



Prediction pathways for innate immune pathology, IBS symptomatology, depression and self-rated health in a general population (the POPCOL Study)

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Background

Recent studies have associated functional gastrointestinal disorders with a subtle pathology which may be due to disturbances in innate immunity (Powell 2010). We hypothesized that high levels of innate inflammatory cells in the lower gastrointestinal tract are directly associated with IBS and IBS related symptoms and indirectly associated with depression, anxiety and poor self-rated health.

Methods

This study included 168 participants (mean age 49 yrs, 56 % women): 86 participants with IBS (Rome II questionnaire) and 82 participants who did not report abdominal pain from 745 colonoscopy participants of the PopCol study, a questionnaire and colonoscopy survey of persons randomly selected from the adult general population in Stockholm, Sweden (Kjellström 2014) in which a questionnaire for abdominal symptoms were sent out to 3347 persons randomly drawn from the Swedish population registry containing all Swedish residence. Out of the 2293 responders to the questionnaire, 1643 were invited by phone to consult with a gastroenterologist and complete further questionnaires. Out of the 1244 who responded, 745 additionally accepted to have colonoscopy including biopsies.

Intraepithelial lymphocytes (IELs) per 100 enterocytes and eosinophils (EOS) per five non-overlapping high power fields (HPF) were counted by light microscopy; immunocytochemistry (CD117) was performed for mast cells (MC) per 5HPF. Mean scores of IELs, mast cells and eos in caecum, transverse and sigmoid colon were used.

Results

Based on the findings from the association analyses with statistically significant association between MC and passing flatus, nausea and smoking ($p < .05$, Table 1) and between EOS and depression ($p = .03$) including a trend between EOS and self-rated health ($p = .07$, Table 2), a causal model path model which hypothesizes 1. MC and EOS being associated with 2. passing excessive flatus and nausea (Abdominal Symptom questionnaire) and smoking status which, in turn, is associated with 3. elevated depression (HADS) and poor self-rated health (excellent to poor) was tested using path analysis implemented in the MPlus software (Figure 1). Although the associations between MC and IBS-symptoms and smoking, as well as between passing flatus and nausea and depression and self-rated health remained in the model, there were no statistically significant indirect associations between MC, EOS and depression and self-rated health (MC-depression: 0.09 $p = .48$; EOS-depression 0.05 $p = .41$; MC-self-rated health: 0.08 $p = .63$; EOS-self-rated health: 0.07 $p = .38$).

Conclusion

In the present study we could not support an indirect association between innate immune cells in the colon and depression or self-rated health. However, a direct association between EOS and depression and self-rated health should be further investigated.

References

Powell, N. (2010). "Gastrointestinal eosinophils in health, disease and functional disorders." *Nat Rev Gastroenterol Hepatol* 7(3): 146-156.
Kjellstrom, L. (2014). "A randomly selected population sample undergoing colonoscopy: prevalence of the irritable bowel syndrome and the impact of selection factors." *Eur J Gastroenterol Hepatol* 26(3): 268-275.

Table 1. Associations between IBS, IBS symptoms and immune cells adjusted for smoking status, age and sex, presented as OR.

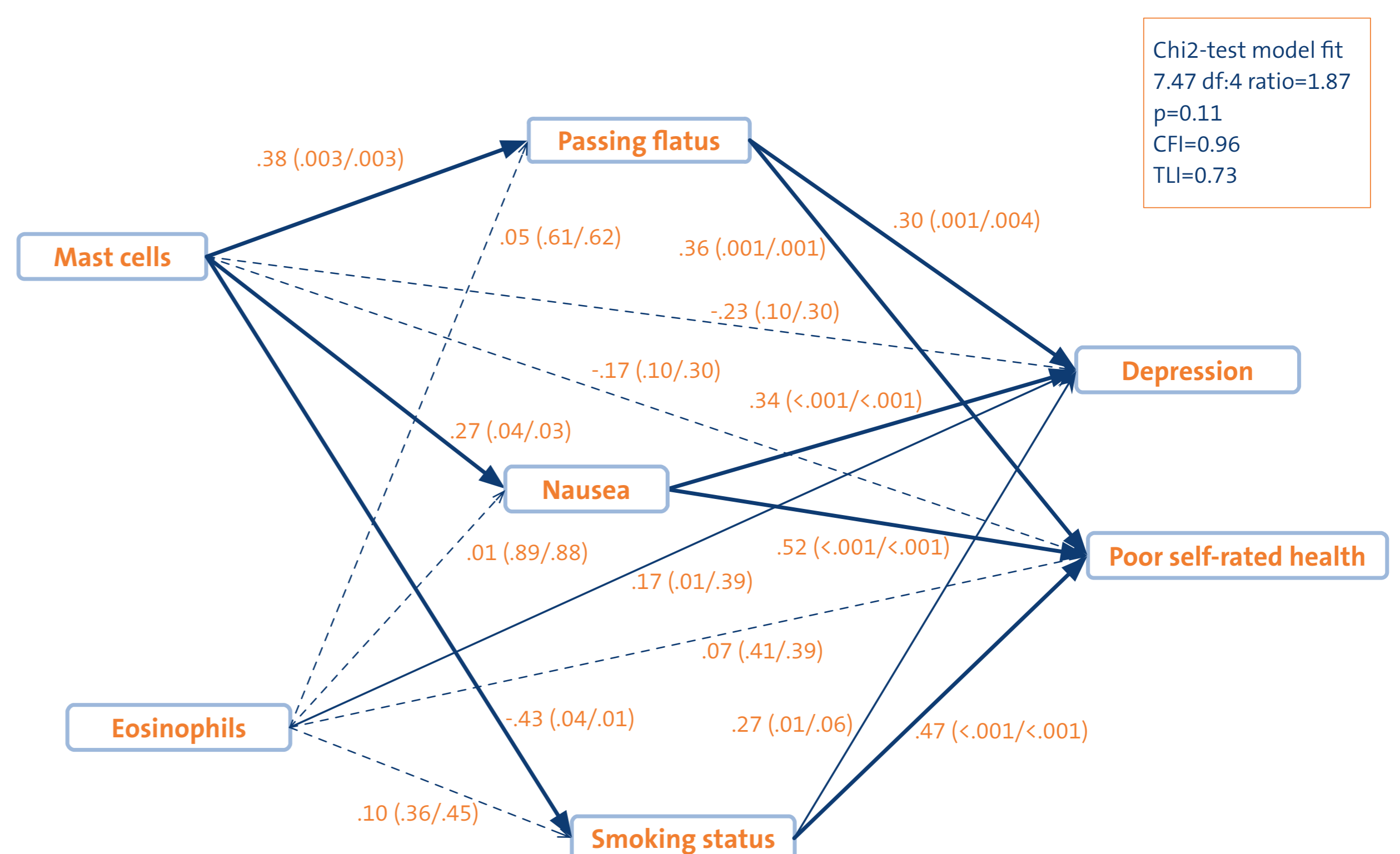
	Mast cells		Eosinophils		Lymphocytes	
	OR	95%CI	OR	95%CI	OR	95%CI
IBS	1.00	.99-1.00	1.01	.98-1.04	1.05	.97-1.13
Abdominal pain and Discomfort	1.17	.80-1.72	1.02	.73-1.40	1.22	.88-1.70
Bloating	1.25	.86-1.85	0.95	.69-1.32	0.92	.67-1.27
Diarrhea	1.06	.76-1.50	1.09	.80-1.49	0.94	.69-1.28
Constipation	0.91	.59-1.40	1.03	.73-1.47	0.89	.62-1.27
Passing flatus	2.04**	1.27-3.29	1.11	.81-1.51	0.91	.67-1.24
Nausea	1.56*	1.02-2.39	1.05	.75-1.47	1.10	.79-1.55
Smoking	0.42*	.20-.85	1.22	.81-3.22	1.30	.85-3.36

* $p < .05$; ** $p < .01$

Table 2. Associations between anxiety, depression and self-rated health. Beta coefficients, p-value/bootstrapped p-value.

Mast cells			
Anxiety	.067	0.58/0.50	
Depression	-.15	0.20/0.15	
Self-rated health			-.066 0.43/0.37
Eosinophils			
Anxiety	-.076	0.49/0.49	
Depression	.275	0.01/0.03	
Self-rated health			.14 0.09/0.07
IELs			
Anxiety	.07	0.53/0.55	
Depression	-.04	0.69/0.71	
Self-rated health			.028 0.73/0.72

All associations are adjusted for age, sex and smoking



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