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# Letter to the editor: Are thyroid function abnormalities only related to antipsychotic treatment in patients with severe mental disorders?

*Dear Editor,*

We have read with interest the article recently published by Vedal et al. in the Journal of Psychiatric Reaserch, in which it has been demonstrated, in a naturalistic study, that patients with severe mental disorders, such as schizophrenia and bipolar disorder, may have thyroid functions abnormalities, notably lower free thyroxin level (fT4), in association with the usage of atypical antipsychotic drugs such as olanzapine and quetiapine (Vedal et al., 2018). We have previously reviewed the medical literature until 2010 in the domain of thyroid functions abnormalities in patients receiving antipsychotic drugs and found that antipsychotic drugs may have numerous types of impact on the thyroid gland (Bou Khalil and Richa, 2011). While it is commonly known that patients with severe mental disorders frequently manifest thyroid function abnormalities even before antipsychotic drugs intake, it is still unclear to what extent can thyroid function variations be considered as an adverse drug effect or a comorbidity to the mental disorder. However, in order to better understand this frequent encounter, it would be interesting to mention all causes related to the severe mental disorder or to the antipsychotic drug intake per se which lead to thyroid function abnormalities.

Among typical antipsychotic drugs, phenothiazines can specifically induce a hypothyroid state through their deiodination effect. They may lead to a hyperthyroid state if they induce a thyroiditis. Typical antipsychotic drugs, whether they were phenothiazines or not, can induce autoimmune thyroid abnormalities (anti-thyroid peroxidase [anti-TPO] and antithyroglobulin increment) via their dopamine antagonism and subsequent hyperprolactinemia. Atypical antipsychotic drugs can, according to their dopamine antagonism profile, moderately interfere with TSH response to TRH. In addition, cyclic tertiary amines such as piperazine and piperidine compounds are incriminated in clinical hypothyroidism in predisposed patients receiving them via a peripheral effect that involves a competition with thyroid hormones in the glucuronidation process in the liver (Bou Khalil and Richa, 2011).

Severe mental disorders may be sometimes accompanied with thyroid function abnormalities regardless of antipsychotic drugs intake. Mood disorders seem to be more represented in this category of mental disorders originally accompanied with a thyroid dysfunction. As a matter of fact, some genetic mutations such as that in the monocarboxylate transporter 8 (MTC8) may lead to neuropsychiatric manifestations as well as to dysthyroidism (Herzovich et al., 2007; Rego et al., 2017). In addition, patients with severe mental disorders may present a diminished thyroid stimulating hormone (TSH) response to thyroid releasing hormone (TRH) (Loosen, 1985).

It is difficult to be able to determine if the treatment with antipsychotic drugs has been the causal factor underlying the appearance of thyroid functions abnormality in a patient with a severe mental disorder. The possible model that seems to better explain this relatively frequent encounter may not be related to the mental disorder alone or to its pharmacologic treatment. As is the case in the appearance of a metabolic syndrome in patients with schizophrenia after atypical antipsychotic drugs intake, patients with severe mental disorders may manifest a gene-environment interaction that may explain the subsequent occurrence of a thyroid abnormality (Brandl et al., 2012). Future studies may be interested in focusing on genetic variability specific to individuals with severe mental disorders that interacts with certain antipsychotic drugs and leads to thyroid function abnormalities.

## Author disclosures

Conflict of interests: I, Dr Rami Bou Khalil, on the behalf of my co-author and myself and in relation to the manuscript entitled: “Are thyroid function abnormalities only related to antipsychotic treatment in patients with severe mental disorders?” certify that we don't have any conflict of interest to declare behind this work.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpsychires.2018.11.011.

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