TABLE 1. Association analysis of *ITGAM* SNPs in NZ, WTCCC and Oxford (UK) samples

			Genotype, *n* (frequency)			Genotypic *P*-value	Minor allele, *n* (frequency)	OR, (95% CI)	Allelic *P*-value
			GG	AG	AA				
NZ	*rs1143679*[a]	Cases	595 (0.818)	126 (0.173)	6 (0.008)	0.88	138 (0.095)	0.95 (0.73, 1.24)	0.72
		Controls	447 (0.813)	97 (0.176)	6 (0.011)		109 (0.099)		
			AA	AT	TT				
WTCCC (UK)[b]	*rs9936831*	Cases	1573 (0.845)	274 (0.147)	14 (0.008)	0.41	302 (0.081)	1.08 (0.93, 1.26)	0.34
		Controls	2507 (0.853)	417 (0.142)	14 (0.005)		445 (0.076)		
			TT	CT	CC				
	rs9888879[c]	Cases	1503 (0.808)	334 (0.179)	24 (0.013)	0.15	382 (0.103)	1.09 (0.95, 1.26)	0.20
		Controls	2404 (0.818)	512 (0.174)	22 (0.007)		556 (0.095)		
			CC	CT	TT				
	rs9888739	Cases	1502 (0.807)	334 (0.179)	25 (0.013)	0.46	384 (0.103)	1.07 (0.93, 1.23)	0.33
		Controls	2397 (0.816)	512 (0.174)	29 (0.010)		570 (0.097)		
			CC	CT	TT				
	rs11860650[c]	Cases	1493 (0.802)	343 (0.184)	25 (0.013)	0.30	393 (0.106)	1.07 (0.94, 1.22)	0.33
		Controls	2380 (0.810)	532 (0.181)	26 (0.009)		584 (0.099)		
Meta-analysis			Major homozygous	Heterozygous	Minor homozygous				
(NZ, WTCCC and	*rs1143679* and	Cases	2682 (0.813)	583 (0.177)	34 (0.010)	0.59	651 (0.099)	1.05[e] (0.93, 1.17)	0.51
Oxford cases)	rs*9888879*[d]	Controls	2851 (0.817)	609 (0.175)	28 (0.008)		665 (0.095)		
			GG	AG	AA				
NZ[f]	*rs1143679*	RF+ cases	430 (0.811)	94 (0.177)	6 (0.011)	0.38	106 (0.100)		
		RF− cases	93 (0.853)	16 (0.147)	0 (0.000)		16 (0.073)		
		CCP+ cases	220 (0.821)	47 (0.175)	1 (0.004)	0.78	49 (0.091)		
		CCP− cases	106 (0.828)	22 (0.172)	0 (0.000)		22 (0.086)		
Oxford (UK)[a,f]	*rs1143679*	RF+ cases	456 (0.828)	91 (0.165)	4 (0.007)	0.44	99 (0.090)		
		RF− cases	122 (0.808)	29 (0.192)	0 (0.000)		29 (0.096)		

[a]Success rate of genotyping for *rs1143679* was 97.5% in both NZ cases and controls, and Oxford cases. [b]Imputed data. [c]SNPs *rs9888879* and *rs11860650* are in complete LD with *rs12928810* and *rs6565227*, respectively, in the HapMap CEU population. Therefore, the data for the first two are presented here. [d]*rs9888879* is in high LD with *rs1143679* (r^2 approaching 1) [2], and therefore acts as a proxy SNP in WTCCC data for *rs1143679* which cannot be imputed directly. [e]The Breslow–Day test for heterogeneity revealed no evidence for a difference between the NZ and UK sample sets ($P = 0.478$). [f]RF and CCP status data were available for 87.7% (654/746) and 54.7% (408/746) of the NZ cases. RF status data were available for 98.8% (720/729) of the Oxford cases.

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Inflammatory profile in the cerebrospinal fluid of patients with central neuropsychiatric lupus, with and without associated factors

SIR, The ACR classifies neuropsychiatric (NP) manifestations into 19 syndromes [1]. From a classification perspective, the current approach of attributing NP manifestations in SLE patients may be appropriate; however, from a pathogenic standpoint, any misclassification will affect the advance in the knowledge of the pathogenic mechanisms, their diagnosis and treatment. Therefore, it is important to know whether the inflammatory profile in NP manifestations due to lupus, with and without associated factors, is similar. We studied 35 patients (ACR criteria) [2] with central NP manifestations (cNPSLE) with and without associated factors. They were evaluated at hospitalization and 6 months later, with a cerebrospinal fluid (CSF) sample at both times in which IgG ANA, anti-dsDNA, anti-ribosomal-P, aCL, anti-β2 glycoprotein-I and anti-*N*-methyl-D-aspartate receptor antibodies, as well as cytokines IL-2, -4, -6, -10, TNF-α, IFN-γ and -α and chemokines MCP-1, regulated on activation normal T cell expressed and secreted, IL-8, monokine induced by interferon gamma and gamma interferon inducible protein (IP-10) were tested. The study was approved by the Institutional Committee of Biomedical Research, and all patients provided informed consent. Of the

TABLE 1. Prevalence of antibodies and levels of cytokines and chemokines in CSF at hospitalization

	cNPSLE pure, $n=17$	cNPSLE-associated factor, $n=18$	*P*-value
Antibodies positive, *n* (%)			
ANA	11 (65)	9 (50)	0.4
Anti-ribosomal P	10 (59)	6 (33)	0.13
Anti-dsDNA	13 (76)	14 (77)	1.0
aCL (IgG)	3 (18)	1 (6)	0.34
Anti-β2 glycoprotein I (IgG)	0	0	–
Anti-NMDAR*	8 (47)	6 (33)	0.32
Cytokines and chemokines, mean (S.D.)			
IL-6	356.1 (1074.7)	793.7 (2169.04)	0.46
IL-8	510.2 (894.9)	1349.2 (3527.2)	0.34
IP-10	2905.7 (2453.7)	1047.07 (1287.09)	0.009
MCP-1	1168.2 (1683.9)	778.02 (1090.08)	0.42
INF-α	51.7 (58.9)	41.5 (28.9)	0.53

*The NMDAR antibody was measured in 34 patients, 17 patients with pure cNPSLE, and 17 with associated factors. NMDAR: N-methyl-D-aspartate receptor.

35 patients with cNPSLE (18 with and 17 without associated factors), the mean age was 30.6 ± 11.8 years and 86% were females. The NP manifestations present were 14 seizures, 8 acute confusional states, 8 cephalalgia, 3 cerebrovascular events, 1 psychosis and 1 pseudo-tumour cerebri.

At hospitalization, patients with pure NP manifestations had greater disease activity (SLEDAI-2K) [3] (18.1 ± 8.0 *vs* 11.7 ± 9.7; $P = 0.04$). Six months later, disease activity decreased in both groups, but it was only in the group with pure cNPSLE that was statistically significant (14.8 ± 1.9; $P < 0.001$).

The prevalence of all the antibodies studied at the time of hospitalization was similar in patients with pure NP manifestations and in those with associated factors (Table 1). Among the patients with paired CSF samples, no significant difference in the prevalence of antibodies at hospitalization and 6 months later was observed. In those patients who were found to be positive for each antibody at hospitalization, a non-significant decreasing trend in the levels of all the autoantibodies was observed in both groups.

The levels of the studied cytokines and chemokines were similar in both groups, except for IP-10, which showed levels significantly higher in the group with pure NP manifestations (Table 1). In both groups, the level of all cytokines and chemokines decreased after 6 months. However, in patients with pure NP manifestations, a statistically significant decrease was observed only in IL-6 and IP-10 (85.4 ± 116.5 *vs* 2.9 ± 2.4 pg/ml; $P = 0.02$; and 2673.9 ± 2330.4 *vs* 723.3 ± 588.09 pg/ml; $P = 0.01$, respectively); whereas in those patients with NP manifestations with associated factors, only IP-10 decreased significantly after 6 months (1258.3 ± 1492.2 *vs* 651.9 ± 682.2 pg/ml; $P = 0.04$).

At present, no specific test exists that might define whether a given NP manifestation is due specifically to lupus activity or any other concomitant factor. Several inflammatory molecules have been found associated with NP manifestations in SLE [4–7]. Patients with pure NP manifestations seemed to have more intense inflammation as reflected by a significantly higher level of disease activity and of IP-10. These results may suggest that in contrast to patients with pure NP manifestations, the presence of associated factors may trigger the onset of NP manifestations at lower levels of inflammation, but the inflammatory profile in both lupus patients is similar that may be the result of a breach of the blood–brain barrier shared by both groups. The significant decrease observed in lupus activity 6 months after the outbreak of NP manifestations in patients with pure cNPSLE, but not with cNPSLE with associated factors, is consistent with this hypothesis [7]. The high levels of IP-10 seem to be indicative of disease activity in the CNS. Even though in NPSLE patients with associated factors, the levels of IP-10 were significantly lower than in patients with pure NP manifestations, the levels were still higher than that found in non-NPSLE patients. Therefore, IP-10 may be considered as a preponderant chemokine in the development of NPSLE.

Our study has the following limitations: (i) the number of patients is not large enough to derive a definitive conclusion about the differences between central neuropsychiatric (cNP) manifestations pure and with associated factors; (ii) we studied the inflammatory profile of cNP manifestations in general, not specifically, hence we cannot reach any conclusion for any particular NP manifestation; (iii) the attribution of NP manifestations to SLE is complex, thus, some misclassification should be present; and (iv) we included patients with acute and severe cNP manifestation, therefore, our results could not be applied for mild or chronic manifestations.

The results allow us to conclude that the inflammatory profile in the CSF of SLE patients with cNP manifestations with and without associated factors is similar; thus, the current rules for the attribution of cNPSLE manifestations seem to be valid, not only for classification purposes, but also for the study of their pathogenic mechanisms, their diagnosis and their treatment.

Rheumatology key message

- Current rules for attribution of cNPSLE manifestations seem valid for classification, pathogenesis, diagnosis and treatment.

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Lupus podocytopathy

SIR, Approximately one-third of the patients with SLE develop readily detectable renal involvement. Proteinuria is a ubiquitous