have several important implications. First, APOE ε4 appears as strongly associated with amyloid pathology as clinical AD. Second, clinical criteria that incorporate biomarker information on Alzheimer’s pathology give a stronger association with APOE ε4 than clinical diagnosis alone. This is compatible with the presumed higher diagnostic accuracy of the revised clinical approach,1–3 and has also been seen in a series of neuropathologically verified AD cases and controls.7 Third, the approach of combining clinical with biomarker data may increase the power of genetic association studies, as well as the potential to provide insights into the mechanistic pathways through which genetic risk factors may exert their effects.

**CONFLICT OF INTEREST**

The authors declare no conflict of interest.

**ACKNOWLEDGMENTS**

This study was funded by grants from Swedish Brain Power, the Swedish Research Council (projects 14002, 2006-6227, K2010-63P-21562-01-4 and K2011-61X-20401-05-6), the Wolfson Foundation, the Alzheimer’s Association (NIGH-08-90356), the JPND Project BIOMARKAPD, Swedish State Support for Clinical Research (ALFGBG-144341), the Swedish Brain Fund, the Alzheimer Foundation, Sweden, the Dementia Association, Sweden, the National Institute for Health Research (NIHR) Biomedical Research Unit in Dementia based at University College London Hospitals (UCLH), University College London (UCL). The Dementia Research Centre is an Alzheimer’s Research Unit in Dementia based at University College London Hospitals (UCLH), London, UK; 3Clinical Memory Research Unit, Clinical Sciences Malmö, Lund University, Lund, Sweden; 4Department of Neurology and Brain Research Unit, Clinical Research Centre/Mediteknio, University of Eastern Finland, Kuopio, Finland; 5Hansson O, Zetterberg H, Buchhave P, Londos E, Blennow K, Minthon L. Lancet Neurol 2006; 5: 228–234.

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**OPEN**

Long-term inflammation increases risk of common mental disorder: a cohort study

*Molecular Psychiatry* (2014) 19, 149–150; doi:10.1038/mp.2013.35; published online 9 April 2013

The inflammation hypothesis of depression, or more broadly, common mental disorders, proposes that chronic inflammation plays an important role in the pathophysiology of these conditions.1,2 The hypothesis is supported by experiments of inflammatory stimuli, antidepressant trials and studies on depression-related genes and pathogen host defense,2–5 but direct population-based evidence from long-term inflammation is scarce. Because of a lack of studies on the effects of chronically elevated inflammation, assessed over several years using repeat measurements, it has remained unclear whether the association between inflammation and common mental disorder is the consequence of acute or chronic inflammation.

This report is from the Whitehall II cohort study.6 In our analysis of up to 4630 adults without chronic disease, we used repeat measures of inflammatory markers and mental disorder. We measured the proinflammatory cytokine interleukin 6 (IL-6) in 1992, 1997 and 2003 and common mental disorder, based on the General Health Questionnaire (GHQ), in 1997, 2003 and 2008. The IL-6 distribution was categorized as: ≤ 1.0 pg ml−1 (low), 1.1–2.0 pg ml−1 (intermediate) and > 2.0 pg ml−1 (high).
respectively, for a 10-year risk of common mental disorder (total risk, 1.18 (0.94–1.47), 1.38 (1.04–1.83) and 1.56 (1.10–2.21), respectively) for participants with high IL-6 on 0, 1, 2 and 3 occasions had odds ratios of 1.00 (Reference), 1.40 (95% CI: 1.07–1.82), 1.40 (1.07–1.82), 1.40 (1.07–1.82). 

Results show that those demonstrating persistently high IL-6 levels is more marked when the assessment of IL-6 is based on repeat measurements (age- and sex-adjusted odds ratio = 1.40 (95% CI: 1.07–1.82)). P < 0.05, **P < 0.01.

The authors declare no conflict of interest.

ACKNOWLEDGMENTS

KPE, on behalf of the Oxford Department of Psychiatry, receives funding for organization of local continued professional development events from Eisai, Lundbeck, Novartis, Boeringer-Ingelheim, and Pfizer.

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Supplementary Information accompanies the paper on the Molecular Psychiatry website (http://www.nature.com/mp)