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Evaluation of Autoimmune Diseases with Mental Health Disorders: An Original Research

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ABSTRACT

Introduction: Clinical research of immune function, along with the comorbidity of autoimmune diseases, schizophrenia, and bipolar disorder, suggest a likely autoimmune etiology. The aim was to determine the degree to which 30 different autoimmune diseases are antecedent risk factors for bipolar disorder, schizophrenia, and non-affective psychosis.

Materials &Methods: From the registry, 2031 cases of schizophrenia, 907 cases of non-affective psychosis, and 992 cases of bipolar disorder were considered.

Results: Autoimmune diseases were more associated with schizophrenia. These associations also existed for the broader category of non-affective psychosis. The pernicious anemia in the family was associated with raised risk for bipolar disorder, signifying a small role for genetic linkage. Previous Crohn's disease, Guillain-Barre' syndrome, and autoimmune hepatitis are associated with bipolar disorder.

Conclusions: The familial relationship of schizophrenia to a range of autoimmune diseases extends to non-affective psychosis but not to bipolar disorder. The study observations suggest that autoimmune processes not only precede the onset of schizophrenia, but also non-affective psychosis and bipolar disorder.

KEYWORDS: Autoimmune diseases, Mental health diseases, psychosis.

INTRODUCTION

The autoimmune diseases multiple sclerosis (MS) and autoimmune thyroid disease are known to be associated with bipolar disorder. The metabolic slowing related to thyroid hormone deficiency could be related to symptoms of depression. However, there is also a consistent association with psychosis, including a particular association, not always confirmed, with rapid cycling bipolar disorder (1-4). The literature on autoimmune diseases and schizophrenia has been reviewed previously (1). It is particularly rich for celiac disease (5), autoimmune thyroid disease (6), and rheumatoid arthritis (7). In the present study, we aim to determine the degree to which 30

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different autoimmune diseases are antecedent risk factors for bipolar disorder, schizophrenia, and non-affective psychosis.

MATERIAL AND METHODS

The study population was taken from the Institutional Register for bipolar disorder, schizophrenia, or non-affective psychosis. There were 992 cases of bipolar disorder, 2031 cases of schizophrenia, and 907 cases of non-affective psychosis. Information about autoimmune diseases in cohort members and their mothers, fathers, and siblings was obtained. Cohort members and their parents and siblings were classified as having a positive history of one or more of 30 autoimmune diseases (Table 1) if they had been admitted or had been in outpatient care with the relevant diagnosis. The category of 30 autoimmune diseases is included to help judge whether the pattern is general or specific to one or a limited number of autoimmune diseases. For the study of the relative risk for the psychiatric disorders associated with prior autoimmune diseases in the individual, time since an autoimmune disease was included as a time-dependent variable (30), which during follow-up was measured as the number of years since the first contact with a diagnosis of the autoimmune disease.

RESULTS

There are statistically significant and positive associations for the familial relationships for Sjogren's syndrome, dermatopolymyositis, psoriasis, autoimmune hepatitis, iridocyclitis, MS, and type 1 diabetes to schizophrenia (Table 1). For bipolar disorder, only pernicious anemia has a significantly raised risk of 1.7. and for dermatopolymyositis, it is 2.1. There is no increase in the risk of bipolar disorder associated with autoimmune diseases in general, and a slight, but statistically significant increase in the risk of schizophrenia associated with autoimmune diseases primarily.The configuration of risk of bipolar disorder is more for individuals with Autoimmune diseases and psychosis who have had autoimmune hepatitis or Guillain-Barre' syndrome at least five years before to inception but seen are fewer cases to confirm whether the risk may be raised in the concurrent period as well.In Crohn's disease, the risk of bipolar disorder is more in both concurrent and delayed periods. There is a statistically significant increased risk for both the concurrent and delayed periods for the incidence of any autoimmune diseases (relative risks of 1.7 for concurrent and 1.2 for delayed; see Table 2). There is a raised risk of concurrent or delayed diagnosis for schizophrenia for five autoimmune diseases for which there is also a familial association— Sjogren's syndrome, dermatopolymyositis, psoriasis, autoimmune hepatitis, iridocyclitis, MS, and type 1 diabetes —proposing a shared genetic etiology for these diseases with schizophrenia. For thyrotoxicosis, no link to the family background was seen. Crohn's disease and Guillain-Barre' syndrome and schizophrenia have a positive association, with a delay of more than five years in the two diagnoses. In general, the overall effect of autoimmune diseases is a raised risk of 1.4 for concurrent and 1.3 for delayed periods (Table 2).

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TABLE 1. ASSOCIATION OF THE AUTOIMMUNE DISEASES AND MENTAL HEALTH, WITH THE FAMILY MEMBERS.

Autoimmune disease in parent or sibling	ICD-8	ICD-10	Bipolar disorder (n = 6,470)		Schizophrenia (n = 16,722)	
			No. cases	Relative risk[a]	No. cases	Relative risk[a]
Pernicious anemia	281.0	D51.0	23	**1.7**	26	1.1
Autoimmune hemolytic anemia	283.90-91	D59.1	1	–	9	1.6
Idiopathic thrombocytopenic purpura	446.49	D69.3	7	1.3	8	0.8
Thyrotoxicosis	242.00	E05.0	82	1.1	142	1.1
Autoimmune thyroiditis	245.03	E06.3	12	1.4	23	1.3
Type 1 diabetes	249	E10	203	1.0	475	**1.3**
Primary adrenocortical insufficiency	255.1	E27.1	7	1.5	14	1.4
Multiple sclerosis	340	G35	50	1.0	141	**1.3**
Guillain-Barré syndrome	354	G61.0	19	0.9	45	1.1
Iridocyclitis	364	H20	22	0.7	89	**1.4**
Crohn's disease	563.01	K50	45	1.1	81	0.9
Ulcerative colitis	563.19	K51	86	1.0	208	1.2
Autoimmune hepatitis	571.93	K73	13	1.0	45	**1.7**
Primary biliary cirrhosis	571.90	K74.3	4	–	9	1.2
Celiac disease	269.00	K90.0	12	1.4	22	1.2
Pemphigus	694 (x694.05)	L10	0	–	6	2.2
Pemphigoid	694.05	L12	3	–	6	1.7
Psoriasis vulgaris	696.09-10, 696.19	L40 (xL40.4)	65	1.0	158	**1.2**
Alopecia areata	704.00	L63	3	–	14	1.6
Vitiligo	709.01	L80.9	4	–	4	–
Seropositive rheumatoid arthritis	712.19, 712.39, 712.59	M05-M06	135	1.0	273	1.1
Juvenile arthritis	712.09	M08	11	1.7	24	1.3
Wegener's granulomatosis	446.29	M31.3	5	1.3	9	1.4
Dermatopolymyositis	716	M33	5	1.0	20	**2.1**
Polymyalgia rheumatica	446.30-31, 446.39	M31.5-6, M35.3	58	1.0	61	0.8
Myasthenia gravis	733.09	G70.0	8	1.7	10	1.1
Scleroderma	734.0	M34	5	0.7	8	0.6
Systemic lupus erythematosis	734.19	M32.1, M32.9	15	1.1	29	1.0
Sjogren's syndrome	734.90	M35.0	12	0.9	33	**1.5**
Ankylosing spondylitis	712.49	M45.9	16	1.0	36	1.1
Any of 30 autoimmune diseases	–	–	796	1.0	1,205	**1.2**

TABLE 2. ASSOCIATION OF THE AUTOIMMUNE DISEASES AND MENTAL HEALTH, WITH THE FAMILY MEMBERS CALCULATED FROM THE TIME OF THE DIAGNOSIS.

Autoimmune disease[b]	Bipolar disorder (n = 9,920)			Schizophrenia (n = 20,317)		
		Relative risk[a]			Relative risk[a]	
	No. cases[c]	Concurrent[d]	Delayed[e]	No. cases[c]	Concurrent[d]	Delayed[e]
Thyrotoxicosis	28/16	**1.9**	1.5	28/18	**1.9**	**2.1**
Thyroiditis	1/0	–	–	3/1	–	–
Type 1 diabetes	28/39	1.3	1.1	59/49	**1.7**	1.0
Primary adrenocortical insufficiency	2/2	–	–	1/2	–	–
Multiple sclerosis	18/12	**2.0**	1.0	11/8	1.0	0.8
Guillain-Barré syndrome	3/8	–	**2.4**	4/10	–	**2.2**
Iridocyclitis	11/11	1.8	1.8	17/10	**1.8**	1.3
Crohn's disease	16/22	**1.9**	**1.8**	11/28	0.7	**1.7**
Ulcerative colitis	31/23	**1.8**	1.0	28/35	1.0	1.2
Autoimmune hepatitis	0/7	–	**3.0**	12/15	**5.4**	**5.6**
Celiac disease	3/0	–	–	4/5	–	1.8
Psoriasis vulgaris	22/13	**2.3**	0.9	28/23	**2.0**	1.4
Seropositive rheumatoid arthritis	26/13	**1.8**	0.8	12/12	0.8	0.8
Juvenile arthritis	1/3	–	–	2/12	–	1.4
Polymyalgia rheumatica	4/1	–	–	0/1	–	–
Scleroderma	0/1	–	–	1/2	–	–
Systemic lupus erythematosis	3/4	–	–	5/2	2.0	–
Sjogren's syndrome	2/2	–	–	6/1	**3.8**	–
Ankylosing spondylitis	1/4	–	–	4/4	–	–
Any of 30 autoimmune diseases	182/176	**1.7**	**1.2**	228/238	**1.4**	**1.3**

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DISCUSSION

From the study, we found an association between autoimmune diseases and schizophrenia. There are no significant familial associations at all with autoimmune diseases, and for any autoimmune disease, no increase in risk at all. The results are also constant, with prior research failing to demonstrate substantially dissimilar risk patterns between schizophrenia and non-affective psychosis. The earlier positive familial associations for pernicious anemia, autoimmune hemolytic anemia, thyrotoxicosis, thyroiditis, celiac disease, and rheumatoid arthritis are not statistically significant. For MS, iridocyclitis, and autoimmune hepatitis, there are significant familial associations not seen in the earlier study, possibly due to the larger sample in the current work. There is partial confirmation in the relationships with concurrent autoimmune diagnosis and nonaffective psychosis for thyrotoxicosis and celiac disease. The positive association of bipolar disorder with ulcerative colitis, psoriasis, and rheumatoid arthritis are the strongest candidates for an explanation by ascertainment bias since there is no research proposing common etiology and since the relationship is only by diagnoses which befall in close temporal association, but this non-causal explanation is vitiated by the association with Crohn's disease, which is moderately strong and significant in both the concurrent and delayed periods. The delayed association with Guillain-Barre' syndrome is baffling, as it is for schizophrenia. The strongest results in the investigation of comorbidities in cases of schizophrenia and bipolar disorder are for Guillain-Barre' syndrome and autoimmune hepatitis. Guillain-Barre's syndrome results point to an etiologic pathway related to infectious agents (8-10) connected in prior research to schizophrenia (11). The results on the familial association are compromised because the parents and siblings may not have lived through the age of onset for the autoimmune diseases. The pattern of results is strongest and includes the most prior autoimmune diseases, for the situation in which the autoimmune diagnosis ensued within the five years before the diagnosis of the three categories of psychosis (concurrent).Nevertheless, the results suggest the possibility that the start of psychosis—with bipolar disorder—in some cases arises in linking with a contemporary inflammatory process associated with these autoimmune diseases. An infection has been deliberated as a possible factor in the neurodevelopmental process for decades (12-14). More recently, the role of the infection, inflammation, and autoimmune processes as part of the process starting or being involved in episodes in adults (15-17). For the individual and familial association between psychosis and autoimmune diseases, genetic markers in the HLA region have frequently been associated with schizophrenia in linkage. Some of the identical immune-related markers in schizophrenia have also been established in bipolar disorder. This has led some to recommend future research on monitoring of immune markers during illness, and we further assume that an autoimmune process may operate before the onset of psychosis (18).

CONCLUSION

From the study, it is evident that there may be an association between autoimmune diseases and the person's mental status. Further studies and the markers are suggested for the exact association of the two.

REFERENCES

1. Bauer MS, Whybrow PC, Winokur A. Rapid cycling bipolar affective disorder. I. Association with grade I hypothyroidism. Arch Gen Psychiatry 1990; 47: 427–432.

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Received 25 April 2021; Accepted 08 May 2021.

2. Oomen HA, Schipperijn AJ, Drexhage HA. The prevalence of affective disorder and in particular of a rapid cycling of bipolar disorder in patients with abnormal thyroid function tests. Clin Endocrinol 1996; 45: 215–223.
3. Cassidy F, Ahearn EP, Carroll BJ. Thyroid function in mixed and pure manic episodes. Bipolar Disord 2002; 4: 393–397.
4. Bauer M, Heinz A, Whybrow PC. Thyroid hormones, serotonin and mood: of synergy and significance in the adult brain. Mol Psychiatry 2002; 7: 140–156.
5. Kalaydjian AE, Eaton W, Cascella N, Fasano A. The gluten connection: the association between schizophrenia and celiac disease. Acta Psychiatr Scand 2006; 113: 82–90.
6. DeLisi LE, Boccio AM, Riordan H et al. Familial thyroid disease and delayed language development in first admission patients with schizophrenia. Psychiatry Res 1991; 38: 39–50.
7. Eaton W, Hayward C, Ram R. Schizophrenia and rheumatoid arthritis: a review. Schizophr Res 1992; 6: 181–192.
8. Stowe J, Andrews N, Wise L, Miller E. Investigation of the temporal association of Guillain-Barre syndrome with influenza vaccine and influenza like illness using the United Kingdom General Practice Research Database. Am J Epidemiol 2009; 169: 382–388.
9. Sivadon-Tardy V, Orlikowski D, Porcher R et al. GuillainBarre syndrome and influenza virus infection. Clin Infect Dis 2009; 48: 48–56.
10. Vucic S, Kiernan MC, Cornblath DR. Guillain-Barre syndrome: an update. J Clin Neurosci 2009; 16: 733–741.
11. Yolken RH, Torrey EF. Are some cases of psychosis caused by microbial agents? A review of the evidence. Mol Psychiatry 2008; 13: 470–479.
12. Muller N, Schwarz MJ. A psychoneuroimmunological perspective to Emil Kraepelins dichotomy: schizophrenia and major depression as inflammatory CNS disorders. Eur Arch Psychiatry Clin Neurosci 2008; 258(Suppl. 2): 97–106.
13. Mednick S, Machon RA, Huttunen MO, Bonett D. Adult schizophrenia following prenatal exposure to an influenza epidemic. Arch Gen Psychiatry 1988; 45: 189–192.
14. Brown AS, Susser ES. In utero infection and adult schizophrenia. Ment Retard Dev Disabil Res Rev 2002; 8: 51–57. Autoimmune diseases and psychosis 645
15. Rothermundt M, Arolt V, Bayer TA. Review of immunological and immunopathological findings in schizophrenia. Brain Behav Immun 2001; 15: 319–339.
16. Hanson DR, Gottesman II. Theories of schizophrenia: a genetic-inflammatory-vascular synthesis. BMC Med Genet 2005; 6: 7.
17. Fan X, Goff DC, Henderson DC. Inflammation and schizophrenia. Expert Rev Neurother 2007; 7: 789– 796.
18. Strous RD, Shoenfeld Y. The mosaic of schizophrenia: has the time arrived to monitor the illness with biomarkers? Clin Biochem 2008; 41: 353–354.