The Relationship Between Plasma Cytokine Levels and Response to Selective Serotonin Reuptake Inhibitor Treatment in Children and Adolescents with Depression and/or Anxiety Disorders

Maya Amitai, MD,1,2,3 Michal Taler, PhD,2,4 Miki Carmel, PhD,2,4 Elena Michaelovsky, PhD,2,4 Tamar Eliat, MA,1 Maya Yabloniski, MA,5 Naama Orpaz, MD,6 Alon Chen, PhD,3,7 Alan Apter, MD,1,2 Abraham Weizman, MD,2,4,8 Silvana Fennig, MD,1,2

Abstract

Objective: In adults there is growing evidence that antidepressant (AD) treatment results in a decline in inflammatory cytokines. This is the first report, to our knowledge, of the relationship between response to selective serotonin reuptake inhibitor (SSRI) treatment for anxiety and/or depression and cytokine levels in children and adolescents.

Methods: Forty-one patients who met Diagnostic and Statistical Manual for Mental Disorders, 4th ed. (DSM-IV) criteria for major depressive disorder (MDD) or anxiety disorders participated in study. Their ages ranged from 9 to 18 (14.12 ± 2.30) years. The patients were treated with fluoxetine for 8 weeks. Plasma concentrations of tumor necrosis factor (TNF)-α, interleukin (IL)-6, and IL-1β were measured by enzyme linked immunosorbent assays (ELISA) before and after fluoxetine treatment. Clinical response was measured with several scales, including the Children’s Depression Rating Scale–Revised (CDRS-R), the Beck Depression Inventory (BDI), and the Screen for Child Anxiety Related Emotional Disorders (SCARED).

Results: The overall response rate was 56%. Antidepressant treatment significantly reduced TNF-α levels ($p = 0.037$), with no significant changes in the levels of IL-6 and IL-1β. All three proinflammatory cytokines were significantly ($p < 0.05$) higher in SSRI-refractory than in SSRI-responsive patients.

Conclusions: Higher levels of TNF-α, IL-6, and IL-1β might predict nonresponse to fluoxetine treatment in children.

Introduction

Affective and anxiety disorders are among the most common childhood psychiatric disorders (Ipser et al. 2009; Mills et al. 2013). Despite the high percentage of these debilitating disorders, their pathogenesis is incompletely understood. Selective serotonin reuptake inhibitors (SSRIs) are generally considered first-line treatment for both depression and anxiety in this age group. However, it has been reported that 30–40% of all patients who receive a sufficient dose and duration of treatment fail to respond (Maalouf and Brent 2012). Currently there is no way of knowing in advance which of the patients will respond. This means that many young people are being exposed to an agent that will not be useful and may have serious adverse events.

In recent years, there has been a growing recognition of the relationship between inflammatory processes and psychiatric disorders, especially depression (Dantzer et al. 2008; Miller et al. 2009; Kim et al. 2014; Rosenblat et al. 2014). In adults, accumulating evidence suggests that major depressive disorder (MDD) may be associated with immune system dysregulation (Miller et al. 2009; Kim et al. 2014). There are a limited number of studies on the association between inflammatory processes and neuropsychiatric disorders in children and adolescents, with the highest correlation demonstrated in autism spectrum disorder (ASD) (Mitchell and Goldstein 2014). Previous studies investigating inflammatory abnormalities related to depression and anxiety in this special population have yielded conflicting and inconclusive results (Mills et al. 2013; Kim et al. 2014).

There is growing evidence that antidepressant (AD) treatment may influence the production of pro-and anti-inflammatory cytokines. Recent findings in adult patients indicate that there may be attenuation/normalization of overactive inflammatory processes.
following AD treatment (Miller et al. 2009; Hannestad et al. 2011; Hodes et al. 2015). To date, reports regarding the effects of SSRIs on cytokine levels are inconsistent in adults, and do not exist in the pediatric population.

The purpose of the present study was to determine whether plasma levels of proinflammatory cytokines can predict response to treatment and/or altered after fluoxetine treatment in children and adolescents with depression and/or anxiety disorders. Our hypotheses, based on adult literature, were that fluoxetine will demonstrate anti-inflammatory properties as reflected by a decrease in proinflammatory cytokines, and that such effect will be associated with a favorable treatment response. Moreover, we hypothesized that depressed and anxious patients with increased inflammatory cytokines will exhibit treatment resistance.

Methods

Study design

Our inclusion criteria included: Age between 7 and 18 years, and a diagnosis of major depression or anxiety disorder according to the Diagnostic and Statistical Manual of Mental Disorders, 4th ed., Text Revision (DSM-IV-TR) (American Psychiatric Association 2000). Anxiety disorders included generalized anxiety disorder (GAD), separation anxiety disorder (SAD), social anxiety disorder, panic disorder (PD), and specific phobia (SP). The diagnosis of major depression or anxiety disorder was the presence of at least moderate severity, with a Clinical Global Impressions–Severity (CGI-S) score of ≥4 (a level consistent with accepted guidelines for the use of antidepressants in children and adolescents) (Bernstein and Shaw 1997; Birmaher et al. 1998). Exclusion criteria included mental retardation, organic brain syndrome, ASD, history of hypomania or mania, psychosis, eating disorder, posttraumatic stress disorder (PTSD), and substance use. Subjects with a major neurological disorder or a major medical illness were excluded. We included treatment-naïve subjects because the likelihood of response declines with the number of previous treatment trials.

Evaluation

Subjects were assessed at intake, and at 2, 4, 6, and 8 weeks. Diagnostic evaluation was conducted using the Hebrew version of the Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime version (K-SADS-PL) (Kaufman et al. 1997; Shaefer et al. 1997). Overall clinical severity and improvement were assessed using the CGI-S and CGI-Improvement (CGI-I) subscales, respectively (Guy 1976). Continuous measures of depression and anxiety were obtained using the Children’s Depression Rating Scale–Revised (CDRS-R) (Poznanski et al. 1984), the Beck Depression Inventory (BDI) (Smucker et al. 1986), and the Screen for Child Anxiety Related Emotional Disorders (SCARED) (Birmaher et al. 1997, 1999).

Procedure

The study was approved by the Schneider Children’s Hospital Institutional Review Board, and informed consent was obtained by the subjects and their parents. After a confirmatory diagnostic assessment, all subjects received fluoxetine. Starting dosage for all patients was 10 mg/day for 1 week, which then was increased to 20 mg/day through week 4. If the degree of improvement was minimal (CGI-I ≥ 3) then the dosage of fluoxetine was increased from 20 to 40 mg/day on week 5.

Cytokine analysis

Blood samples were collected from all subjects prior to starting treatment and after 8 weeks of fluoxetine treatment. From each participant in the research, blood samples were collected between 9 a.m. and 11 a.m. and plasma was separated for determination of tumor necrosis factor (TNF)-α, interleukin (IL)-6, and IL-1β. Measurements of the cytokines for all participants were conducted in duplicate by enzyme linked immunosorbent assays (ELISA) in the same run, to avoid interassay variability. All cytokines were assessed with a sandwich ELISA based on a monoclonal-monoclonal antibody pair and a biotin-streptavidin amplification system (Siemens Medical Solutions Diagnostics, Los Angeles, CA), following the manufacturers protocol. The laboratory staff was blinded to the clinical data, and the clinician team was blinded to the laboratory data.

Statistics

Paired t test, Mann–Whitney test, and general linear model with repeated measures were used as appropriate. Associations between laboratory values and demographic and clinical variables were analyzed using Spearman correlation or χ² test, as appropriate. The level of significance was set at 5%. All analyses were two tailed. All results are expressed as mean ± SD. The Statistical Package for the Social Sciences was used to create a database and perform the statistical analyses (SPPS, version 17 for Windows Inc., Chicago, IL).

Results

Subjects

Forty-one subjects (22 [54%] males and 19 [46%] females, age 14.12 ± 2.30 years) were included in the analysis. Of the 41 subjects, 24 (59%) had a diagnosis of MDD. The other 17 (41%) had a diagnosis of anxiety disorder (GAD [n = 13], social anxiety disorder [n = 6], PD [n = 6], SAD [n = 8], SP [n = 11]; some of the subjects had more than one anxiety disorder). Nine (22%) had a combined diagnosis of depressive disorder and anxiety disorder.

Table 1. Comparison of Demographic/Clinical Variables of Responders and Nonresponders to Fluoxetine

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Responders (n = 23)</th>
<th>Nonresponders (n = 18)</th>
<th>p value (χ², t test or Mann–Whitney test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male)</td>
<td>14 (61%)</td>
<td>8 (44%)</td>
<td>χ² = 1.10, p = 0.30</td>
</tr>
<tr>
<td>Age (years)</td>
<td>13.70 ± 2.43</td>
<td>14.67 ± 2.20</td>
<td>p = 0.17</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>21.10 ± 4.14</td>
<td>21.37 ± 4.07</td>
<td>p = 0.90</td>
</tr>
<tr>
<td>DSM-IV-TR diagnosis (n)</td>
<td>9</td>
<td>8 (44%)</td>
<td>χ² = 7.74, p = 0.02</td>
</tr>
<tr>
<td>Anxiety</td>
<td>12 (52%)</td>
<td>3 (17%)</td>
<td></td>
</tr>
<tr>
<td>Comorbid</td>
<td>2 (9%)</td>
<td>7 (39%)</td>
<td></td>
</tr>
<tr>
<td>CGI-S</td>
<td>5.22 ± 0.39</td>
<td>5.00 ± 0.69</td>
<td>p = 0.24</td>
</tr>
<tr>
<td>BDI</td>
<td>16.80 ± 8.28</td>
<td>20.33 ± 11.50</td>
<td>p = 0.39</td>
</tr>
<tr>
<td>CDRS-R</td>
<td>59.17 ± 20.63</td>
<td>55.06 ± 20.10</td>
<td>p = 0.49</td>
</tr>
<tr>
<td>SCARED</td>
<td>26.90 ± 10.19</td>
<td>33.61 ± 14.26</td>
<td>p = 0.14</td>
</tr>
</tbody>
</table>

BDI, Beck Depression Inventory; BMI, body mass index; CDRS-R, Children’s Depression Rating Scale – Revised; CGI, Clinical Global Impressions – Severity; Comorbid, depression and anxiety disorder; DSM-IV-TR, Diagnostic and Statistical Manual of Mental Disorders, 4th ed., Text Revision; SCARED, Screen for Child Anxiety Related Emotional Disorders.
Clinical response

Twenty-three subjects (56%) received a rating of “very much improved” or “much improved” on the CGI-I, and were identified as responders. The demographic and clinical data of the responders and nonresponders are shown in Table 1. Eight of the responders were treated with a dose of 40 mg/day. The mean CDRS decreased from 59.17 (SD = 20.63) to 34.93 (SD = 14.34) (paired t = 7.07, df = 40, p < 0.0001), and mean BDI score decreased from 18.50 (SD = 9.85) to 10.10 (SD = 10.42) after the treatment period (paired t = 6.10, df = 40, p < 0.0001). Mean SCARED score decreased from 29.83 (SD = 12.50) to 21.49 (SD = 15.61) after the treatment period (paired t = 4.07, df = 40, p < 0.0001).

Cytokines

Levels of TNF-α significantly decreased following SSRI treatment (paired t: 5.58 ± 6.51 vs. 3.55 ± 3.07, t = 2.13, df = 40, p = 0.037). No significant differences were observed in the levels of IL-6 and IL-1β (Table 2). No correlation was found between pretreatment cytokine levels and age, gender, diagnosis, or body mass index (BMI) (data not shown). There was also no correlation between pretreatment cytokine levels and levels of anxiety or depression as measured by the scales’ scores (data not shown).

Responders versus nonresponders

There were no significant difference in baseline characteristics, including age (p = 0.17), gender (p = 0.30), and BMI (p = 0.90) between the responder and nonresponder groups. With regard to diagnosis, a more favorable response rate was observed in the depressed group than in the anxiety group (see Table 1). Also, no significant difference was found regarding the pretreatment scales’ scores (see Table 1). Pretreatment cytokines were significantly higher in the nonresponse groups in all the three cytokines measured (Table 3 and Fig. 1).

Posttreatment cytokine levels remained higher in the nonresponse group; however, this difference was significant only in

**Table 2. Pre- and Posttreatment Cytokine Levels in the Whole Sample (n=41)**

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Pretreatment Mean ± SD</th>
<th>Posttreatment Mean ± SD</th>
<th>p value (paired t test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNF-α (pg/mL)</td>
<td>5.58 ± 6.51</td>
<td>3.55 ± 3.07</td>
<td>t = 2.13, df = 40, p &lt; 0.0001</td>
</tr>
<tr>
<td>IL-6 (pg/mL)</td>
<td>0.35 ± 0.17</td>
<td>0.31 ± 0.12</td>
<td>t = 1.26, df = 40, p = 0.037</td>
</tr>
<tr>
<td>IL-1β (pg/mL)</td>
<td>0.62 ± 0.34</td>
<td>0.76 ± 1.08</td>
<td>t = 1.00, df = 37, p = NS</td>
</tr>
</tbody>
</table>

Boldface is statistically significant.

**Table 3. Pretreatment Cytokine Levels in the Responders versus Nonresponders**

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Responders Mean ± SD</th>
<th>Nonresponders Mean ± SD</th>
<th>p value (Mann–Whitney test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNF-α (pg/mL)</td>
<td>3.81 ± 3.04</td>
<td>7.85 ± 8.84</td>
<td>p = 0.04</td>
</tr>
<tr>
<td>IL-6 (pg/mL)</td>
<td>0.28 ± 0.10</td>
<td>0.42 ± 0.20</td>
<td>p = 0.006</td>
</tr>
<tr>
<td>IL-1β (pg/mL)</td>
<td>0.51 ± 0.23</td>
<td>0.76 ± 0.40</td>
<td>p = 0.007</td>
</tr>
</tbody>
</table>

Boldface is statistically significant.

IL-1β, interleukin 1β; IL-6, interleukin 6; TNF-α, tumor necrosis factor – α.

*FIG. 1. Pretreatment cytokine levels in the responders versus nonresponders: Tumor necrosis factor (TNF)-α levels; Interleukin (IL)-6 levels; IL-1β levels. *p < 0.05.*
TNF-α and IL-6 (Table 4). No significant difference in the changes in cytokine levels before and after treatment was found between responders and nonresponders to the fluoxetine treatment (see Table 4).

Discussion

This is the first study demonstrating that SSRI therapy is associated with cytokine changes in depressed and/or anxious children and adolescents ($n = 41$). In this study, we excluded subjects with medical conditions that can affect inflammatory pathways. We also excluded subjects with a history of trauma, because of recent reports on the modulatory effect of trauma on the immune system (Bucker et al. 2015). Our main results demonstrate that after 8 weeks of treatment with fluoxetine, the levels of the proinflammatory cytokine TNF-α significantly decreased, whereas there was no significant change in the levels of IL-6 and IL-1β.

In adults, there is conflicting evidence regarding cytokine levels after treatment with AD (Kim et al. 2014). Previous studies in MDD in adults report that treatment with AD significantly reduced plasma levels of proinflammatory cytokines. Eller et al. (2008) suggested that proinflammatory cytokines might induce depressive symptoms, and that this increase may be attenuated by ADs (Eller et al. 2008). In 2008, Yoshimura et al showed that treatment with ADs significantly reduced plasma levels of IL-6 and TNF-α (Yoshimura et al. 2009). However, in 2013, the same author suggested that pretreatment plasma levels of IL-6 were significantly higher in the SSRI responders than in the nonresponders (Yoshimura et al. 2013). A meta-analysis by Hamnestad et al. (2011) showed that SSRs may reduce the levels of IL-6 and TNF-α (Hamnestad et al. 2011). Another meta-analysis showed a significant decrease in IL-6 after treatment (Hiles et al. 2012). Therefore, our findings are in accord with the majority of evidence in adults suggesting that treatment with SSRIs reduces proinflammatory cytokine levels.

Another finding of our study was that patients with higher pretreatment cytokine levels failed to respond to treatment with SSRIs. We found that all the levels of the three cytokines predicted treatment response, but were significantly lower at baseline in responders than in nonresponders (see Fig. 1). These results suggest that higher cytokine levels are associated with refractoriness of depression and anxiety to treatment, and that plasma proinflammatory cytokine levels might be a predictor for response to SSRIs.

This finding is in accordance with other studies finding a similar effect of ADs in depressed adults. Yoshimura et al (2009) found that plasma IL-6 level, but not plasma TNF-α level, was higher in SSRI-refractory than in SSRI-responsive depressed patients (Yoshimura et al. 2009). O’Brien et al. (2007) reported that patients with SSRI-resistant depression had significantly higher production of the proinflammatory cytokines IL-6 and TNF-α than did normal controls, and assumed that suppression of proinflammatory cytokine expression did not occur in depressed patients who failed to respond to SSRIs, and is necessary for clinical remission and recovery (O’Brien et al. 2007). Eller et al. (2008) reported that a higher level of TNF-α might predict a nonresponse to treatment with escitalopram (Eller et al. 2008). However, other studies failed to find such effect. The reason for the discrepancy between these studies is unclear, and may be related to the numerous methodological dissimilarities among studies.

As mentioned, numerous studies in adults have suggested that major depression is accompanied by immune dysregulation (Dantzer et al. 2008; Dowlati et al. 2010). In children and adolescents there are fewer studies but accumulating data indicate a relationship between inflammatory markers and depression (Mills et al. 2013; Kim et al. 2014). There are a number of reasons why studies regarding the relationship between the immune system and depression/anxiety disorders should be conducted in pediatric populations. There may be differences in the neurobiology of adolescent MDD and anxiety disorders compared with that in adults. Increased understanding of the role of cytokines may lead to new therapeutic targets with improved outcomes in pediatric MDD and anxiety disorders. In adults, the relationship between depression and inflammatory markers is confounded by obesity, smoking, and other lifestyle factors that can have a strong effect on both depressive/anxiety presentation and inflammatory response, factors that are less common in children.

Although changes in cytokine levels following SSRI treatment have not been studied in depressed children and adolescents, one study found that unmedicated depressed adolescents have higher IL-6 levels than medicated adolescents (Henje Blom et al. 2012). Our study is the first, to our knowledge, to show the effect of SSRI treatment on proinflammatory cytokine levels in children and adolescents. As in adults, our findings suggest that fluoxetine appears to have some suppressive activity on proinflammatory cytokine expression. Our results suggest that the role of cytokines in AD treatment in youth is similar to that in adults. However, depression in children and adolescents is associated with different immune and inflammatory changes than those seen in adult depression, with contradictory findings of natural killer (NK) cell activity, and differences in proinflammatory cytokines such as IL-1β and TNF-α (Mills et al. 2013). An improved understanding of the role of

---

**Table 4. Comparison of Responders and Nonresponders in the Alterations (Δ) of the Various Variables Following Fluoxetine Treatment**

<table>
<thead>
<tr>
<th>Week</th>
<th>Responders</th>
<th>Nonresponders</th>
<th>p</th>
<th>p Time</th>
<th>p Response</th>
<th>p Time by response</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>16.80 ± 8.28</td>
<td>59.17 ± 20.63</td>
<td>Δ</td>
<td>20.33 ± 11.50</td>
<td>33.61 ± 14.26</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>8</td>
<td>4.70 ± 3.55</td>
<td>29.96 ± 7.83</td>
<td>Δ</td>
<td>17.00 ± 12.23</td>
<td>30.28 ± 17.24</td>
<td>&lt;0.005</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TNF-α (pg/mL)</th>
<th>IL-6 (pg/mL)</th>
<th>IL-1β (pg/mL)</th>
<th>p Time</th>
<th>p Response</th>
<th>p Time by response</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.81 ± 3.04</td>
<td>0.28 ± 0.10</td>
<td>0.51 ± 0.23</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2.33 ± 1.20</td>
<td>0.28 ± 0.13</td>
<td>0.61 ± 0.54</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1.48 ± 3.02</td>
<td>−0.003 ± 0.18</td>
<td>0.10 ± 0.35</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>5.10 ± 3.97</td>
<td>0.34 ± 0.11</td>
<td>0.96 ± 1.54</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>−0.8 ± 0.20</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>0.16</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>0.31</td>
<td>0.17</td>
<td>0.76</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Boldface is statistically significant.

BDI, Beck Depression Inventory; CDRS-R, Children’s Depression Rating Scale – Revised; IL-1β, interleukin 1β; IL-6, interleukin 6; SCARED, Screen for Child Anxiety Related Emotional Disorders; TNF-α, tumor necrosis factor – α.
cytokines in pediatric MDD and anxiety disorders and in response to SSRI treatment may lead to a better understanding of the pathophysiology and treatment options in depressed/anxious children and adolescents.

Limitations

There were some limitations and weakness in this study. First and foremost, our treatment group consisted of children and adolescents with depression and/or anxiety disorders. Even though the pharmacological treatment for these disorders is the same (usually SSRIs), there might be different neurobiological mechanisms responsible for the different clinical phenotypes, which may confound our findings. Second, our study lacks a corresponding group of control subjects, such as an untreated depressed/anxiety group or a nondepressed/unanxious healthy cohort. Third, the sample size was small and heterogeneous, which may have restricted the statistical power and have the potential for a type I error. Fourth, we lacked important information such as the length of the episode and whether the episode’s duration predicted response. Finally, there are numerous other cytokines of interest that were not investigated in our study (e.g., anti-inflammatory cytokines). Therefore, further research is needed to test the preliminary results achieved in this study.

However, the strength in our study lies in the fact that all the subjects were drug naïve, and treated with the same protocol.

Conclusions

Together, our data suggest that similarly to in adults, inflammatory processes may play a role in response to AD treatment in children and adolescents. Our findings suggest that high levels of TNF-α, IL-6, and IL-1β may be involved in the refractoriness to treatment of anxiety and depression, and that plasma levels of these proinflammatory cytokines might serve as biological markers for prediction of response to SSRIs. Further research in larger samples is needed to confirm our preliminary results.

Clinical Significance

Current best practice for AD treatment in depressed and anxious children and adolescents involves trial and error, and it can take months to identify an effective AD for the 30–40% of children and adolescents who do not respond to an initial AD. Identifying biomarkers to predict early response could be of high impact on the treatment of depressed and anxious children and adolescents. Our findings suggest that proinflammatory cytokines may predict response to treatment with fluoxetine, and, therefore, may serve as possible biomarkers that would be early predictors of response and could help to maximize the benefit–risk ratio for the use of SSRIs, and speed the matching of treatment to patient. Currently, cytokine levels are not used as potential predictors of response to antidepressants. Further research is warranted to explore the role of cytokines in the response of pediatric population to SSRIs. One hopes that the expansion of the current state of knowledge regarding the involvement of cytokines in the pathophysiology and pharmacotherapy of pediatric depression will lead to progression in the field, and eventually to the inclusion of circulating cytokine levels as putative biomarkers of treatment response.

Disclosures

No competing financial interests exist.

References


Address correspondence to:
Maya Amitai, MD
Department of Psychological Medicine
Schneider Children’s Medical Center of Israel
Petach Tikva
Israel

E-mail: maya47@zahav.net.il
1. Zhewu Wang, M. Rita I. Young. 2016. PTSD, a Disorder with an Immunological Component. *Frontiers in Immunology* 7. [CrossRef]