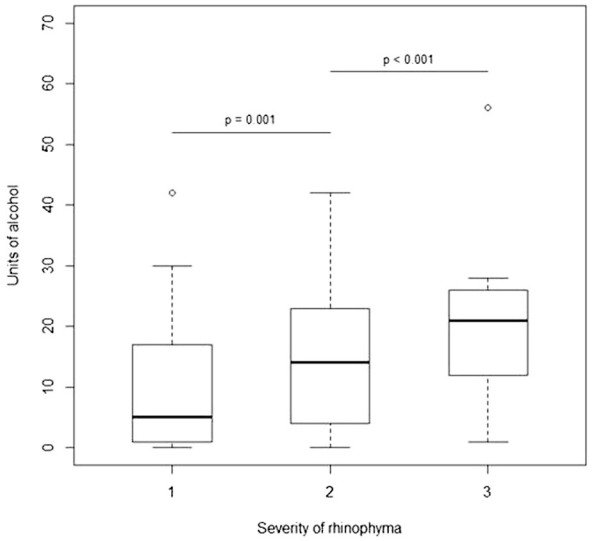

Fig 1. Alcohol intake according to severity of rhinophyma.

median weekly alcohol intake.[5] Our study shows a highly significant association with alcohol, with the OR increasing as intake goes up, and a correlation between the amount of alcohol consumed and severity of rhinophyma. There is an association with telangiectasia, and cases of phyma developed at the surface of hemangiomas or capillary malformation, suggesting a critical role of vascular changes. As alcohol is a strong inducer of flushing and vasodilatation, it might play a role in the vascular background necessary for skin thickening on the nose. A genetic predisposition for rosacea exists, but a family background of rhinophyma had been suggested only in case reports. We show that male sex and family history are major risk factors; genetic predisposition is probably critical, as alcohol is not sufficient to induce rhinophyma. Moreover, only a minority of patients with rosacea develop phymas (ie, skin hypertrophy with large sebaceous glands), which might also be related to alcohol abuse.

Association of rosacea with diabetes is controversial. Our study suggests a significant link with rhinophyma; no satisfactory explanation has yet been found, except for a comparison with abnormal growth and leakage of capillaries in diabetic microangiopathy, resulting in edema and functional tissue impairment, as is observed in rosacea. This remains to be explored.

Our study is, to our knowledge, the first to provide convincing epidemiologic arguments to support the age-old supposition of a link between alcohol and rhinophyma and suggests—at least in predisposed individuals—a possible causal role.

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Drugs used for neurologic and psychiatric conditions increase the risk for bullous pemphigoid: A case–control study

To the Editor: The association between neurologic diseases and bullous pemphigoid (BP) is well established.[1] However, it has not yet been established whether drugs that affect the nervous system can influence the onset of BP. The aim of this

Table I. Demographics of bullous pemphigoid patients and basal cell carcinoma controls

Characteristic	Cases, n = 3397, n (%)	Controls, n = 12,941, n (%)*
Sex		
Female	2028 (59.7)	7766 (60.0)
Male	1369 (40.3)	5175 (40.0)
Mean age, years	76.6	76.7

*Age, sex, and year of diagnosis matched in a 1:4 ratio. Due to the availability of drug reimbursement data, 579 patients had fewer than the intended 4 controls.

Table II. Proportions of bullous pemphigoid patients and basal cell carcinoma controls exposed to drugs significantly associated with bullous pemphigoid

Drug for neurologic or psychiatric condition*	Group	Total	N (%)	OR (95% CI)	Adjusted OR (95% CI)†
Carbamazepine	Cases	3397	90 (2.6)	2.26 (1.73-2.95)	1.57 (1.12-2.20)
	Controls	12,941	154 (1.2)	Reference	Reference
Pregabalin	Cases	3397	122 (3.6)	1.26 (1.02-1.55)	1.24 (1.00-1.53)
	Controls	12,941	383 (3.0)	Reference	Reference
Biperiden	Cases	3397	16 (0.5)	2.59 (1.37-4.92)	2.94 (1.42-6.09)
	Controls	12,941	24 (0.2)	Reference	Reference
Levodopa and decarboxylase	Cases	3397	110 (3.2)	2.20 (1.74-2.79)	1.85 (1.10-3.12)
Inhibitors	Controls	12,941	196 (1.5)	Reference	Reference
Levomepromazine	Cases	3397	44 (1.3)	3.08 (2.06-4.61)	2.84 (1.81-4.48)
	Controls	12,941	54 (0.4)	Reference	Reference
Perphenazine	Cases	3397	34 (1.0)	2.23 (1.46-3.42)	1.82 (1.09-3.06)
	Controls	12,941	57 (0.4)	Reference	Reference
Periciazine	Cases	3397	15 (0.4)	4.79 (2.24-10.3)	7.55 (2.91-19.6)
	Controls	12,941	12 (0.1)	Reference	Reference
Haloperidol	Cases	3397	49 (1.4)	2.94 (2.01-4.30)	3.00 (1.93-4.65)
	Controls	12,941	63 (0.5)	Reference	Reference
Melperone	Cases	3397	41 (1.2)	3.50 (2.29-5.34)	4.00 (2.46-6.49)
	Controls	12,941	45 (0.3)	Reference	Reference
Quetiapine	Cases	3397	97 (2.9)	2.13 (1.66-2.75)	1.62 (1.20-2.18)
	Controls	12,941	178 (1.4)	Reference	Reference
Sulpiride	Cases	3397	13 (0.4)	2.56 (1.25-5.25)	2.37 (1.12-5.00)
	Controls	12,941	19 (0.1)	Reference	Reference
Risperidone	Cases	3397	172 (5.1)	3.06 (2.49-3.75)	3.04 (2.38-3.89)
	Controls	12,941	225 (1.7)	Reference	Reference
Hydroxyzine	Cases	3397	134 (3.9)	17.3 (11.5-26.0)	17.3 (11.5-26.0)
	Controls	12,941	37 (0.3)	Reference	Reference
Diazepam	Cases	3397	130 (3.8)	1.35 (1.10-1.66)	1.33 (1.08-1.63)
	Controls	12,941	372 (2.9)	Reference	Reference
Chlordiazepoxide	Cases	3397	18 (0.5)	2.16 (1.21-3.85)	2.15 (1.20-3.84)
	Controls	12,941	32 (0.2)	Reference	Reference
Oxazepam	Cases	3397	244 (7.2)	1.38 (1.19-1.61)	1.34 (1.15-1.56)
	Controls	12,941	688 (5.3)	Reference	Reference
Lorazepam	Cases	3397	73 (2.1)	1.58 (1.19-2.08)	1.48 (1.11-1.95)
	Controls	12,941	177 (1.4)	Reference	Reference
Nitrazepam	Cases	3397	38 (1.1)	1.84 (1.24-2.72)	1.84 (1.24-2.72)
	Controls	12,941	79 (0.6)	Reference	Reference
Temazepam	Cases	3397	326 (9.6)	1.36 (1.19-1.55)	1.35 (1.18-1.55)
	Controls	12,941	955 (7.4)	Reference	Reference
Zopiclone	Cases	3397	567 (16.7)	1.14 (1.03-1.27)	1.13 (1.02-1.26)
	Controls	12,941	1945 (15.0)	Reference	Reference
Amitriptyline	Cases	3397	75 (2.2)	1.62 (1.23-2.13)	1.60 (1.20-2.12)
	Controls	12,941	180 (1.4)	Reference	Reference
Doxepin	Cases	3397	60 (1.8)	2.26 (1.64-3.12)	2.33 (1.66-3.27)
	Controls	12,941	103 (0.8)	Reference	Reference
Citalopram	Cases	3397	317 (9.3)	1.87 (1.63-2.16)	1.83 (1.58-2.12)
	Controls	12,941	681 (5.3)	Reference	Reference
Sertraline	Cases	3397	43 (1.3)	1.73 (1.20-2.48)	1.68 (1.13-2.48)
	Controls	12,941	96 (0.7)	Reference	Reference
Escitalopram	Cases	3397	107 (3.1)	1.69 (1.34-2.14)	1.62 (1.26-2.09)
	Controls	12,941	249 (1.9)	Reference	Reference
Mianserin	Cases	3397	37 (1.1)	1.72 (1.16-2.54)	1.78 (1.15-2.74)
	Controls	12,941	82 (0.6)	Reference	Reference
Mirtazapine	Cases	3397	195 (5.7)	1.36 (1.15-1.61)	1.30 (1.09-1.56)
	Controls	12,941	559 (4.3)	Reference	Reference

Continued

Table II. Cont'd

Drug for neurologic or psychiatric condition*	Group	Total	N (%)	OR (95% CI)	Adjusted OR (95% CI)†
Venlafaxine	Cases	3397	47 (1.4)	1.85 (1.30-2.63)	2.15 (1.41-3.27)
	Controls	12,941	98 (0.8)	Reference	Reference
Duloxetine	Cases	3397	28 (0.8)	1.86 (1.18-2.94)	1.81 (1.07-3.06)
	Controls	12,941	59 (0.5)	Reference	Reference
Donepezil	Cases	3397	111 (3.3)	2.03 (1.61-2.57)	1.40 (1.02-1.94)
	Controls	12,941	220 (1.7)	Reference	Reference
Rivastigmine	Cases	3397	87 (2.6)	2.46 (1.87-3.23)	2.11 (1.47-3.03)
	Controls	12,941	141 (1.1)	Reference	Reference
Galantamine	Cases	3397	48 (1.4)	2.38 (1.66-3.41)	1.75 (1.07-2.85)
	Controls	12,941	79 (0.6)	Reference	Reference
Carbachol	Cases	3397	8 (0.2)	2.74 (1.10-6.81)	2.82 (1.12-7.12)
	Controls	12,941	11 (0.1)	Reference	Reference
Memantine	Cases	3397	142 (4.2)	2.98 (2.38-3.73)	2.34 (1.67-3.26)
	Controls	12,941	200 (1.5)	Reference	Reference

CI, Confidence interval; *OR*, odds ratio.

*Statistically significant results (defined by a *P* value $< .05$) from analyses of all drugs from the Anatomical Therapeutic Chemical classification system main group N, nervous system (excluding N01-N02).

†Adjusted for diagnoses of the following neurologic and psychiatric conditions: Alzheimer disease, vascular dementia, other/unspecified dementia, Parkinson's disease, multiple sclerosis, subarachnoid hemorrhage, intracerebral hemorrhage, cerebral infarction, epilepsy, schizotypal and delusional disorder, schizophrenia, bipolar affective disorder, major depressive disorder, neurotic, stress-related and somatoform disorders, personality disorders, delirium due to known physiologic conditions, other mental disorders due to known physiologic conditions, personality and behavioral disorders due to known physiologic conditions, unspecified mental disorder due to known physiologic conditions.

study was to determine if patients who receive drugs to treat neurologic and psychiatric diseases have an altered risk for BP.

We searched the Finnish Care Register for Health Care database for all patients who received a diagnosis of BP during 1987-2013. The search returned data for 4524 patients, and because of drug reimbursement data available, the present analysis could include data from only 3397 patients who received diagnoses during 1997-2013. A total of 66,138 basal cell carcinoma (BCC) patients were identified; 12,941 of these patients were randomly selected to be matched to the BP population by age, sex, and year of diagnosis in a 4:1 ratio. Characteristics of study populations are shown in Table I.

The associations between the use of each drug for neurologic and psychiatric diseases purchased in the previous 2 years and BP incidence were evaluated by using a conditional logistic regression model; odds ratios and 95% confidence intervals are presented. The associations that were statistically significant are shown in Table II. Drugs that particularly elevated the risk for BP included periciazine, melperone, haloperidol, biperiden, and risperidone. At the drug-class level, the butyrophenone derivates and the antidementia anticholinesterases were the only groups in which all constituent drugs were significantly associated with an increased risk for BP. Hydroxyzine seemed to be associated with a remarkable increase in the risk for BP, but this finding probably reflects use of hydroxyzine to treat pruritus that manifested as a prediagnosis BP symptom, rather than hydroxyzine predisposing patients to BP. The mean time interval between the first purchase of these drugs and diagnosis of BP was >1 year (data not shown), except for hydroxyzine (263 days).

The use of dipeptidyl peptidase-4 inhibitors, especially vildagliptin, has recently been shown to markedly increase the risk for BP.[2] Certain neuroleptics, aldosterone antagonists, and loop diuretics have also been reported to be risk factors for BP.[3,4] The present study demonstrates that use of many of the selected neurologic and psychiatric drugs is more common among BP patients than controls, and exposure to these medications increases the risk for BP. Because odds ratios were adjusted for the several psychiatric and neurologic diagnoses that the studied drugs are used for, these findings cannot be explained solely by the appearance of psychiatric and neurological conditions as BP comorbidities. As previously seen with dipeptidyl peptidase-4 inhibitors, the time interval between first drug exposure and the diagnosis of BP was rather long.[5] However, considering their pharmacological properties and the chemical structures of the drugs that were most strongly associated with BP, no definite similarities were apparent. Our findings suggest that the use of

drugs that affect the nervous system might contribute to the onset of BP, but additional studies are required to clarify this association.

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Table I. Study demographics

Characteristics	Value*
Sex	
Male	118 (71.1)
Female	48 (28.9)
Age, y, median (range)	51 (6-78)
Region	
Europe	77 (46.4)
North America	49 (29.5)
Africa	20 (12.0)
Asia	9 (5.4)
South America	6 (3.6)
Oceania	5 (3.0)
Education	
Without primary	1 (0.6)
Primary	11 (6.6)
Secondary	70 (42.2)
University	84 (50.6)
History of skin cancer	
Absent	127 (84.1)
Nonmelanoma skin cancer	20 (13.2)
Melanoma	4 (2.6)
Data missing	15
Phototype	
I	5 (3.1)
II	71 (43.6)
III	63 (38.7)
IV	23 (14.1)
V	1 (0.6)
Missing	3
No. organs transplanted, median (range)	1 (1-2)
Organs transplanted	
Kidney	79 (47.6)
Lung	12 (7.2)
Heart	31 (18.7)
Liver	33 (19.9)
Bone marrow	13 (7.8)
Pancreas	1 (0.6)

*Values are n (%) except where indicated.

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Sun exposure risks in athletes who were recipients of solid organ and bone marrow transplants

To the Editor: In recent decades, there has been an up to 3 times increase in incidence of skin cancer in the world population.[1] It is estimated that solid organ transplant recipients receiving immunosuppressive therapy have a 3-5 times higher risk of developing neoplastic diseases, such as cutaneous nonmelanoma carcinomas squamous cell carcinoma (SCC) and basal cell carcinoma (BCC), than the general population.[2] Risk factors that contribute to neoplastic development in transplant patients include the following: age at transplant, intensity and duration of immunosuppression, history of sun exposure, history of skin cancer before transplant, and frequency of sunburn in childhood. The main predictors of sunburn are skin phototype, age, sex, and education level.[3]

Athletes who practice outdoor sports and are recipients of bone marrow or organ transplant are possibly at higher risk of developing photo-induced