

September 7, 2016

## **28263-manuscript revision**

V. Ajdacic-Gross et al.: 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

Dear Editors

Dear Reviewers

On behalf of my co-authors, I would like to thank you for the reviews and supportive suggestions.

Reviewer #1 has made several suggestions.

- Could the authors tell something about the clinical relevance. Could those results already be translated in a diagnostic assessment (for example standard blood sampling ?)

This is a challenging suggestion. However, this study had a macro focus on the most general risk factors and on aggregate CMD variables. It would be premature to expect translational benefits, since much more detailed information would be required on the level of subtypes of each CMD and equally a much better understanding of involved immune system mechanisms. Nevertheless, we are convinced that this will be reached much earlier than most scholars do believe.

- Why no 'psychotic-group' and rationale for 4 groups ?  
Inclusion of subjects with schizophrenia or schizoaffective disorder was not promising because of low frequencies. Epidemiological population studies are not well suited to assess subjects with these disorders. We added the following sentence to the paragraph : "Disorders with low frequencies (schizophrenia, schizoaffective disorders) or inadequately fitting in with the major groups (obsessive-compulsive disorder, personality disorders, eating disorders) were not included in the analyses."

The grouping of disorders is similar to conventional grouping approaches. It deviates only in so far, as early and late onset anxiety disorders were separated. This allowed us to take a glance on disorders with similar age at onset (neurodevelopmental and early anxiety disorders on the one hand, mood and late anxiety disorders on the other hand).

- Which questionnaires have been used to assess childhood adversity and

traumatic experiences. Please mention this in the manuscript.

The childhood adversity items were introduced in PsyCoLaus from the childhood section of a preliminary version of the SADS-LA. Since there are no further sources available and published in this connection we explicitly quoted the questions in the paragraph on Covariates:

"Childhood adversities dichotomized into any vs. none if one of the following questions was confirmed:

- did your parents fight frequently amongst themselves? (interparental violence);
- did your parents ever do anything that frightened you (like lock you in a closet)? (fear of maltreatment by parents);
- did any of the following occur before your 16th birthday: .... put in foster care? (foster care);
- overall, how would you characterize your childhood (N/A, happy, either happy not unhappy, unhappy, very unhappy)? categorized as yes, if unhappy or very unhappy (unhappy children)."

The trauma items stem from the SADS-LA. We added the following sentence in the paragraph on Covariates: "The questions were taken from the French version of the SADS-LA (see above) and dichotomized into any vs. none."

Reviewer #2 made no recommendations for changes.

Reviewer #3 made no recommendations for changes.

### **Further issues**

Language polishing:

"growing up in a children's home" was changed into "growing up in a foster home".

The title length exceeds 12 words. Since shortening the title would mask the message we preferred to keep the long version of the title.