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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Psychiatry

ESPS manuscript NO: 28263

Title: Infectious, atopic and inflammatory diseases, childhood adversities and familial aggregation are independently associated with the risk for mental disorders: Results from a large Swiss epidemiological study

Reviewer's code: 00631881

Reviewer's country: Belgium

Science editor: Fang-Fang Ji

Date sent for review: 2016-07-01 13:33

Date reviewed: 2016-07-12 22:11

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

Very interesting study. Some minor remarks : - Could the authors tell something about the clinical relevance. Could those results already be translated in a diagnostic assessment (for example standard blood sampling ?) - Why no 'psychotic-group' and rationale for 4 groups ? - Which questionnaires have been used to assess childhood adversity and traumatic experiences. Please mention this in the manuscript.

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Name of journal: World Journal of Psychiatry

ESPS manuscript NO: 28263

Title: Infectious, atopic and inflammatory diseases, childhood adversities and familial aggregation are independently associated with the risk for mental disorders: Results from a large Swiss epidemiological study

Reviewer's code: 01761104

Reviewer's country: Taiwan

Science editor: Fang-Fang Ji

Date sent for review: 2016-07-01 13:33

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

This study examined the associations between mental disorders and infectious, atopic, inflammatory diseases while adjusting for other risk factors. The authors used data from PsyCoLaus, a large Swiss Population Cohort Study (N=3720; age range 35–66). A French version of the semi-structured Diagnostic Interview for Genetic Studies (DIGS) was used in the PsyCoLaus study to assess a broad spectrum of lifetime DSM-IV Axis I criteria. The DIGS allowed for gathering additional information on the course and chronology of comorbid features. However, the brief phobia section of the DIGS was replaced by the corresponding sections from the Schedule for Affective Disorders and Schizophrenia - Lifetime Version (SADS-L) in the current study. All diagnoses are lifetime diagnoses. Lifetime diagnoses of mental disorders were grouped into the following categories: neurodevelopmental, anxiety (early and late onset), mood and substance disorders. They were regressed on infectious, atopic and other inflammatory diseases adjusting for sex, educational level, familial aggregation, childhood adversities and traumatic experiences in childhood. A multivariate



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logistic regression was applied to each group of disorders. In a complementary analysis interactions with sex were introduced via nested effects. As a result, associations with infectious, atopic and other chronic inflammatory diseases were observable together with consistent effects of childhood adversities and familial aggregation, and less consistent effects of trauma in each group of mental disorders. Streptococcal infections were associated with neurodevelopmental disorders (men), and measles / mumps / rubella-infections with early and late anxiety disorders (women). Gastric inflammatory diseases took effect in mood disorders (both sexes) and in early disorders (men). Similarly, irritable bowel syndrome was prominent in a sex-specific way in mood disorders in women, and, moreover, was associated with early and late anxiety disorders. Atopic diseases were associated with late anxiety disorders. Acne (associations with mood disorders in men) and psoriasis (associations with early anxiety disorders in men and mood disorders in women) contributed sex-specific results. Urinary tract infections were associated with mood disorders and, in addition, in a sex-specific way with late anxiety disorders (men), and neurodevelopmental and early anxiety disorders (women). In conclusions, infectious, atopic and inflammatory diseases are important risk factors for all groups of mental disorders. The sexual dimorphism of the associations is pronounced. Importance: There is an increasing awareness that infectious diseases, atopies and inflammatory conditions contribute to the risk for neurodevelopmental disorders (ND) and common mental disorders (CMD). This is the first study to apply a comprehensive epidemiological perspective on the associations of major groups of ND and CMD with infectious, atopic and inflammatory diseases. The findings add to the evidence that infectious, atopic and inflammatory diseases make up an important group of risk factors for neurodevelopmental and common mental disorders. They contribute independently of further major risk factors such as childhood adversities, traumatic experiences and familial aggregation. Each group of mental disorders (neurodevelopmental, early and late anxiety, mood, substance) attracts different combinations of risk factors. The sexual dimorphism of the associations is pronounced. In addition, the authors provided very reasonable hypotheses. A hypothesized biological mechanism that acts as a common denominator in this group of risk factors involves imbalances, e.g. within the development of the immune system interfering with critical stages of brain development. In agreement with epidemiological research, the microglia pathway offers new perspectives for the understanding of the sex-ratios in mental disorders. Microglia numbers in males and fem



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Name of journal: World Journal of Psychiatry

ESPS manuscript NO: 28263

Title: Infectious, atopic and inflammatory diseases, childhood adversities and familial aggregation are independently associated with the risk for mental disorders: Results from a large Swiss epidemiological study

Reviewer's code: 02465274

Reviewer's country: United States

Science editor: Fang-Fang Ji

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
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		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

Intriguing approach to the biology of major psychiatric disorders. Gender differences are critically important for the further efforts to understand the role of inflammation.