Letters to the Editor

645

Rheumatology 2006;45:645–646
doi:10.1093/rheumatology/kel033
Advance Access publication 8 February 2006

β2-Glycoprotein I IgA antibodies and ischaemic stroke

Sir, Regarding the article by Kahles et al., recently published in this journal [1], we would like to point out that our previous paper, published in 2003 [2] and not referred to by Kahles et al., had already shown an association of IgA antibodies to β2-glycoprotein I (β2gpl) with ischaemic stroke. Like Kahles et al., we conducted a case-control study with multivariate analysis. This also allowed us to evaluate risk association after adjustment for known risk factors for stroke. Our data showed that the presence of IgA anti-β2gpl antibodies was independently associated with the risk of acute cerebral ischaemia (adjusted odds one of a number of reference points for the motor control system that informs the predicted sensory feedback, or efference copy. Other factors, including joint position sense, the environment, previous experience and emotional factors, inevitably influence the efference copy. If any one of these becomes altered or distorted, the individual is rendered more vulnerable to an inaccurate or distorted sensory prediction. It is possible that some of these factors are differentially weighted and hence it is not surprising that the level of pain experienced has been shown to be significantly correlated with the level of cortical reorganization in some patients with phantom limb and in CRPS populations [6, 7]. In addition, functional MRI data show a dramatic increase in activity in the somatosensory cortex, as well as other cortical areas involved in cognitive and motor processing, when pin-prick hyperalgesia is induced in the CRPS-affected limb compared with the unaffected limb [8].

The authors have declared no conflicts of interest.

Rheumatology [2]. Our position was primarily one of caution that alternative explanations for both the results and the mechanisms underpinning them should not be excluded. Some of our concerns, for example selection bias, were allayed, but some remain. For example, while we appreciate that abnormal sensations stopped immediately when normal visual input was restored and that this suggests a direct relationship between the experimental condition and the abnormal sensations, the cogency of this finding would be strengthened if the onset of abnormal sensation occurred immediately too. Our contention that further work is required to determine how the experimental condition was related to the abnormal sensations still stands.

We agree, and it is well established, that many factors from across domains may impact on motor commands and their efference copies [3], and that changes in cortical reorganization (that is, the response profile of S1 neurons) cannot be solely responsible for pain. Furthermore, while S1 holds maps of the superficial and deep surfaces of the body, the understanding of the relationships between cutaneous afferent activity, proprioception and motor control is not well developed [4].

In summary, it is possible that mirror use in healthy volunteers is sufficiently incongruent to evoke abnormal sensations yet the same mirror use in patients is sufficiently congruent to alleviate these sensations. However, it seems critical to acknowledge that on the basis of current data this hypothesis can neither be accepted nor refuted.

The authors have declared no conflicts of interest.


Sir, Thanks for the opportunity to comment on McCabe et al.’s response to our Editorial [1] concerning their earlier paper in

G. L. MOSELEY, S. C. GANDEVIA

Department of Human Anatomy and Genetics and fMRIB Centre, University of Oxford, Oxford, UK and 1Prance of Wales Medical Research Institute and University of New South Wales, Sydney, Australia

Accepted 6 January 2006

Correspondence to: G. L. Moseley.
E-mail: lorimer.moseley@ndm.ox.ac.uk

ratio 4.6; 90% confidence interval 1.5–14.3; P = 0.025). β2glycoprotein IgA antibodies in patients with ischaemic stroke brings about a possible link of autoimmunity with thrombophilia and/or atherosclerosis.

G.L.N. is an employee of INOVA Diagnostics Inc. He does not hold any stock or equity interest in the company.

H. L. STAUB, C. A. VON MUHLEN, G. L. NORMAN
Rheumatology Department, Saint Lucas Hospital, Pontificial Catholic University of Rio Grande do Sul, Porto Alegre, Brazil and 
INOVA Diagnostics, San Diego, CA, USA
Accepted 06 January 2006

Correspondence to: H. L. Staub, Rheumatology Department, Saint Lucas Hospital, Pontificial Catholic University of Rio Grande do Sul, Av. Ipiranga 6690/220, Porto Alegre Rio Grande do Sul 90610-000. Brazil. E-mail: henriquestaub@terra.com.br


Rheumatology 2006;45:646–647
doi:10.1093/rheumatology/kel035
Advance Access publication 20 February 2006

β2-Glycoprotein I IgA antibodies and ischaemic stroke: reply

Sir, We appreciate the interest of Staub et al. in our recent article [1] and welcome their comment. We apologize for not referring to their paper published in Arquivos de Neuropsiquiatría in 2003 [2], in which they analysed the frequency of different phospholipid antibodies and antibodies to heat-shock proteins in patients with ischaemic stroke. They reported significantly higher positive test results for heat-shock protein 65 IgG and anti-β2-glycoprotein IgA in cases than in controls.

In accordance with our results, elevated titres of anti-β2-glycoprotein IgA appear to be associated with ischaemic stroke. In our study this was also the case after correction for multiple comparison. Additionally, we were able to show significantly higher titres of anti-phosphatidylserine IgG in patients with ischaemic stroke compared to healthy controls.

Moreover, we tested for an association of a broad panel of phospholipid antibodies within stroke subtypes with special regard to cryptogenic stroke. We found a trend for positivity for lupus anticogulant and anti-phosphatidylinositol IgM in patients with cryptogenic stroke compared with those with a determined cause of stroke, which was not significant after modified Bonferroni correction for multiple comparison.

Establishing a causal link between cerebral ischaemia and elevated anti-β2-glycoprotein IgA titres on the one hand and atheroma plaques containing β-2-glycoprotein on the other hand requires at least the separation of strokes into their aetiological subtypes. Such a link remains to be elucidated.

However, we fully agree with Dr Staub and colleagues that anti-β2-glycoprotein IgA is associated with ischaemic stroke. The results of our recent study may serve as the base for upcoming prospective studies, which should focus on the relevant phospholipid antibodies found to be associated.

The authors have declared no conflicts of interest.

T. KAHLES, M. HUMPICH, M. SITZER, E. LINDHOFF-LAST
University Hospital, Department of Neurology, JW Goethe University, Frankfurt/Main, Germany
Accepted 06 January 2006

Correspondence to: T. Kahles, University Hospital, Department of Neurology, JW Goethe University, Schleusenweg 2–16, ZNN, D-60528 Frankfurt/Main, Germany. E-mail: t.kahles@em.uni-frankfurt.de


Rheumatology 2006;45:646–647
doi:10.1093/rheumatology/kel035
Advance Access publication 20 February 2006

Can research quality be estimated from journal titles?

Sir, In the article by Wooding et al. [1] the method used to estimate the impact of each individual paper published as the result of receiving an Arthritis Research Campaign grant is not clearly stated. However, if it was calculated indirectly from the impact factor of the journal of publication, the approach used to rank authors, I have serious concerns about the value of the information derived.

To investigate the reliability of this approach I have used a database of papers published from the (now defunct) MRC Clinical Research Centre (CRC) between 1972 and 1985, as listed in the CRC’s bi-annual (later annual) reports. The data collected for each individual paper included the journal of publication, number of pages and total citations for that paper. Single-page papers were excluded as possibly being abstracts.

There were 20 journals that published more than 20 CRC papers each scoring more than 10 citations (mean 34) among several hundred journals used overall by CRC scientists, who were working in clinical and translational research relevant to many clinical disciplines. The distribution of the total citations received in the first 20yr after publication by the 680 papers was found to be logarithmic, after subtracting nine citations from each (to correct for self-citation), the highest score being well over 1000. After log-transformation, analysis of variance was used to relate total score to journal, and journal was found to account for only 10% of the variance in the data. The residuals were exponentially distributed, so that after log transformation the s.d. was 0.5. This means that the estimated mean and 95% confidence interval for predicting the citation count of an individual Lancet or Nature article (net of an estimated nine self-citations) was 42 (4.2, 420) and for the lowest scoring journal it was 10 (1, 100).

Estimating confidence intervals for the data published by Wooding et al. is impossible because they quote citations received annually. The CRC data showed clearly that clinical research had a much longer citation half-life than translational research for a similar number of total citations, or in other words had less early impact that was more sustained. This is appropriate for work