Role of the serotonin transporter gene in susceptibility to mood disorders in children of depressed parents
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Introduction
Depression is a disabling condition that adversely affects a person's social, academic, and occupational life. The most common age of onset is between 20 and 30 years, with a later peak between 30 and 40 years (Kessler et al., 2003). In Egypt, around 2.7% of people suffer from major depression (Ghanem et al., 2009). Children also suffer from depression, a condition that requires the attention of health services for prevention and treatment. As many as three in 100 young children and nine in 100 adolescents have serious depression (Park and Goodyer, 2000).

Parental depression is among the strongest predictors of depression and other psychiatric disorders in offspring (Weissman et al., 1987; Beardslee et al., 1998; Warner et al., 1999; Bureu et al., 2009; Murray et al., 2012). In general, children of depressed parents were estimated to be at a two- to four-fold risk of developing depressive disorders (Hammen et al., 1990; Kramer et al., 1998). Likewise, these children are at risk for other internalizing, and externalizing problems, in addition to academic and social failure (Lewinsohn et al., 2003).

According to the report from the Institute of Medicine (England, 2009), at least 15 million children are living with a depressed parent in the USA. Moreover, the number of children exposed to parental depression is much larger when the entire span of childhood is considered, rather than a single year, and when other forms of parental mood disorders are included. Many parents who recover from an episode of depression continue to experience subclinical levels of depressive symptoms, with their children repeatedly exposed to associated disruptions in parenting (Brennan et al., 2003).

In contrast, the elevated risk of psychopathology and functional impairment in the offspring of depressed parents does not prevent many of these children from functioning well over the life course without developing depression or other mental disorders (Lewandowski et al., 2013; Lewandowski et al., 2014). The term 'resilience' has been used to describe positive adaptation in the face of circumstances involving a high likelihood of maladjustment (Luthar et al., 2006). In fact, it is the balance of risk factors and protective resources that determines outcome (Solantaus-Simula et al., 2002a, 2002b).

Objectives
The aim of the study was to explore psychological and behavioral disturbances in a sample of Egyptian children with depressed parents and investigate the potential role of the short (s) alleles of the serotonin transporter-linked polymorphic region in developing depressive symptoms in both parents and their offspring.

Subjects and methods
The study included 20 families with depressed parents and their offspring (age 6–18 years), who were compared with 20 control families with healthy parents. The Child Behavior Check List was filled by parents for children to detect syndromal and subsyndromal symptoms of mood disorders and other psychiatric disorders in the offspring. Blood samples were drawn from all groups and PCR analysis was conducted to investigate the polymorphism of interest.

Results
The children of depressed parents scored higher than the children of control parents in almost all Child Behavior Check List internalizing and externalizing problem parameters. A significantly higher percentage of depressed parents (70%) were found to carry the risk allele (s) compared with control parents (35%) (P = 0.03). A similar, but nonsignificant, pattern of asymmetric allele distribution was also found among the offspring of the two groups (77.3 vs. 50%).

Conclusion
Parental depression must be recognized as a major risk factor of psychiatric morbidity in children. Greater emphasis should be placed on developing large-scale effective preventive interventions for families with parental depression.

Keywords:
children, depression, 5-HTTLPR, parental, polymorphism
Over the past years, data have accumulated on several samples of depressed parents and their offspring. Weissman et al. (2005) followed a sample of offspring of depressed and nondepressed parents over 20 years, and all the offspring are now adults and have their own children. At the last assessment, rates of diagnosis of mood disorders and other disorders were three-fold in the new adult offspring compared with the comparison group (Weissman et al., 2006). Lower maternal overprotection, greater offspring self-esteem, and higher intelligence quotient (IQ) were associated with greater odds of resilient outcome in the cohort (Lewandowski et al., 2013).

An integrative model of the transmission of risk from depressed mother to child that incorporates biological and environmental factors was proposed (Goodman and Whitaker, 2002). The transmission of risk of depression from parent to child has been shown to be a bidirectional process. That is to say, although parental behaviors influence child outcome, the child's behavior likewise influences the parent. Similarly, Goodman and Gotlib's integrative model is strengthened by the bidirectionality inherent in its structure, in that the mechanisms for transmission of risk are proposed to overlap and interact with one another (Forbes et al., 2008). Applying this model to the heritability of depression, a child who inherits a certain genetic makeup from a depressed parent has the raw materials for developing depressive symptoms, but only when certain environmental effects come into play does the combination of gene and environment create the end product – namely, a depressive disorder (Hammen et al., 2010).

The serotonin transporter gene is known as the 'depression risk-gene'. It was reported that individuals carrying one or two short (s) alleles of the serotonin transporter-linked polymorphic region (5-HTTLPR) exhibit certain personality traits that predispose them to depression (Brown and Harris, 2008). In 2003, it was reported that s-carriers exhibit more depressive symptoms, full-blown depressive syndrome, and suicidal tendencies after exposure to stressful life events. Thus, this gene has become the most investigated genetic variant in psychiatry and also has been known as a mood-regulating gene (Hariri et al., 2002; Brody et al., 2009). Evidence for gene–environment interaction (G'E) involving the polymorphism in the promoter of the serotonin transporter genotype (5-HTTLPR) and adult depression was first reported using data from the Dunedin birth cohort (Caspi et al., 2003). The short (s) less active allele was associated with a greater risk for adult depression in the presence of a history of either childhood maltreatment or multiple life events in a 5-year period before onset. The sl heterozygote showed intermediate predisposition between the ss and ll homozygotes. The finding is consistent with the research on the role of serotonin in animals and humans (Uher and McGuffin, 2008).

The current study aimed to study the differential rates of syndromal and subsyndromal symptoms of mood disorders in children of depressed parents in comparison with children of healthy controls. We also aimed to investigate the potential association between the short allele (s) of the serotonin transporter gene and the occurrence of depression in both parents and their offspring.

Subjects and methods

This paper is adapted from a thesis titled ‘Role of Serotonin Transporter Gene in Susceptibility to Mood Disorders in Children and Adolescents of Depressed Parents’, which was submitted by the last author to the Faculty of Medicine, Tanta University, as partial fulfillment of a Master’s Degree in Neuropsychiatry. The study included the offspring of 20 families with depressed parents, recruited from both outpatient and inpatient sections of the department, who were compared with the offspring of 20 healthy control families. Control families were recruited from among those coming to the neurology clinic for minor neurological complaints (e.g. back pain, peripheral neuritis, etc.). Parents were included if they had offspring between the ages of 6 and 18 years and accepted to participate in the study with a written consent. Parents were excluded if they suffered from mental retardation (IQ<70), schizophrenia, or schizoaffective or any mental disorders due to general medical conditions. Parents suffering from significant neurological conditions that could affect their collaboration with the study, such as multiple sclerosis or epilepsy, were also excluded. Families with depressed parents had the additional inclusion criterion of including at least one parent who met the Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-IV) lifetime diagnosis of major depressive disorder (MDD), whereas control families had the additional exclusion criterion of having at least one parent who met such a diagnosis. No exclusion for any psychiatric disorders was made in the offspring. Children with medical, neurological, or low IQ or with any condition that interfered with the interviews were not assessed face to face.

After acquiring informed consent, all patients were subjected to full psychiatric history and mental status examination, in addition to physical and neurological examination. The Fahmy and El-Sherbini scale (Fahmy and El-Sherbini, 1983) was used to collect demographic
Role of serotonin transporter gene: Eldod et al. 75

and socioeconomic data. The Arabic version of Mini International Neuropsychiatric Interview ‘M.I.N.I’ was carried out to confirm the diagnosis of MDD in depressed parents and to exclude such a diagnosis in control parents (Sheehan et al., 1998). This was translated and validated in Arabic (Ghanem et al., 1999). The Child Behavior Check List (CBCL) was filled by parents for school-aged children to detect syndromal and subsyndromal symptoms of mood disorders or other psychiatric disorders in the offspring (El Defrawy et al., 1995; Achenbach and Dumenci, 2001).

Blood samples were drawn from all groups (parents and offspring) after obtaining informed consent. DNA was extracted from 200 ml of frozen blood using the Qiagen Dneasy Kit (Qiagen, Hilden, Germany; Cat. #695061). Oligonucleotide primers flanking the 5-HTTLPR and corresponding to the nucleotide positions −1416 to −1397 (strp5, 5-GGC GTT GCC GCT CTG AAT GC) and -910 to -888 (strp3, 5-GAC GGA CTG AGC TGG ACA ACC AC) of the 5-HTT gene 5-flanking regulatory region were used to generate 484 or 528 bp fragments. PCR amplification was carried out in a final volume of 30 μl consisting of 50 ng of genomic DNA, 50 ng of each of sense and antisense primers, 15 μl of Taq PCR Master mix (Qiagen; Cat. #201445), 10% dimethyl sulfoxide, and 1 mol/l betaine. Annealing was carried out at 61 °C for 30 s, extension at 71 °C for 1 min, and denaturation at 95 °C for 30 s for a total of 35 cycles. The PCR products were electrophoresed through 5% polyacrylamide gel (acrylamide/bis-acrylamide ratio 19 : 1) at 60 V for 60 min. A 100 bp marker was used to measure the PCR product size for the L and S alleles.

Statistical analysis of the present study was conducted using the mean, SD, and the χ²-test, with SPSS V.18 (IBM corporation, Armonk, New York, USA). Fully informed consent was taken from the parents. Participants and the ethical committee of the faculty of Medicine in Tanta University, which approved the study, were informed of any unexpected risks that could accrue during the course of the research.

Results

Of the total sample of parents with depression (n = 20), 6 (30%) were male and 14 (70%) were female. The age of depressed parents ranged from 25 to 45 years with a mean of 32.7 and SD of 2.1 years. Regarding the control parents (n = 20), 5 (25%) were male and 15 (75%) were female. The age of control parents ranged from 30 to 60 years with a mean of 44.8 years and SD of 8 years. Comparison of the two groups showed that depressed parents were significantly younger than the controls (P = 0.001), but there were no significant differences between the two groups regarding sex or socioeconomic status as estimated by the Fahmy and El-Sherbini score (P = 0.2, 0.4) (Table 1 and Fig. 1).

As regards offspring groups, the children of depressed parents (n = 22) were aged 10.6 years on average with an SD of 2.2 years. Twelve children were girls (54.5%) and 10 were boys (44.5%). The children of control parents were aged 9.4 years on average with an SD of 2.7 years. Most of those children were girls (85%, compared with 15% boys). Differences between the two groups did not reach statistical significance in any of the demographic variables (P ≥ 0.05). The children of depressed parents showed less school, social, and total competence scores on CBCL (P ≤ 0.05). Differences in participation in scholastic activities were not significant (P = 0.09) (Table 2 and Fig. 2).

| Table 1 Comparison between depressed and control parents |
|-------------------------------|----------------|----------------|
| Variables                      | Depressed      | Control        |
|                               | parents (n = 20)| parents (n = 20)| Statistics | P-value |
| Age                           | 32.7 ± 2.1     | 44.8 ± 8       | t = 5.8    | 0.001   |
| Sex (female, %)               | 70             | 75             | χ² = 2.3   | 0.2     |
| SES                           | 21.8 ± 7.1     | 23.9 ± 7.9     | t = 0.9    | 0.4     |
| SES, socioeconomic status.    |                |                |            |         |

Figure 1

Comparison between depressed and control parents.

Figure 2

Differences between offspring of depressed parents and offspring of control parents (6–18 years old) regarding sociodemographic data and CBCL competence parameters. CBCL, Child Behavior Check List.
With the exception of thought problems and problems of inattention, the children of depressed parents scored higher than the children of control parents in all CBCL problem parameters. These include internalizing problems such as anxiety symptoms, depressive symptoms, psychosomatic symptoms, and social symptoms in addition to externalizing symptoms such as rule-breaking behavior and aggressive behavior (all \( P \leq 0.05 \)). However, depressive and psychosomatic symptoms were characterized by highly significant differences (\( P \leq 0.001 \)) (Table 3 and Fig. 3).

When CBCL DSM-oriented scales were explored, the above-mentioned differences in symptom scales were found to translate into corresponding psychiatric disorders. Internalizing problems manifested themselves in the form of affective disorders, anxiety disorders, somatic (somatoform) disorders, and post-traumatic stress disorders. In contrast, externalizing disorders were manifested in the form of oppositional disorder and conduct disorder. All \( P \)-values were significant (\( \leq 0.05 \)), except those for somatic and post-traumatic disorders, which were highly significant (\( \leq 0.001 \)). Notably, children of depressed parents scored higher than control children on sluggish cognitive tempo score despite the absence of a corresponding difference in attention score between the two groups (Table 4 and Fig. 4).

When the genotyping results of parent groups were compared, a higher percentage (70%) of depressed parents were found to carry the risk allele (s) compared with control parents (35%). The difference between the two groups was statistically significant (\( P = 0.03 \)). A similar pattern of allele distribution was also found among the offspring of the two groups. Seventeen (77.3%) children of depressed parents carried the s allele as compared with 10 (50%) control offspring. However, the difference between the two offspring groups approached but did not reach the level of statistical significance (\( P = 0.07 \)) (Table 5 and Fig. 5).

**Discussion**

We report higher internalizing and externalizing behavioral problems, in addition to lower levels of scholastic and social competence, in children of depressed parents. Internalizing problems, which took the form

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**Table 2 Differences between offspring of depressed parents and offspring of control parents (6–18 years old) regarding sociodemographic data and CBCL competence parameters**

<table>
<thead>
<tr>
<th>CBCL subscale</th>
<th>Offspring of depressed parents (n = 22)</th>
<th>Offspring of control parents (n = 20)</th>
<th>Statistics</th>
<th>( P )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>10.6 ± 2.2</td>
<td>9.4 ± 2.7</td>
<td>( t = 1.6 )</td>
<td>0.1</td>
</tr>
<tr>
<td>Sex (female, %)</td>
<td>54.5</td>
<td>85</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participation in activities</td>
<td>27.01 ± 2.3</td>
<td>31.7 ± 4.2</td>
<td>( \chi^2 = 3.1 )</td>
<td>0.08</td>
</tr>
<tr>
<td>Social competence</td>
<td>34.5 ± 5.1</td>
<td>41.8 ± 11.5</td>
<td>( t = 2.8 )</td>
<td>0.03</td>
</tr>
<tr>
<td>School competence</td>
<td>40.8 ± 5.3</td>
<td>74.5 ± 13.0</td>
<td>( t = 0.3 )</td>
<td>0.04</td>
</tr>
<tr>
<td>Total competence</td>
<td>33.3 ± 8.5</td>
<td>79.1 ± 13.1</td>
<td>( t = 0.3 )</td>
<td>0.04</td>
</tr>
</tbody>
</table>

\( \text{CBCL, child behavior check list; } \text{P-value less than 0.05 is considered statistically significant (shown in bold).} \)}

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**Figure 3**

Differences between offspring of depressed parents and offspring of control parents (6–18 years old) regarding CBCL problem parameters. CBCL, Child Behavior Check List.

**Figure 4**

Differences between offspring of depressed parents and offspring of control parents (6–18 years old) regarding CBCL DSM-oriented disorders. CBCL, Child Behavior Check List; DSM, Diagnostic and Statistical Manual of Mental Disorders.
of depressive and psychosomatic symptoms, were more prominent than externalizing ones. The main psychometric tool utilized in this study was the CBCL, a cost-efficient and time-efficient screening instrument for a dimensional assessment of competences as well as behavioral and emotional problems in offspring at high risk for psychopathology (Biederman et al., 1993, 2001, 2005; Faraone et al., 2005). We also report that both depressed parents and their children were more likely to be carrying one or two short (s) alleles of the 5-HTTLPR despite the fact that the difference in the offspring group did not reach the level of statistical significance.

To our knowledge, this is the first Arab and Egyptian study on the impact of parental depression on the mental and behavioral well-being of the offspring. Our results replicate and support previously reported results, which state that children of depressed parents are especially at risk for the development of various psychiatric and behavioral disturbances (Warner et al., 1999; Weissman et al., 2005; Pilowsky et al., 2006; Bruder-Costello et al., 2007). In a survey on a large number of mothers (n = 1357), adolescents whose mothers showed chronic, elevated, and stable subclinical latent depressive symptoms reported more internalizing and externalizing problems and acknowledged engaging in more risky behavior than did children of never depressed mothers (Campbell et al., 2009).

Table 3 Differences between offspring of depressed parents and offspring of control parents (6–18 years old) regarding CBCL problem parameters

<table>
<thead>
<tr>
<th>CBCL subscale</th>
<th>Offspring of depressed parents (n = 22)</th>
<th>Offspring of control parents (n = 20)</th>
<th>Statistics</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety symptoms</td>
<td>57.7 ± 5.8</td>
<td>51.6 ± 3.4</td>
<td>t = 3.4</td>
<td>0.03</td>
</tr>
<tr>
<td>Depressive symptoms</td>
<td>60.5 ± 12.2</td>
<td>51.8 ± 2.5</td>
<td>t = 2.8</td>
<td>0.009</td>
</tr>
<tr>
<td>Psychosomatic symptoms</td>
<td>57.6 ± 7.6</td>
<td>50.1 ± 3.2</td>
<td>t = 2.0</td>
<td>0.003</td>
</tr>
<tr>
<td>Social problems</td>
<td>56.1 ± 5.3</td>
<td>51.7 ± 2.8</td>
<td>t = 2.5</td>
<td>0.05</td>
</tr>
<tr>
<td>Thought problems</td>
<td>51.3 ± 1.3</td>
<td>50.2 ± 0.4</td>
<td>t = 0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>Symptoms of inattention</td>
<td>53.9 ± 5.1</td>
<td>52.1 ± 2.9</td>
<td>t = 1.2</td>
<td>0.3</td>
</tr>
<tr>
<td>Rule-breaking behavior</td>
<td>55.5 ± 6.03</td>
<td>50.2 ± 0.4</td>
<td>t = 3.2</td>
<td>0.02</td>
</tr>
<tr>
<td>Aggressive behaviors</td>
<td>54.4 ± 5.3</td>
<td>50.7 ± 1.1</td>
<td>t = 2.2</td>
<td>0.04</td>
</tr>
<tr>
<td>Internalizing problems</td>
<td>57.7 ± 10.9</td>
<td>41.3 ± 7.9</td>
<td>t = 11.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Externalizing problems</td>
<td>48.3 ± 12.4</td>
<td>38.8 ± 7.5</td>
<td>t = 4.5</td>
<td>0.006</td>
</tr>
<tr>
<td>Total problems</td>
<td>51.2 ± 10.9</td>
<td>33.8 ± 11.2</td>
<td>t = 10.5</td>
<td>0.001</td>
</tr>
</tbody>
</table>

CBCL, child behavior check list; P-value less than 0.05 is considered statistically significant (shown in bold).

Table 4 Differences between offspring of depressed parents and offspring of control parents (6–18 years old) regarding CBCL DSM-oriented disorders

<table>
<thead>
<tr>
<th>CBCL subscale</th>
<th>Offspring of depressed parents (n = 22)</th>
<th>Offspring of control parents (n = 20)</th>
<th>Statistics</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affective disorder</td>
<td>55.8 ± 8.0</td>
<td>53.2 ± 5.1</td>
<td>t = 1.7</td>
<td>0.09</td>
</tr>
<tr>
<td>Anxiety disorder</td>
<td>56.3 ± 6.4</td>
<td>50.7 ± 0.5</td>
<td>t = 1.6</td>
<td>0.04</td>
</tr>
<tr>
<td>Somatic disorders</td>
<td>54.1 ± 5.5</td>
<td>50.0 ± 0.4</td>
<td>t = 3.6</td>
<td>0.009</td>
</tr>
<tr>
<td>ADHD</td>
<td>52.3 ± 3.2</td>
<td>50.8 ± 1.2</td>
<td>t = 0.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Oppositional defiant disorder</td>
<td>55.3 ± 6.2</td>
<td>50.8 ± 1.9</td>
<td>t = 3.3</td>
<td>0.03</td>
</tr>
<tr>
<td>Conduct disorder</td>
<td>55.6 ± 6.1</td>
<td>50.7 ± 1.5</td>
<td>t = 3.9</td>
<td>0.02</td>
</tr>
<tr>
<td>Sluggish cognitive tempo</td>
<td>55.3 ± 7.9</td>
<td>52.0 ± 2.9</td>
<td>t = 1.3</td>
<td>0.09</td>
</tr>
<tr>
<td>OCD</td>
<td>51.3 ± 1.7</td>
<td>52.7 ± 5.2</td>
<td>t = 0.2</td>
<td>0.5</td>
</tr>
<tr>
<td>PTSD</td>
<td>59.4 ± 5.15</td>
<td>50.8 ± 1.5</td>
<td>t = 3.9</td>
<td>0.008</td>
</tr>
</tbody>
</table>

ADHD, attention deficit hyperactivity disorder; CBCL, child behavior check list; DSM, diagnostic and statistical manual of mental disorders; OCD, obsessive–compulsive disorder; PTSD, post-traumatic stress disorder; P-value less than 0.05 is considered statistically significant (shown in bold).
et al. (2003), who stated that individuals with one or two copies of the short allele of the 5-HTTLPR polymorphism exhibited more depressive symptoms, yielded no evidence that the serotonin transporter promoter polymorphism confers increased risk of depression in conjunction with negative life events. Another meta-analysis also yielded no evidence that the serotonin transporter genotype, alone or in interaction with stressful life events, is associated with an elevated risk of depression (Risch et al., 2009). This discrepancy in results might be due to a variety of factors, including ethnicity and sample size.

Over the past years there has been considerable progress in delineating the gene-by-environment interplay in determining the range of outcomes in children. In addition, progress has been made in identifying the risk mechanisms and moderators that underlie the transmission of disorder and in developing effective prevention programs (Beardslee et al., 2011). Molecular genetics has focused on finding specific genes that may affect outcomes. Our genetic results agree with the conclusion made by Caspi et al. (2003), who stated that individuals with one or two copies of the short allele of the 5-HTT promoter polymorphism exhibited more depressive symptoms, diagnosable depression, and suicidality in relation to stressful life events compared with individuals homozygous for the long allele. Other studies (Karg et al., 2011) have shown that the s allele of the 5-HTTLPR polymorphism confers increased risk of depression in conjunction with negative life events. In addition, a recent study (Starr et al., 2012) suggested that the association between stress, depression, and the 5-HTTLPR genotype may be bidirectional, as the short allele may contribute to stress generation in addition to stress reactivity. Less evident difference between the offspring groups in the current study may reflect the need for genetic and environmental factors in this group for full-blown depressive syndrome to be evident in the offspring.

Father–child conflict has been found to mediate the contribution of paternal depression to the offspring’s internalizing and externalizing symptoms (Kane and G, 2009). Parental disengagement, responsiveness, unpredictability, expressed emotion, and hostility have been found to affect the offspring in the context of parental depression (Lovejoy et al., 2000; Frye and Garber, 2005; Feng et al., 2007; Dietz et al., 2008) as has parent–child conflict (Kane and G, 2009). Increased chronicity and severity of parental depression have long been shown to increase the likelihood that children will become ill (Brennan et al., 2000, 2003; Campbell et al., 2009). In contrast, lower maternal overprotection, greater offspring self-esteem, and higher IQ were associated with greater odds of resilient outcome defined by consistently high functioning (Lewandowski et al., 2014).

Table 5 Genetic distribution among parent and offspring groups

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Depressed parents (n = 20) [n (%)]</th>
<th>Control parents (n = 20) [n (%)]</th>
<th>Statistics</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LL</td>
<td>6 (30)</td>
<td>13 (65)</td>
<td>$\chi^2 = 4.9$</td>
<td>0.03</td>
</tr>
<tr>
<td>S Allele</td>
<td>14 (70)</td>
<td>7 (35)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genotype</td>
<td>Offspring of depressed parents (n = 22) [n (%)]</td>
<td>Offspring of control parents (n = 20) [n (%)]</td>
<td>Statistics</td>
<td>P-value</td>
</tr>
<tr>
<td>LL</td>
<td>5 (22.7)</td>
<td>10 (50)</td>
<td>$\chi^2 = 3.4$</td>
<td>0.07</td>
</tr>
<tr>
<td>S Allele</td>
<td>17 (77.3)</td>
<td>10 (50)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

LL, homozygote; S allele, homozygote (SS) or heterozygote (SL).
with parental depression is needed (NRCalOMP, 2009). Moreover, prevention efforts should be integrated into primary care and school systems. Prevention offers one of the best ways of addressing health disparities, another key public health concern.

Finally, it is important to highlight the limitations of this study. First, the small size of the sample might limit the generalization of the results on Egyptian children or children with depressed parents in general. This small number did not allow the differential evaluation of psychiatric and behavioral problems in different age categories of children – for example school-aged children versus adolescents. Second, the information collected in this study was obtained only from parent reports; no teacher reports were obtained as most of the families were interviewed on only one occasion. Thus, inaccurate reporting due to parents’ underestimation or overestimation of the symptoms might have occurred. Third, subjects were not formally evaluated through a structured or semistructured interview. The high validity and reliability of the well-known tool CBCL might decrease but does not suffice to replace a formal psychiatric interview. The validity of CBCL in diagnosing psychiatric disorders was questioned, especially in chronically ill children. Furthermore, other confounding factors, such as family conflicts, parenting styles, and medications received by children, were not taken into account.

Conclusion
Children with depressed parents suffer from high internalizing and externalizing problems. These internalizing problems tend to present in the form of depressive and psychosomatic symptoms, whereas externalizing problems tend to appear in the form of oppositional and conduct problems. The S allele of the 5-HTTLPR polymorphism was found to be disproportionately represented in both depressed parents, and to a lesser extent in their offspring. More effort needs to be exerted for the early identification and management of psychological morbidity in children with depressed parents.

Acknowledgements
Conflicts of interest
There are no conflicts of interest.

References

Role of serotonin transporter gene Eldod et al. 79


