Interpersonal sensitivity and functioning impairment in youth at ultra high risk for psychosis.

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Abstract

Background
A personality trait that often elicits poor and uneasy interpersonal relationships is interpersonal sensitivity. The aim of the present study was to explore the relationship between interpersonal sensitivity and psychosocial functioning in individuals at ultra high risk for psychosis as compared to help-seeking individuals who screened negative for an ultra high risk of psychosis.

Methods
A total sample of 147 adolescents and young adult who were help-seeking for emerging mental health problems participated in the study. The sample was divided into two groups: 39 individuals who met criteria for an ultra high risk mental state (UHR), and 108 (NS). The whole sample completed the Interpersonal Sensitivity Measure (IPSM) and the Global Functioning: Social and Role Scale (GF:SS; GF:RS). Mediation analysis was used to explore whether attenuated negative symptoms mediated the relationship between interpersonal sensitivity and social functioning.

Results
Individuals with UHR state showed higher IPSM scores and lower GF:SS and GF:RS scores than NS participants. A statistically negative significant correlation between two IPSM subscales (Interpersonal Awareness and Timidity) and GF:SS was found in both groups. Our results also suggest that the relationship between the aforementioned aspects of interpersonal sensitivity and social functioning was not mediated by negative prodromal symptoms.

Conclusion
This study suggests that some aspects of interpersonal sensitivity were associated with low level of social functioning. Assessing and treating interpersonal sensitivity may be a promising therapeutic target to improve social functioning in young help-seeking individuals.

Key words: Ultra High Risk; interpersonal sensitivity; social functioning; negative prodromal symptoms.
Introduction

Psychosocial functioning impairment is a core feature in schizophrenia and it is generally more enduring and devastating than the positive symptoms (Carpenter et al, 1988; Harvey et al, 2010). It includes deficits in social and interpersonal function and role and occupational function (Kim et al, 2013). Compromised psychosocial functioning is seen in the early stages of the disorder and it has been found to be difficult to reverse after onset of the psychotic disorder (Tandon and Maj, 2008). Studies examining predictors of transition to psychosis in young individuals at ultra high risk of psychosis (UHR), consistently demonstrated that functioning is more impaired in individuals who later convert to psychosis compared to those who do not develop a psychotic episode (Yung et al, 2004, 2006; Cornblatt et al, 2007; Cannon et al, 2008; Velthorst et al, 2010; Cornblatt et al, 2012; Fusar–Poli et al, 2009). Moreover, some UHR individuals who begin follow-along studies with poor functioning continue to show poor functioning after several years, even when their positive symptoms never cross the threshold into full psychotic severity (Yung et al, 2007; Addington et al, 2011; Schlosser et al, 2012). Thus, although they do not convert to full-blown psychosis over brief follow-up periods, these “false positives” are still in need of clinical intervention (Fulford et al, 2013; Fusar-Poli et al, 2013).

Several early studies have focused on the relationships between psychosocial functioning impairment and negative symptoms within UHR sample (Dworkin et al, 1993; Cornblatt et al, 2003). More recently, Corcoran and colleagues (2011) reported data on 56 young people at UHR for psychosis, showing that negative symptoms were related to poor social functioning. Fulford et al (2013) showed that more severe negative and disorganized symptoms were related to poorer psychosocial functioning in UHR samples. Many studies were also conducted to evaluate the relationship between temperament and character and clinical profiles of psychopathologies, psychosocial functioning, and some aspects of psychological health in patients with psychosis and also during the prodromal phase of this illness (Guillelm et al, 2001; Hori et al, 2008; Song et al, 2013). A particular personality trait, called “interpersonal sensitivity”, is defined as undue and
excessive awareness of and sensitivity to the behaviour and feelings of others (Boyce and Parker, 1989). Boyce and Parker (1989) proposed that this personality trait is a characteristic of the “depression-prone” personality. However, early studies indicated high interpersonal sensitivity and problems with self-confidence as being part of the subjective symptoms and observable behavioural changes occurring during the prodromal phase of schizophrenia (Subotnik & Nuechterlein, 1988; Häfner et al, 1992; Hambrecht et al, 1994). More recent studies have confirmed an association between interpersonal sensitivity, avoidant coping strategies, persecutory ideations and depressive symptoms in the ultra-high-risk and non-clinical samples (Valmaggia et al, 2007; Green et al, 2011; Masillo et al, 2012; Joo et al, 2012). These findings suggest that individuals who have problems in interpersonal sensitivity tend to modify their behaviour to comply with others' expectation in an attempt to minimize the risk of criticism or rejections. Furthermore, the association found between high interpersonal sensitivity and avoidant coping strategies, such as social withdrawal (McCabe et al, 1999; Freeman et al, 2008; Masillo et al, 2012) and the possible alterations in expression of emotions and self of highly sensitive individuals to comply with others’ expectation, may bring forth the hypothesis of a connection between negative prodromal symptoms and interpersonal sensitivity. Therefore, greater knowledge concerning interpersonal sensitivity and its relationship with prodromal psychopathology, especially negative symptoms, could enhance our understanding of the role of subjective symptoms and personality traits occurring during the prodromal phase of psychosis and their relationship with psychosocial functioning.

Aims of the study

The aims of the present study were: (i) to assess interpersonal sensitivity in the UHR (ii) to explore the relationship between interpersonal sensitivity and psychosocial functioning during the prodromal phase of psychosis; (iii) to evaluate the potential mediation role of negative prodromal psychotic symptoms on the aforementioned relationship. Based on previous evidence (Valmaggia et
al, 2007; Masillo et al, 2012), we hypothesized that UHR individuals would report higher interpersonal sensitivity than other help-seeking participants who do not meet UHR criteria for psychosis. We also anticipated that higher levels of interpersonal sensitivity would be associated with low level of social functioning. Finally we hypothesized that this relationship would be mediated by the presence of negative psychotic symptoms.

Methods

Participants

The original intake sample consisted of 147 adolescents and young adults involved in the early detection project “Liberiamo il futuro” (Release the future). The study was described in details by Masillo et al. 2014. Briefly, the main aim of the “Liberiamo il Futuro” is to identify subjects at high-risk for developing a psychosis. “Liberiamo il Futuro” sources of referral includes general practitioners (GPs) and other primary care services, school and university counselling services, the justice system (i.e., prisons and youth detention centres), youth accommodation centres, as well as families/caregivers and young people themselves.

The inclusion criteria were: age between 12 and 35 years; IQ ≥ 70; sufficient knowledge of the Italian language; the disorder is not secondary to or correlated with a general medical condition; willingness and ability to provide free written informed consent (the informed consent was provided by parents or guardian in case of minors). Adolescents and young adults referred to “Liberiamo il Futuro”, were initially screened using a self-report screen for prodromal symptoms in adolescents and young adults, the Prodromal Questionnaire (PQ, Lowey et al., 2005).

Following the screening phase the sample was divided into two groups: a UHR group of 39 individuals who scored 18 or higher on the positive symptoms PQ subscale and met UHR criteria
using the Structured Interview for Prodromal Syndromes (SIPS, Miller et al, 2002, 2003); and a Negative Screening (NS) group of 108 individuals who scored 17 or lower in the positive symptoms PQ subscale and were therefore not assessed with the SIPS).

In the UHR sample, 26 (66.7%) individuals were under 18 years old; in the NS sample 67 (62%) were under 18 years of age.

**Ethical approval**

The study was given ethical approval by the local research and ethics committee and conforms to the provision of the Declaration of Helsinki.

**Assessment Instruments**

Socio-demographic and anamnestic variables were recorded during a clinical assessment using a non-standardized questionnaire.

*Interpersonal Sensitivity Measure (IPSM)*

To measure interpersonal sensitivity, we used the Italian version (Masillo et al, 2014) of the Interpersonal Sensitivity Measure (IPSM; Boyce & Parker, 1989), a 36-item self-report questionnaire. Self-statements are rated on a four-point scale (1=very unlike self, 4=very like self). The level of interpersonal sensitivity is calculated by summing up the scores for each item. The factor structure of the IPSM consists of the following five components: (1) “interpersonal awareness” (seven items, range 1–28; this component defines a sensitivity to interpersonal interactions, and includes the perceived impact an individual has on another and the consequences of receiving a negative or critical response); (2) “need for approval” (eight items, range 8–32; it contains items reflecting a wish to make others happy and keep the peace, together with a wish that
others will like, and not reject, the subject); (3) “separation anxiety” (eight items, range 8–32; this third component defines the distress experienced when faced with the actual or perceived separation form important others); (4) “timidity” (eight items, range 8–32; it identifies the lack assertiveness to prevent upsetting others); and (5) “fragile inner-self” (five items, range 5–20; it suggests the sense of having an inner or core self that is unlikeable and needs to be hidden from others).

The IPSM has been found to have good internal consistency (a values from 0.85 to 0.86), test–retest reliability (r=0.70), and it was found to correlate with clinical judgment ratings of interpersonal sensitivity (r=0.72).

**Prodromal Questionnaire (PQ)**

To assess prodromal psychotic symptoms we used the Prodromal Questionnaire (PQ; Loewy et al. 2005), a self-report screening questionnaire that aims to identify individuals who may benefit from a clinical diagnostic interview. The 92 true/false items can be divided into four major subscales: (1) positive symptoms (e.g. unusual thinking and perceptual abnormalities); (2) negative symptoms (e.g. flat affect and social isolation); (3) disorganized symptoms (e.g. odd behaviour); and (4) general symptoms (e.g. depression and diminished role functioning). A score of eighteen or more positive symptoms on the PQ has been found to predict UHR as assessed by the SIPS (Structured Interview for Prodromal Symptoms, Miller et al, 2002, 2003) with 82% sensitivity and 49% specificity (Lowey et al, 2012).

**Global Functioning: Social and Role Scales**

Social and role functioning was assessed using the Global Functioning: Social and Global Functioning: Role scales (Cornblatt et al, 2007). These rater-scored measures were designed to represent parallel, well-anchored scales that account for age and phase of illness and detect functional changes over time (Cornblatt et al, 2007). In addition, the scales avoid confounding functioning with psychiatric symptoms. The GF: Social Scale assesses peer relationships, peer
conflict, age-appropriate intimate relationships, and involvement with family members. The GF: Role Scale rates performance and amount of support needed in one’s specific role (i.e., school or work). For both scales, scores range from 1 to 10 (10 = superior functioning to 1 = extreme dysfunction). Ratings for each of the two GF scales were based on available clinical information, which included clinician reports, telephone and face to face follow-up assessments. High inter-rater reliabilities (Fujii et al, 2003) were reported using this approach, along with construct and predictive validity (Cannon et al, 2008; Cornblatt et al, 2007).

Statistical analysis

Descriptive statistics including means and standard deviations for continuous variables and absolute and relative frequencies for categorical variables were calculated. Group differences in categorical variables were examined using the $\chi^2$ test. Mann–Whitney U tests were conducted to explore the impact of the UHR on interpersonal sensitivity (as measured by the IPSM) and on the psychosocial functioning (as measured by the GF: role and social scale). This analysis was conducted on the whole sample divided into the aforementioned two groups. The association between interpersonal sensitivity and psychosocial functioning was investigated using a Spearman’s correlation, according to group membership. The effect size was calculated using Cramer’s V for $\chi^2$ test and Rosenthal’s $r$ for Mann-Whitney U tests.

A mediation analysis was conducted, separately for each group, to examine the mediating role of negative prodromal symptoms on the relationship between interpersonal sensitivity and social functioning. For testing mediation, we followed the procedures and conceptual understanding provided by Hayes (2009). Analysis were performed in three steps: in step 1 regression analysis was run to test univariate main effect of interpersonal sensitivity on social functioning; in step 2 regression analysis was run to test the effect between predictor and mediator; in step 3 the mediator was then included as covariate. Mediation analysis was used to estimate direct an indirect effect of interpersonal sensitivity (independent variable) on social functioning (dependent variable with
negative prodromal symptoms as a mediating variable. Significance of medication was investigated using bootstrapping and confidence intervals at 95% significance level. The level of statistical difference was set at \( p<0.05 \) and all reported significance values were two-tailed. Statistical analyses were performed using SPSS version 18 (SPSS Inc., USA).

**Results**

A total of 39 UHR and 108 NS individuals were included in the present study. Socio-demographic characteristics of the sample are presented in Table 1. There were no significant differences between groups in age, sex, education, employment status, and referral reasons. However, UHR participants were more likely than the NS group to have received a psychological intervention or pharmacological treatment.

As illustrated in Table 2, there were statistically significant differences between groups in IPSM total score (\( U=1430.0, p=0.003, r=0.245 \)), interpersonal awareness (\( U=1277.5, p=0.000, r=0.300 \)) and separation anxiety (\( U=1304.5, p=0.000, r=0.290 \)). UHR and NS reported statistically significant different scores in GF: role (\( U=1355.0, p=0.001, r=-0.279 \)) and GF: social scale (\( U=1279.0, p=0.000, r=-0.306 \)) scores. There were also statistically significant differences between groups in PQ total (\( U=1402.5, p=0.002, r=0.255 \)), positive (\( U=1348.0, p=0.001, r=0.275 \)), negative (\( U=1613.5, p=0.030, r=0.179 \)), general (\( U=1625.0, p=0.034, r=0.175 \)) and disorganized (\( U=1524.0, p=0.010, r=0.212 \)) scores.
The relationship between interpersonal sensitivity and functioning scales scores are shown by group in Table 3. High sensitivity to interpersonal interactions (interpersonal awareness) and timidity were associated with lower level of social functioning (as measured by GF: Social scale) in both groups. In the NS participants a statistically significant correlation between fragile inner-self IPSM subscale and social functioning (as measured by GF: Social scale) was found. Role functioning (as measure by GF: Role scale) was not significantly related to interpersonal sensitivity level in either groups.

We also found statistically significant correlations between interpersonal sensitivity and negative prodromal symptoms (as measured by PQ) in both groups. In the UHR group, the higher the sensitivity to interpersonal interactions ($r_s=-0.292$, $p=0.002$), the anxiety about separation from significant others ($r_s=0.480$, $p=0.002$) and the sense of having an inner or core self that is unlikeable and needs to be hidden from others ($r_s=0.320$, $p=0.047$), the higher the level of negative prodromal symptoms. A statistically significant correlation was also found between timidity IPMS subscale and PQ negative subscale in the NS group ($r_s=0.204$, $p=0.035$).

Considering the aforementioned significant association between interpersonal sensitivity and negative prodromal symptoms, a mediation analysis was conducted to examine the mediating role of negative prodromal symptoms on the relationship between interpersonal sensitivity and social functioning. Using the Hayes model, we examined the estimated strength of the indirect effect from predictor (IPMS) to the outcome (GF: Social Scale) through the mediator (PQ negative), and the $p$-value to determine the level of significance (Fig.1). In the UHR sample we found that interpersonal sensitivity was related to social functioning ($\beta=-0.088$, $p=0.020$). Interpersonal sensitivity was also
related to negative prodromal symptoms \((\beta = 0.475, p=0.001)\). Testing the mediation role of negative prodromal symptoms, we found that the direct effect of interpersonal sensitivity on social functioning was no longer significant \((\beta = -0.076; p=0.084)\) but the indirect effect was also not significant because the interval of confidence included zero \((\beta = -0.011, \text{BootLLCI}= -0.059, \text{BootULCI}=0.023)\). Thus, our results showed that the relationship between interpersonal sensitivity and social functioning was not mediated by negative prodromal symptoms. Negative prodromal symptoms had a role on the relationship between interpersonal sensitivity and social functioning even though it was not statistically significant.

-- Figure 1--

In the NS sample we found that interpersonal sensitivity was related to social functioning \((\beta =-0.044, p=0.020)\). Interpersonal sensitivity was also related to negative prodromal symptoms \((\beta =0.229, p=0.006)\). Testing the mediation role of negative prodromal symptoms, we found that the direct effect of interpersonal sensitivity on social functioning remained statistically significant \((\beta = -0.043; p=0.018)\); moreover the indirect effect was not significant \((\beta = -0.001, \text{BootLLCI}= -0.009, \text{BootULCI}=0.007)\).

**Discussion**

This study explored the possible relationship between interpersonal sensitivity and psychosocial functioning in UHR people. Before discussing the results, it is important to highlight that the study was cross-sectional and therefore it is impossible to infer causality. Without longitudinal follow-up data we cannot draw any conclusion on whether interpersonal sensitivity is a predictive or an independent factor for the functioning impairment.

The first aim of the present study was to assess the impact of the UHR for psychosis state on interpersonal sensitivity. In line with previous studies (Valmaggia et al, 2007; Masillo et al, 2012)
we found that UHR subjects showed high sensitivity to interpersonal interaction, high vigilance to others’ behaviour in an attempt to gauge their response, as well as high level of anxiety about separation from significant others. The NS group had IPSM scores similar to those reported within previous general population studies (Otani et al, 2008; Green et al, 2011) and healthy control sample (Masillo et al, 2012).

The Role and Social Functioning scores reported by UHR participants in our study were comparable to those reported by previous studies (Cornblatt et al 2007). Furthermore, our results showed that UHR subjects reported statistically significant lower social role and social functioning level than the NS sample.

One interesting result was that in both groups a low role functioning level was not associated with being overly sensitive; one possible explanation is that activities such as studying or working do not inevitably imply a social contact, except for formal interactions. As Boyce and Parker (1989) stated, high interpersonal sensitivity often elicits poor and uneasy interpersonal relationships. Moreover, previous studies found an association between interpersonal sensitivity and maladaptive problem-solving styles, such as social withdrawal, habituation or adaptation to illness, and “self-treatment” with alcohol or drugs (McCabe et al, 1999; Masillo et al, 2012). Perceived self-deficiencies in relation to others and feelings of a fragile and bothersome core-self (personality aspects explored by IPSM) may contribute both to the development of maladaptive coping strategies and to social anxiety and isolation (Freeman et al, 2008). This may explain the relationship between some aspects of interpersonal sensitivity and social functioning showed by our results. Also, in line with previous studies, high sensitivity to interpersonal interactions (interpersonal awareness) and timidity were negatively associated with social functioning in both groups.

Interpersonal awareness includes the perceived impact an individual has on another and the consequences of receiving a negative response. Thus, one possible explanation of the connection between interpersonal awareness and restrictions of social contacts may be the fear of receiving critics or to be rejected. Individuals with high level of timidity lack assertiveness and often do
something they do not want to do rather than offend or upset someone. This inability to obtain reinforcement from the environment may be connected, as our results showed, to lack of social meeting and social isolation. It is also noteworthy that other IPSM subscales, such as separation anxiety and need for approval, were not related to social functioning impairment; one possible explanation is that these aspects may lead to look for friends and interpersonal relationships, in order to reinforce personal weakness and to avoid struggles with separations. Fragile inner-self was related to social functioning, but only in the NS subgroup. The fragile inner-self subscale suggests the sense of having an inner self that is unlikeable and needs to be hidden from others. The presence of significant correlation between interpersonal sensitivity aspects and social functioning both in the UHR and NS groups may suggest a lack of specificity. The young age of our sample (mean age around 18 years) could be one possible explanation. It is well known that adolescents often struggle to achieve an integrated and coherent sense of self, consolidating the many different aspects of their private and social persona; thus, finding a relationship between being overly sensitive to interpersonal interactions and social functioning impairment is not necessarily specific of an higher risk to develop psychosis, even if our UHR sample showed significantly higher level of interpersonal sensitivity and lower level of social functioning.

Social functioning impairment is an independent predictor of longitudinal outcome within UHR people (Velthorst et al, 2010; Fusar Poli et al, 2009) and tends to be resistant to treatment, both pharmacological and social (Cornblatt et al, 2012). It is also reflected by a considerably decreased subjective quality of life (Ruhrmann et al, 2008; Bechdolf et al, 2005). Numerous studies have shown that negative symptoms contribute significantly to psychosocial functioning impairment in UHR individuals (Piskulic et al, 2012; Valmaggia et al, 2013; Fulford et al, 2013).

In our study, interpersonal awareness, separation anxiety and fragile inner-self IPSM subscales, were correlated with higher levels of attenuated negative prodromal symptoms. However, mediation analysis did not reveal a significant role of attenuated prodromal negative symptoms on the relationship between interpersonal sensitivity and social function impairment in both groups.
Attenuated negative symptoms suggested reduced emotions and blunting of affects; on the contrary, as shown by previous studies, interpersonal sensitivity was found to be closely linked to depressive psychopathology more than to flat affects (Boyce et al, 1991; Boyce & Mason, 1996; Masillo et al, 2012). Thus, the association between interpersonal sensitivity and negative prodromal symptoms shown by our results, may be due mainly to their correlation with social functioning rather than to a psychopathological relationship. This seems to confirm a direct link between interpersonal sensitivity and social functioning impairment during the high risk phase of psychosis. On the one hand, pervasive feelings of insecurity, low self-esteem and hyper-attentiveness to the reactions and behaviours of others are psychopathological aspects that may contribute to social withdrawal. On the other hand, difficulties in communication and relations with the peer group could exacerbate the sensitivity to interpersonal interactions and feelings of having a fragile core-self. Assessing levels of interpersonal sensitivity and planning targeted psychotherapeutic interventions (Nelson et al, 2009; Bell and Freeman, 2014) in order to struggle potential difficulties in interpersonal relationships may be a therapeutic action to stop the afore-mentioned vicious cycle and to avoid a poor long-term outcome (Nelson et al, 2013).

The important role of a subjective symptoms, such as interpersonal sensitivity, in the UHR individuals may lead to some other considerations. Many studies revealed that in addition to attenuated psychotic symptoms, people who meet UHR criteria usually present with a mixed bag of psychopathology, in particular anxiety, depression and substance use (Yung et al, 2007; Woods et al, 2009; Fusar-Poli et al, 2014) and that co-morbid diagnoses of anxiety or depression were associated with impaired global functioning (Fusar-Poli et al, 2014). Considering these data, some researchers hypothesized that the UHR period should be seen as heterogeneous, capturing some individuals with an admixture of affective and psychotic symptoms and some with a true vulnerability to schizophrenia/psychotic disorder alone (Nelson et al, 2013) and suggested that there is much more to be “prevented” (Fusar-Poli et al, 2014).

Interpersonal sensitivity is strictly linked to affective psychopathology, both in persons with
depression and during prodromal phase of psychosis (Boyce et al, 1991; Boyce & Mason, 1996; Masillo et al, 2012). At a cross-sectional level, our results confirmed that a proportion of UHR individuals could be those from the general population with affective psychopathology and the co-presence of Psychotic like Experiences (Yung et al, 2009) and that some “transitions” to psychosis may represent the poor social outcome of these subjects (Fusar Poli et al, 2013). It is of course possible that our UHR sample was at risk for an affective psychosis as the instruments and methods we used are not sensitive enough to differentiate during this a-specific and initial phase between affective and non-affective psychosis risk (Fusar-Poli et al, 2013). Evaluating if high level of interpersonal sensitivity are linked to the development of a depressive spectrum disorder or if it can signal a fragile an un-structured sense of self that can more easily bring to a schizophrenic breakout may represent an important part of the diagnostic and therapeutic process (Nelson et al 2009).

Limitations

Our results should be interpreted in view of the limitations of this study. As mentioned before, a major limitation is the lack of follow-up data to evaluate whether interpersonal sensitivity is a predictive, or independent, factor for the social functioning impairment during the prodromal phase of psychosis. In future studies we intend to explore the correlations between baseline interpersonal sensitivity level and outcomes in terms of psychopathology and social functioning. Furthermore, the UHR group was relatively small compared to the NS group, however our samples were similar to those of previous studies which used a similar methodology (Fusar-Poli et al 2012, Fusar-Poli et al, 2013; Rietdijk et al 2014).

A further limitation was that prodromal negative symptoms were assessed by a self-reported questionnaire (PQ) rather than by clinical interviews; this weakens the strength of the results because it is possible that participants misinterpreted some questions. Using PQ, instead of clinical interviews, as screening instruments, was also a limitation. Unfortunately, community mental health services often lack resources and time to perform long screening interviews. However, previous
studies have found that a two stage approach whereby only people who screen positive on the PQ are interviewed face to face to be an efficient and valid method to detect UHR individuals (Loewy et al., 2005, 2011, 2012; Rietdijk et al., 2010, Jarrett et al 2012).

**Conclusions**

Confirming previous studies, we found that being an individual extremely sensitive to interpersonal interactions was a subjective psychological feature manifest during the UHR phase for psychosis and distinguished ultra-high-risk participants from other help-seekers. Furthermore we found that high interpersonal sensitivity level were strongly associated with social functioning impairment. We also found that negative prodromal symptoms had a role on the relationship between interpersonal sensitivity and social functioning but it was not statistically significant.

Assessing levels of interpersonal sensitivity and planning targeted psychotherapeutic interventions in order to fight potential difficulties in interpersonal relationships may be a therapeutic action to stop the vicious cycle between interpersonal “hyper-sensitivity” and social withdrawal and to avoid a poor long-term outcome. To better manage the diagnostic and therapeutic process, during the a-specific and heterogeneous phase of a mental illness, clinical judgement seems to be essential.
Acknowledgments

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The present study did not receive any specific financial support. Sapienza University of Rome provided a PhD scholarship for three authors (AM, MB and GDK) and allowed other trainees in Psychiatry (JFL, MC, AS, LD) to spend part of their training working for the present study; Rome H Mental Health Department supported this study by organizing clinical supervision on the early detection work.

Declaration of Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethical Standard

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1964, as revised in 2008.
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Fig. 1
Indirect effect of interpersonal sensitivity on social functioning through negative prodromal symptoms among UHR subjects.

Note:
Indirect Effect = -.012;
Boot LLCI = -.059; Boot ULCI = .023.
$p = .020$. ** $p = .001$
IPSM = InterPersonal Sensitivity Measure
PQ = Prodromal Questionnaire
GF: Global Functioning Social Scale
Table 1. Socio-demographic characteristics of the sample

<table>
<thead>
<tr>
<th></th>
<th>UHR (n=39)</th>
<th>Negative Screening (n=108)</th>
<th>Total (n=147)</th>
<th>Test</th>
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<th>Effect size</th>
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<td>Male</td>
<td>21 (53.8%)</td>
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<td><strong>Educational Level n (%)</strong></td>
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<td>Primary school</td>
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<td>26 (24.1%)</td>
<td>36 (24.5%)</td>
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<td>Junior high school</td>
<td>20 (51.3%)</td>
<td>47 (43.5%)</td>
<td>67 (45.6%)</td>
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<td>Senior high school</td>
<td>9 (23.1%)</td>
<td>35 (32.4%)</td>
<td>44 (29.9%)</td>
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<td><strong>Employment Status n (%)</strong></td>
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<td>Student</td>
<td>31 (79.5%)</td>
<td>79 (73.1%)</td>
<td>110 (74.8%)</td>
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<td>37 (25.2%)</td>
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<td>“Neurotic” symptoms</td>
<td>32 (82.1%)</td>
<td>82 (75.9%)</td>
<td>114 (76.6%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(anxiety, depression,</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>relational problem)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conduct disorder/</td>
<td>7 (17.9%)</td>
<td>26 (24.1%)</td>
<td>33 (22.4%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scholastic problems</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>**Previous psychiatric</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>treatments n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>18 (46.2%)</td>
<td>71 (65.7%)</td>
<td>89 (60.5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychotherapy</td>
<td>13 (33.3%)</td>
<td>29 (26.9%)</td>
<td>42 (28.6%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychotropic drugs</td>
<td>8 (20.5%)</td>
<td>8 (7.4%)</td>
<td>16 (10.9%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>and psychotherapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age, mean (S.D.)</strong></td>
<td>17.36 (5.58)</td>
<td>18.51 (6.26)</td>
<td>18.20 (6.09)</td>
<td>t=-1.011</td>
<td>p=0.314</td>
<td></td>
</tr>
</tbody>
</table>

UHR= Ultra High Risk
Table 2. Comparisons between Ultra High Risk (UHR) and Negative Screening (NS) participants with regard to psychosocial and self-reports measures

<table>
<thead>
<tr>
<th>Measure</th>
<th>UHR</th>
<th>Negative Screening</th>
<th>Sig.*</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Median</td>
<td>SD</td>
<td>Min</td>
</tr>
<tr>
<td>IPSM total</td>
<td>97.21</td>
<td>98.00</td>
<td>18.69</td>
<td>47</td>
</tr>
<tr>
<td>Interpersonal awareness</td>
<td>21.00</td>
<td>22.00</td>
<td>5.36</td>
<td>7</td>
</tr>
<tr>
<td>Need for approval</td>
<td>23.08</td>
<td>24.00</td>
<td>3.91</td>
<td>14</td>
</tr>
<tr>
<td>Separation Anxiety</td>
<td>23.15</td>
<td>24.00</td>
<td>5.52</td>
<td>8</td>
</tr>
<tr>
<td>Timidity</td>
<td>19.44</td>
<td>18.00</td>
<td>5.20</td>
<td>8</td>
</tr>
<tr>
<td>Fragile Inner-Self</td>
<td>10.54</td>
<td>9.00</td>
<td>4.48</td>
<td>2</td>
</tr>
<tr>
<td>GF: Role Scale</td>
<td>5.85</td>
<td>6.00</td>
<td>1.87</td>
<td>1</td>
</tr>
<tr>
<td>GF: Social Scale</td>
<td>6.15</td>
<td>6.00</td>
<td>1.26</td>
<td>3</td>
</tr>
<tr>
<td>PQ total</td>
<td>37.54</td>
<td>39.00</td>
<td>18.19</td>
<td>1</td>
</tr>
<tr>
<td>PQ positive</td>
<td>17.15</td>
<td>17.00</td>
<td>9.97</td>
<td>0</td>
</tr>
<tr>
<td>PQ negative</td>
<td>8.38</td>
<td>7.00</td>
<td>4.89</td>
<td>0</td>
</tr>
<tr>
<td>PQ general</td>
<td>7.26</td>
<td>8.00</td>
<td>3.39</td>
<td>0</td>
</tr>
<tr>
<td>PQ disorganized</td>
<td>4.74</td>
<td>5.00</td>
<td>3.10</td>
<td>1</td>
</tr>
</tbody>
</table>

* evaluated with the Mann–Whitney U test.

UHR= Ultra High Risk; IPSM=InterPersonal Sensitivity Measure; GF= Global Functioning, Role Scale and Social Scale; PQ= Prodromal Questionnaire
Table 3. Correlation between the IPSM and functioning scales scores (by group)

<table>
<thead>
<tr>
<th>Scale</th>
<th>UHR</th>
<th></th>
<th>NS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( r_s )</td>
<td>Sig.</td>
<td>( r_s )</td>
<td>Sig.</td>
</tr>
<tr>
<td>GF: Social Scale</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interpersonal awareness</td>
<td>-.325</td>
<td>.020</td>
<td>-.241</td>
<td>.012</td>
</tr>
<tr>
<td>Need for approval</td>
<td>-.046</td>
<td>.782</td>
<td>-.023</td>
<td>.810</td>
</tr>
<tr>
<td>Separation Anxiety</td>
<td>-.203</td>
<td>.216</td>
<td>-.043</td>
<td>.656</td>
</tr>
<tr>
<td>Timidity</td>
<td>-.363</td>
<td>.023</td>
<td>-.205</td>
<td>.033</td>
</tr>
<tr>
<td>Fragile Inner-Self</td>
<td>-.203</td>
<td>.216</td>
<td>-.650</td>
<td>.000</td>
</tr>
<tr>
<td>IPSM total</td>
<td>-.241</td>
<td>.140</td>
<td>-.179</td>
<td>.064</td>
</tr>
<tr>
<td>GF: Role Scale</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interpersonal awareness</td>
<td>-.044</td>
<td>.791</td>
<td>-.069</td>
<td>.478</td>
</tr>
<tr>
<td>Need for approval</td>
<td>.211</td>
<td>.197</td>
<td>.006</td>
<td>.995</td>
</tr>
<tr>
<td>Separation Anxiety</td>
<td>.149</td>
<td>.365</td>
<td>.126</td>
<td>.195</td>
</tr>
<tr>
<td>Timidity</td>
<td>.091</td>
<td>.581</td>
<td>.116</td>
<td>.233</td>
</tr>
<tr>
<td>Fragile Inner-Self</td>
<td>.195</td>
<td>.235</td>
<td>.096</td>
<td>.322</td>
</tr>
<tr>
<td>IPSM total</td>
<td>.211</td>
<td>.197</td>
<td>.087</td>
<td>.368</td>
</tr>
</tbody>
</table>

UHR= Ultra High Risk; IPSM=InterPersonal Sensitivity Measure; GF= Global Functioning, Role Scale and Social Scale; PQ= Prodromal Questionnaire; NS= Negative Screening