UNIVERSITÀ
DEGLI STUDI
FIRENZE

DOTTORATO DI RICERCA IN SCIENZE CLINICHE

CICLO XXIX

COORDINATORE Prof. Francesco Annunziato

Efficacy of cognitive behavioural therapy
for individuals at ultra-high-risk of first episode of psychosis:
a randomised controlled trial

Settore Scientifico Disciplinare M-PSI/08

Dottorando
Dott. Pozza Andrea

Tutor
Prof. Dèttore Davide

Coordinatore
Prof. Annunziato Francesco

Anni 2014/2016

Contents

Summary

Background

Growing attention has been dedicated by researchers and practitioners to early identification and intervention on young individuals considered as at ultra-high-risk (UHR) of a first psychosis episode. Cognitive behavioural therapy (CBT) has shown to be the first-line treatment strategy. However, there is a small number of trials on its efficacy. UHR groups who do not make transition frequently report poor functioning and secondary symptoms, such as depression and anxiety. Existing trials focused on psychosis prevention as a dichotomous outcome without sufficiently targeting additional outcomes. Despite it has been linked with frank psychosis, worry has not been considered as outcome.

Objectives

Primary objective of the current study was (a) to assess whether a CBT modular protocol was able to reduce or delay risk of transition to psychosis in a group of UHR help-seeking individuals after 6 months (post-treatment) and 14-months (follow-up) compared with treatment as usual as a control condition. Secondary objectives were (b) to compare the CBT intervention with the control condition on secondary outcomes, including depression, anxiety, worry and global functioning.

Methods

Participants were included if they were 16-35-year old and met criteria for At-Risk-Mental State (ARMS) at the Comprehensive Assessment of At-Risk-Mental States (CAARMS). Fifty-eight individuals recruited from mental health services (mean age= 25.51, SD= 6, 67.20% males) were randomly assigned to CBT or control condition. The CBT modular protocol consisted of 30 weekly sessions with multiple components including engagement and goal setting, psychoeducation on psychotic experiences, (meta)cognitive restructuring, intervention on depression, worry, social anxiety and skills. Kaplan-Meier survival statistics were used to analyse the primary outcome. Participants lost to follow-up were coded conservatively as non-converters. In the group that did not make transition, secondary outcomes were analysed by ANCOVA.

Results

Overall, 7 participants (12.10%) at post-treatment and 11 (19%) at 14-month follow-up cumulatively made the conversion to psychosis. In the CBT group, the number of individuals who made cumulative conversion to psychosis (n= 4, 10.30%) at 14-month follow-up was lower than in the control group (n= 8, 27.60%), despite this difference was at a borderline significance level (Log rank test $\chi 2_{(1)}= 3.66$, $p= 0.05$). In the CBT group, a higher number of participants achieved remission than in the control group on secondary outcomes at post-treatment (75% vs 38.10% for both depression and anxiety) [$\chi^2_{(1)}= 6.25$, $p< 0.05$] and also at follow-up. However, a significantly greater effect of CBT than control condition on depression, anxiety, worry and functioning was not found when these outcomes were considered as continuous.

Conclusions

CBT seems to be an option of intervention able to reduce drop out among UHR individuals and to some extent also prevent the risk of a first episode with some benefits on secondary outcomes such as anxiety and depression when levels on these outcomes are clinically significant. Further research is required to examine additional strategies targeting worry and functioning. Clinical implications, limitations and future directions are discussed.

Riassunto

Premessa

L'identificazione precoce di giovani considerati a alto rischio di un primo episodio di psicosi è un tema che sta ricevendo attenzione crescente da parte di ricercatori e clinici. La terapia cognitivo comportamentale (TCC) si è dimostrata il trattamento di prima linea. Tuttavia, ad oggi esiste un numero ridotto di studi sulla sua efficacia. I soggetti a alto rischio tendono frequentemente a riportare ridotto funzionamento e sintomi secondari, come ansia e depressione. Gli studi esistenti si sono focalizzati prevalentemente sulla prevenzione del rischio di psicosi senza indagare sufficientemente ulteriori indici di esito. Inoltre, il rimuginio non è stato considerato come misura di esito, nonostante sia associato ai disturbi psicotici conclamati.

Obiettivi

L'obiettivo primario del presente studio è stato (a) valutare se un protocollo di TCC modulare fosse in grado di ridurre o ritardare il rischio di sviluppo di psicosi in un gruppo di soggetti afferenti ai servizi di salute mentale dopo sei mesi (post-trattamento) e 14 mesi (follow-up) a confronto con treatment as usual come controllo. Gli obiettivi secondari sono stati (b) confrontare la TCC con il controllo su misure di esito secondarie, come la depressione, l'ansia, il rimuginio, il funzionamento globale.

Metodi

I partecipanti sono stati inclusi se avevano età compresa tra 16 e 35 anni e soddisfacevano i criteri per uno stato mentale a rischio alla Comprehensive Assessment of At-Risk-Mental States (CAARMS). Cinquantotto soggetti reclutati da servizi di salute mentale (età media= 25.51, DS= 6, 67.20% maschi) sono stati randomizzati a TCC o gruppo di controllo. Il protocollo modulare di TCC includeva 30 sedute settimanali con componenti multiple, ovvero ingaggio, definizione degli obiettivi, psicoeducazione sulle esperienze psicotiche, ristrutturazione (meta)cognitiva, interventi sulla depressione, rimuginio, ansia e abilità sociali. Sono state calcolate le statistiche di sopravvivenza Kaplan-Meier per analizzare l'obiettivo primario. Nel gruppo che non ha sviluppato psicosi, le misure di esito secondarie sono state analizzate con ANCOVA.

Risultati

Complessivamente, 7 partecipanti (12.10%) e 11 (19%) hanno sviluppato psicosi al post-trattamento e follow-up rispettivamente. Nel gruppo TCC, il numero di soggetti che ha sviluppato psicosi a follow-up in modo cumulativo è stato inferiore (n= 4, 10.30%) a quello del gruppo di controllo (n= 8, 27.60%), sebbene questa differenza sia risultata per un livello di significatività borderline (Log rank test $\chi 2_{(1)}= 3.66$, $p= 0.05$). Nel gruppo TCC, un numero più alto di soggetti ha raggiunto la remissione rispetto al gruppo di controllo sulle misure secondarie (75% vs 38.10% sia per depressione che ansia) [$\chi^2_{(1)}= 6.25$, $p< 0.05$]. Tuttavia, non si è rilevato un effetto significativamente più elevato della TCC su depressione, ansia, rimuginio e funzionamento quando questi indici sono stati considerati come variabili continue.

Conclusioni

La TCC sembra essere una forma di intervento in grado di ridurre il drop out nei soggetti a alto rischio di psicosi ed in una certa misura prevenire il rischio di un primo episodio con benefici anche su misure di esito secondarie, quali ansia e depressione quando i loro livelli sono considerati come variabili continue. Si richiedono ulteriori ricerche che indaghino strategie aggiuntive per il rimuginio e il funzionamento. Si discutono le implicazioni dei risultati, i limiti e le prospettive future.

Introduction

Despite its low incidence of 0.03 per 100 persons every year (Kirkbride et al., 2012), psychosis represents the third most costly brain vulnerability with direct and indirect healthcare economic costs of about 93 billion in the European countries (Mangalore & Knapp, 2007; Olesen, Gustavsson, Svensson, Wittchen, & Jönsson, 2012). Once thought to be inevitably progressive, psychosis can have very heterogeneous outcomes (Harrison et al., 2001). During the last two decades, a wide international movement of researchers and practitioners has sought to apply principles of practice based on early detection and treatment that are well established for other branches of medicine, such as cancer and cardiovascular diseases (Marshall & Rathbone, 2011). Increasing efforts have been put into developing early detection and prevention strategies before the development of a first episode of psychosis.

In patients with first psychotic episode only 20% will completely recover from a single episode and 70-80% will have a relapsing and chronic course with lifelong vulnerability and social impairment (Alvarez-Jiménez et al., 2011). Clinical observations have suggested that a relevant part of first-episode psychosis patients (about 70%) report having suffered from mental problems including attenuated or intermittent psychotic symptoms and increasing psychosocial impairment for an average 5-year period prior to the onset of psychosis (Schultze-Lutter, Ruhrmann, Berning, Maier, & Klosterkötter, 2010).

Initially, the early psychosis movement focused on timely recognition and phase-specific treatment of first-psychosis episode. However, it was recognized that for most patients a prolonged period of attenuated symptoms and impaired functioning precedes the first episode. Much of the disability associated with psychosis develops much longer before the onset of frank symptoms and is difficult to reverse, even if the first psychotic episode is successfully treated. This pre-onset period has been named as prodromal phase (Hafner et al., 2003; Yung, 2003; Yung & McGorry, 1996).

About half of individuals diagnosed with psychotic disorders have sought mental health care prior to onset of psychosis (Rietdijk et al., 2011). Screening for psychosis among help-seeking populations with psychiatric symptoms in mental health, or even in primary care settings, is very important given that psychosis can be underestimated if individuals receive professional help for symptoms other than

psychotic symptoms (van der Gaag, Nieman, & van den Berg, 2013). Several studies reported a high rate of individuals meeting criteria for a psychotic disorder, who had not been detected by clinicians, suggesting that practitioners are not often aware of psychotic manifestations in individuals who seek help for other kinds of mental problems (Boonstra et al., 2011; Marshall et al., 2005).

In the last subsequent decade, growing interest has been dedicated to the development of early identification and intervention strategies for young people who experience the prodromal states of psychosis. Two main approaches were developed when identifying individuals in a CHR state (Fusar-Poli et al., 2013): the ultra-high-risk criteria (UHR) that focus on detecting an imminent risk of psychosis (Yung et al., 1996) and the basic symptom criteria that focus on the detection of the earliest possible specific symptoms (Schultze-Lutter, 2009). As many as 4–8% of adolescents and young adults seeking mental health care may meet CHR criteria (Ising et al., 2012; Rietdijk et al., 2014).

Chapter 1: The at-risk-mental state (ARMS)

1.1.Psychotic-like experiences are normal

Population-based studies have shown that the dichotomous disease model of psychotic disorders can be integrated into a model of psychosis as an extended phenotype across clinical and non-clinical expressions, where at one end of the continuum lies schizophrenia, in the middle are non-psychotic mental disorders with psychotic-like experiences (PLEs), and at the other extreme lie PLEs in healthy, non-help-seeking individuals (Kaymaz et al. 2012; van Os & Linscott, 2012). Schizophrenia only represents the poorest outcome segment of this much wider spectrum of psychotic manifestations, which have a lifetime prevalence of 3.50% (van Os, Hanssen, Bijl, & Vollebergh, 2001).

Psychotic features are not uncommon in the general population, and psychotic symptoms are experienced not only by patients with full psychotic disorders but also by patients with non-psychotic disorders and part of the general population (van Os et al., 2001). Having one of psychotic symptoms was reported in about 25% (n= 5877) of the American population (Kendler, Gallagher, Abelson, & Kessler, 1996), 17.50% (n= 7076) of the Dutch population (van Os et al., 2001), and in 17.50% (n= 2548) of the German population (Spauwen, Krabbendam, Lieb, Wittchen, & van Os, 2003). In an English-Italian cohort study (Ohayon, 2000), where hypnagogic and hypnopompic hallucinations were considered, the percentage increased to about 40% (n= 13057). The incidence of subthreshold psychotic characteristics tends to be about 100 times as high as in the population as the incidence of a psychotic disorder (Hanssen, Bak, Bijl, Vollerbergh, & van Os, 2005). In a population-based survey (n= 7076), about 18% of participants reported one or more psychotic symptoms, while 0.40% had a schizophrenic psychotic disorder and 1.10% an affective psychotic disorder (Hanssen et al., 2005). After three years, the group with one or more symptoms was symptom-free in 84% of the cases; psychotic symptoms were enduring among 8%, while another 8% had a transition into psychosis (Hanssen et al., 2005).

PLEs include a variety of types (Kelleher & Cannon, 2011). One group consists of sensory experiences which are not shared by other present people and refer to hearing sounds (such as voices, noises), unexplained visual experiences (such as visions, seeing ghosts), unusual bodily experiences (such as feeling touched) or smell that nobody else seems to smell (van der Gaag, Nieman, & van den

Berg, 2013). Other kinds include distorted self-experiences, which regard a distorted sense of self. Most of these feelings include one or more of the following (Nelson, Thompson, & Yung, 2012; Yung et al., 2009):

- a diminished sense of basic self, such as sense of inner void, lack of identity, being different from others;
- a decreased ability to be affected by people, situations and events;
- different kinds of depersonalization experiences, such as decreased or temporally delayed sense of "mineness" to experience, a pervasive sense of distance between the self and experience;
- different feelings of derealisation, such as an impression that the external environment has somehow transformed, is unreal or strange or experiencing the world as if seen through fog;
- intense reflectivity: the tendency to take oneself or parts of oneself or elements of the external environment as objects of intense reflection (such experience can include also thinking about one's own experiences);
- perplexity: difficulty automatically grasping the meaning of the everyday events.

1.2.The staging model of psychosis and the clinical high risk status (CHR)

McGorry and colleagues (2006) criticized diagnostic systems highlighting that they include categories, such as schizophrenia and depression, that are too broad and poorly informative for prognosis and treatment decision-making (McGorry et al., 2006). The authors believed that DSM-IV-TR (American Psychiatric Association, 2000) or ICD-10 (World Health Organization, 1993) consist of artificial constructions based on cross-sectional symptom sets confused with course of illness variables (McGorry et al., 2007). Clinical features that occur early in the course are not distinguished from those that become apparent as a disorder persists (McGorry et al., 2006). Different from conventional diagnostic practice, clinical staging models, originally developed for medical conditions such as autoimmune or cardiovascular diseases, aim to define the extent of progression of disease at a specific time point, and consequently conceptualize conditions along the continuum of the illness course (Hasselbach, 1993). Such models are able to differentiate early and milder clinical phenomena from those that accompany illness progression and chronicity (McGorry et al., 2007). They make practitioners more capable of selecting treatments specific to earlier stages, and assume that such interventions will be both more effective and less harmful than treatments delivered later in the course (McGorry et al., 2007).

McGorry and colleagues (2006) developed a clinical staging theoretical model of psychosis and mood disorders, within which biological markers can be progressively introduced to build a clinicopathological model. The staging model of psychosis is presented in Table 1.1.

Table 1.1. Staging model of psychosis (McGorry et al., 2006).

Clinical stage	Definition	Target populations for recruitment	Potential interventions	Indicative biological and endophenotypic markers
0	Increased risk of psychotic or severe mood disorder. No symptoms currently	1st degree teenage relatives of probands	Improved mental health literacy, family education, drug education, brief cognitive skills training	Trait marker candidates and endophenotypes, e.g. Smooth Pursuit Eye Movements, P 50, Niacin sensitivity, Binocular rivalry, Prepulse inhibition, Mismatch negativity, Olfactory deficits, etc.
1a	Mild or non-specific symptoms, including neurocognitive deficits of psychosis or severe mood disorder. Mild functional change or decline	Screening of teenage populations, referral by primary care physicians, referral by school counsellors	Formal mental health literacy, family psychoeducation, formal CBT, active substance abuse reduction	Trait and state candidates where feasible according to sample size
1b	Ultra-high-risk: moderate but subthreshold symptoms, with moderate neurocognitive changes and functional decline to caseness (GAF<70)	Referral by educational agencies, primary care physicians, emergency departments, welfare agencies	Family psychoeducation, formal CBT, active substance abuse reduction, atypical antipsychotics agents for episode, antidepressant agents or mood stabilizers	Niacin sensitivity, folate status, MRI and MRS changes, HPA axis dysregulation
2	First episode of psychotic or severe mood disorder Full threshold disorder with moderate-severe symptoms, neurocognitive deficits and functional decline (GAF 30-50)	Referral for primary care physicians, emergency departments, welfare agencies, specialist care agencies, drug and alcohol services	Family psychoeducation, formal CBT, active substance abuse reduction, atypical antipsychotics agents for episode, antidepressant agents or mood stabilizers, vocational rehabilitation	Continue with markers of illness state, trait and progression
3a	Incomplete remission from FEP Could be linked or fast-tracked to stage 4	Primary and specialist care services	As for "2" with additional emphasis on medical and psychosocial strategies to achieve full remission	Continue with markers of illness state, trait and progression
3b	Recurrence of relapse of psychotic or mood disorder which stabilizes with treatment at a level of GAF, residual symptoms, or neurocognition below he best level achieved following remission from first episode	Specialist care services	As for "3a" with emphasis on long-term stabilization	Continue with markers of illness state, trait and progression
3c	Multiple relapses, provided worsening in clinical extent and impact of illness is objectively present	Specialist care services	As for "3b" with emphasis on long-term stabilization	Continue with markers of illness state, trait and progression
4	Severe, persistent or unremitting illness as judged on symptoms, neurocognition and disability criteria Note: could fast track to this stage at first presentation through specific clinical and functional criteria (from stage 2) or alternatively by failure to respond to treatment (from stage 3a)	Specialist care services	As for "3c" but with emphasis on clozapine, other tertiary treatments, social participation despite ongoing disability	Continue with markers of illness state, trait and progression

Note. CBT= cognitive behavioural therapy, FEP = first episode psychosis, GAF= Global Assessment of Functioning, HPA= Hypothalamic-pituitary axis, MRI= magnetic resonance imaging, MRS= magnetic resonance spectroscopy.

1.3.The Ultra-High Risk of psychosis criteria (UHR)

The ultra-high-risk of psychosis criteria (UHR) define a condition identifying three subgroups of CHR individuals:

(a) those reporting attenuated psychotic symptoms (APS);

(b) those having brief limited intermittent psychotic episodes (BLIPs) below DSM-IV's duration criteria for a brief psychotic episode;

(c) those individuals who have genetic vulnerability, consisting of familial risk or presence of a schizotypal personality disorder combined with recent decline in functioning during the last years (McGorry et al., 2009).

An age range of 15–30 years was also included in the identification approach, as this age group has been found to have the highest risk for psychosis (McGorry et al., 2009). APS can include at least any of ideas of reference, odd beliefs or magical thinking, such as ideas of grandiosity, paranoid ideation and unusual perceptual experiences, thinking and speech (McGorry et al., 2009). BLIPs can include presence of at least any of hallucinations, delusions, and formal thought disorders (McGorry et al., 2009). Presence of a genetic risk factor can consist of family history of psychosis in first-degree relatives, schizotypal personality disorder in combination with a recent significant decline in psychosocial functioning. UHR criteria are met if at least one of BLIPs, APS or genetic risk factors are met.

As suggested by Debbané and colleagues (2015), APS were modelled both on "psychotic-like experiences" defined by Chapman and Chapman (1980) as delusional and hallucinatory phenomena in that some insight is still maintained, and on the five positive DSM-III-R prodromal symptoms of schizophrenia (American Psychiatric Association, 1987) that are phenomenologically equal to the positive symptoms in the definitions of the clinical manifestation of schizotypy in the ICD-10 category of schizotypal personality disorder (World Health Organization, 1994).

As many as 4–8% of adolescents and young adults seeking mental health care may meet UHR criteria (Ising et al., 2012; Rietdijk et al., 2014). Individuals with APS consistently account for the majority of the UHR population (Debbané et al., 2015). The temporal relationship between CHR subgroups and early psychosis across time windows and phase-specific interventions is provided in Figure 1.1.

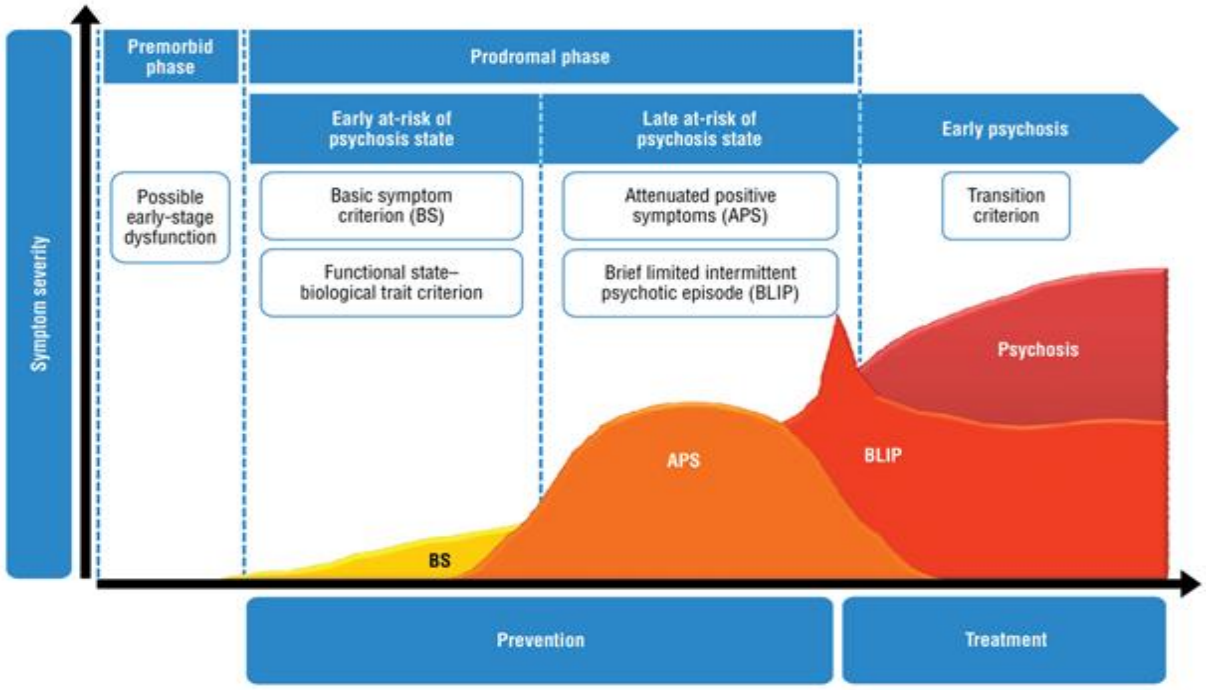


Figure 1.1. CHR groups across time windows and phase-specific interventions (source: Fusar-Poli et al., 2012).

1.4.The Basic Symptoms criteria (BS)

A similar early detection strategy complementary to the UHR approach was created in Germany: the basic symptoms criteria (BS; Klosterkotter et al., 2001). BS were conceptualized as subtle, subjectively experienced subclinical disturbances in drive, affect, thinking, speech, (body) perception, motor action, central vegetative functions, and stress tolerance (Gross, 1989; Huber & Gross, 1989). They can occur and have been reported in every stage of the psychosis illness, such as in the prodromal phase to the first episode, in prodromes to relapse, in residual states, and even during psychotic episodes per se (Gross, 1989).

BS are different from what is considered to be one's ''normal'' mental self. Being subjective, they remain predominately private and apparent only to the affected person (Gross, 1989). They are rarely observable to others, although the patient's self-initiated coping strategies (including avoidance behaviours and social withdrawal) in response to his/her BS may be recognizable to others. Being self-experiences, BS differ from negative symptoms as they are currently understood and appear as functional deficits observable to others (Parnas et al., 2005). BS are also distinct from frank psychotic symptoms that are experienced by the patient as real, normal thinking, and feeling. In contrast, BS are spontaneously and immediately recognized by the affected person as disturbances of his/her own mental processes. Insight that something is wrong with one's thinking is present, yet some

experiences might be so new and strange that they remain nearly inexplicable. The rare, highly introspective person may be able to articulate what is happening, but any detailed description of these experiences usually requires help in the form of guided questioning (Schultze-Lutter et al., 2007). The ability to experience BS with insight and to cope with them often attenuates with progressive illness and emerging psychotic symptoms but is restored upon remission (Gross, 1989). Thus, an evaluation of BS is often hindered by acute and/or prominent psychotic symptoms.

BS were considered as the earliest subjectively experienced symptoms of psychosis and the most immediate symptomatic expression of its neurobiological correlates — thus the term ‘‘basic’’ (Huber & Gross, 1989). According this model, early symptoms would occur in three developmental forms: ‘‘uncharacteristic’’ BS affecting drive, volition, and affect, concentration and memory (level 1); ‘‘characteristic’’, qualitatively peculiar BS, especially of thinking, speech (body) perception, and motor action (level 2); and psychotic symptoms per se (level 3) (Gross, 1989). Upon onset at level 1, BS would gradually increase in number and severity and, in most cases, ultimately develop into psychotic symptoms. Temporary improvements, however, are possible. In some cases, level 1 and/or level 2 BS will remit completely and spontaneously before reaching the threshold for psychotic symptoms. These symptomatic phases without conversion to a frank psychotic episode can reproduce true prodromal stages and are called ‘‘outpost syndromes’’ because they precede the subsequent prodrome. The emergence of level 2 or characteristic BS and their conversion to level 3 psychotic symptoms can be triggered by everyday stressful situations and demands that overstrain an already pathologically vulnerable information processing capacity (Gross, 1989). Given favourable environmental and individual conditions, such as a supportive social network, effective social and problem solving skills or coping successfully with pressure such as passing difficult exams, BS can be compensated for at any state almost completely as long as their number and/or severity do not overextend personal resources and coping strategies (Gross, 1989).

A list of cognitive and perceptual BS associated with psychosis is presented in Table 1.2.

Table 1.2. Cognitive and perceptual basic symptoms associated with psychosis (Klosterkotter et al., 2001).

Thought interference An intrusion of completely insignificant thoughts hindering concentration/thinking (“I can’t help thinking about other things, which is very distracting”)
Thought perseveration An obsessive like repetition of insignificant thoughts or mental images (“I always have to mull over what I just said. I can’t stop thinking about what I might have said wrong or what I could have added although I really don’t think that anything was wrong with what I said”)
Thought pressure A self-reported ‘‘chaos’’ of unrelated thoughts (“If I am stressed out my mind gets chaotic and I have great problems thinking straight. Too many thoughts come up at once’’)
Thought blockages either with or without intrusion of a new thought A sudden loss of the thread or train of thoughts (“Sometimes my thoughts just stop, are suddenly gone, like being cut off’’)
Disturbance of receptive language Paralysis in the immediate comprehension of simple words/sentences, either read or heard, that can result in giving up reading or avoiding conversations (“I often can’t get the meaning of common words when I am reading’’)
Disturbance of expressive speech Problems in producing appropriate words, sometimes also experienced as a reduction in active vocabulary (‘‘Sometimes I think it must appear as if English were really my second language, like I don’t know English very well because I have difficulties expressing myself. I forget the words’’)
Disturbances of abstract thinking An unusual basic symptom seen when asking the patient to explain sayings or idioms (“Sometimes I get puzzled if a certain object or event only stands as a metaphor for some more general, abstract or philosophical meaning’’)
Inability to divide attention Difficulty dividing attention between simultaneous nondemanding tasks that each draw primarily upon a different sense that would not usually require a switching of attention (‘‘Doing two things at once has become impossible even with the simplest things. I always have to concentrate on one thing at a time, like if I prepare a sandwich, I cannot do anything else, like watch a film’’)
Captivation of attention by details of the visual field that catches and holds the look (“Sometimes an object really seems to stand out from the rest of what I see. My eyes then fix on it. It’s like being spellbound, even though I don’t want to look at it at all’’)
Decreased ability to discriminate between perception and ideas, true memories and fantasies (“I thought about my grandparents. Then a weird thing happened: I couldn’t remember if knew my grandparents properly, if they were real or if they were just in my imagination. Did I know them, or had I made them up?’’)
Unstable ideas of reference with insight (“When I was listening to the radio the idea that the lyrics had some special meaning for me suddenly popped up into my head. Off course I knew straight away that it was just my imagination, a kind of weird thing. I did not have to think twice about it to know that’’)
Derealization A decreased emotional and gestalt connection with the environment (“Sometimes, I feel disconnected from the world around me, like I’m under a glass cover’’)
Visual or acoustic perceptual disturbances with insight Unlike hallucinations or schizotypal perceptual distortions, basic symptom perceptual observations are not regarded as real but are immediately recognized as a sensory or subjective problem. The knowledge that the misperception, eg, a wrong colouring, distorted shape or changed sound quality/intensity, has no counterpart in the real world is immediate and unquestioned (“People suddenly seemed changed and had different hair colours’’)

1.5. Prognostic accuracy

Available studies in the literature reported a wide variety of transition rates of UHR criteria. The first published study (Yung et al., 1998) using UHR criteria found a transition rate of 40% to threshold psychotic disorder within one year. Another early study examining psychosis conversion in

individuals meeting CHR criteria reported a 45% two-year conversion rate (Yung et al., 2004). These findings were subsequently replicated by several international groups (Riecher-Rossler et al., 2007; Mason et al., 2004; Miller et al., 2002). Using a combination of studies, Ruhrman and colleagues (Ruhrmann, Schultze-Lutter, & Klosterkötter, 2003) reported an average one-year transition rate of 36.70% in CHR individuals who did not receive antipsychotic medications. The North America Prodrome Longitudinal Study (NAPLS; Addington et al., 2007) consisted of cohorts of 291 individuals recruited from eight North American centres. The UHR criteria predicted a group for early transition to psychosis with a large RR of 405. However, a limitation of the study was that treatments were not controlled and varied across centres.

Investigations of the accuracy of BS in predicting the onset of psychosis within 12 months after baseline assessments revealed that presenting with at least two of nine cognitive disturbances cluster of BS resulted in a transition rate to psychosis of 23.90% within twelve months, an additional 22.40% within the second year and a further 14.90% within the third year (Lencz et al., 2003). Thus, the twelve-month transition rate of the cognitive disturbances cluster of BS is comparable with that observed among individuals classified as CHR for APS (twelve-month transition rate of 26.50% for APS alone) (Lencz et al., 2003).

In conclusion, both approaches (BS and UHR) as well as the instruments specifically developed for their assessment, have shown the ability to detect a considerably increased CHR for psychosis with pooled 1–3-year conversion rates to psychosis ranging from 15% to 29% for UHR (Fusar-Poli et al., 2012; Kempton et al., 2015) and from 14% to 50% for BS criteria, and sufficient prognostic accuracy of their assessment, in particular in ruling out psychosis risk (Fusar-Poli et al., 2015). Indeed, there is evidence that about 23% of patients with CHR who disengage from CHR services (drop-outs) will later develop psychosis (Green et al., 2011). However, these figures are not stable but were shown to vary not only with the follow-up time but also with characteristics of the group in which CHR state is assessed, for example, with age composition or referral source (Fusar-Poli et al., 2015; Schimmelmann et al., 2015).

A meta-analysis (Fusar-Poli et al., 2012) provided a summary Kaplan-Meyer estimate of psychosis risk in CHR samples (mainly by UHR criteria), and indicated that most transitions occurred within the first 2 years. There was a consistent transition risk, independent of the psychometric instruments used, of 18% after 6 months of follow-up, 22% after 1 year, 29% after 2 years, and 36% after 3 years (Fusar-Poli et al., 2012). Transition risks from the meta-analysis of Fusar-Poli and colleagues (2012) are provided in Figure 1.2.

The sensitivity and specificity of CHR assessments have recently been estimated at meta-analytical level. The prognostic sensitivity for psychosis prediction at 38 months was 96% (95% CI: 92%-98%),

while the prognostic specificity for psychosis prediction at 38 months was 47% (95% CI: 38%-57%) (Fusar-Poli et al., 2015). These values indicate that CHR assessments have an outstanding ability to rule out psychosis risk and an only modest ability to rule in subsequent psychosis (Fusar-Poli et al., 2015).

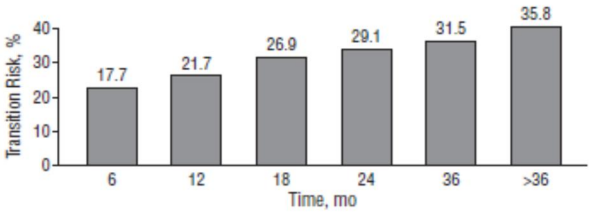
Recent studies and meta-analyses (Kempton et al., 2015; Schultze-Lutter et al., 2015; Wiltink et al., 2015) found considerably lower transition risks as compared to earlier research on CHR status. Subsequent studies consistently found lower two-year conversion rates ranging from 15 to 30% (Demjaha et al., 2012; DeVylder et al., 2014; Katsura et al., 2014; Lee et al., 2014; Liu et al., 2011; Nelson et al., 2013; Riecher-Rossler et al., 2009; Ruhrmann et al., 2010; Woods et al., 2009; Ziermans et al., 2011). It was suggested that this risk dilution was partially caused by increasing attention paid to early symptoms by clinicians and early intervention but also by an increase of false positive related to higher awareness of the UHR phase. In addition, it was hypothesized that risk dilution was caused by changes in referral pathways and inclusion of younger age groups and, consequently, in changes of the populations (ie, pre-test risk of psychosis) from which CHR patients are selected (Cornblatt et al., 2015). Thus, recruitment strategies might have an important role in the accuracy of predicting psychosis onset using CHR criteria. The individual risk of developing psychosis after being tested for CHR criteria depends upon the underlying risk of the disease of the population from which the person is selected (pre-test risk of psychosis), and thus on recruitment strategies. Yet, the impact of recruitment strategies on pre-test risk of psychosis is unknown (Fusar-Poli et al., 2015).

In a recent meta-analytic study, Fusar-Poli and colleagues (2015) included 11 studies for a total of 2519 individuals. Findings indicated that pre-test risk for psychosis in help-seeking individuals was 15%. A thorough examination of the studies highlighted that recruitment strategies were heterogeneous and opportunistic (Fusar-Poli et al., 2015). Heterogeneity was largely accounted for by intensive outreach campaigns primarily targeting the general public along with higher proportions of self-referrals, which diluted pre-test risk for psychosis in patients undergoing CHR assessment. The average 15% risk of pre-test risk of psychosis in these help-seeking samples is significantly higher than the comparable 0.1% risk of psychosis in the general population over the same period (Fusar-Poli et al., 2015). Since recruitment strategies can significantly increase psychosis risk in help-seeking individuals even before they undergo CHR assessment (pre-test risk of psychosis), it is not only the criteria themselves that determine the post-test risk of transition to psychosis but also the process of preselection of samples, such as the defined populations of origin of these samples, which creates substantial enrichment in risk (Fusar-Poli et al., 2015).

Recently, some researchers claimed the potential value of symptom-based risk prediction to clinical practice. The majority of published studies examining symptoms and risk prediction likewise have

reported that items reflecting disordered thought content unusual ideas (Katsura et al., 2014; Nelson et al., 2013; Salokangas et al., 2013; Wilcox et al., 2014), suspiciousness (Riecher-Rossler et al., 2009; Salokangas et al., 2013), bizarre thoughts (Ruhrmann et al., 2010), odd beliefs/magical thinking and problems distinguishing fantasy and reality (Mason et al., 2004), unstable ideas of reference (Klosterkotter et al., 2001), derealization (Klosterkotter et al., 2001) are more severe in converters than nonconverters.

In the NAPLS Study, Perkins and colleagues (2015) developed a classifier that included those items of the Scale of Psychosis-Risk Symptoms (McGlashan, Walsh, & Woods, 2010), that best distinguished individuals who converted to psychosis from nonconverters in the dataset of obtained cases. Results demonstrated that the severity of unusual thought content, referential thinking and suspiciousness are key high-risk symptoms in the prediction of transition to psychosis (Perkins et al., 2015). With two exceptions (Klosterkotter et al., 2001; Mason et al., 2004), most other studies have likewise failed to find perceptual disturbances as predictive (DeVylder et al., 2014; Katsura et al., 2014; Nelson et al., 2013; Riecher-Rossler et al., 2009; Ruhrmann et al., 2010; Salokangas et al., 2013; Thompson et al., 2013; Velthorst et al., 2009; Wilcox et al., 2014).



No. of Studies	Follow-up, mo	Transition Risks, 95% CI
9	6	17.7 (12.3-24.9)
13	12	21.7 (16.6-27.8)
4	18	26.9 (19.5-35.9)
12	24	29.1 (23.2-35.7)
6	36	31.5 (23.8-35.0)
4	>36	35.8 (29.6-42.5)

P<.001 for all.

Figure 1.2. Transition risk from subclinical symptoms to full psychosis as a function of time windows (Fusar-Poli et al., 2012).

1.6. Should CHR be inserted in the DSM5? Strength and weakness

In the recent DSM5 (American Psychiatric Association, 2013), the diagnostic category of attenuated psychosis syndrome (APS) has been identified and relegated to the research appendix because of lack of consensus among researchers on the validity of this category as a syndrome and for the

inconclusiveness of data supporting its diagnostic reliability (Addington, Penn, Woods, Addington, & Perkins, 2008; Fusar-Poli et al., 2015).

During the preparation of DSM5, the Psychotic Disorders Work Group proposed the creation of a new diagnostic category to serve as a placeholder for the ARMS concept (Fusar-Poli, Carpenter, Woods, & McGlashan, 2014). The proposal was firstly termed Psychosis Risk Syndrome (PRS) and was then criticized as a premature and confusing category. Subsequent field research showed that individuals at risk already needed treatment for their current psychiatric symptoms and not only the potential preventive effect of early intervention on a "risk syndrome" (Phillips, 2013). Thus, the new category proposal was reconsidered as a mental disorder per se. It was renamed attenuated psychosis syndrome (APS), according to the term assigned to one subgroup of patients identified by the high-risk mental state research criteria (Yung & Nelson, 2011). Although other sets of high-risk criteria existed, most at-risk patients identified in specialized research centres presented APS as their main medical complaint. The syndrome differed from full-blown psychosis due to the subthreshold (attenuated) intensity or frequency of presented symptoms (Fusar-Poli et al., 2014).

On one side of the debate, opponents of the APS category argued that this diagnosis could undesirably stigmatize and generate unnecessary treatment to young people whose majority would never transition to psychosis (Mittal, Dean, Mittal, & Saks, 2015). Identifying APS as an official diagnostic category could also determine inappropriate allocation of the already scarce resources destined to mental health (Regier, Kuhl, Kupfer, & McNulty, 2010). Potential inadequate prescription of antipsychotic medication, with their harmful effects of weight gain and increased cardiovascular risk, could cause a profound impact on the life of identified population. Moreover, stigmatizing effects could be unpredictable on the individually and socially perceived sense of autonomy and responsibility of diagnosed patients (Yung, Nelson, Thompson, & Wood, 2010). Researchers in the field recognized the possibility of stigma, discrimination and inappropriate prescription of antipsychotics as one element of the risk-benefit analysis of APS inclusion in DSM5, given that current evidence does not support antipsychotics as more effective than other more benign treatments (Yung et al., 2012).

On the other hand, supporters of the APS inclusion in the DSM5 believed that it could increase access to adequate treatments for people having this condition (Corcoran, First, & Cornblatt, 2010). Moreover, associated symptoms could be treated, including anxiety, depression, social withdrawal, and work/academic impairment, even for those individuals who would never develop psychosis (Corcoran et al., 2010). Also, clinical recognition of APS could hypothetically reduce the rates of misdiagnoses, improving the process of differential diagnosis, promoting better case management and providing proper reimbursement (Corcoran et al., 2010).

Some advocates of APS inclusion also argued that this move could enhance the exchange and acquisition of new knowledge in the field of high-risk mental states (Carpenter & van Os, 2011; Sadler, 2013). APS inclusion would also bring psychiatry in line with other fields of medicine that identify risk factors for the purposes of instituting preventative interventions (Corcoran et al., 2010). Consistent with the necessity of identifying ARMS as a category in the DSM5, a large recent meta-analysis performed by Fusar-Poli and colleagues (2015) indicated that individuals at CHR had impaired functioning and quality of life compared with healthy controls, and that no significant difference emerged between the CHR groups and groups of patients with full-blown psychosis. Among the groups at CHR, those individuals who had conversion to psychosis showed poorer functioning than those who did not have the transition at baseline prior entering treatments (Fusar-Poli et al., 2015).

1.7.Time matters: the Duration of Untreated Psychosis (DUP)

Duration of Untreated Psychosis (DUP) is generally determined as the time from the onset of psychotic symptoms to the initiation of treatment or first clinical presentation, when a diagnosis of first episode psychosis may be given (Norman & Malla, 2001). Ising and colleagues (2011) found 1.4% of the help-seeking population presenting with a nonpsychotic disorder to actually have a psychotic disorder. An UHR syndrome was diagnosed in 4.0% of the help-seeking population. The high rate of the interviewed participants that met the criteria for a psychotic disorder, but that had not been detected by clinicians, suggested that mental health professionals are often unaware of the presence of psychotic symptoms in patients who seek treatment for other mental disorders, as it has also been demonstrated by other authors (Boonstra et al., 2011; Nieman et al., 2009).

A systematic review including 24 studies evidenced a median DUP of 6-21 weeks (Anderson, Fuhrer, & Malla, 2010). Other recent data (Addington et al., 2016) suggested that in community settings length of DUP may be greater than in academic settings (median DUP= 74 weeks; 68% of participants had DUP of greater than six months). Patients with a longer DUP have more symptoms at first presentation, and longer DUP may be associated with a reduced response to antipsychotic medications as measured by severity of global psychopathology, positive and negative symptoms, demoralization, depression, and functional outcomes (Perkins et al., 2005). Neuroimaging studies have also indicated that prolonged untreated illness is associated with more pronounced structural brain abnormalities, whereas this is less prominent earlier in the course of the disorder (Lieberman et al., 2005).

In conclusion, treatment delay can be viewed as a complex behavioural phenomenon moderated by a variety of factors, including illness-related predictors (e.g., mode of onset of psychosis, age at onset, premorbid functioning), patient-related issues (e.g., marital status, premorbid substance use), family-related factors such as family coping, health system-level variables like health insurance status, and environmental factors such as abuse and neglect during childhood/adolescence, and even neighbourhood disorder.

Some studies aimed to examine predictors of longer DUP (Compton & Broussard, 2011). Evidence showed that single marital status, greater negative symptoms, a gradual onset of psychosis, childhood/adolescence maltreatment, living in poverty, poor family functioning, not having health insurance, the family's report of financial problems were significant predictors of longer DUP (Bonstra et al., 2009; Broussard et al., 2013; Compton et al., 2008, 2011; Haar et al., 2016; O'Donoghue et al., 2016; Pek et al., 2006).

Regarding cannabis use, most of the studies examining DUP among cannabis users and non-users reported a shorter DUP in users (Burns, 2012); other data suggested a relationship between substance use and a longer DUP (Broussard et al., 2013). Some recent evidence showed variations in DUP between age of onset of psychosis, highlighting that the DUP among individuals with adolescent-onset psychosis was approximately twice than the length of DUP among individuals with adult-onset (Dominguez et al., 2013). Additionally, DUP among cases with onset of psychosis in adolescence appeared largely different as a function of ethnic group: White adolescents had a median DUP of 454 days, Black 103 days and Asian 28.5 days (Dominguez et al., 2013).

A recent systematic review of 33 observational studies (Penttilä, Jääskeläinen, Hirvonen, Isohanni, & Miettunen, 2014) investigated the relation between DUP and long-term outcomes. Findings indicated a significant association between longer DUP and poorer general symptom outcomes, more severe positive and negative symptoms and failure to achieve remission, as well as decreased social functioning. In addition, there was no significant correlation between DUP and quality of life or hospitalization (Penttilä et al., 2014). The correlation between DUP and poor outcomes appeared stronger in longer follow-up periods (Penttilä et al., 2014). However, the relatively high withdrawal rate in the primary studies and variation in the methods of defining DUP and increased the risk of selection and information bias for this systematic review.

1.8. Beyond psychosis risk, towards a broad model of psychopathology staging

The goal of prospectively identify the prodromal phase is a challenge complicated by the nonspecific nature of prodromal symptoms (McGorry et al., 2009). It is necessary to consider that psychosis is

just one possible outcome of the CHR state: remission, transition to a non-psychotic disorder and persistence of the high-risk state account for most of outcomes at follow-up. One possible explanation is that a relevant part of individuals referred to services for CHR individuals are experiencing transient psychotic experiences (Nelson & Yung, 2009). While they fulfil CHR criteria, these experiences may not underlie impending psychotic illness (Nelson & Yung, 2009). Psychotic experiences often occur in the general population, but they persist in only a small proportion of the people who report them (Lin et al., 2011), and an even smaller proportion develop a psychotic disorder (van Os, Linscott, Myin-Germeys, Delespaul, & Krabbendam, 2009). Rather, psychotic experiences may be related to other forms of psychopathology, such as depression, anxiety and OCD (Wigman et al., 2011; Wigman et al., 2012), which are common in individuals with CHR (Fusar-Poli, Nelson, Valmaggia, Yung, & McGuire, 2014; Salokangas et al., 2012; Yung et al., 2007; Velthorst et al., 2009; Woods et al., 2009). Preliminary research with small samples found high rates of mood disorders at 6-month (Lam, Hung, & Chen, 2005) and 12-month follow-up assessments (Simon & Umbricht, 2010). Anxiety disorders are also common. In a large sample, Addington and colleagues (2011) reported that, of the individuals who did not make transition to psychosis, 29% had a mood disorder and 38% had an anxiety disorder after 1 year. These rates dropped to 15% and 32%, respectively, by 2-year follow-up (Addington et al., 2011). Substance use disorders were also prevalent, but their number was reduced after 2 years.

It is also possible that at-risk individuals who have not transitioned to psychosis continue to experience attenuated psychotic symptoms and meet at-risk criteria (McGorry et al., 2002). Rates of attenuated psychotic symptoms at 1-year follow-up vary from 23% to 42% (Haroun, Dunn, Haroun, & Cadenhead, 2006; Simon & Umbricht, 2010). At 2 year-follow-up, attenuated symptoms have been evident in 35-40% (Addington et al., 2011; McGorry et al., 2002) of at-risk samples and in 25% and 50% at 3 years (Velthorst et al., 2011; Lemos-Goràldez et al., 2009). Continued attenuated symptoms could represent an extended prodrome with transition to psychosis yet to occur. Alternatively, young people with attenuated symptoms may not be prodromal, but their ongoing symptoms may be distressing and disabling and may be comorbid with threshold or subthreshold mood or anxiety disorder. Lin and colleagues (2015) evaluated a large cohort of 226 young individuals at follow-up that had been identified as UHR individuals in the 2-14 years previously at the Personal Assessment and Crisis Evaluation (PACE) clinic. Results indicated that the presence of attenuated psychotic symptoms was significantly associated with mood disorder and with any nonpsychotic disorder over the follow-up period, but not with anxiety and substance use disorders (Lin et al., 2015). The proportion of participants still APS at follow-up that were at or above the threshold for UHR was 28.3% for the entire cohort, those without mood disorder at baseline, 32.8% developed one. Of those with an anxiety disorder at baseline (39.9%), 40.7% experienced persistent or recurrent anxiety. Of

those without anxiety disorder at baseline, 29.5% developed one. Substance use disorders were present at baseline for 21.9% (of the 192 with available baseline substance use diagnoses). Of them, over half (52.4%) showed persistent or recurrent substance use disorder over follow-up. Of those without substance use disorder at baseline, 22.0% developed a substance use disorder. Mood disorders were the most common diagnosis during follow-up. Major depressive disorder was especially common. This was followed by high rates of anxiety disorders, cannabis dependence, and alcohol abuse (Lin et al., 2015).

The CHR state seems to predict much broader outcomes than schizophrenia/psychotic disorders alone, suggesting that there is much more to be "prevented", increasing the public health relevance of the strategy (Fusar-Poli, Yung, & McGorry, 2013). It is important to note that those who do not transition to psychosis are not healthy "false-positives", but are help-seeking individuals suffering from a range of mental and social role functioning problems, and are carrying a poor prognosis for a range of adverse sequela (Yung et al., 2010). A recent meta-analysis (Kaymaz et al., 2012) suggested that although the relative risk for transition to a mental disorder is highest for (rare) psychosis outcomes, the absolute number of preventable cases is much higher for (more common) non-psychotic outcomes, including anxiety and depressive disorders. Fusar-Poli, Yung and McGorry (2013) observed that the CHR paradigm might be extended beyond the context of subthreshold psychotic symptoms in the prediction of psychotic outcomes, but broadly to the context of non-specific subthreshold mental distress predicting both psychotic and non-psychotic outcomes. The authors believed that a wider model should be introduced in early detection and intervention, focusing on a general syndrome of early mental distress requiring non-specific interventions to prevent more severe stages of psychopathology, that may develop in more specific, and relatively treatment-resistant, syndromes later benefits a much narrower population (Fusar-Poli et al., 2013). A picture of this model is presented in Figure 1.3 (source: Fusar-Poli et al., 2013). Early intervention on mental distress therefore may more efficiently prevent transition to mental disorders in general. In comparison, only a small fraction of individuals would benefit from exclusive focus on CHR states and prevention of schizophrenia (Fusar-Poli et al., 2013).

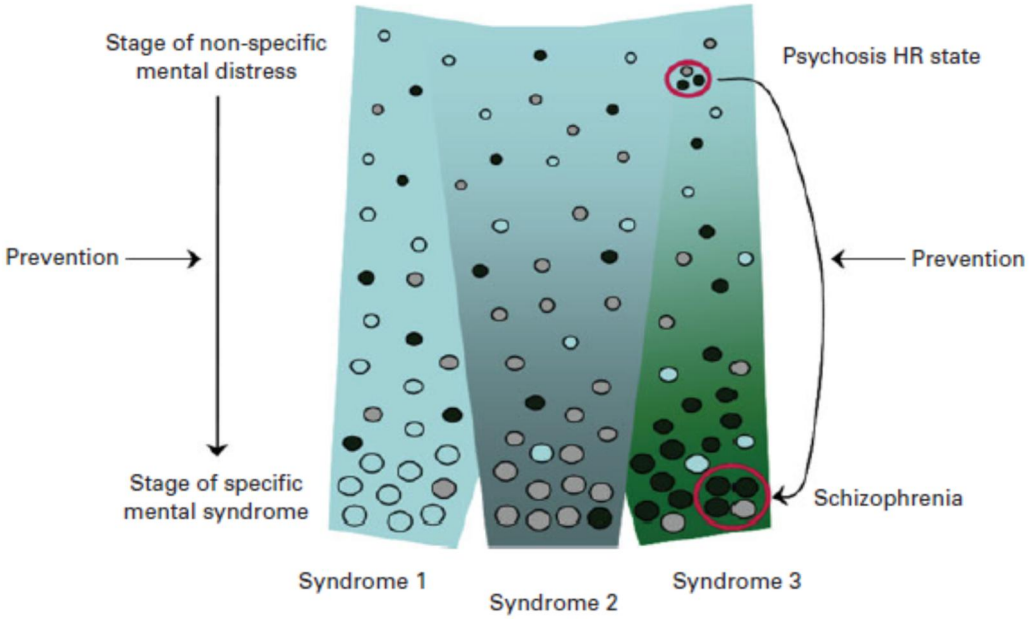


Figure 1.3. Broad model of staging and prevention (source: Fusar-Poli et al., 2013). Psychiatric disorders develop from non-specific states of mental distress gradually developing into full syndromes of anxiety (syndrome 1), depression (syndrome 2) and psychosis (syndrome 3). Note: HR= High risk.

Chapter 2: Correlates of CHR states

2.1. The role of gender

Psychosis is a condition with heterogenous clinical expressions and outcomes, that presents differently in men and women. Gender differences of chronic and first-episode psychosis have long been recognized in the literature (Abel, Drake, & Goldstein, 2010; Køster et al., 2008). Thereby, men and women often require different intervention strategies regarding doses and/or types of medications, staging of interventions, and array of treatments offered (Smith, 2010). Men with psychosis tend to show a higher propensity to negative symptoms, lower social functioning, earlier age at onset and co-morbid substance abuse, whereas women display more affective symptoms (Usall et al., 2003). However, other research found inconsistent evidence about gender-related differences in psychosis symptom expression (Cotton et al., 2009; Morgan et al., 2008). A recent meta-analysis conducted by Fusar-Poli and colleagues (2015) did not evidence gender as a moderator of worse quality of life and functioning in UHR individuals compared with healthy controls.

As suggested by Barajas and colleagues (2015), a variety of factors may account for this inconsistency, including medication status (higher doses of typical antipsychotics contributing to negative symptomatology), diagnostic stringency (use of stricter criteria excluding women with affective symptoms), age at onset (negative symptoms are more prominent in younger men than in younger women), and sampling bias (inadequate sample size or overrepresentation of men).

Recent research examined the role of gender as a potential moderator of the heterogeneity in the clinical manifestations also of UHR states (Amminger et al., 2006). Van Os and colleagues (2009) formulated the continuum hypothesis, which stated that gender differences would be equally present over the entire psychosis continuum, including also the UHR phase. It has been also hypothesized that men and women are vulnerable to different "types" of psychotic disorders or that psychosis develops differently in men and women. In a study (Amminger et al., 2006) evaluating individuals with UHR for psychosis by gender, it was found that female gender was one of the independent significant predictors of affective psychosis, which is in accordance with the higher prevalence of affective disorders in women (Blazer et al., 2014). In contrast, other studies of individuals with UHR for psychosis did not find gender differences in the expression of symptoms (Cocchi et al., 2014).

Willhite and colleagues (2008) investigated gender differences in the clinical symptom presentation of UHR individuals. Sixty-eight UHR individuals were assessed at baseline, and twenty-seven returned for follow-up assessments approximately 6 and 12 months later. Findings did suggest differences in demographic variables, symptoms or functioning at baseline across gender (Willhite et al., 2008). Males were found to have significantly higher levels of negative symptoms and marginally lower levels of functioning when baseline and follow-up time points were considered collectively. Additionally, females reported higher levels of social support at baseline. Differences in negative symptoms were found to mediate differences in functioning between male and female patients (Willhite et al., 2008).

Rietschel and colleagues (2015) investigated gender differences in clinical symptoms and functioning in 239 UHR individuals of which 80 were females. Men displayed more pronounced negative symptoms, higher rates of past substance abuse disorders and higher deficits in social functioning. No gender difference was found for depression, which affected almost 50% of the cohort, or age at onset for the fulfilment of UHR criteria.

Barajas and colleagues (2015) provided a recent systematic review of available evidence on gender related differences in the clinical expression of UHR symptoms. Overall, results indicated that UHR men have more severe negative symptoms than women, being more difficult to detect them across current risk criteria for psychosis focused on positive attenuated symptoms. Inconsistent results were found in relation to transition to psychosis: some studies did not show gender differences and others indicated a greater risk for conversion to psychosis in men (Barajas et al., 2015). It might be suggested that differential precipitating factors exist as a function of gender, which are involved in conversion to psychosis and their identification should be useful in clinical practice (Barajas et al., 2015). Most of the studies suggested that differences between men and women in the expression of psychosis extended across a continuum, from the subthreshold forms of illness to the psychosis onset, mainly in aspects of clinical expression (such as more negative symptoms in men) and social functioning (such as premorbid and psychosocial functioning, worse in men). However, the small number of studies and their significant methodological limitations did not allow for firm conclusions. The limited evidence about cognitive impairment in prodromal phase per gender indicated a differential sex effect that varied by risk status (Barajas et al., 2015).

Few studies with inconsistent findings investigated whether differences related to gender would be extended to those individuals who are in the UHR status. In addition, it is important to note that findings could be complicated by the fact that more women than men seek help for psychological or medical problems (van Os et al., 2009).

In a study on a general population sample, Maric, Krabbendam, Vollebergh., de Graaf and van Os (2003) observed that subclinical positive psychotic symptoms were more prevalent in women, while subclinical negative psychotic symptoms were more prevalent in men. In contrast, in a meta-analysis Van Os and colleagues (2009) found slightly increased odds ratios for men regarding prevalence rates, whereas the incidence rate was minimally higher for women. Spauwen and colleagues (2003) analysed a representative Dutch population sample (aged 17 to 28), with their focus being on possible gender differences before and after the age of 21. They found that the incidence of subclinical psychotic experiences was higher in men aged 17 to 21, but then became comparable with that of women when those men reached 22 to 28 years of age (Spauwen et al., 2003).

In a recent study, as part of the North American Prodrome Longitudinal Study (NAPLS; Walder et al., 2013), no gender differences were found in conversion rates at 2.5-year follow-up (26.5% women; 24.5% men) in UHR adolescents and young adults. Lemos-Giráldez and colleagues (2009) reported that the conversion rate to psychosis was 22.95% in the three-year follow-up period without statistical gender differences (22.5% men versus 23.8% women). In addition, in a study with UHR help-seeking people, Ziermans and colleagues (2011) showed that at the end of the follow-up period (2 years) 15.6% of UHR adolescents had experienced a psychotic transition, with a higher proportion of men. Furthermore, Nordentoft and colleagues (2006) found that, among young adults with a diagnosis of schizotypal disorder, men had a fourfold greater risk for conversion to schizophrenia one year after enrolment when compared to women. However, the findings of this study may not be directly comparable to the entire UHR population, which includes a wider definition of psychosis risk.

On the other hand, Goldstein and colleagues (2011) demonstrated that there are sex-specific patterns of transmission of psychosis. Among fathers with psychoses most offspring who developed psychosis were female (15.2% females versus 3.1% males); in contrast, among mothers with psychosis 18.8% of their male offspring developed psychosis compared with 9.5% of their daughters.

Inconsistency of findings across the studies might be attributed to differences in methodological aspects, including the lack of consensus among the studies in the definition of CHR states as well in the screening tools used to detection the prodromal phase (Barajas et al., 2015).

Consistent significant gender differences have not been found in DUP: it is shorter in women than in men in most of the studies (Thomas & Nandhra, 2009; Thorup et al., 2007) although in other it was shorter in men (Køster, Lajer, Lindhardt, & Rosenbaum, 2008). It is likely that more women seek help for psychological or medical problems than men. In addition, it has been hypothesized this would be dependent on females' higher ability to recognize distress and emotional problems, which may influence a prompt self-referral after onset, and hence a shorter DUP (Galdas, Cheater, & Marshall, 2005). Young males, in particular, are influenced by negative attitudes and beliefs about mental

disorders, with higher stigmatizing attitudes associated with lower use of both clinical and non-clinical sources of support (Eisenberg, Downs, Golberstein, & Zivin, 2009). Additional detection strategies, especially targeted at males, should be developed, not only to improve the quality of research but also above all to prevent the development of more severe forms of the disease.

2.2. CHR across age cohorts

Some research has investigated potential age-related differences in the clinical manifestations of ARMS comparing groups of early adolescents, adolescents and young adults (Schultze-Lutter et al., 2015). Transition risk in help-seeking UHR groups aged 12-18 years appeared lower than those observed in adult or mixed-age samples (Schultze-Lutter et al., 2015; Wells & Tiffin, 2014; Ziermans et al., 2011), which might indicate a lesser predictive accuracy of UHR criteria in this age group (Schultze-Lutter et al., 2015). Additionally, though not assessing the UHR criteria with specific instruments, community studies of children and adolescents found high prevalence rates of APS, particularly hallucinations, with a spontaneous remission in approximately 75% of cases (Rubio et al., 2012).

Fusar-Poli and colleagues (2012) conducted a meta-analysis of 27 longitudinal studies (n= 2502) investigating predictors of psychosis transition in CHR samples. Findings from meta-regressions indicated that age cohort moderated conversion probability, showing a modest yet significant increase of transition risk with increasing age of patients at CHR (β=0.07; 95% CI: 0.05-0.09; Q=27.94; p<.001) (Fusar-Poli et al., 2012).

More recently, Gerstenberg and colleagues (2016) examined the prevalence of BS and APS in 13- to 35-year-old individuals seeking help in an early recognition program. Participants presenting APS criteria were compared with participants meeting only BS criteria across different characteristics. Co-occurrence of BS and APS was compared across 13–17, 18–22 and 23–35 years age groups. Compared to BS, APS status was associated with younger age (18.30 ± 5.0 vs 23.20 ± 5.60 years) with age-related differences in the prevalence of APS (ranging from 80.30% in 13- to 17-year-olds to 33.3% in 23- to 35-year-olds). Within the group with APS, fewer adolescents fulfilled combined risk criteria of APS and BS compared to the older age groups (Gerstenberg et al., 2016).

Other authors (Schimmelmann, Michel, Martz-Irngartinger, Linder, & Schultze-Lutter, 2015) investigated UHR symptoms in a large sample of individuals aged 8-40 years. Individuals with APS were younger than those without APS. Compared to persons aged 20-24 years, those aged 8-12 and 13-15 years were more likely to report APS, while all other age groups (i.e., 16-17, 18-19, 25-29, 30-40) were not. When only perceptual abnormalities were considered, odds ratios in individuals aged

8-12 and 13-15 increased while no effect was found in the adult groups and in the 16-17-year olds. Conversely, when only non-perceptive APS were considered, the model was non-significant, suggesting that individuals across all age groups were equally likely to report non-perceptive APS (Schimmelmann et al., 2015). When the UHR onset/worsening requirement was considered, the age effects on the prevalence of APS increased. Again, only individuals aged 8-12 and 13-15 years were more likely to meet the requirement, as compared to the 20-24-year-olds (Schimmelmann et al., 2015).

2.3. Substance use and CHR status

Several epidemiological studies have reported associations between substance use, generally cannabis, and increased risk of developing frank psychotic symptoms (Kuepper et al., 2011; Moore et al., 2009). Alcohol was the next most frequently reported kind of substance use behaviour with frequency rates ranging between 17% and 44% across the studies (Auther et al., 2012; Corcoran et al., 2008; Dragt et al., 2012; Ruhrman et al., 2007). In relation to diagnoses of alcohol abuse, rates ranged from 10% of samples to 30% (Corcoran et al., 2008; Kristensen & Cadenhead, 2007; Ruhrman et al., 2010). Some studies evidenced that prevalence of tobacco/nicotine lifetime use ranged from 16% to 34% (Auther et al., 2012; Kristensen K, Cadenhead, 2007). However, the available limited data showed that use of substances other than cannabis, alcohol and tobacco/nicotine, is very heterogenous in CHR populations, being present only in a CHR subgroup. The use of other substances was also noticeably lower compared with cannabis: the use of hallucinogens was reported as the highest (7% - 19%) (Auther et al., 2012; Phillips et al., 2002).

Addington and colleagues (2014) conducted a systematic review of 10 longitudinal cohort studies investigating the role of substance use in conversion to psychosis. Only two studies indicated a significant association between cannabis and nicotine use and transition to psychosis within one year (Corcoran et al., 2008; Kristensen & Cadenhead, 2007). In the study conducted by Kristensen and Cadenhead (2007), 12% of 48 CHR individuals made the transition to psychosis, with 5 of these individuals meeting criteria for current cannabis abuse, thus showing a significant association between cannabis use and conversion to psychosis. However, because this study was also examining psychophysiological and neuropsychological variables, individuals with current cannabis dependence had been excluded from the study to avoid the risk of affecting the psychophysiological and neuropsychological test measures.

In a large sample (n= 291), Cannon and colleagues (2008) highlighted a transition rate of 35% during a 2.5-year follow-up and reported that a history of any substance use disorder was one of five

predictors of conversion to psychosis. Another study (Auther et al., 2012) did not find any association between age of cannabis onset and age of psychosis onset. However, two studies (Dragt et al., 2010; Korver et al., 2010) found that a younger age of onset of cannabis use resulted in a younger age of psychotic symptom onset.

One review on predictors of psychosis in UHR individuals showed that a history of substance abuse was one of the risk factors associated with an increased probability of developing psychosis (Fusar-Poli et al. 2013). However, findings from subsequent research and reviews appeared inconsistent (Addington et al., 2014; Buchy, Perkins, Woods, Liu, & Addington, 2014; Dragt et al., 2012), despite a larger number of studies to date has not reported a role for substance use in later conversion to psychosis.

Kraan and colleagues (2015) performed a systematic review of seven prospective studies reporting lifetime cannabis use in UHR individuals (n = 1171). Of these studies, five also examined current cannabis abuse or dependence. Lifetime cannabis use was not significantly associated with transition to psychosis (OR= 1.14, 95% CI: 0.856–1.524, p= 0.37). A second meta-analysis yielded an OR of 1.75 (95% CI: 1.135–2.710, p< 0.01), indicating a significant association between current cannabis abuse or dependence and transition to psychosis (Kraan et al., 2015).

2.4. The role played by stressful life events

Some research focused on stressful life events in individuals at CHR and their role in transition to psychosis. Kraan and colleagues (2014) performed a series of meta-analyses investigating prevalence rates of childhood traumatic events and recent life events in CHR groups compared with healthy groups. Findings showed that the prevalence scores of childhood trauma were significantly higher in CHR patients (86.8%: 95% CI 77%–93%) than in healthy controls (47%-60%) (Kraan et al., 2014).

Furthermore, it has been observed that CHR participants experience their first trauma at an earlier age compared to healthy controls, and that both the incidences of trauma, and the age at which trauma occurred were significant predictors of having a CHR status (Russo et al., 2014). On the other hand, Sahin and colleagues (2013) reported that not only is the frequency of childhood trauma higher among high-risk participants compared to healthy controls, but also that childhood trauma was related to baseline severity of positive symptoms. Others have found that the intensity of perceptual abnormalities are higher among groups that have experienced physical abuse and other trauma compared to those without a history of trauma (Velthorst et al., 2013) and that CHR participants who report experiencing childhood trauma have poorer premorbid functioning compared to controls (Tikka et al., 2013). Yung and colleagues (2015) recently found that childhood maltreatment, as

assessed by the Childhood Trauma Questionnaire (Bernstein et al., 2003), was a significant predictor of poor functioning in CHR groups, as well as those who eventually transition.

Prevalence rates of trauma among CHR appeared consistent with the reported prevalence rates of 85% in patients diagnosed with schizophrenia (Larsson et al., 2013). However, in contrast with hypotheses, CHR patients experienced a significantly less number of life events compared with healthy controls; yet, this series of meta-analyses was based only on a narrow pool of studies (Larsson et al., 2013).

Other research focused on perceived discrimination among the CHR sample (n= 540) recruited in the of the NAPLS-2 study. CHR individuals endorsed significantly more perceived discrimination compared to healthy controls, and this was associated with negative schemas about the self and others (Saleem et al., 2014). Subsequently, a recent study investigated the role of discrimination in an enriched sample of 764 CHR individuals recruited in the NAPLS (Stowkowy et al., 2016). Results showed that the CHR group reported having experienced significantly more trauma, bullying, and endorsed more items on perceived discrimination relative to controls. Trauma and bullying were not found to contribute to the prediction of psychosis; yet, individuals who reported higher levels of perceived discrimination had a greater chance of conversion to psychosis (Stowkowy et al., 2016).

2.5. Schizotypy in CHR status

Schizotypy is a clinical comprised of three factors, which broadly correspond to the positive, negative and disorganized dimensions of schizophrenia, respectively (Nelson et al., 2013). The positive dimension is the Cognitive-perceptual factor, which includes magical thinking, unusual perceptual experiences, ideas of reference and paranoia (Nelson et al., 2013). Another Disorganized factor consists of odd behaviours and weird speech. The third one is the Interpersonal factor, which resembles the negative dimension of schizophrenia and includes constricted affect, social anxiety, lack of close personal relationships, and suspiciousness (Nelson et al., 2013).

Debbané and colleagues (2015) conducted a review of 18 prospective studies examining the evidence for a link between schizotypal traits and conversion to psychosis in 4 different types of samples: general population, clinical risk samples according to UHR and/or BS criteria, genetic (familial) risk, and clinical samples at-risk for a nonpsychotic schizophrenia-spectrum disorders. Four samples (n=7282) were included. All studies consistently showed that schizotypal dimensions significantly predicted later development of either psychotic disorders or schizophrenia spectrum disorders (Debbané et al., 2015). More specifically, findings revealed that the positive dimension was mainly related to the later onset of psychosis, while the negative dimension (especially anhedonia) was rather

selectively associated with the emergence of nonpsychotic schizophrenic-spectrum disorders. Information on the disorganization dimension was missing since none of these general population studies had assessed this dimension (Debbané et al., 2015).

Irrespective of whether self-report questionnaires or clinical semi-structured interviews were adopted in the assessment of schizotypal traits, there was some, though not consistent, indication that schizotypal dimensions could be involved in the transition to psychosis in individuals already identified at CHR prior to and independently from schizotypy assessment.

Overall, contrary to the evidence drawn from population-based samples, CHR studies showed that the positive dimension of schizotypy was of poor value in terms of increasing the predictive accuracy of psychotic disorders in samples already considered to be prone to psychosis for UHR and/or BS criteria (Debbané et al., 2015). Rather, when schizotypy was differentially assessed, the interpersonal, negative dimension seemed to explain additional variance and to assist the detection of converters to psychosis (Seeber & Cadenhead, 2005). However, except for one study on CHR patients (Ruhrman et al., 2010), all studies had relatively short follow-up time that might not have been sufficient to detect onset of psychosis in patients with more pronounced schizotypy.

Three studies investigated the development of psychosis in patients with a clinical picture of schizotypy, such as a schizotypal or schizoid personality disorder, involved follow-up assessments for 2–20 years but did not provide information on psychometric schizotypy dimensions (McGlashan, 1984; Nordentoft et al., 2006; Wolff, 1991).

In the study by Nordentoft and colleagues (2006) on adult in- and outpatients diagnosed with schizotypal personality disorder, the conversion rates to a psychotic disorder varied between 25% and 48% (Nordentoft et al., 2006). Suspected schizotypal personality disorder in children however seldom led to the later development of a psychotic disorder (only 6.25%). Despite a relation between schizotypal personality disorder and psychosis risk is clearly indicated, future studies of this clinical group should therefore provide dimensional scores of schizotypy to clarify the possible patterns of associations between schizotypal personality disorder and emerging psychotic disorders.

Four studies (Carter, Parnas, Cannon, Schulsinger, & Mednick, 1999; Erlenmeyer-Kimling et al., 1993; Johnstone, Ebmeier, Miller, Owens, & Lawrie, 2005; Shah et al., 2012) on samples at genetic risk for psychosis included a total of 637 offsprings (first- or second-degree relatives) of patients diagnosed with schizophrenia, and covered follow-ups between 8 and 25 years. Like general population studies, schizotypy dimensions were found to be significantly related with the later onset of psychosis in genetic high-risk samples (Carter et al., 1999). However, no clear pattern of associations between schizotypal dimension and psychotic disorders emerged. Yet, substantially different assessment methods were employed over the 20-year span covered by these studies (1993

and 2012) that may have contributed to the heterogeneity of findings. The most recent study by Shah and colleagues (2012) underscored the pre-eminence of schizotypy amongst a variety of predictive risk factors from etiological (degree of relatedness to family member with schizophrenia: genetic risk), to environmental (cannabis use, obstetric complications, welfare), and cognitive (intelligence quotient, perseveration, verbal fluency) assessments. In a multivariate structural equation model, only baseline ratings on the Chapman scales (Chapman, Chapman, & Kwapil, 1995) (Magical Ideation, Perceptual Aberration, and Social Anhedonia Scales) were directly and positively related to conversion to psychotic disorders (Shah et al., 2012).

Therefore, Debbané and colleagues (2015) hypothesized the interactions between dimensions of schizotypy, clinical expressions of schizotypy, symptomatic CHR criteria, and overt psychosis. The model is presented in Figure 2.1. Schizotypal traits during adolescence could represent a developmental link between early risk factors and later development of psychotic disorders (Debbané et al., 2015). Specifically, consistent with Meehl's hypotheses (Meehl, 1962), it was assumed that a distribution of schizotypal characteristics in the general population from absence to clinically significant manifestations in terms of schizotypal personality disorder to the most extreme psychotic expression, with increasing severity of schizotypy being associated with higher levels of distress and/or functional impairment. APS might appear at as a clinical manifestation or as an exacerbation of the underlying schizotypy, in particular of features of the cognitive-perceptual and, though to a lesser degree, the disorganization dimension (Debbané et al., 2015). The occurrence of APS might be triggered by aberrations in information processing at neurobiological level, that are perceived and expressed as basic symptoms, in particular of cognitive-perceptive basic symptoms and cognitive disturbances (Debbané et al., 2015).

Thus, CHR individuals with high levels on schizotypy measures might need for a tailored adaptation early intervention approach, including techniques which should not only address positive symptoms of schizotypy or APS but also aberrant information processing style of reality (Debbané et al., 2015). Moreover, standard care interventions might not be optimally suited to address the needs of patients with pronounced negative features of the interpersonal dimension not captured by CHR criteria whose personality traits are characterized by enduring social withdrawal and poverty of interpersonal relationships (Debbané & Barrantes-Vidal, 2015). However, more longitudinal research on the complex relationships between early and intermediate risk indicators for psychosis is needed to examine this assumption.

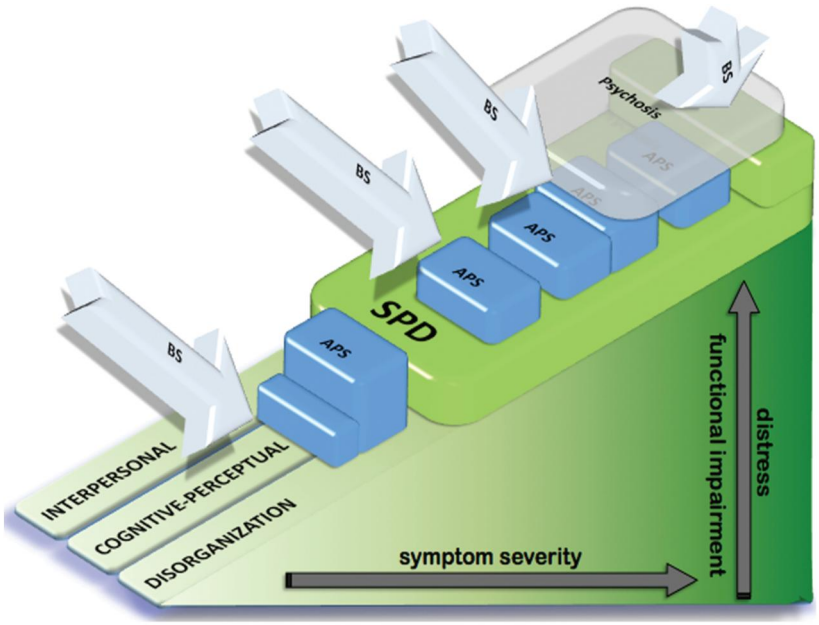


Figure 2.1. Model of the assumed relationship and interactions between dimensions of schizotypy, clinical expressions of schizotypy, symptomatic CHR criteria, and overt psychosis (source: Debbané et al., 2015)

2.6. Emotion recognition and regulation in CHR status

Emotion recognition is the ability to recognize other people's feelings (Brüne, 2005). Although most of studies observed deficits in emotion recognition in CHR individuals when compared to healthy controls (Amminger et al., 2012; Comparelli et al., 2013; Kohler et al., 2014; van Rijn et al., 2011; Wölwer et al., 2012), mixed findings have been reported, with some studies not evidencing a deficit (Gee et al., 2012; Seiferth et al., 2008; Thompson et al., 2012) and others showing selective deficits in a sub-set of negative emotions (Amminger et al., 2011). Those studies that did not report a significant deficit in emotion recognition tended to have smaller samples, typically less than 20 participants.

Compared to healthy controls, CHR individuals had deficits in social cognition similar to those observed in patients at the first episode of psychosis and patients who have a more chronic course of schizophrenia (Green et al., 2012). Such deficiencies were reported in several domains of social cognition, such as theory of mind, emotion recognition, social perception and attributional style (Addington & Barbato, 2015).

Several studies, using a variety of tasks, have shown that theory of mind, is impaired among CHR individuals (Hur et al., 2013; Thompson et al., 2012), although few studies have not observed this outcome (Brüne et al., 2011; Stanford et al., 2011). In most of these studies, participants were asked to read short stories or cartoons and perform a first or second order mental state attribution, which

means inferring the mental state of a character in the story, or inferring the character's beliefs about another character.

Another important aspect of theory of mind is the ability to process counterfactual information, for example detecting sarcasm or lies. In everyday social interactions, sarcasm and lie detection entails going beyond the literal meaning of a message by using social cues. Most studies examining emotion recognition in CHR individuals have focused on prosody and facial affect processing (Brüne, 2005). The only study to date examining how CHR individuals process counterfactual information reported impaired detection of sarcasm and lies (Green et al., 2012).

Social perception generally refers to the awareness of cues and rules that occur in social situations. Three studies have examined social perception in individuals at CHR as compared to healthy controls (Couture et al., 2008; Thompson et al., 2012), although they investigated different aspects of social perception. Findings from the PREDICT study (Couture et al., 2008) showed that CHR individuals had biased complex social judgements compared to healthy controls and to a help-seeking control sample (Healey et al., 2013). Green and colleagues (2012) looked at perception of social relationships and demonstrated poorer performance for the CHR group compared to the control group. Thompson and colleagues (2012), using the Managing Emotions branch of the Mayer–Salovey–Caruso Emotional Intelligence Test (MSCEIT; Mayer et al., 2002), did not evidence that their CHR sample had impairment. Although the Managing Emotions section of the MSCEIT includes questions about perception of social or interpersonal situations, the MSCEIT is usually considered a measure of emotional intelligence, that is, the ability to understand and manage emotions and to problem-solve on the basis of them (Mayer et al., 1999), and therefore may not necessarily measure social perception.

Attributional style is an individual's tendency when inferring the cause of an event. A few studies have looked at attributional style in CHR individuals (An et al., 2010; DeVylder et al., 2013; Thompson et al., 2013). Although DeVylder and colleagues (2013) did not evidence an attributional bias in individuals at CHR compared to controls, An and colleagues (2010) reported a perceived hostility bias and Thompson and colleagues (2013) found a significantly more externalized locus of control for the CHR group compared to controls. However, it should be noted that most of these studies were under-powered due to small sample sizes. More recently, in a large multi-site cross-sectional cohort study, the North American Prodromal Longitudinal Study-2 (NAPLS-2; Barbato et al., 2015), large groups of CHR individuals and healthy controls completed measures of social cognition, such as The Awareness of Social Inference Test (TASIT; McDonald et al., 2006), measures of theory of mind, facial emotion recognition, and social perception, respectively. Results indicated that social cognition was not associated with positive and negative symptom severity, but it was associated with age and intelligence quotient. Individuals at CHR demonstrated poorer performance

on all measures of social cognition. However, after controlling for age and intelligence quotient, the group differences remained significant for measures of theory of mind and social perception, but not for facial emotion recognition. In conclusion, theory of mind and social perception seemed to be impaired in individuals at CHR for psychosis.

However, in the current literature there is still a lack of longitudinal studies investigating the role of emotion recognition as potential predictors of transition to psychosis.

2.7. The role of comorbidity in CHR status

Although the rates of transition to psychosis have declined in recent years, leading to debates on the validity of the UHR state and legitimacy of its treatment (Fusar-Poli et al., 2013), studies have highlighted the existence of a significant proportion of nonpsychotic psychiatric comorbidity in the UHR population, where participants fulfil the criteria for both UHR and at least one nonpsychotic mental disorder (Fusar-Poli et al., 2014a; Hui et al., 2013; Kwon et al., 2012; Salokangas et al., 2012; Woods et al., 2009). Additionally, comorbidity has been associated with lower global functioning and more severe psychopathology (Fusar-Poli et al., 2014a). Comorbidity rates in UHR populations are comparable to those in schizophrenia (Buckley et al., 2009). However, evidence that comorbidity might influence transition to psychosis has been equivocal (Fusar-Poli et al., 2014; Salokangas et al., 2012).

Lim and colleagues (2015) followed for one year 163 CHR individuals who were assessed through the CAARMS. Baseline comorbidity patterns showed that about 80% of participants recorded at least one lifetime comorbid diagnosis while about 50% had at least one current comorbid diagnosis. The most frequent diagnoses were depressive and anxiety disorders. Within these categories, the most common depressive and anxiety disorders were major depressive disorder and obsessive–compulsive disorder (OCD), respectively (Lim et al., 2015). Fourty-two percent of participants reported one lifetime comorbid diagnosis, whereas 37% reported more than one diagnosis. Thirty-two participants reported one current comorbid diagnosis and 17% reported more than one current comorbid diagnosis (Lim et al., 2015). In addition, the authors found that UHR individuals with comorbidity had more severe symptoms, higher distress and lower functioning with no differences in general cognition (Lim et al., 2015). Lower functioning was associated with current comorbidity. There were no differences in the comorbidity rates between those who developed psychosis (6.7%) after one year and those who did not.

2.8. Cognitive biases in CHR status

A great body of research highlighted the role of cognitive biases as vulnerability and maintenance factors in schizophrenia, particularly delusions **(**Bell et al., 2006**;** Moritz & Woodward, 2007). Patients rarely are aware when they gather data and make decisions based on biases (Bell et al., 2006). In experimental research, Freeman and colleagues (2006) reported that despite adopting a marked data-gathering bias, patients viewed themselves as reflective decision-makers able to adequately weigh the pros and cons of different perspectives. Moritz and Woodward (2007) developed a metacognitive training for patients with schizophrenia aimed at reducing the most powerful biases playing a role in the symptoms.

Growing attention has been dedicated to the recognition of cognitive biases also in ARMS conditions (Broome et al., 2007). Improvement of the patients' awareness can be an important target of the psychological intervention with individuals at CHR (van der Gaag et al., 2013).

2.8.1. Jumping to conclusions

Cognitive models propose that psychotic symptoms arise from faulty appraisals of anomalous or ambiguous experiences, driven by emotional processes and cognitive biases (Garety et al., 2007; van der Gaag, 2006). A key contributing factor to the formation of these appraisals is a ''data gathering'' or Jumping to Conclusions (JTC) bias (van Dael et al., 2006), a tendency to use less information to reach a decision. This can be studied using a probabilistic reasoning task, in which a participant guesses which of the two jars a series of coloured beads is drawn from. Compared with healthy controls, patients with psychotic disorders tend to make their decision after seeing fewer beads, demonstrating a so-called JTC bias (Moritz & Woodward, 2005), and this bias is related to the intensity and conviction of delusional ideation (Fine, Gardner, Craigie, & Gold, 2007).

Thus, it was hypothesized that JTC tendencies and misattribution of the source of self-generated material could increase the likelihood that subclinical psychotic experiences will develop into a psychotic disorder (Garety et al., 2007). It is also present in the first-degree relatives of patients with schizophrenia, in non-clinical delusion-prone participants, and in people with a ARMS for psychotic disorders tend to make their decision after seeing fewer beads, demonstrating a so-called JTC bias (Broome et al., 2007; Liney, Peters, & Ayton, 1998; van Dael et al., 2006), and this bias is related to the intensity and conviction of delusional ideation (Fine et al., 2007).

In a study by Broome and colleagues (2007), 35 UHR individuals and 23 healthy volunteers participated in a modified version of the "beads" reasoning task with different levels of difficulty.

When task demands were high, the at-risk group made judgements on the basis of less information than the control group. Within both groups, JTC was directly correlated with the severity of abnormal beliefs and intolerance of uncertainty. In the UHR group it was also associated with impaired working memory, whereas in the control group poor working memory was associated with a more conservative response style (Broome et al., 2007).

A self-recognition deficit such as faulty appraisal of ambiguous auditory verbal experiences, is thought to contribute to auditory verbal hallucinations (Allen, Aleman, & McGuire, 2007), and can be studied using an on-line Verbal Self-Monitoring (VSM) paradigm. The VSM task requires participants to make source judgments (i.e. self/other) about externally presented distorted speech trials. Relative to healthy controls, individuals with schizophrenia, affective psychosis or a ARMS (Johns, Gregg, Allen, & McGuire, 2006) tend to misidentify their own distorted speech as being non-self in origin, particularly if they experience auditory verbal hallucinations (Johns & McGuire, 1999). In a prospective study, Winton-Brown and colleagues (2014) followed twenty-three individuals with ARMS for about a mean of 30 months administering measures of clinical symptoms and cognitive tasks that engage VSM and probabilistic reasoning. Findings showed a relation between JTC performance and PANSS delusion and hallucination item scores at follow-up, despite it appeared only at a trend level. This supported increasing evidence that the JTC bias relates most specifically to delusion. In contrast, VSM task performance did not relate to symptoms either at follow-up nor in terms of the respective longitudinal changes between baseline and follow-up. Neither task performance at baseline nor the change in performance over time was significantly related to the later onset of psychosis. Because the number of participants who developed psychosis was small (n = 5), the possibility that this was related to limited statistical power, cannot be excluded. There was a trend for more conservative baseline (i.e. normal) JTC scores to relate to greater functional status at follow-up, and baseline PANSS scores also related to GAF at follow-up. However, these associations were not significant when considered in a multivariate regression model, which identified baseline anxiety ratings as a significant independent predictor: individuals who had low levels of anxiety at baseline were more likely to have a good functional outcome (Winton-Brown et al., 2014). In addition to the low power, a limitation of the study was the use of a very heterogenous follow up time point (mean follow up= 31 months, SD= 19).

2.8.2. Negative expectation bias

Subthreshold negative symptoms, such as lack of motivation starting new activities and feelings of emptiness, and impaired cognitive performances, such poor capacity to plan, are common among

people suffering from ARMS. Furthermore, when they experience initial cognitive deficits such as poor sustained attention and memory, they can lose faith in themselves. Grant and Beck (2009) have found a relation between negative symptoms defeatist beliefs. In ARMS individuals, it has been shown that negative performance beliefs are endorsed to a greater extent than in healthy controls. These beliefs were associated with negative symptoms independently from depression and positive symptoms (Perivoliotis, Morrison, Grant, Frech, & Beck, 2009). Beck and colleagues identified a series of six beliefs that are defined as follows:

- Social aversion: "I attach very little importance to having close friends";
- Negative expectancies about performance: "If you cannot do something well, there is little point in doing it all";
- Low expectancies for pleasure: "It is more work than it is worth";
- Low expectancies for success: "I am not going to be enough";
- Low expectancies owing to stigma: "What do you expect? I am mentally ill";
- Beliefs about limited resources: "I do not have enough energy".

Such beliefs would perpetuate disengagement as a safety behaviour and lead to a worse outcome and a diminished social functioning.

2.8.3. Metacognitive factors

Metacognitive beliefs may guide information and attention processes, increasing affective and symptomatic reactions to stressful events. Cognitive self-consciousness (CSC; i.e., a preoccupation with one's thoughts) may increase awareness of metacognitive beliefs, potentially triggering the onset of psychotic symptoms. Morrison, French and Wells (2007) administered the Metacognition Questionnaire (MCQ; Wells & Cartwright-Hatton, 2004) to 73 patients with a psychotic disorder, 43 UHR individuals, 188 healthy controls. Results indicated that patients with psychotic diagnoses and those at risk scored higher on metacognitive belief dimensions than non-patients. Patients with psychosis showed higher positive metacognitive beliefs than the CHR patients, indicating a greater range of unhelpful metacognitions overall, when compared to non-patients (Morrison et al., 2007).

In an experimental study (Palmier-Claus, Dunn, Taylor, Morrison, & Lewis, 2012) the role of metacognitive beliefs as moderator of affective and symptomatic reactions to stress in UHR individuals was analysed. A small group of individuals with ARMS completed a self-report diary when prompted by an electronic wristwatch several times each day for 6 days (experience sampling).

Metacognitive beliefs moderated the association between affective, but not symptomatic, responses to social stress. CSC preceded the subsequent occurrence of hallucinations in individuals who reported strong beliefs about the need to control their thoughts (Palmier-Claus et al., 2012).

2.8.4. Self-monitoring bias

Verbal self-monitoring refers to the bottom-up cognitive process of self-monitoring. However, the paradigm also measures the top-down decision-making process of appraising ambiguous sensory stimuli (Johns et al., 2010). Both cognitive processes seem to be involved in the external attribution of inner speech and the generation of auditory hallucinations.

Cognitive models of auditory hallucinations propose that they arise from a deficit or bias in source monitoring, whereby verbal thoughts are not recognized as self-generated and are misidentified as externally generated voices (Keefe et al. 1999). Patients with schizophrenia showed poor self-monitoring on a range of cognitive and motor tasks, and this impairment seems to be more marked in patients who have current positive symptoms (Farrer & Franck, 2007). Self-monitoring of speech in patients with schizophrenia has been examined in a series of studies using a paradigm in which online auditory verbal feedback is manipulated while participants speak out loud (Johns et al. 2006). If defective self-monitoring contributes to the development of hallucinations and other positive symptoms, then this impairment should be present in individuals who are at high risk of developing psychosis, before the onset of severe symptoms.

Two previous studies have examined self-monitoring in CHR groups, with mixed results (Vermissen et al., 2007a, 2007b). On a task measuring self-monitoring of actions, Versmissen et al. (2007b) found poor self-monitoring in a genetic high-risk group (first-degree relatives of patients with psychosis) and a psychometric UHR group. They also found a positive association between self-monitoring errors and level of delusional ideation, but no relationship between errors and severity of hallucinations. However, Versmissen et al. (2007a) found no evidence of impairments in the same UHR groups using a shortened version of the verbal self-monitoring task that has been associated with deficits in patients with schizophrenia.

Impaired verbal self-monitoring is evident in people with ARMS, although the deficit seems to be less marked than in patients with schizophrenia (Johns et al., 2010). In an experimental study, Johns and colleagues (2010) tested 31 individuals with ARMS and 31 healthy volunteers. Participants read single adjectives aloud while the source and pitch of the online auditory verbal feedback was manipulated, then immediately identified the source of the speech they heard (Self/Other/Unsure). Response choice and reaction time were recorded. When reading aloud with distorted feedback of

their own voice, ARMS participants made more errors than controls (misidentifications and unsure responses). ARMS participants misidentified the source of their speech as "Other" when the level of acoustic distortion was severe, and misidentification errors were inversely related to reaction times (Johns et al., 2010).

2.9. Biomarkers of CHR status

A variety of candidate biomarkers has been recently identified, suggesting that the CHR status is associated with brain abnormalities at the neuroanatomical, functional, and chemical levels (Allen et al., 2012; Bodatscht et al., 2011; Fusar-Poli et al., 2011; Fusar-Poli, 2012, Fusar-Poli et al., 2012; Schmidt et al., 2013). The longitudinal investigation of individuals at high-risk for schizophrenia using structural magnetic resonance imaging (MRI) has provided insights into brain changes during the period of transition from ARMS to the psychosis state (Pantelis et al., 2005). Overall, these alterations seem to be similar to, but less severe than those in the full-blown disease (Fusar-Poli et al., 2007). More specifically, MRI studies comparing UHR individuals with a subsequent full-blown illness to those without a later disease transition showed reduced grey matter in prefrontal, temporal, cingulate, insular, and subcortical brain structures in the former group (Smieskova et al., 2010).

Growing evidence suggested also that reduced size of the hippocampus was a potential premorbid marker of illness, particularly reduced left hippocampal volume identified in first-episode psychosis and bilaterally smaller hippocampi in patients diagnosed with schizophrenia (Velakoulis et al., 1999). In a small cross-sectional study combining UHR individuals (both those converting to psychosis with those not converting), this group had smaller volumes than a healthy comparison population (Phillips et al., 2002). However, subsequent analyses of the high-risk group by psychosis outcome found that those individuals who subsequently developed psychosis had normal hippocampal volumes, while those who did not develop a psychosis had reduced volume of the hippocampus (Phillips et al., 2002). In a larger study involving 473 participants, comprised of 89 patients with chronic schizophrenia, 162 with first-episode psychosis, 135 UHR patients and 87 healthy controls (Velakoulis et al., 2006). In addition to hippocampal volumes this study included separate estimates of amygdala volumes. Patients with chronic schizophrenia had bilaterally smaller hippocampi but normal amygdala volumes, while first episode schizophrenia patients had smaller left hippocampal volumes and normal amygdala volumes. The hippocampal/amygdala volumes of first-episode schizophreniform patients and both UHR groups did not differ from those of controls. In contrast, patients with affective psychoses exhibited larger amygdalae but normal hippocampal volumes. Thus, in first-episode and established schizophrenia patients, the hippocampi were reduced but amygdalae were normal, while

in affective and other psychoses the hippocampi were normal and amygdalae were enlarged. These findings are broadly consistent with the meta-analyses mentioned above in patients with established schizophrenia (Steen et al., 2006), which have identified reduced hippocampal volume as one of the more robust structural imaging findings in schizophrenia.

In a voxel-based morphometry imaging study, increasing duration of illness was significantly associated with loss of volume in the right medial temporal, medial cerebellar and bilateral anterior cingulate grey matter regions (Velakoulis et al., 2002). Different from data obtained on patients with schizophrenia (Heckers, 2001), the UHR group as well as first-episode patients did not exhibit any reduction on magnetic resonance spectroscopy in hippocampal N-acetylaspartate, compared with controls, which is a marker of neuronal integrity (Wood et al., 2003), Therefore, these findings were at odds with the dominant neurodevelopmental theories of schizophrenia that, on the basis of an early and static neurodevelopmental disturbance, predict that patients at all stages of schizophrenia should exhibit the same degree of structural change (Weinberger & Marenco, 2003). However, these studies had the limitation of a cross-sectional design.

A voxel-based morphometry study examined brain structural changes over the transition phase to illness (Pantelis et al., 2003). Twenty-one of the 75 UHR individuals who had a baseline magnetic resonance scan were followed up with a second scan, either immediately post-psychosis (UHR-P group) or after at least 12 months had elapsed for those not developing psychosis (UHR-NP group). Comparison between baseline and follow-up scans for the two groups indicated that in the UHR-P group, four regions of the left hemisphere were reduced, involving a left inferior frontal region, a left medial temporal region (that included the parahippocampal gyrus), a left inferior temporal region, and the mid-cingulate bilaterally. Both UHR-P and UHR-NP showed a reduction of grey matter volume in the left cerebellum (Pantelis et al., 2003). It should be noted, however, that there are a number of methodological limitations to this study, including small sample size in the longitudinal arm, the use of relatively thick slices that may hinder detection of subtle changes, the use of voxel-based morphometry that has been criticized as not optimal for structural imaging (including inadequacy in dealing with registration of brains between individuals due to variation in cortical folding), the lack of a control group and possible medication related effects (Crum, Griffin, Hill, & Hawkes, 2003). Despite these limitations, this was the first study to demonstrate progressive brain structural changes (grey matter loss) in individuals who were developing active psychotic illness followed longitudinally from before illness onset.

In a subsequent voxel-based morphometry follow-up study, Job and colleagues (Job et al., 2005) examined brain changes over two years in young high-risk adults compared with healthy controls. The CHR group exhibited significant reductions in grey matter density in temporal lobe, right frontal

and right parietal lobes, which were not observed in the healthy comparison group. Comparing those individuals with transient or isolated psychotic symptoms versus those with no such symptoms showed progressive changes in left temporal lobe regions, including the hippocampus (Job et al., 2005). CHR individuals who later developed schizophrenia (3 at time of second scan, 5 developing schizophrenia subsequent to the second scan) showed reductions in the left inferior temporal lobe, left uncus and right cerebellum. Importantly, these participants were all neuroleptic-naïve, indicating that medication did not explain these changes.

2.9.1. Dopamine sensitization

Laruelle, Kegeles and Abi-Dargham (2003) suggested that frontal dopamine activation can inhibit dopamine sensitization in the medial brain. Sensitization regards the process by which a cellular receptor becomes more likely to respond to a stimulus. Thus, dopamine sensitization refers to the process by which the dopamine system responds fiercely to the release of dopamine. Abi-Dargham and colleagues (2000) proposed that D2 receptor blockade, if sustained, might allow for an extinction of this sensitization process with potential re-emergence upon treatment discontinuation.

A biological substrate of the salience network may be anterior cingulate cortex and anterior insula. Reduced activation in these areas is shown to be related to reality distortion (Palanyappanan et al., 2010; Palanyappan et al., 2013).

Howes and Kapur (2009) proposed that the locus of dopamine deregulation is primary at the presynaptic dopaminergic control level and that this deregulation is the final common pathway to psychosis. The abnormal release of dopamine lead to an aberrant assignment of salience to innocuous stimuli. It is argued that psychotic symptoms, especially delusions and hallucinations, emerge over time as the individual's own explanation for the experience of aberrant salience (Kapur, 2003). Psychosis, is therefore, aberrant salience driven by dopamine and filtered through the individual's existing cognitive and sociocultural schemas (Howes & Kapur, 2009).

Salience is like a highlighter in the perceptual field that makes certain stimuli emerge in the centre in the perceptual field and are experienced as extremely important.

2.9.2. The hypothalamic–Pituitary–Adrenal (HPA) function

Consistent research evidence has shown the link between the activity of the Hypothalamic-Pituitary-Adrenal (HPA) function and psychotic disorders. Elevated cortisol levels were found in patients with first episode and recent onset (Modelli et al., 2010), and increased activity of systemic cortisol

metabolism in patients with psychosis (Steen et al., 2010). In addition, higher levels of cortisol and more pronounced cortisol reactivity to daily stressors have been observed in relatives of patients with schizophrenia (Yildirim, Dogan, Semiz, & Kilicli, 2011). Recently, a study of first-episode patients revealed no differences from controls in cortisol, but the magnitude of the decrease in cortisol over 12 weeks was associated with the decline in severity of positive and negative symptoms (Garner et al., 2011).

Poor work has been conducted to explore the activity of the HPA function in the CHR state. As stress response is believed to play a role in triggering symptoms, indices of the biological response to stress are important during the prodromal phase. In one study assessing pituitary volume through magnetic resonance imaging, the CHR individuals who later converted to psychosis had a significantly larger baseline pituitary volume compared with those who did not (Garner et al., 2005). The authors concluded that the larger pituitary volume may be indicative of increased HPA activation (Garner et al., 2005). However, in another study conducted by the same research group on 18 CHR individuals, cortisol levels were not significantly associated with global psychopathology, psychotic symptoms, or pituitary and hippocampal volumes, but positively correlated with ratings of depression and anxiety (Thompson et al., 2007).

These investigators also conducted a study in which they administered the dexamethasone corticotrophin releasing hormone test to a small group of 12 individuals at CHR at baseline (Thompson et al., 2007). Three of the 12 developed psychosis within 2 years. Due to the small sample size, statistical analyses were not conducted, but the authors reported that participants who did not develop psychosis showed a trend toward higher cortisol levels at the latter stages of the test, when compared to the three participants who did develop psychosis (Thompson et al., 2007).

Other studies with larger samples have indicated that CHR individuals reported higher cortisol levels (Mizrahi et al., 2012; Walker et al., 2010; Weinstein, Donald, Schiffman, Walker, & Bonsall, 1999).

Findings from a recent study showed that CHR youth who convert to a psychotic disorder had significantly increased cortisol levels in the year preceding onset (Walker et al., 2010). Of the 56 included CHR young participants, 14 subsequently developed a psychotic disorder. Multiple saliva samples were obtained to enhance cortisol estimation reliability. As in previous studies of HPA activity in adolescence, an age-related increase in cortisol secretion was also observed, suggesting that the developmental period of peak risk for prodromal onset is also characterized by greater stress sensitivity.

Another recent study assessed a group of UHR individuals and a group of patients with psychosis using positron emission tomography to index percent change in receptor binding between conditions (stress versus control) in the limbic, associative, and sensorimotor striatum (Mizrahi et al., 2012). The

stressor was a challenging mental arithmetic task. Compared to healthy controls, CHR and patients with psychosis had more pronounced dopamine response in the associative and sensorimotor striatum, as well as a greater cortisol response to the stressor. Further, there was a significant association between the increases in cortisol and DA (Mizrahi et al., 2012).

Recently, in the context of the large multicentre NAPLS study, Walker and colleagues (2013) followed 256 CHR individuals and 141 healthy controls, all of whom underwent baseline assessment and measurement of salivary cortisol. Findings indicated that the CHR group had higher cortisol levels. There were modest, positive correlations of cortisol with baseline symptom severity, and baseline cortisol was higher among those who transitioned to psychotic level symptoms when compared to healthy controls and CHR participants who remitted (Walker et al., 2013).

Chapter 3: Assessment procedures for the detection of CHR individuals

3.1. Screening interviews

In a recent meta-analysis, Fusar-Poli and colleagues (2015) included 12 studies assessing help-seeking individuals referred to CHR services and assessed through a CHR interview. Findings indicated an excellent overall prognostic performance in terms of the area under the curve (AUC) at 38-month follow-up, which appeared comparable to other preventive approaches in medicine. However, excellent AUC values were mainly mediated by an outstanding ability of the instruments to rule out psychosis, then high sensitivity but only moderate overall specificity, which suggested some need to further improvement of prediction tools (Fusar-Poli et al., 2015).

3.1.1. Bonn Scale for the Assessment of Basic Symptoms (BSABS)

In the 1960s Huber and Gross developed the Bonn Scale for the Assessment of Basic Symptoms (BSABS; Gross, 1987) on basis of the primary symptoms of schizophrenia according to Bleuler (1950). Further analyses of the BS resulted subsequently in a set of predictive criteria based on nine cognitive disturbances, the BSABS-P (Schültze-Lutter & Klosterkötter, 2002), an instrument able to cover the earliest signs of psychosis.

3.1.2. Structural Interview for Prodromal Syndromes (SIPS)

The SIPS (McGlashan et al., 2001; Miller et al., 2002) is a structured diagnostic interview used to diagnose the three prodromal syndromes and may be thought of as analogous to the Structured Clinical Interview for DSM-IV (SCID; First et al., 1997) or other structured diagnostic interviews. The SIPS includes the SOPS, the Schizotypal Personality Disorder Checklist (American Psychiatric Association, 1994), a family history questionnaire (Andreasen et al. 1977), and a well-anchored version of the Global Assessment of Functioning scale (GAF; Hall 1995). The SIPS also covers operational definitions of the three prodromal syndromes (the Criteria of Prodromal Syndromes [COPS]) and an operational definition of psychosis onset (Presence of Psychotic Syndrome [POPS]).

As part of the SIPS, the COPS and the POPS are applied to the information from the positive symptoms of the SOPS, the schizotypal personality disorder Checklist, and the family history questionnaire to diagnose a prodromal syndrome or the presence of psychosis. The SOPS is a 19-item scale designed to measure the severity of prodromal symptoms and changes over time. It may be conceptualized as analogous to the Positive and Negative Syndrome Scale (PANSS; Kay, Flszbein, & Opfer, 1987), the Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1962), and other established severity rating scales for patients who are fully psychotic. The SOPS contains four subscales for Positive, Negative, Disorganization, and General Symptoms constructs. There are five Positive, six Negative, four Disorganization, and four General Symptoms items. The Negative, Disorganization, and General Symptoms rated on the SOPS are not currently part of making prodromal diagnoses according to the COPS but are useful in describing the severity of the diagnosis once established.

3.1.3. Comprehensive Assessment of At-Risk Mental States (CAARMS)

The Comprehensive Assessment of At-Risk Mental States (CAARMS, Yung et al. 2005) is a well-established instrument to classify individuals at UHR for developing a psychotic disorder. The CAARMS is assessed in an interview that takes approximately one to 2 hours, and needs to be conducted by a specifically trained mental health professional, which is usually not widely available outside of specialized services. The CAARMS was used to determine if a patient was either psychotic (or had life time diagnosis of a psychotic disorder), UHR for psychotic disorder, or neither of both prior categories. It allows to identify 3 UHR groups:

- Individuals with a family history of a psychotic disorder in a first-degree relative and non-specific symptoms for at least one month associated with a significant decrease in functioning;
- Individuals with attenuated psychotic symptoms (APS), such as sub-threshold with respect to intensity of symptoms;
- Individuals with Brief Limited Intermittent Psychotic Symptoms (BLIPS), symptoms of psychotic intensity that are infrequent with a total duration of less than seven days.

The CAARMS is composed by seven sections:

1) Positive symptoms (four items)
2) Cognitive change attention/concentration (two items)
3) Emotional disturbance (three items)
4) Negative symptoms (three items)

5) Behavioural change (four items)
6) Motor/physical change (four items)
7) General psychopathology (eight items)

The positive symptoms items are the main items on the basis of which individuals are included in the ARMS state. The four positive symptoms are:

1.1 unusual content of thoughts

1.2 Non-bizarre ideas

1.3 Perceptual disturbance

1.4 Disorganized speech

These items are scored with anchor points on intensity (0-6 point Likert scale) and frequency/duration (0-6 point Likert scale). In addition, dates of start and end of symptoms are annotated as well as the level of distress (0-100) and relationship with drug use (0-2). It is very important to ascertain the combination of intensity and frequency/duration of the positive symptoms if an individual has APS, BLIPS, psychosis and/or above below the threshold symptoms. ARMS groups according to CAARMS are presented in Table 3.1.

Table 3.1. ARMS groups identified by the CAARMS.

		Intensity	frequency
Attenuated psychotic symptoms subthreshold intensity group	Unusual thought content	3-5	3-6
	Non-bizarre ideas	3-5	3-6
	Perceptual abnormalities	3-4	3-6
	Disorganized speech	4-5	3-6
Attenuated psychotic symptoms subthreshold frequency group	Unusual thought content	6	3
	Non-bizarre ideas	6	3
	Perceptual abnormalities	5-6	3
	Disorganized speech	6	3
Brief limited intermittent psychotic symptoms group	Unusual thought content	6	4-6
	Non-bizarre ideas	6	4-6
	Perceptual abnormalities	5-6	4-6
	Disorganized speech	6	4-6

Note. ARMS= At-risk mental state, CAARMS= Comprehensive Assessment of At-Risk-Mental State.

3.1.4. Early Recognition Inventory based on IRAOS (ERIraos)

The instrument Early Recognition Inventory based on IRAOS (ERIraos) has been developed with the aim to cover comprehensively a detailed assessment of APS, BLIPS and BS into one measure. Pioneer work by Häfner and colleagues elucidated the early course of schizophrenia in a retrospective assessment (ABC study IRAOS; Maurer, Hörrmann, Trendler, Schmidt, & Haefner, 2006). ERIraos

assesses the 10 cognitive-perceptive basic symptoms (COPER symptoms) ("Thought perseveration of past events", "Disturbance of receptive speech", "Thought interference", "Pressing and racing thoughts", "Thought block", "Decreased ability to discriminate between ideas, perception, fantasy and true memories", "Derealisation, Depersonalisation", "Unstable ideas of reference (subject-centrism)", "Disturbances of optic perceptions", "Disturbances of acoustic perceptions") and additionally the item "Disturbances of olfactory, gustatory, sensible, somatic and tactile perceptions; Impaired bodily sensations (coenaesthesia)" that showed predictive validity for a transition to psychosis in the German Research Network on Schizophrenia (GRNS study; Schultze-Lutter et al., 2010). This scale consists of 50 symptoms, including BS, APS and BLIPS. For each of the 50 symptoms subjects are asked to refer (A) if this specific symptom was present in the past four weeks, (B) if it already occurred within the last 12 months, (C) if there was a deterioration during the last 12 months, and (D) if there is a current emotional strain regarding this symptom (score range 0–200, cut-off = 30). The absence of an increased risk of psychosis is assumed, when no BLIPS, no APS or less than two basic symptoms and no transgression of the cut-off score is presented. Early ARMS is defined by a transgression of the cut-off or the presence of at least two basic symptoms, while a late ARMS is defined by the presence of at least one BLIPS or APS, independent of the score achieved. The patients are further evaluated by the instruments Global Assessment of Functioning (GAF; Startup, Jackson, & Bendix, 2002) to evaluate the psychological, social and occupational functioning, the Personal and Social Performance Scale (PSP; Morosini et al., 2000), which focuses on socially useful activities, personal and social relationships, self-care and disturbing and aggressive behaviour, and the Schizotypal Personality Questionnaire – Brief (SPQ-B; Raine & Benishay, 1995), which is a brief, self-report screening instrument for schizotypal personality features. Finally, the associated instruments of the ERIraos "Alcohol and drug consumption", and "Mental illness in the family" are applied.

3.1.5. Schizophrenia Proneness Instrument-Adult version (SPI-A)

Schizophrenia Proneness Instrument-Adult version (SPI-A) is composed by 34 items comprising 6 subscales of 5 to 6 items each, based on a 7-point severity scale with maximum of occurrence within the last three months as the guiding criterion ("Symptom absent"= 0, "Present daily"= 6): (a) "affective dynamic disturbances" including impaired stress tolerance, a change in general mood and a decrease in general as well as positive emotional responsiveness; (b) "cognitive-attentional impediments" including some cognitive basic symptoms that were found to be less specific to individuals later developing psychosis, such as attention and short-term memory deficits as well

concentration problems; (c) "cognitive disturbances" comprising of the more peculiar cognitive basic symptoms found to be rather specific to prodromal individuals (Klosterkötter et al., 2001), such thought interference and blockages, indecisiveness with regard to minor choices; (d) "disturbances in experiencing self and surroundings", including self-reported pressure of thoughts unrelated to each other and unstable ideas of reference; "body perception disturbances" comprising of coenesthetic phenomena, such as unusual perceptive experiences related to the body in a non-delusive way; (f) "perception disturbances" with hypersensitivity to optic and acoustic stimuli, micro-/macropsia, changes in the perception of the intensity/quality of acoustic stimuli.

3.1.6. Schizophrenia Proneness Instrument-Child and Youth version (SPI-CY)

The Schizophrenia Proneness Instrument, Child and Youth version (SPI-CY; Schultze-Lutter et al., 2012) was developed to assess BS in 8- to 18-year-old individuals. The tool is designed to assess Risk criterion "Cognitive-perceptive basic symptoms" (COPER), including at least any of the following 10 basic symptoms with a SPI-CY score of ≥3 (i.e., several times in a month or weekly) within the past 3 months: (a) decreased ability to discriminate between ideas and perception, fantasy and true memories (B1), (b) unstable ideas of reference (B2), (c) visual perception disturbances (B3, O1, O3), (d) acoustic perception disturbances (B4.2, B5), (d) derealisation (B7), (e) thought interference (D9), (f) thought pressure (D10), (g) disturbance of receptive speech (D11), (h) thought perseveration (D14), (i) thought blockages (D15). The measure evaluates also the high-risk criterion "Cognitive Disturbances" (COGDIS), consisting of at least 2 of the following 9 basic symptoms with a SPI-CY score of ≥3 (i.e., several times in a month or weekly) within the past 3 months: (a) unstable ideas of reference (B2), (b) disturbances of abstract thinking (D7), (c) inability to divide attention (D8), (d) thought interference (D9), (e) thought pressure (D10), (f) disturbance of receptive speech (D11), (g) disturbance of expressive speech (D12), (h) thought blockages (D15), (i) captivation of attention by details of the visual field (O2).

The SPI-CY consists of 4 subscales, each including 8 to 19 items rated on a 7-point severity scale according to their maximum frequency during the past 3 months:

- Adynamia: decreased drive; impaired stress tolerance; affective changes; and unspecific concentration, memory, and thought disturbances;
- Perception Disturbances: disturbances in visual, acoustic, and body perception; derealisation; unstable ideas of reference; disturbances in apprehension of perceptions; and decreased ability to discriminate between ideas and perception. All but 2 are included in BS criteria, particularly COPER;

- Neuroticism: reduced desire for social contact; increased emotional responsiveness to the misfortunes of strangers; irritability; obsessive compulsive and phobic phenomena; depersonalization; and bodily sensations of circumscribed pain and of touch being negatively experienced;
- Thought and Motor Disturbances: 8 thought disturbances that are part of BS criteria; 6 other thought and memory disturbances; 3 cognitive motor disturbances; decreased spontaneity; and disturbances in social skills.

Findings from the Age, Beginning and Course Schizophrenia Study (ABC-study; Maurer et al., 2006) identified different ARMS-subgroups, the so-called pre-psychotic and psychotic prodromal states (Rausch et al., 2013).

In conclusion, the CAARMS, ERIraos and SPI-A are aimed to comprise different subgroups according to prodromal states and time windows (Figure 3.1).

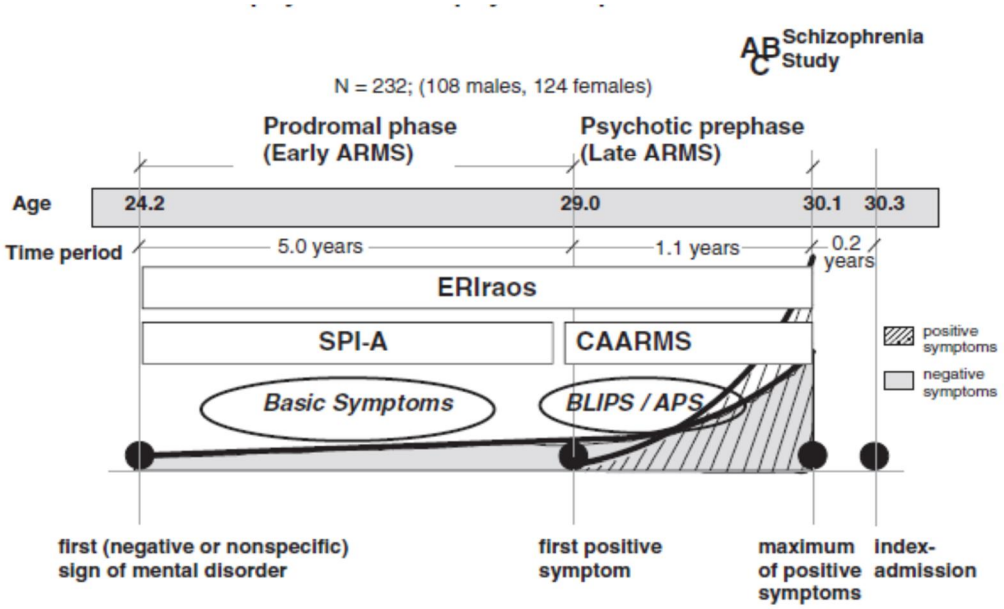


Figure 3.1. ARMS groups, related diagnostic scales and time windows (source: Rausch et al., 2013).

3.2. Self-report tools

For several reasons, however, clinical interviews targeting CHR status are not considered suitable for contexts beyond tertiary settings. Interviews targeting CHR status are typically lengthy, and clinicians must receive training to become familiar with the constructs, rating scales, and diagnostic criteria (McGlashan et al., 2010). The development of brief, easy to-use instruments that can be implemented

for clinical use is a crucial step toward establishing and disseminating evidence-based care for individuals most vulnerable to psychosis.

Brief self-report questionnaires have the potential to screen populations of interest and may ultimately aid in the detection of far more CHR individuals than would be possible through clinician- or self-referrals to specialized programs, offering a potential solution to the challenge of sample ascertainment for CHR research programs.

A key question remains whether and how the criteria for the psychosis risk syndrome can be applied in populations with a lower a priori probability of psychosis risk, outside the specialized clinics (Carpenter & van Os, 2011). As the incidence of UHR is low and the early signs and symptoms are non-specific, this approach is only likely to succeed if an adequate diagnostic screening instrument is available, with which individuals with suspected UHR symptoms can be identified for further in-depth diagnostic interviews. The test should have a high specificity (to maximize the proportion of actual negatives which are correctly identified as such) and also a good sensitivity (to maximize the proportion of actual positives which are correctly identified as such) (Wilson & Jungner, 1968). In addition, the screening should be acceptable to clinicians and the population to be screened, and the procedure should be cost effective and feasible in routine mental health care.

A variety of self-report screening tools have been developed to detect more efficiently for the ARMS (Kline et al., 2012). In several of these measures, item content focuses on symptoms associated with the attenuated symptom construct such as unusual perceptions and sensations, difficulty concentrating, affective changes, superstitious beliefs, or abnormally suspicious thoughts (e.g., Heinimaa et al., 2003; Loewy et al., 2005; Ord et al., 2004).

3.2.1. Prodromal Questionnaire (PQ)

The Prodromal Questionnaire (PQ; Loewy et al., 2005) is a 92-item self-report screening questionnaire that assesses the presence of APS on a two-point scale (true/false). On average, it takes 20 minutes to complete. The items are divided into four major subscales: positive symptoms (45 items), negative symptoms (19 items), disorganized symptoms (13 items), and general symptoms (15 items). Positive symptoms are grouped in three subscales: (1) unusual thought content, delusional ideas and paranoia (22 items); (2) perceptual abnormalities and hallucinations (17 items); and (3) conceptual disorganization (6 items).

As part of the Dutch Early Detection and Intervention Evaluation study (EDIE-NL; Riedijk et al., 2010), Ising and colleagues (2012) administered the PQ in the context of a two-stage screening procedure in the consecutive help-seeking population for nonpsychotic disorders accessing secondary

mental health care services. Participants were 3533 individuals aged 18–35 years who were screened with the PQ. Individuals with scores above the cut-off were then assessed with the CAARMS to investigate possible psychosis risk status. In line with other researchers (Loewy et al., 2011), people were selected if they were with PQ-positive symptom scores in the top 20% of the distribution for further investigation using the criterion was 18 or more PQ-positive symptom items. A 16-item list was selected. For use as a screening instrument, a cut-off score of 6 or more symptom items was found to identify ‘‘caseness’’ (UHR/psychosis) best with a sensitivity of 87%, resulting in a specificity of 87% and PPV of 44%. Total score on the PQ-16 was significantly correlated with the CAARMS diagnosis. Cronbach's alpha for the total score on the PQ-16 was 0.77. The newly developed PQ-16 has good concurrent validity with both the interview-based CAARMS diagnoses in our population and also in comparison to the original PQ. A cut-off of 6 or more symptoms on the PQ-16 has a high true positive rate (87%) and high specificity (87%) when differentiating UHR/psychosis from those with no CAARMS diagnosis. The 16-item PQ consists of 9 items out of the perceptual abnormalities/hallucinations subscale, 5 items including unusual thought content/delusional ideas/paranoia, and 2 negative symptoms. If the individual scores above the cut-off, a semi-structured interview, like the CAARMS, is recommended to ascertain whether he/she fulfil the UHR criteria.

3.2.2. Community Assessment of Psychic Experience (CAPE)

The Community Assessment of Psychic Experience (CAPE; Konings et al., 2006) is a 42-item self-report questionnaire that proved to be stable, reliable and valid for self-reported PLES in the general population. Mossaheb and colleagues (2012) investigated whether the CAPE could be used as a screening tool to detect individuals at an increased risk for developing psychosis in a clinical help-seeking population. A cut-off value of 2.80 for the positive dimension identified UHR individuals in a clinical population with a high sensitivity (83%).

3.2.3. PRIME Screen

The PRIME Screen (Miller et al., 2004) is based on items from the Structured Interview for Prodromal Syndromes (SIPS), which was also developed by Miller et al. (2003). This screening questionnaire consists of 12 items covering positive symptoms and utilizes a self-rated scoring system of between 0 (“Definitely disagree”) and 6 (“Definitely agree”). In the developmental phase of the PRIME Screen, Miller et al. (2004) reported that it showed a sensitivity of 0.90 and had a perfect specificity,

but these results were obtained using small samples (n=36) and the predictive validity was not examined.

3.2.4. Basel Screening Instrument for Psychosis (BSIP)

The Basel Screening Instrument for Psychosis (BSIP; Riecher-Rössler et al., 2008) is modelled on the Brief Psychiatric Rating Symptom Scale (BPRS; Overall & Gorham, 1962). It is a 46-item checklist used in combination with the BPRS Three symptoms of the BPRS are used for the assessment of APS: hallucinations, unusual thought content, and suspiciousness. Four symptoms of the BPRS are used for the assessment of BLIPS: hallucinations, unusual thought content, suspiciousness, and conceptual disorganisation.

3.2.5. Early Detection Primary Care Checklist (PCCL)

The research group of Paul French developed a short tool, the Early Detection Primary Care Checklist (PCCL; French et al., 2012). The measure was completed by primary care practitioners who referred positive screens for specialized psychiatric assessment (UK adolescents and young adults ages 14–34). With regard to CAARMS CHR/psychosis diagnoses, the PCCL was found to have excellent sensitivity (0.96) but poor specificity (0.10). An optimized 6-item version yielded a sensitivity of 0.88 and specificity of 0.47; an optimized 20-item version sensitivity of 0.89 and specificity of 0.60 (French et al., 2012).

3.3. The European Psychiatric Association guidelines on early detection

Recently, according the European Psychiatric Association (EPA) guidelines (Schultze-Lutter et al., 2015), the following three CHR criteria should be alternatively used in the early detection of psychosis when past or current psychosis and causation by a somatic condition have been excluded:

- at least any one attenuated psychotic symptom, that meets the additional requirements of either SIPS or early CAARMS, such as (1) unusual thought contents or delusional ideas not held with full conviction, including ideas of reference not immediately rectified by cognition, (2) perceptual aberrations or hallucination with remaining insight, or (3) disorganized communication or speech that is still comprehensible and responds to structuring in the interview;

- at least any two self-experienced and self-reported cognitive basic symptoms rated irrespective of their appearance in the interview, such as (1) interference of completely insignificant thought contents, (2) blockage of thoughts not explained by lack of concentration or attention, (3) thought pressure by thoughts unrelated to a common topic, (4, 5) disturbances of receptive or expressive speech in everyday use of native language, (6) inability to divide attention between tasks relating to different senses and generally not requiring full attention each such as making a sandwich and talking to someone, (7) disturbance in the immediate recognition and understanding of any kind of abstract, figurative or symbolic phrases or contents, (8) subjective experience of self-reference that are almost immediately rectified by cognition, and (9) captivation of attention by insignificant details of the visual field that impairs paying attention to more relevant stimuli. These features should have not been evident in what the patient considers his/her premorbid stage, have occurred at least on a weekly basis for some time in the past 3 months and are not an effect of drug use;
- at least any one transient psychotic symptom, such as delusion, hallucination, formal thought disorder that meet the additional requirements of either SIPS or early CAARMS.

Additionally, the EPA guidelines state that a genetic vulnerability related to a family history of psychosis in at least one first-degree relative should not be used as a clinical indicator of a CHR per se, even if accompanied by functional decline. Rather, it should be regarded as a general risk factor indicating an already increased pre-CHR assessment risk for psychosis that should be carefully considered in CHR individuals (Schultze-Lutter et al., 2015). Patients not presenting the above CHR criteria but a genetic risk and other mental problems should however be encouraged to present again for a CHR assessment, should they note the onset of mental problems resembling CHR symptoms (Schultze-Lutter et al., 2015).

In line with the general EPA guidance on prevention of mental disorders whose aims include reduction of the burden of mental disorders by improvement in quality of life and productivity of individuals, the EPA considers that a significant decline in occupational and/or social functioning should not be an obligate requirement in the above CHR criteria for the lack of evidence for an improvement of prediction by this addition. However, it should be considered as an indication of an imminence of risk of conversion and CHR patients with a significant functional decline should be considered at high need for treatment (Schultze-Lutter et al., 2015).

The EPA considers that the above CHR criteria should only be applied in persons already distressed by mental problems and seeking help for them or persons seeking clarification of their current risk for a vulnerability for psychosis, e.g., by genetic risk. Any clinical screening of other persons seems

not warranted by current scientific evidence. In late adolescence, however, the CHR criteria seem to be as applicable as in adults.

The EPA considers that a trained specialist (psychiatrist, clinical psychologist or equivalent mental health professional) with sufficient experience in CHR should carry out the assessment; if referral to a specialist is not possible, the responsible clinician should consult a trained specialist on the case (Schultze-Lutter et al., 2015).

Moreover, the EPA guidelines also did not include the basic symptom criterion COPER because of its large overlap with COGDIS and, compared to COGDIS, its poorer evidence due to the reduced number of available studies (Kosterklötter et al., 2001) and meta-analytic data not supporting the assumption that it would improve prediction of psychosis in help-seeking samples.

Furthermore, the EPA working group evidenced that a "one-fits-all" detection approach most likely does not account for noticeable heterogeneity of conversion rates even in CHR samples of equal intake criteria (Schultze-Lutter et al., 2015). Future early detection approaches should therefore define different CHR groups that are identified, for example, by a risk stratification approach, which might consider most likely level of functioning but also other potential predictors such as neurocognitive or neurobiological abnormalities (Schultze-Lutter et al., 2015).

Chapter 4: Preventing or delaying psychosis: interventions for CHR states

4.1. Cognitive behavioural therapy (CBT) protocols

French and Morrison (2004) developed a cognitive behavioural therapy (CBT) protocol based on 26 weekly sessions over 6 months following the principles of the cognitive therapy manual by Aaron T. Beck (1976). This kind of intervention is structured, problem-oriented and time-limited; it encourages collaborative empiricism, uses guided discovery and homework tasks. It is based on the cognitive model most appropriate to the disorder that is prioritised on a problem list agreed between the therapist and the patient. Therefore, if a transient or an attenuated psychotic symptom is prioritised, the case conceptualisations (and subsequent treatment strategies) are based on Morrison's recent integrative model of hallucinations and delusions (Morrison, 2001). This model emphasises the culturally unacceptable interpretations that people with psychosis make for events, in addition to their responses to such events and their beliefs about themselves, other people and control strategies. The central feature of the approach to the prevention of psychosis involves normalising the interpretations that people make, helping them to generate and evaluate alternative explanations, decatastrophising their fears of impending madness and helping them test out such appraisals using behavioural experiments and cognitive restructuring. However, if the problem prioritised was an anxiety disorder (such as panic, social phobia, obsessive–compulsive disorder or generalised anxiety) or depression, then the appropriate models are employed (e.g., Beck et al, 1979; Clark, 1986; Clark & Wells, 1995; Wells, 1995). The case formulation model of French and Morrison (2004) is provided in Figure 4.1. The purpose of the model is to facilitate the collaborative development of idiosyncratic case formulations, from intervention strategies ca be derived (Smethurst, French, & Morrison, 2013). In the manual sequence of treatment components included definition of a list of problems and goals, normalization interventions, practice of skills and coping through in-session role-playing exercises, cognitive restructuring through in- and out-session behavioural experiments, examination of advantages/disadvantages, generating alternative explanations and survey planning, planning of activities to reduce social isolation and increase pleasure emotions (French & Morrison, 2004). All the CBT components are delivered also in the form of homework assignment. The manual also included a relapse prevention module, where the therapist and the patient collaboratively develop a

"blueprint". This step involves the review of all the skills that he/she has learnt during the therapeutic course and how will apply them in the future. The patient is encouraged to image all the obstacles that he/she could face in the future and discuss with therapist how to manage them. The patients is also invited to identify all potential trigger situations and warning signs of distress (Smethurst, French, & Morrison, 2013).

Bechdolf and colleagues (2007) developed a novel Integrated Psychological Intervention (IPI) package for CHR youth. IPI includes individual CBT, group therapy focusing on skills training, cognitive remediation for concentration, attention, vigilance, and memory, and psychoeducational multifamily groups providing family members with information on the CHR state. McFarlane and colleagues (1992) adapted Family-Aided Assertive Community Treatment (FACT), historically used in the treatment of severe schizophrenia, for use with CHR youth. The principal psychosocial ingredient of FACT is psychoeducational multifamily group treatment, designed to educate families on biomedical aspects of psychopathology and use the family as leverage in assisting the client in goal setting and problem solving.

More recently, van der Gaag and colleagues (2012) developed a CBT protocol, based on the protocol by French and Morrison (2004), that was enriched with psychoeducation on dopamine sensitivity and cognitive biases involved in early psychosis. Psychoeducation provides information on how this affects perception (aberrant salience for trivial stimuli) and thinking (more intrusions, more causal reasoning over coincidences, stronger data-gathering bias). Furthermore, exercises were added to experience cognitive biases; becoming aware of cognitive biases may lead to corrected secondary appraisals (van der Gaag et al., 2012).

The biases addressed are the following domains: (a) data-gathering bias, mainly characterized by jumping to conclusions distortions; (b) selective attention to threatening stimuli; (c) confirmatory bias, moderating delusion formation; (d) negative expectation bias, leading to increased distress levels, as well as underrating of one's capacities; (e) covariance bias, in which the chance of a causal relationship between independent events is overrated (van der Gaag et al., 2013).

The use of written materials is considered as necessary for compensate attention and memory deficits. Activity scheduling is a relevant component of the treatment in order to develop more activities and to strengthen the feeling of satisfaction and joy. The involvement of family members can be very helpful in these patients to help transfer behaviour outside in real-life contexts, to help with homework and to prevent unnecessary conflicts (van der Gaag et al., 2013).

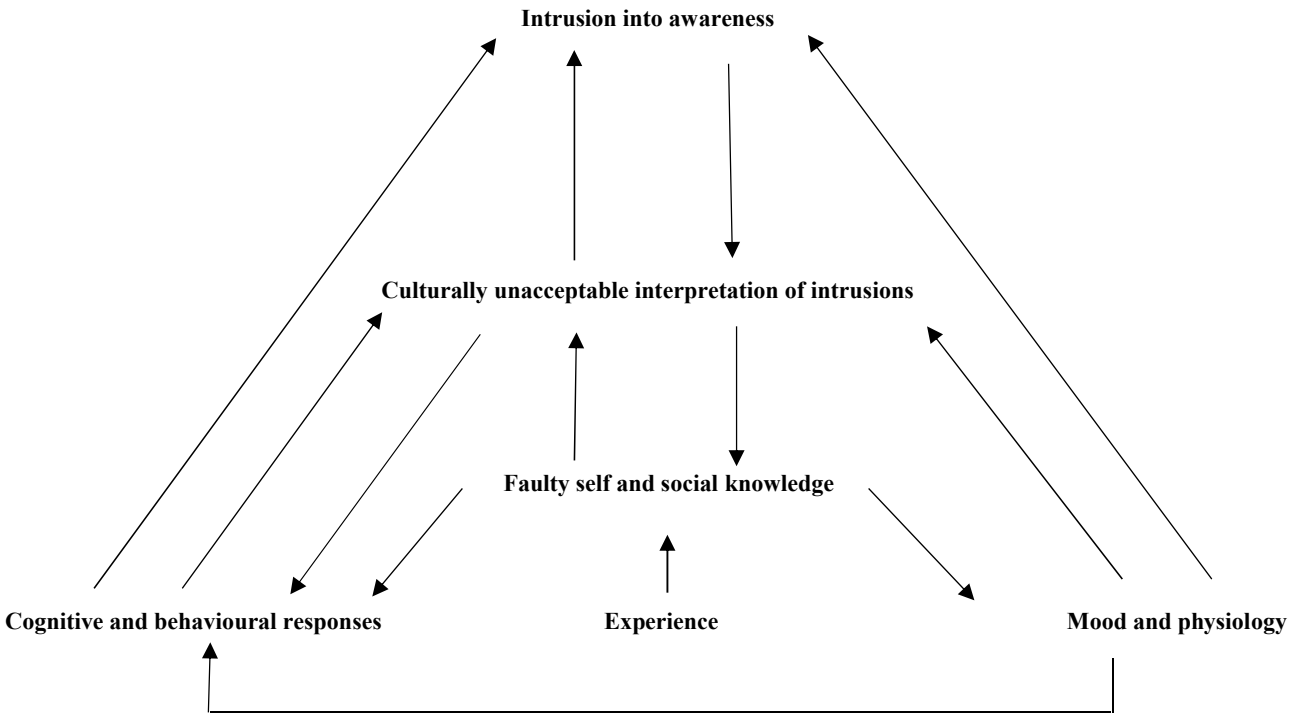


Figure 4.1. Case formulation model in the CBT protocol of French and Morrison (2004).

4.2. Family-based psychological treatments

Some researchers have hypothesized that early intervention on CHR groups would be strengthened by involving family members in treatment, as individuals at CHR are often adolescents living with their parents, and parental involvement may enhance the young person's access to mental health services (Schlosser et al., 2010). Moreover, the evolution of APS may be affected by family contextual variables. For example, levels of expressed emotion (EE), such as criticism, hostility, or overprotectiveness, in parents were associated with the severity of APS in CHR youth over 6 months (Schlosser et al., 2010). Levels of parental EE may escalate in reaction to the functional deterioration of an offspring with emerging psychosis but may also become a stressor for the offspring (McFarlane & Cook, 2007; Miklowitz, 2004).

Miklowitz and colleagues (2014) developed and evaluated a protocol of family-based psychological treatment. Treatment consisted of 18 1-hour sessions family sessions (12 weekly and 6 biweekly sessions over six months) including psychoeducation about early warning signs of psychosis, trigger situations, stress management techniques (including relaxation exercises), communication enhancing training, and problem-solving training. During communication enhancement training, participants

rehearsed skills for expressing positive feelings, active listening, requesting changes in another person's behaviour, communication clarity, and expressing negative feelings (Miklowitz et al., 2014). Last sessions were dedicated to practice of problem-solving, where participants learned to break down larger problems (e.g., "We have to stop fighting") into smaller ones (e.g., "We need to use lower tones of voice"), generate and evaluate solutions, and develop a solution implementation plan. Overall, the intervention was aimed to reduce EE, criticism, enhance warm, assertive communication between family members, promote active listening skills thus reducing irritability, anger, and complaints (Miklowitz et al., 2014).

Landa and colleagues (2015) developed a group and family-based cognitive behavioural therapy program consisting of 15 weekly sessions, where CHR adolescents and their family members are provided with CBT skills individually or in small groups. The aims of the program are directed at enhancing family and peer support, reducing isolation feelings, normalizing PLES, facilitating positive thinking and decision-making skills, and reduce cognitive biases. In a recent preliminary uncontrolled study on a small UHR group screened by the CAARMS (n= 6), all enrolled participants remitted from ARMS, showed significant decreases also in depression, cognitive biases and improvements in functioning (Landa et al., 2016). Family members showed significant improvements in use of CBT skills, more effective communication with their offspring, and greater confidence in their ability to help (Landa et al., 2016).

4.3. Pharmacological treatments

Growing research focused on the use of low-dose use of antipsychotics as a potential treatment strategy to reduce risk of development of a first episode of psychosis (e.,g, McGorry et al., 2013). Preliminary data (Tsujino et al., 2013; Woods et al., 2009) examined the use of aripiprazole or perospirone, a combined serotonin (5-HTdopamine antagonist and 5HT1A receptor agonist). However, these trials were based on an uncontrolled design. Further, RCTs investigated the potential benefit of 5-15 mg/die of olanzapine versus placebo (McGlashan et al., 2006) or the combination of low-dose risperidone with CBT versus placebo + supportive therapy (McGorry et al., 2013).

Recently, on the basis of poor evidence in favour of antipsychotics, some researchers have argued that there are several problems associated with using antipsychotic medication in a CHR group. The risks associated with using pharmacological interventions with false-positive cases are considerable, adherence to antipsychotic medication regimens within this group is variable (McGorry et al, 2002) and the ethical position has caused some debate. In particular, it has been suggested (Bentall & Morrison, 2002) that use of antipsychotic medication is problematic because these drugs have harmful

and stigmatising side-effects, their effect on the developing brain in adolescents is unknown, and because they target psychotic experiences, which may not be the priority for people at high risk.
According van der Gaag and colleagues (2013), trials with anti-psychotic medications may focus on prescription of low doses of the second-generation antipsychotics associated with low metabolic impact and possibly improved adherence rates and fewer side effects. Anti-psychotic medication can also be offered as a second line intervention after failed or partial treatment response in CBT. The finding that effects wane over time for both pharmacological and psychosocial interventions might point to the need for more elaborate interventions or booster sessions to preserve the results (van der Gaag et al., 2013).

4.4. Nutritional supplements

Eicosapentaenoic acid increases glutathione is the brain's principal antioxidant protective factor (Berger et al 2007). There is evidence that acute psychotic symptoms are associated with glutathione deficiency and, hence, oxidative stress. Some evidence suggested that long-chain o-3 (o-3) polyunsaturated fatty acids (PUFAs) could add some benefit. A recent randomized placebo-controlled trial (Amminger et al., 2010) found a 4.9% rate of transition to acute psychosis in UHR patients treated with PUFAs as compared with a psychosis transition rate of 27.5% in individuals who received placebo in addition to standard care, indicating that supplementation with o-3 PUFAs may reduce the risk of transition to psychosis. Lower levels of o-3 PUFAs correlate with more severe negative symptoms in UHR patients (Amminger & McGorry, 2012) and that decreased levels of fatty acids (that is, nervonic acid, o-3 PUFAs) may serve as biomarkers predicting the conversion to psychosis in UHR subjects (Amminger et al., 2011). However, the pharmacological and neurochemical mechanisms of o-3 PUFA action remain incompletely understood

4.5. Efficacy of CHR interventions: what RCTs say

Efficacy of CBT as an adjunct to routine treatments has been widely demonstrated in acute psychosis (Drury et al, 1996; Zimmermann, Favrod, Trieu, & Pomini, 2005) and in cases of chronic, persistent psychotic symptoms (Tarrier et al, 1998, 2000; Sensky et al, 2000), as well as in relapse prevention (Gumley et al, 2003). Growing attention has been focused on the identification of effective strategies for individuals at CHR (Seidman & Nordentoft, 2015). Some promising results have been produced. In a first study, 59 participants at CHR were randomized to six months of active treatment (Risperidone 1–3 mg/day plus a CBT protocol) or to a needs-based intervention (McGorry et al.,

2002). By the end of treatment, significantly fewer individuals in the active treatment group had progressed to a first-episode of psychosis (9.7% vs 36%). A second, more rigorous study (McGlashan et al., 2006), was a randomized, double-blinded trial of 60 help-seeking prodromal patients comparing the efficacy of an antipsychotic (Olanzapine) vs placebo in preventing or delaying the onset of psychosis. Although not statistically significant, at one-year follow-up 16% of olanzapine-treated participants had converted to psychosis compared with 35% of placebo-treated participants (McGlashan et al., 2006). Olanzapine was associated with significantly greater symptomatic improvement in prodromal symptoms than placebo (McGlashan et al., 2006).

Morrison and colleagues (2002, 2004) conducted the Early Detection and Intervention Evaluation (EDIE) trial, a single-blinded randomized trial which aimed to identify the CHR group. Participants were randomly allocated to a monthly monitoring condition or CBT plus monthly monitoring. Eligible participants were recruited from a variety of settings, including primary care teams, student counselling services, accident and emergency departments, specialist services (e.g. community drug and alcohol teams, child and adolescent psychiatry and adult psychiatry services) and voluntary sector agencies (such as carers' organisations). Individuals were included if they were aged between 16 and 35 years old and met the criteria used in Yung and colleagues (1998). Sixty individuals were included, of these twenty-three were assigned to monitoring condition and 37 to CBT. The randomised participants were monitored at monthly intervals using the Positive and Negative Symptoms Scale (PANSS; Kay, Flzsbein, & Opfer, 1987) for a period of 12 months following initial assessment. The CBT intervention was based on the manual of French and Morrison (2004). Fourty-eight participants had APS, 6 transient psychotic symptoms and 4 were included on the basis of a family history and recent deterioration. In the CBT condition, withdrawal rate was 14%. Using PANSS-defined transition as the dependent variable, results showed that the main effect of cognitive therapy was significant (OR= 0.04, 95% CI 0.01–0.71, $p<0.028$), suggesting that there was a 96% reduction in the odds of making a transition in the CBT group compared with those who received monitoring alone, after adjustment for age, gender, family history and baseline PANSS score. In addition, CBT improved positive symptoms with some benefits maintained at 3-year follow-up. However, CBT had not an effect on functioning and distress, assessed by the Global Assessment of Functioning (GAF; Startup, Jackson, & Bendix, 2002) and the General Health Questionnaire (GHQ; Goldberg & Hiller, 1979).

Another trial compared eicosapentoic acid (EPA) with placebo (Amminger et al., 2010) for twelve months. At 12 months 4.9% (2/41) of individuals in the EPA group compared to 27.5% (11/40) in the placebo group developed psychosis. Furthermore, there were significant group differences in positive and negative symptoms at 12 weeks and 12 months in favour of the treatment group. 94% completed

the twelve-week intervention period. Omega 3 fatty acids proved safe to administer as an alternative therapy and did not cause side effects other than mild gastrointestinal symptoms (Amminger et al., 2007). Of note is the relatively high percentage of individuals accepting to participate in a trial involving substances that are normally found in the human body (67% consent for omega 3) compared with RCTs involving antipsychotics (35% in the PACE study) (Phillips et al., 2009).

Addington and colleagues (2011) compared the efficacy of a 20-sessions CBT protocol based on the manual of French and Morrison (2004) with supportive therapy in 51 individuals aged between 14 and 30 years. There were no conversions in those who received CBT and three in the supportive therapy group, but this was not a significant difference. All three conversions had a final diagnosis of schizophrenia. Two of the conversions occurred approximately 15 weeks after baseline, and the third occurred 10 weeks after baseline. Participants in both treatment groups made significant improvements in attenuated positive symptoms, anxiety and depression and neither treatment impacted negative symptoms nor poor functioning. Although both groups had improved at six months, there were no differences in positive symptoms between the groups. However, an examination of the change in positive symptoms over the first 5 months demonstrated that the CBT group had an earlier and thus faster reduction in their positive symptoms. It should be considered that in this trial participants in the CBT condition received an inadequate dose of CBT treatment - for many of the CBT cases, the intervention focused primarily on engagement and less on the strategies that are the core of CBT. Furthermore, the number of sessions was limited which may have accounted for less time spent on core CBT strategies. In addition, the study was underpowered, and the sample was clearly too small to detect a difference although all effects were in the predicted direction. Finally, the conversion rates were much lower than expected, and for a few the final conversion status is unknown. Approximately 40% of the sample did not complete the 18-month follow-up. Several of these young people left the study when they felt they had made some improvement.

Recently, van der Gaag and colleagues (2012) conducted a randomized controlled trial, the Dutch Early Detection Intervention Evaluation (EDIE-NL), where CBT for individuals at CHR was compared as add-on with treatment as usual in a group of help-seeking people at mental health services. Both the experimental and the control group were treated with evidence-based active treatment for the axis 1 or 2 disorder from which they were suffering. The experimental group was given an add-on treatment that focused on subclinical psychosis (van der Gaag et al., 2012). CBT for UHR people had a maximum provision of 26 weekly sessions. The mean number of sessions was 10: 16 patients had no sessions at all; 21 had 1–5 sessions; 16 had 6–11 sessions; and 45 had 12–25 sessions. Patients were eligible for inclusion if the following criteria were met: (1) age 14–35 years; (2) a genetic risk or CAARMS scores in the range of the ARMS; and (3) an impairment in social

functioning (a score on the SOFAS of 50 or less, and/ or a reduction by 30% on the SOFAS for at least 1 month in the past year). Patients were excluded if they met any of the following criteria: (1) current or previous use of antipsychotic medication with ⩾15 mg cumulative haloperidol equivalent; (2) severe learning impairment; (3) problems due to an organic condition; (4) insufficient competence in the Dutch language; and (5) history of psychosis. Two hundred and one were included and randomized to conditions. Each patient was treated during 6 months and followed-up during 18 months. In the survival analyses, those who were lost to follow-up were conservatively considered as non-transitions. The Kaplan-Meier curves showed a significant difference between individuals assigned to CBT and control patients. The odds ratio was 0.522 (95% CI: 0.188–0.948). In the CBT condition, 5 patients at 6 months, 9 patients at 12 months, and 10 patients at 18 months cumulatively made the transition to psychosis. In the TAU condition, 14 patients at 6 months, 20 patients at 12 months, and 22 patients at 18 months made the transition to psychosis. Overall, 16.3% of the patients developed a psychotic episode. After transition to psychosis, the DSM-IV diagnoses were schizophrenia, paranoid type (19); schizophrenia, disorganized type (2); psychotic disorder not otherwise classified (3); brief psychotic disorder (1); schizo-affective disorder (1); depression with psychotic features (4); and bipolar disorder (2). All patients who transitioned fulfilled the PANSS criteria for psychosis (14 had 1 positive symptom intensity of 4; 12 had an intensity score of 5; 5 had an intensity score of 6; and 1 person had missing data). With regard to at risk status at 18-month follow up, the CBT group had a higher remission rate of ARMS (70.4% remission of ARMS; 17.3% ARMS; 12.3% psychosis) than the TAU group (57.0% remission of ARMS; 19.4% ARMS; 23.7% psychosis. The number needed to treat for preventing transition to psychosis was 9.

Subsequently, Ising and colleagues (2016) reported the EDIE-NL trial data obtained through 4-year follow-up assessments on 113 participants who consented to complete measures of the original 196. The number of participants assigned to the CBT group developing psychosis increased from 10 at 18-month follow-up to 12 at 4-year follow-up, whereas it did not change in the treatment as usual condition (n = 22) still suggesting a clinically meaningful and statistically significant effect (incidence rate ratio= 12/22 = 0.55) in favour of CBT (Ising et al., 2016). In addition, significantly more participants remitted from their UHR status in the CBT condition (76.3%) compared with the treatment as usual (58.7%). Finally, conversion to psychosis was associated with more severe psychopathology and social functioning at 4-year follow-up (Ising et al., 2016).

In another recent study, the detection and evaluation of psychological therapy (DEPTh) trial (Stain et al., 2016), 57 young individuals (mean age=16.5) suffering from a CHR state were randomly allocated to CBT (n=30) or non-directive reflective listening (n=27). Rate of transition to psychosis was 5%, rather lower than in previous trials; the 3 transitions occurred in the CBT condition (baseline,

2 months, 5 months respectively). The non-directive reflective listening condition was associated with significantly greater reduction in distress associated with psychotic symptoms as compared to CBT. There were no significant treatment effects on frequency and intensity of psychotic symptoms, global, social or role functioning (Stain et al., 2016).

4.6. Evidence from meta-analytic studies

Some meta-analytic studies were conducted to assess the efficacy of interventions for people at CHR. A first meta-analysis was conducted using the data from five randomized controlled trials (Preti & Cella, 2010). The pooled relative risk was 0.36, meaning that the risk of a first psychotic episode was reduced by 64%, and statistically significant. Heterogeneity was absent, meaning that differences across the primary studies could be attributed to random sample error rather than to systematic factors (Preti & Cella, 2010).

The Cochrane group conducted another systematic review and meta-analysis using six studies, but did not pool the data (Marshall & Rathbone, 2011). The most recent meta-analysis was based on seven studies (Fusar-Poli et al., 2013) and reported a relative risk of 0.34 (95% CI: 23–7; $p< 0.001$), indicating the interventions were successful in reducing the risk of a first psychotic episode in a statistically significant way by 66%. These outcomes were associated with a number needed to treat of 6 indicating that 6 UHR individuals needed to receive treatment for preventing one more transition to psychosis compared to treatment as usual (Fusar-Poli et al., 2013).

Van der Gaag and colleagues (2013) performed a meta-analysis of 10 randomized controlled trials published by 2012. In the three trials examining antipsychotic medication, a statistically significant pooled RR of 0.55 was found with a NNT of 7. In the five trials evaluating CBT, a pooled RR of 0.52 was observed. Six studies included measures of social, occupational or global functioning; however, there was no significant difference favouring experimental conditions (van der Gaag et al., 2013).

A main limitation of the meta-analysis was the risk of publication bias, low number of primary studies and that some studies were under-powered. The authors concluded that although the effects are encouraging, more research is needed. The focus on transition to psychosis must be broadened with the clinical staging idea (McGorry and Van Os, 2013). The UHR group who does not transition is still not functioning well and is suffering from anxiety or depression and limitations in social role functioning. This requires that a broader set of outcome measures must be used in a next generation of prevention studies in psychosis. After all, the UHR group is not only psychosis-prone, but more general psychopathology-prone and at risk for compromised social functioning (Yung et al., 2010).

Miklowitz and colleagues (2014) conducted a trial where CHR adolescents and young adults were randomly assigned to 18 sessions of family-focused therapy in 6 months or 3 sessions of family psychoeducation. One hundred and two were followed for six months. Participants assigned to the family focused therapy showed greater improvements in attenuated positive symptoms than those allocated to family psychoeducation. Negative symptoms improved independently of psychosocial treatments. Changes in psychosocial functioning depended on age: individuals over 19 years showed more role improvement in family focused therapy, whereas participants between 16 and 19 years showed more role improvement in family psychoeducation (Miklowitz et al., 2014). Individuals at high risk and their family members who participated in the family focused therapy demonstrated greater improvement from baseline to 6-month reassessment in constructive communication and decreases in conflictual behaviours during family interactions than those in family psychoeducation (O'Brien et al., 2014). Participants in family focused therapy showed greater increases from baseline to 6 months in active listening and calm communication and greater decreases in irritability and anger, complaints and criticism, and off-task comments compared to participants in family psychoeducation (O' Brien et al., 2014). These changes occurred equally in high-risk participants and their family members.

4.7. The European Psychiatry Association on early intervention guidelines

In the context of the European Psychiatry Association (EPA) working group on early psychosis, Schmidt and colleagues (2015) produced a guidance paper on early intervention in CHR states evaluating the efficacy of interventions that aim at preventing the conversion to psychosis and/or a deterioration of functional outcome. In a preliminary step, the authors performed a meta-analysis of 15 randomized controlled trials on intervention for individuals at CHR conducting a systematic literature search by 2014. Regarding pharmacological treatments, the working group found six studies, two uncontrolled studies and four RCTs. The mean therapy duration was 6.83 months (SD= 4.31, range = 2–12), the mean follow-up period was 15.29 months (SD= 16.23, range = 2–48), and the drop-out rate ranged between 13.0 and 55.0%. These trials investigated the efficacy of aripiprazole (Woods et al., 2009) and perospirone (Tsujino et al., 2013) using an uncontrolled design, and, as RCTs, olanzapine versus placebo (McGlashan et al., 2006), "risperidone plus CBT" versus need-based intervention (McGorry et al., 2002), "amisulpride plus needs based intervention" versus needs-based intervention (Ruhrman et al., 2007), and "risperidone plus CBT" versus "placebo plus supportive therapy" (McGorry et al., 2013). Only one pharmacological study did not use

antipsychotic medication but a neuroprotective approach, and investigated the effect of PUFAs in CHR individuals compared to placebo through a randomized design.

Among the psychological interventions, the authors found nine studies (Schmidt et al., 2015). Mean therapy duration was 6.87 months (SD= 3.7, range = 2–12), a mean follow-up period of 16.67 months (SD= 10.40, range = 2–36), and a drop-out rate between 15.0 and 45.0%. Five interventions used CBT techniques such as normalization, behavioural experiments, and cognitive restructuring to improve stress- and symptom-management. These compared CBT with monitoring (Morrison et al., 2004, 2012), supportive therapy (Addington et al., 2011), supportive therapy with placebo (McGorry et al., 2013), and other evidence-based interventions for the disorders patients sought help (van der Gaag et al., 2012). One uncontrolled study evaluated cognitive remediation therapy in CHR patients (Hooker et al., 2014). Moreover, a multi-family psycho-educational group program was evaluated first in one uncontrolled study (O'Brien et al., 2007), and next in a RCT with enhanced care as control condition (Miklowitz et al., 2014). One of the included RCTs (Bechdolf et al., 2012) combined all of the aforementioned approaches with social skills training and compared this integrated psychological intervention with supportive therapy.

Findings of the meta-analysis suggested that early interventions can significantly reduce conversion rates in adult CHR patients at short- to medium term follow-up (Schmidt et al., 2015). However, the effect of these interventions may only be specific for conversion rates but not for functional outcome because the experimental conditions did not achieve larger functional improvements than the control conditions. This indicates that patients have functionally benefited from control interventions to a similar degree. This may be due to that this particular patient group is quite heterogeneous, for example, with regard to their individual vulnerability, their developmental status, their level of functional impairments, different environmental factors, and the prevalence of comorbid mental health issues (Kirkbride et al., 2006).

Another point was that this meta-analysis provides preliminary evidence that early intervention programs are less effective in reducing conversion to psychosis in youth compared to adult patients. This may be due to the lower conversion rates generally found in children and adolescents (Schultze-Lutter et al., 2015) but needs to be interpreted cautiously due to the lack of studies consisting of youth samples, in particular with regard to conversion rates. However, together with the result that youth also achieved lower functional improvements than adults, this suggests that current intervention programs do not sufficiently address the special needs and developmental stage of younger CHR patients.

Finally, the EPA guidance considers that the current evidence on the efficacy of psychological and pharmacological interventions in children and young adolescents is not sufficient to justify primarily

preventive interventions (Schmidt et al., 2015). The EPA considers that psychological, specifically CBT, as well as pharmacological interventions are able to prevent or at least postpone a first psychotic episode in adult CHR patients. In line with the general EPA guidance on prevention of mental disorders, the EPA considers that an early intervention in patients presenting with CHR should not only aim to prevent the first episode of an affective or non-affective psychotic disorder but also the development or persistence of functional impairment. The EPA guidance considers that any intervention in CHR should also address current individual needs and other mental disorders present (comorbidities), specifically depression and anxiety, according to their respective treatment guidelines (Schmidt et al., 2015). Where psychological interventions have proved ineffective, they should be complemented by low dose second-generation antipsychotics in adult CHR patients if severe and progressive CHR symptomatology (APS with only minimal or clearly declining insight, or BLIPS in higher or increasing frequency) is present and with the primary aim to achieve a degree of symptomatic stabilization that is required for psychological interventions to be effective. Thus, any long-term antipsychotic treatment with a primarily preventive purpose is not recommended (Schmidt et al., 2015).

In conclusion, CBT is regarded as the first-choice intervention for the prevention of conversion to psychosis but it might be complemented by pharmacological interventions with low dose second-generation antipsychotics for symptomatic stabilization, if risk symptoms limit the efficacy of CBT (Schmidt et al., 2015).

4.8. "One size does not fit all": towards modular treatments

Along with efficacy trials, some pioneer research is starting analysing active therapeutic processes involved in CBT for UHR populations. In a recent Delphi study of expert opinion (Morrison & Barratt, 2010), the essential therapeutic components of cognitive behavioural therapy for psychosis produced consensus regarding the importance of goal setting (development of a problem list and goals of therapy in a collaborative, shared and problem-orientated fashion, which requires the development of a problem list and shared goal), an idiosyncratic case formulation based on the cognitive model, and provision of normalising information, evidential analysis and testing beliefs by modification of safety behaviours.

In the context of a secondary data analysis of the Early Detection and Intervention Evaluation trial (EDIE-2; Morrison et al., 2012), Flach and colleagues (2015) investigated whether specific therapeutic active components of the cognitive model (a shared problem list, case formulation, homework tasks) acted as processes increasing the effect of therapy. Interestingly, receiving all

aspects of therapy was associated with a significant reduction of symptom severity by 20 points compared to those who receive only some or none of the components; however, this effect showed a borderline significance level (Flach et al., 2015). When each aspect of therapy is considered separately as a mechanism of CBT, there is no longer a significant direct effect of randomisation on the severity of symptoms. There was no direct effect of randomisation on outcomes, suggesting that allocation to therapy per se is not sufficient to produce change, rather it is the quality of the therapy providing gains in clinical outcomes (Flach et al., 2015). When the therapeutic components were analysed, agreement on problems and goals was not associated with better outcomes. The lack of an effect of having a problem list might be that it is a necessary, but not sufficient, condition for achievement of clinical improvement (Flach et al., 2015). There was instead a significant additional decrease in the symptom score estimated for case formulation (estimated 23 points decrease) and the proportion of sessions involving homework (estimated 26-point decrease). Thus, the inclusion of active therapeutic components in therapy seemed to improve outcomes although the estimate was again at a trend level of significance (Flach et al., 2015).

In a recent paper, Thompson and colleagues (2015) reviewed the therapeutic components of psychosocial treatments that have demonstrated efficacy in the intervention for CHR. The authors noted that all the trials assessing psychosocial interventions for CHR included the following common therapeutic components (Thompson et al., 2015).:

- Assessment;
- Engagement;
- Safety planning;
- Individualized case formulation;
- Cognitive behavioural strategies;
- Psychoeducation;
- Treating comorbidity;
- Improving social skills;
- Integration with other services to help meet client needs and support their goals outside of psychotherapy.

It could be believed that a comprehensive treatment for CHR should include all these core aspects delivered in appropriate modules. Assessment with valid reliable tools is a very important first step in order to develop the participant's awareness of symptoms and help him/her to self-monitor them over time, including a collaborative sharing of baseline data from psychometric scales and tracking progress during therapy (Kline & Schiffman, 2014). Engagement - as the reciprocal process in which rapport and trust are built with the patient - may be considered as extremely important for young

individuals suffering from a CHR status, particularly for those reporting increased suspicion and social isolation that could precedes frank psychosis (French & Morrison, 2004). Strong engagement may facilitate better treatment adherence and further steps of care increasing willingness to consent to higher levels of care when necessary (e.g., medication, hospitalization).

Thompson and colleagues (2015) identified the most commonly used therapeutic components of psychoeducation delivered in the recent RCTs for UHR individuals (e.g., Bechdolf et al., 2007; Ising et al., 2016; Miklowitz et al., 2014; Morrison et al., 2004, 2012; van der Gaag et al., 2012). A summary of the components is presented in Table 4.1. In addition, during the therapy progress a central role is played also by a clinical case formulation (Thompson et al., 2015). Most of RCTs on psychological interventions for UHR individuals included this core aspect of therapy (e.g., Addington et al., 2011; Bechdolf et al., 2012; Morrison et al., 2004, 2012; Kim et al., 2011), which involves a thorough understanding of the role of thoughts and beliefs in the development and maintenance of APS, continuative engagement sessions until clinical formulation is established, consider unique concerns, experience, and strengths of the participant, and a focus on "bridging" participants' and families' goals with the goals of therapy.

In the review by Thompson and colleagues (2015), development of cognitive and behavioural strategies has been found the central component on 10 RCTs of psychological treatments for CHR states. A detailed description of the core therapeutic processes involved in all the RCTs of CBT for UHR participants is provided in Table 4.2 as illustrated by Thompson and colleagues (2015).

Finally, another main target of interventions is treatment of comorbid conditions, that can improve the outcomes as evidenced by RCTs (e.g, Bechdolf et al., 2007; Yung et al., 2011). This area of therapy includes assertiveness and social skills training techniques (e.g, Bechdolf et al., 2007). Interpersonal relationship impairments are relatively common among individuals at CHR and may be an important moderator of risk for future psychosis (Addington et al., 2008; Cornblatt et al., 2011), making these skills a potentially important target for early intervention. Among adults with schizophrenia, social skill deficits predict poor occupational functioning (Dickinson et al., 2007); for younger people, poor social skills may lead to problems making friends or dealing with bullies (Yung et al., 2011). Social communication skills can be delivered both in individual and group settings to improve social network (Thompson et al., 2015).

In conclusion, it could be considered that CHR individuals show a variety of levels of symptom intensity, persistence, and distress (Thompson et al., 2015). For some, APS may be the primary target of therapy because of associated distress and impairment. For others, however, it may be useful to monitor these symptoms over time while targeting other areas of concern, such as social impairment, employment/education difficulties, comorbidities (Thompson et al., 2015). A modular approach to

treatment that is adapted from evidence-based interventions and designed to be flexible, tailored and sensitive to the needs of the individual may improve clinicians' ability to effectively treat this unique population.

Table 4.1. The most commonly used psychoeducation components in trials for CHR (Thompson et al., 2015)

Psychoeducation components
Psychoeducation provides information about mental health, coping, and CHR
Family involvement provides education to relatives
Identifying the participant's unique constellation of symptoms and teaching basic classification of symptoms (e.g., anxiety versus negative symptoms) to develop a context for effective communication
Education on the CHR neurobiology and guiding through appropriate interpretation of information
Education on environmental risk and protective factors includes discussing the role of the social climate, sleep patterns, and substance use
Discussion of role of stress response and coping
Presentation of the cognitive model (e.g., beliefs, attributions) promotes understanding of relation between thoughts, emotions, and behaviours
Normalization includes understanding symptoms as extensions of normal experiences, discussing fear as an understandable response, presenting data regarding prevalence of psychotic-like experiences, and making efforts to reduce stigma
Multiple families are brought together for psychoeducational sessions
Handouts (i.e., mood charts, symptom lists) are provided and participants/families are asked to keep records of symptoms, stress levels, mood.

Note. CHR= clinical high risk.

Table 4.2. Core therapeutic processes of CBT interventions in RCTs for CHR states (Thompson et al., 2015).

CBT processes	RCTs studies
Evaluation and testing of cognitive distortions and metacognitive beliefs Beliefs about thought processes, such as appraisals of cognitions, are collaboratively identified and tested through thought and behavioural experiments	Addington et al., 2011; Bechdolf et al., 2007, 2012; Kim et al., 2011; McGorry et al., 2013; Morrison et al., 2004, 2012; van der Gaag et al., 2012; Yung et al., 2011
Evaluation and testing of core beliefs Maladaptive beliefs about the client's self that influence the interpretation of his/her surroundings are collaboratively identified and tested through thought and behavioural experiments	Addington et al., 2011; Bechdolf et al., 2007, 2012; Kim et al., 2011; McGorry et al., 2013; Morrison et al., 2004, 2012; van der Gaag et al., 2012; Yung et al., 2011
Generating and evaluating alternative explanations Adaptive alternatives to dysfunctional appraisals, assumptions, and beliefs are collaboratively developed	Addington et al., 2011; Bechdolf et al., 2007, 2012; Kim et al., 2011; McGorry et al., 2013; Morrison et al., 2004, 2012; van der Gaag et al., 2012; Yung et al., 2011
Addressing and modifying safety behaviours Behavioural responses to distress that maintain symptoms are identified and modified by collaboratively generating healthier responses	Addington et al., 2011; Bechdolf et al., 2007, 2012; Kim et al., 2011; McGorry et al., 2013; Morrison et al., 2004, 2012; van der Gaag et al., 2012; Yung et al., 2011

Note. CBT= cognitive behavioural therapy, CHR= clinical high risk, RTCs= randomised controlled trials.

4.9. Strengths of psychological interventions

Treating young people in the putative prodromal phase does cause some concern that they may be exposed to unnecessary and potentially harmful treatments. For example, there have been some concerns about the use of antipsychotic medication (Bentall & Morrison, 2002). Thus, psychological interventions might be expected to be promising in this pre-psychotic period particularly when the symptoms are less severe and also less specific. Antipsychotic medication is effective in reducing the rate of transition to psychosis by 45%, but antipsychotics are associated with high attrition rates, e.g. 54.8% in the McGlashan et al. (2006) and McGorry et al. (2002) studies, and 37.2% in the McGorry et al. (2013) study. In addition, McGlashan and colleagues reported an 8.8 kg weight gain. The conclusion of the recent study by McGorry and colleagues (2013) was that antipsychotic medication should not be offered as a first-line treatment in CHR patients. After all, the data on antipsychotic

medication in CHR patients are based on small trials and more evidence is needed to demonstrate efficacy and safety.

French and Morrison (2004) present several arguments to support why CBT may be a beneficial psychological intervention for this clinical high-risk group. It addresses the range of symptoms and concerns present in the clinical high-risk period and teaches potentially effective strategies to protect against the impact of environmental stressors that may contribute to the emergence of psychosis.

Chapter 5: The CHiRis study (*Challenging High Risk of psychosis*): efficacy of cognitive behavioural therapy for individuals at ultra-high risk for first episode of psychosis. A randomised controlled trial

5.1. Introduction and rationale

In the last decade, growing attention has been dedicated by researchers and practitioners to early identification and intervention on groups of young individuals, who could be at increased risk of a first episode of psychosis (Fusar-Poli et al., 2014, 2015). Some recent research has been conducted by RCTs to investigate the potential benefits of CBT as a treatment strategy for these conditions (van der Gaag et al., 2013).

On one hand, there appears to be still a small number of trials on the efficacy of treatment options. One point that emerged was that the UHR group, who does not transition, reports still poor functioning and secondary clinical symptoms, such as depression and anxiety (van der Gaag et al., 2013). It has been argued that a broader set of outcomes must be used in a next generation of prevention studies in psychosis, not only focusing on prevention of a first episode of psychosis (van der Gaag et al., 2013). It has been, recently, reported that few UHR trials in the literature focused on such additional outcomes (Stain et al., 2016). Worry is an outcome that has not been considered in previous trials. It refers to a covert process of repetitive negative thinking about the future (Borkovec & Roemer, 1995), which has been consistently studied in anxiety and depressive disorders (Borkovec & Roemer, 1995), but also in frank psychosis and schizophrenia, since it has been investigated as moderator of progression into delusional symptoms (Luzón, Harrop, & Nolan, 2009; Startup, Freeman, & Garety, 2007).

More recently worry has been studied in UHR groups through observational research (e..g., Meneghelli et al., 2016). Hypervigilance of cognitive processes caused by repetitive worry has been hypothesized to be involved in the progression of psychotic symptoms among UHR groups by increasing awareness and potentially triggering the onset of frank psychotic symptoms. In a preliminary study (Palmier-Claus, Dunn, Taylor, Morrison, & Lewis, 2012), 27 UHR individuals completed a self-report diary when prompted by an electronic wristwatch several times each day for a week overall. Cognitive self-consciousness, a cognitive construct like worry, preceded the subsequent occurrence of hallucinations in individuals who reported strong beliefs about the need to control their thoughts (Palmier-Dunn et al., 2012).

Finally, as recently highlighted by some researchers (Thompson et al., 2015), given the heterogeneity

of the clinical picture reported by UHR groups, modular treatments may be improve outcomes of UHR individuals as they can include multiple therapeutic components designed to be tailored for the clients, such as modules to target not only PLES but also anxiety, depression and social skills.

5.1.1. Primary objectives

Primary objectives of the current study were:

(a) to assess whether a CBT modular protocol can reduce or delay risk of transition to psychosis in a group of UHR individuals after 6 months (post-treatment) and 14-months (follow-up), compared with treatment as usual as a control condition. The primary outcome was the number of participants who developed a first episode of psychosis.

(b) to compare the CBT intervention with the control condition on the number of participants who reported a remission status on the ARMS and of those who had subthreshold psychotic symptoms (still ARMS status) at post-treatment and follow-up.

5.1.2. Secondary objectives

Secondary objectives were:

(c) to compare the CBT intervention with the control condition on secondary outcomes, including depression, anxiety, worry and global functioning at post-treatment and follow-up.

5.2. Method

5.2.1. Eligibility criteria of participants

Participants were help-seeking individuals recruited from secondary mental health services of Azienda USL Toscana Centro. They were included if were 16 to 35 years old and met criteria for ARMS at the Comprehensive Assessment of At Risk Mental States (CAARMS; Yung et al., 2006; Yung et al., 2005). Participants were not included if they had diagnosis of a neurological disorder, mental retardation, autism, current or history of psychosis or bipolar disorder, previous psychotic episodes, active suicidal intent, had undergone CBT, were on antipsychotic medications, had insufficient competence in the Italian language. Concomitant antidepressant medications were allowed only if they were kept on a stable dosage for the whole treatment duration. Concurrent psychological treatments also resulted in exclusion.

Participants were identified and contacted through advertisements on leaflets and e-mail messages to general medicine doctors, psychiatrists, psychologists, social workers of public and private services. A series of workshops for mental health professionals were organized by a group of psychologists extensively trained in this topic in order to provide information on identification of signs of ARMS and encourage referrals. Help-seeking individuals at mental health services with a suspicion of clinical picture of a psychotic risk were referred by mental health professionals, then were assessed through the CAARMS by the study staff.

The study also used the following exit/discontinuation criteria: (a) voluntary discontinuation by the participant who was free to leave the study at any time, without prejudice to further treatment; (b) safety reasons as judged by the investigator (ie, the participant met criteria for conversion to a first psychotic episode or developed suicidal intent). Participants who developed a first episode of psychosis entered into routine mental health service treatment pathways.

5.2.2. Baseline measures

Baseline Axis I disorders were assessed through the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I; First et al., 1997; SCID-I Italian version; Mazzi et al., 2000). The module on psychosis was administered at post-treatment and follow-up and used as primary outcome measure. Comorbid personality disorders were investigated through the Structured Clinical Interview for DSM-IV-TR Personality Disorders (SCID-II; First et al., 1997). The SCID-II is a semi-structured clinical interview composed by 140 questions which assess symptoms of diagnostic criteria of personality disorders classified by the DSM-IV-TR. Score on each question are coded by the interviewer on a three-point Likert scale ("Absent symptom"= 1, "Doubt"= 2, "Present"= 3). Assessment of each personality disorder is conducted calculating the sum of scores. The Italian version of the SCID-II (Maffei et al., 1997) had good internal consistency (Cronbach's alpha= 0.79).

5.2.3. Primary outcomes

Primary outcomes were the number of participants who reported a first psychotic episode at post-treatment or follow-up, including also any of psychotic disorders or bipolar disorders according the DSM-IV-TR (American Psychiatric Association, 2000). Diagnosis was assigned through the SCID-I and confirmed by the PANSS. Development of a first psychotic episode was assessed 6 months after baseline (post-treatment) and 14 months after baseline (8-month follow-up from post-treatment) or at

the moment the therapist who was conducting treatment, informed the researchers that a transition had (probably) occurred.

Primary outcomes were also the reduction of subthreshold psychotic symptoms assessed by the CAARMS. The Positive And Negative Syndrome Scales (PANSS; Kay et al., 1989) was used as a measure of psychotic symptoms. The structure of the measure is based on the bidimensional model of Crow (1980), which differentiates positive symptoms from negative ones, and is composed by 7 items assessing positive, 7 assessing negative symptoms and 16 covering general psychopathological symptoms (Kay et al., 1989). The questionnaire is a self-report tool. High scores indicate severe psychotic symptoms.

5.2.4. Secondary outcomes

Secondary outcomes were severity of depressive symptoms, anxiety, worry, and general functioning. The Beck Depression Inventory-second edition (BDI-II; Beck, Steer, & Brown, 1996) was used as a measure of severity of depressive symptoms. The BDI-II is a self-report tool composed by 21 statements assessing cognitive, affective, motivational and physiological characteristics of depression. A cut-off score of 20 was identified to define clinically significant depression. The Italian version (Sica, Ghisi & Lange, 2007) showed excellent internal consistency in clinical and non-clinical samples (Cronbach's alpha was 0.93 and 0.92, respectively). In the current study, internal consistency was ex excellent (Cronbach's alpha= 0.92).

The Beck Anxiety Inventory (BAI; Beck & Steer, 1990) is a 21-item self-report tool designed to assess anxiety symptoms. Items are rated from 0 to 3 scores. The Italian version (Sica et al., 2007) had good internal consistency (Cronbach's alpha= 0.80). A cut-off score of 20 was identified to define clinically significant anxiety. In the current study, internal consistency was ex excellent (Cronbach's alpha= 0.90).

The Penn State Worry Questionnaire (PSWQ; Meyer et al., 1990) was used as a measure of worry and its characteristics of intensity, frequency, persistence and uncontrollability. The PSWQ is a self-report tool composed by 16 items on a five-point Likert scale ("Not at all typical of me"= 1, "Vey typical of me"= 5). High scores indicate severe worry. The Italian version (Morani, Pricci, & Sanavio, 1999) had good internal consistency. In the current study, internal consistency was good (Cronbach's alpha= 0.84).

The Global Assessment of Functioning scale (GAF; Startup, Jackson, & Bendix, 2002) combines the evaluation of symptoms as well as relational, social and occupational functioning on a single axis. The scale runs from 1 to 100 and is divided into 10 equal parts providing defining characteristics,

both symptoms and functioning, for each 10-point interval. A low rating reflects worse symptoms and a poorer level of functioning, whereas a high rating reflects less symptoms and a better level of functioning. The GAF score is known to be a valid measure of global functioning in patients with schizophrenia (Schwartz, 2007).

5.2.5. Feasibility and satisfaction with CBT

Feasibility of the treatment was evaluated by calculating attrition rates for each treatment arm. Satisfaction with treatment was assessed through a satisfaction self-report questionnaire ad hoc developed to measure aspects related to satisfaction, self-efficacy in the self-management of symptoms after the end of the psychotherapeutic course. It is composed by 11 statements (eg, "Did the psychotherapeutic path improve your psychological well-being?") rated on a five-point Likert scale ("Completely"= 5, "Not at all"= 0). In the current study, internal consistency was excellent (Cronbach's alpha= 0.90).

5.2.6. Design

The study was conducted following The Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT 2013; Chan et al., 2013) with a randomised controlled superiority parallel-group single-blinded design. Participants classified as at high risk were randomly assigned to CBT or a control condition. Control condition included 30 weekly individual supportive sessions, consisting of identification of needs and current problems of the participant, validating, empathetic listening and confrontation (i.e, paraphrasing what the participant was telling), and clarification what he/she was saying without the use of active CBT techniques and concepts for PLEs and any secondary symptoms (eg, psychoeducation on PLEs, cognitive restructuring). Supportive sessions in the control condition were delivered by clinical psychologists. The flowchart of participants' progression over study course is presented in Figure 5.1.

Socio-demographic and clinical characteristics were collected before randomisation. Random sequence was created by a computerized program. An independent researcher, not involved in the study assigned participants to treatment arms. Allocation was conducted through a 1:1 blocking procedure. Random sequence was concealed by an independent researcher, who put random numbers into envelopes and kept them in a remote location. Allocation concealment was ensured, as the researcher did not release the randomization code until the patient was recruited into the trial, which

occurred after all baseline measures were administered. Participants were then allocated after providing informed consent

A single-blinding procedure was adopted. Assessment at baseline, 6-month post-treatment, and 14-month follow-up with both clinical interviews and self-report measures were conducted by blind independent assessors. Due to difficulties related to blinding of participants in psychotherapy trials, in the current study a double-blinding procedure was not adopted.

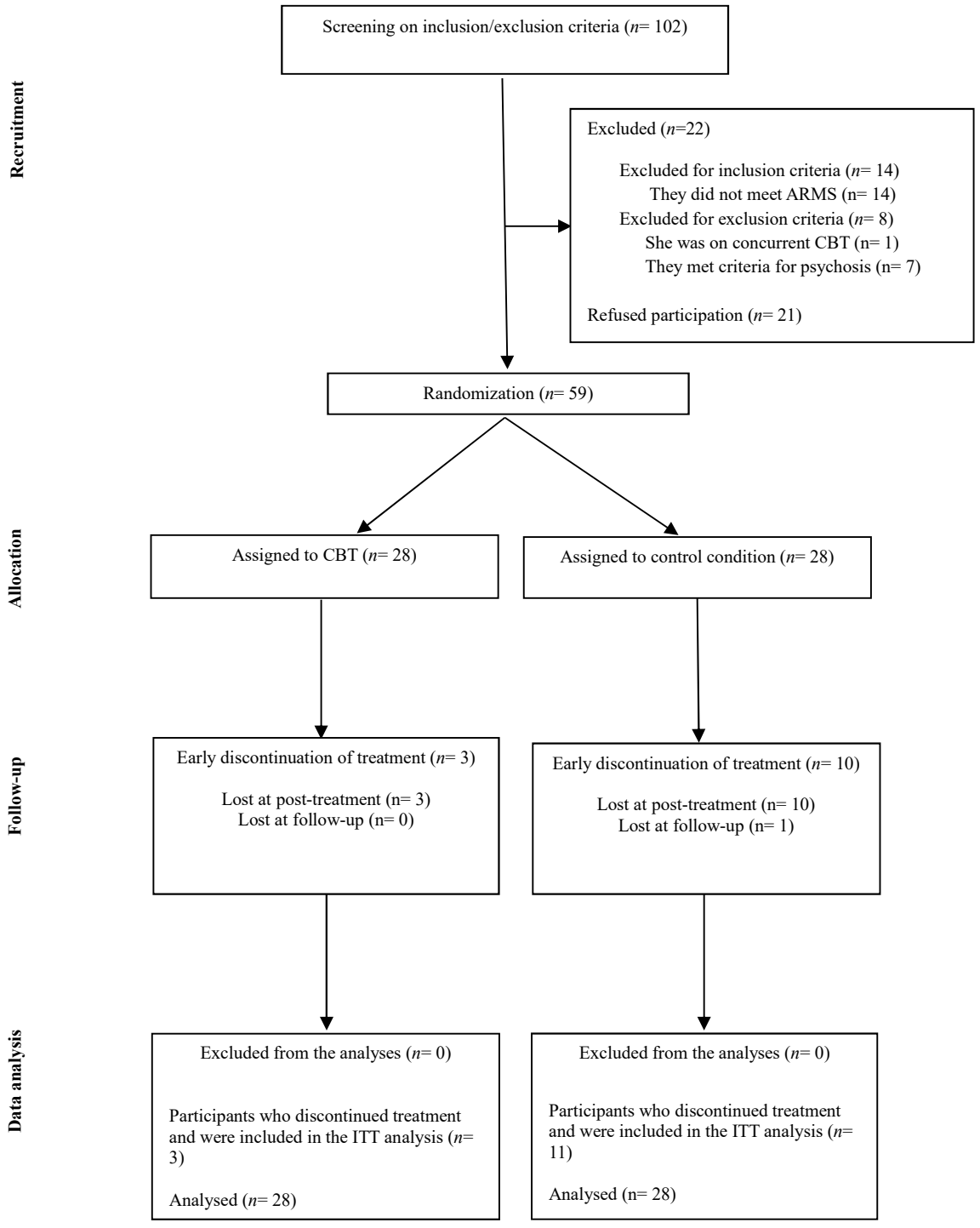


Figure 5.1. CONSORT flowchart of participants through the phases of the trial.

5.2.7. Diagnostic inter-rater reliability

The CAARMS SCID-I and SCID-II were administered by two independent assessors (psychiatrists or psychologists), who were trained by internships in conducting the SCID-I, SCID-II and CAARMS (including observation of experienced trainers conducting the interviews). Assessors were blind to treatment allocation.

All the diagnoses were reached by inter-rater consensus through staff meetings during the enrolment of the participants, in which each case was carefully reviewed for accuracy and between-rater discrepancy was discussed to reach consensus. Inter-rater agreement was reached for all the included participants except for two cases whose ARMS status was not resolved initially. Then, these participants were excluded by consensus of a third independent assessor.

5.2.8. Treatment fidelity

The CBT intervention was delivered by clinical psychologists with four-year training in CBT and extensively trained in the assessment and treatment of UHR states with three years of experience in the CBT treatment of ARMS. Training of therapists included reading of therapy manuals for UHR CBT, attending oral presentations, meetings with international experts, workshops, conferences, courses with international experts in this field, participating in role playing sessions on CBT for CHR supervised through monthly meetings of supervision. Psychologists who delivered CBT were on supervision by at least one expert with 30-year experience in CBT.

Treatment fidelity was assessed by a random selection of a group of CBT sessions which were audiotaped (n= 10). Such sessions were subsequently rated by two other clinical psychologists trained in the CBT protocol who were not involved in the trial. Cohen's kappa estimates of fidelity judgements were all equal or higher than 0.70, suggesting satisfactory inter-rate agreement on fidelity to the protocol (Cohen, 1960).

5.2.9. Procedure

The study was conducted between March 2014 and November 2016. Participants were screened and recruited between June 2014 and September 2015. The CBT manual was created during December 2013 and May 2014. Data analysis was conducted in October 2016.

Participation was voluntary and uncompensated. All participants were offered antidepressant or anxiolytic medication according to needs. However, no anti-psychotic medication was prescribed unless/until participants met criteria for the onset of a psychotic episode. Prescription and

management of medication was the responsibility of medical staff who was in contact with, but not involved in, the study and was blind to group allocation. All the individuals who were included were asked to provide written informed consent to participate after having received a detailed description of the study aims. Individuals being under 18 years old required informed consent from both parents. Participants' identities remained anonymous. Participants had the possibility to withdraw their informed consent at any time with no consequence for their treatment

All materials containing personal information about participants were kept accurately on electronic supports protected by passwords or clinical folders that contained an identification code specific for each participant. On each folder, the name of the participant was not included, but it was kept in another protected site. The research protocol has been approved by the Institutional Ethics Committee. The trial was conducted according to the Helsinki Declaration.

5.2.10. Cognitive behavioural therapy (CBT) protocol

The CBT protocol consisted of 30 individual weekly sessions each lasting about one hour. Treatment lasted for six months overall. The protocol was a modular treatment based on a manual of CBT for young individuals at UHR for psychosis (van der Gaag et al., 2013), whose efficacy has been already assessed in previous trials (Ising et al., 2016; Riedtijk et al., 2010).

The goal of the intervention was to reduce distress provoked by extraordinary experiences (van der Gaag et al., 2013). Therapeutic components were adapted to follow recommendations by Thompson and colleagues (2015) who identified the following core components in RCTs of psychological interventions for CHR states: Assessment, Engagement, Individualized case formulation, Psychoeducation, Cognitive behavioural strategies, Treatment of comorbid conditions (depression, anxiety), Improvement of social skills. The intervention developed by van der Gaag and colleagues (2013) was enriched with additional components targeting depression (e.g, cognitive restructuring and behavioural experiments testing depressive distortions), social skills (e.g, assertiveness training), and worry and generalized anxiety (time for worry, cognitive restructuring of metacognitive distortions of worry advantages and its dangerous effects).

The protocol was divided in different phases including specific therapeutic components: (1) introduction, (2) assessment, (3) engagement and goal setting, (4) normalization of PLEs, (5) cognitive restructuring and metacognitive intervention, (6) skills of emotions management, (7) intervention on depression, (8) intervention on worry, (9) intervention on social anxiety and social skills, (10) relapse prevention, (11) booster sessions. A detailed description of the protocol and therapeutic materials/worksheets is provided in the Appendix at the end of the manuscript.

During the Introduction phase, the therapeutic path is presented including sessions agenda and techniques which will be used. During the Assessment phase, collaborative functional analysis aimed at identified trigger situations; ABC diaries are completed by the participant and the therapist during the session; symptom monitoring is facilitated; automatic thoughts, intermediate and basic assumptions are analysed. Subsequently, in the Engagement phase, working together, the therapist and the participant develop a shared hierarchy of goals for the therapeutic intervention. The therapeutic model is based on the hypothesis that the final common pathway from ARMS to psychosis is largely caused by catastrophic misinterpretations of psychotic-like symptoms which are then exacerbated by a high level of emotional arousal (Riedijk et al., 2010).

During the fifth phase, psychoeducation on extraordinary experiences and PLEs is provided. Young individuals with ARMS often are worried about their extraordinary experiences: they can fear losing control over their minds (Meneghelli et al., 2016). Receiving an exploratory model of extraordinary experiences and learning that there is an adequate treatment is a comforting message, that attenuates distress associated with extraordinary experiences themselves (van der Gaag et al., 2013).

The subsequent phase, Cognitive restructuring and metacognitive intervention, aims to increase the awareness of the individual of the effects of cognitive distortions on emotional experience, physiological responses and behaviours. The intervention aims to enhances monitoring by the young individual of the effects of distortions and help him/her to modify them and their impact on thought, emotions and behaviours. The ABC (activating events, beliefs, consequences) model is provided and is used to help the individual to discover the connection between emotions, thoughts and behaviours. The aim here is learning how activating events can induce beliefs, which can cause response in terms of emotions, somatic signals and behaviours (van der Gaag et al., 2013). Cognitive interventions, such as cognitive restructuring and behavioural experiments are designed to challenge and test dysfunctional beliefs. Those interventions are also developed in order to help the individual stopping avoidance of trigger situations and safety behaviours; in addition, exposure to trigger stimuli is scheduled.

The subsequent three modules, Intervention on depression, Intervention on worry, Intervention on social anxiety and social skills are conceived to target comorbid conditions which are often present among UHR individuals. Intervention on depression starts with completing mood charts, analysing pleasant activities for the young individual, scheduling pleasant activities that are assigned using a self-monitoring diary. In this diary, the individual had to indicate and schedule activities that they have engaged during the subsequent days, to report emotions and thoughts they had and to measure the intensity of these emotions. The rationale for this is to enhance greater awareness of positive emotions and the intensity associated to them, to enhance self-efficacy in the management of daily

living, thus reducing experience of anxiety and depressive symptoms. Such activities are conceived as behavioural experiments, aimed to challenge catastrophic beliefs about capacity to get pleasure from daily activities ("My days always are unemotional", "I never feel emotions"). Different from the protocol of van der Gaag and colleagues (2013), a module on worry is added, introducing psychoeducation on worry, exploring and correcting metacognitive maladaptive assumptions about worry (positive and negative cognitions about worry) and CBT strategies to manage worry (exposures, problem solving, behavioural experiments, relaxation techniques). Intervention on social anxiety integrates principles of assertiveness training, targets self-esteem by role-playing and in-session and out-session exposure. Trigger situations are identified first. Then, distorted beliefs about self, others and the world are analysed with restructuring strategies. Finally, to optimize flexibility of the intervention, the participant and the therapist can expose themselves together in the real-life context of the young UHR individual out of the office. Subsequently, the participant is encouraged to face such situations on his/her own in order to enhance generalizability of the therapeutic process. At the end of the therapeutic course, a relapse prevention module is dedicated to the identification of early warning signs of relapse.

Between-session homework tasks are planned during all the treatment course. At the end of each session, the therapist asks the participant for feedback (e,g, how he/she did feel during the session, potential encountered difficulties, usefulness of the session content). Together, they develop key take-home messages.

A detailed description of the phases and CBT psychotherapeutic components used during each session is provided in Table 5.1.

Table 5.1. Description of the CBT psychotherapeutic components for each session and phase.

Sessions	Phase	Psychotherapeutic components
1	Introduction and goal setting	▪ Defining agenda of the session ▪ Presentation of the ABC model ▪ Discussion of outcomes of interviews and questionnaires completed at pre-treatment ▪ Completing diaries ▪ Setting of therapeutic goals ▪ Presentation of the CBT techniques ▪ Discussion on rationale for homework ▪ Asking the patient for feedback about the session ▪ Take-home messages ▪ Homework
2	Assessment	▪ Review of previous session ▪ Discussion on homework ▪ Defining agenda of the session ▪ Completing diaries ▪ Identification of trigger situations ▪ Symptom monitoring ▪ Exploring automatic thoughts, intermediate beliefs, basic assumptions ▪ Downward arrow ▪ Asking the patient for feedback about the session ▪ Take-home messages ▪ Homework
3	Assessment	▪ Review of previous session ▪ Discussion on homework ▪ Defining agenda of the session ▪ Meeting with parents and family members ▪ Asking the family members for feedback about the session ▪ Take-home messages
4	Engagement	▪ Review of previous session ▪ Discussion on homework ▪ Defining agenda of the session ▪ Case formulation ▪ Asking the patient for feedback about the session ▪ Take-home messages ▪ Homework
5-7	Normalization of psychotic experiences	▪ Review of previous session ▪ Discussion on homework ▪ Defining agenda of the session ▪ Normalizing information and psychoeducation on psychotic-like experiences ▪ Information on dopamine sensitization ▪ Written materials ▪ Flashcards ▪ Asking the patient for feedback about the session ▪ Take-home messages ▪ Homework
8-12	Cognitive restructuring and metacognitive intervention	▪ Review of previous session ▪ Discussion on homework ▪ Defining agenda of the session ▪ Introduction of cognitive distortions ▪ Written materials ▪ Cognitive and metacognitive restructuring ▪ Identifying alternative explanations ▪ Development of more functional thoughts

		▪ Attentional training ▪ Flashcards ▪ Asking the patient for feedback about the session ▪ Take-home messages ▪ Homework
13-15	Cognitive restructuring and metacognitive intervention	▪ Review of previous session ▪ Discussion on homework ▪ Defining agenda of the session ▪ Organizing of hierarchy ▪ Exposure and behavioural experiments ▪ Asking the patient for feedback about the session ▪ Take-home messages ▪ Homework
16	Skills for emotions management	▪ Review of previous session ▪ Discussion on homework ▪ Defining agenda of the session ▪ Normalizing information and psychoeducation on emotions and bodily sensations ▪ Written materials on emotions ▪ Asking the patient for feedback about the session ▪ Homework
17	Skills for emotions management	▪ Review of previous sessions ▪ Defining agenda of session ▪ Discussion on homework ▪ Relaxation techniques (diaphragmatic breath, muscular progressive relaxation) ▪ Written materials ▪ Flashcards ▪ Asking the patient for feedback about the session ▪ Take-home messages ▪ Homework
18-19	Intervention on depression	▪ Review of previous session ▪ Discussion on homework ▪ Defining agenda of the session ▪ Cognitive bias of depression ▪ Cognitive restructuring of depression bias ▪ Daily mood graph ▪ Behavioural experiments ▪ Behavioural activation ▪ Pleasant activities ▪ Flashcards ▪ Asking the patient for feedback about the session ▪ Take-home messages ▪ Homework
20-21	Intervention on depression	▪ Review of previous session ▪ Discussion on homework ▪ Defining agenda of the session ▪ Intervention on procrastination ▪ Self-instructional training ▪ Asking the patient for feedback about the session ▪ Take-home messages ▪ Homework
22-25	Intervention on worry	▪ Review of previous session ▪ Discussion on homework ▪ Defining agenda of the session ▪ Problem solving ▪ Time for worry ▪ Flashcards

		▪ Asking the patient for feedback about the session ▪ Take-home messages ▪ Homework
26-29	Intervention on social anxiety	▪ Review of previous session ▪ Discussion on homework ▪ Defining agenda of the session ▪ Psychoeducation on assertiveness and social skills ▪ Completing assertiveness diaries ▪ Role playing on social skills ▪ Exposure on social cues and trigger situations ▪ Assertiveness exercises ▪ Exercises to strengthen self-esteem ▪ Flashcards ▪ Asking the patient for feedback about the session ▪ Take-home messages ▪ Homework
30	Relapse prevention	▪ Overview of the psychotherapeutic course and key points ▪ Asking the patient for feedback about the session ▪ Relapse prevention
31	Booster session	▪ Review of the psychotherapeutic course ▪ Review of case formulation ▪ Review of psychoeducation on psychotic-like experiences ▪ Review of cognitive and metacognitive restructuring ▪ Completing ABC diaries on recent trigger situations ▪ Asking the patient for feedback about the session ▪ Take-home messages ▪ Booster homework
32	Booster session	▪ Review of the assertiveness concept ▪ Completing ABC diaries on recent trigger situations ▪ Asking the patient for feedback about the session ▪ Take-home messages ▪ Booster homework

5.2.9. Homework tasks compliance

Compliance with homework tasks (defined as completion of homework written worksheets, reading psychoeducation materials, listening of relaxation audiotaped records, performing between-session exposures and behavioural experiments) was recorded as present at each session if a review of the homework tasks assigned in the previous session was added in the notes.

5.2.10. Data analysis

Comparisons between the CBT and the control groups on baseline sociodemographic and clinical characteristics were conducted through ANOVA or non-parametric statistics (chi squared, Kruskal-Wallis, Mann-Whitney U test).

The primary outcome was analysed using Kaplan-Meier survival statistics. Participants lost to follow-up were coded conservatively as non-converters. Survival curves were compared using the log-rank test.

Data at post-treatment and follow-up on secondary outcomes were analysed using the intention to treat approach that was applied with the last observation carry-forward technique (Newell, 1992). Analyses on secondary outcomes were conducted on the group of participants who did not make a transition to psychosis during the study period. These analyses cannot be done by linear mixed-modelling analysis because the missing values after a transition were not random: in the control group, a higher number of participants developed a psychosis episode as compared as the those in CBT group.

Changes over time were analysed by univariate tests of ANCOVA of the data at post-treatment (6 months) and follow up (14 months), with baseline scores as covariate of the people who were non-transitions at that measurement moment. Eta Squared (η^2) were calculated as effect sizes (Olejnik & Algina, 2003). Values of 0.01, 0.06, 0.14 suggest low, moderate, and large effect sizes, respectively (Cohen, 1988).

Chi square linear-by-linear test was performed to assess the discrete outcomes, such as ARMS status (in remission, at risk, psychosis).

Numbers needed to treat were calculated for prevention of transition and attaining remission status. For all the analyses, statistical significance was set at a 0.01 or 0.05 p-value. Statistical analyses were conducted with the Statistical Packages for the Social Sciences software (SPSS, version 21.00).

5.3. Results

5.3.1. Baseline socio-demographic characteristics in the total study group

A total of 58 participants were included in the study. In the total study group, mean age was 25.71 years (SD= 6.00, range 16-35). Thirty-nine individuals (67.20%) were males. Fifty-one (87.90%) were born in Italy. Individuals who were born in another country were 7 participants (12.10%); in this subgroup, mean duration of stay in Italy was 16.71 years (SD= 8.28, range= 8-26). One participant was born in Eastern Europe (Romania), three in Central or Northern Europe (one in France, one in Switzerland, one in the Netherlands), two in Africa (one in Ethiopia, one in Iran), one in Southern America (Bolivia). Nineteen (32.80%) were students, 27 (46.60%) were unemployed, 12 (20.60%) were employed. Twenty-nine (50%) had high-school license. Participants were referred from mental health professionals of secondary mental health services. Specifically, thirty-four participants (58.60%) were recruited from Struttura Operativa Semplice 5, 5 (8-60%) from Struttura Operativa Semplice 6, 3 (5.10%) from Struttura Operativa Semplice 2-4, 6 (10.30%) from Unità Funzionale di Salute Mentale Adulti (UFSMA) zona Mugello, 2 (3.40%) from Unità Funzionale Salute Mentale Infanzia e Adolescenza (UFSMIA) of Florence, 3 (5.10%) from Unità Funzionale Salute Mentale Adulti e Unità Funzionale Salute Mentale Infanzia e Adolescenza of Prato, 5 (8-60%) from private mental health professionals (psychiatrists and psychologists) working in Florence or Prato and coworking with those public secondary mental health services.

A detailed overview of baseline socio-demographic characteristics is provided in Table 5.2.

5.3.2. Comparison of baseline socio-demographic characteristics in CBT and control groups

Mean age in the CBT group was not significantly different from age in the control group ($F_{(1, 56)}$= 0.13, p= 0.71). Groups were not significantly different also on gender [$\chi^2_{(1)}$= 0.78, p= 0.78], area of residence in Italy [$\chi^2_{(1)}$= 2.07, p= 0.15], birth country [Kruskal-Wallis $\chi^2_{(1)}$= 0.15, p=0.69], marital status [$\chi^2_{(1)}$= 0, p= 1], education level [Kruskal Wallis $\chi^2_{(1)}$= 2.06, p= 0.15], employment status [$\chi^2_{(1)}$= 2.06, p=.07], birth country (immigrant status) [$\chi^2_{(1)}$= 0.16, p= 0.68].

Table 5.2. Baseline socio-demographic characteristics of total study group and conditions groups.

	Total group (*n*= 58)	**CBT (*n*= 29)**	**Control condition (*n*= 29)**	$\chi^2_{(df)}$ / $F_{(df)}$
	M (SD; range)	*M (SD; range)*	*M (SD; range)*	
Age (years)	25.71 (6; 16-35)	25.41 (6.12; 16-35)	26 (5.97; 16-35)	$0.13_{(1, 56)}$
	n (%)	*n (%)*	*n (%)*	
Gender				$0.78_{(1)}$
Males	39 (67.20)	19 (65.50)	20 (69)	
Females	19 (32.80)	10 (34.50)	9 (31)	
Area of residence in Italy				$2.07_{(1)}$
Centre	56 (96.60)	29 (100)	27 (93.10)	
South	2 (3.40)	0	2 (6.90)	
Birth country				$0.15_{(1)}$
Italy	51 (87.90)	26 (89.70)	25 (86.20)	
Eastern Europe	1 (1.70)	0	1 (3.40)	
Central or Northern Europe	3 (5.20)	0	3 (10.30)	
Africa	2 (3.40)	2 (6.90)	0	
Southern America	1 (1.70)	1 (3.40)	0	
Marital status				$0_{(1)}$
Single	54 (93.10)	27 (93.10)	27 (93.10)	
Married	4 (6.90)	2 (6.90)	2 (6.90)	
Employment status				$3.23_{(1)}$
Student	19 (32.80)	12 (41.40)	7 (24.10)	
Employed	12 (20.70)	7 (24.10)	5 (17.20)	
Unemployed	27 (46.60)	10 (34.50)	17 (58.60)	
Education level				$2.06_{(1)}$
Mid school license	20 (34.50)	7 (24.10)	13 (44.80)	
High school license	29 (50)	17 (58.60)	12 (41.40)	
Degree	9 (15.50)	5 (17.20)	4 (13.80)	

5.3.3. Baseline clinical characteristics

In the total study group, 58 participants (100%) reported APS for intensity, 58 (100%) reported APS for frequency, 3 (5.20%) had BLIPS and 8 (13.80%) had a family history of psychosis or schizotypal personality disorder. Twenty (34.50%) had any of anxiety disorders, 27 (46.60%) had any of unipolar mood disorders. The most prevalent axis I disorders were Dysthymia (n= 18, 31%), Obsessive compulsive disorder (n= 12, 20.70%), Major depressive disorder (n= 8, 13.80%), and Panic disorder (n= 7, 12.10%). Sixty-three percent had a BDI-II score above the cut-off (20), showing clinically significant depression symptoms. Sixty-one had a BAI score above the cut-off (20). Twenty-seven (46.60%) had a comorbid personality disorder. The most prevalent personality disorders were

schizoid/schizotypal personality (n= 14, 24.10%) and avoidant personality (n= 6, 10.30%). Thirty-two (55.20%) were on concomitant antidepressants, 10 (17.20%) were on anxiolytic benzodiazepines. The two groups were not significantly different for the number of participants having an unipolar mood disorder [$\chi^2_{(1)}$= 0.62, p= 0.43], any of anxiety disorders [$\chi^2_{(1)}$= 0.30, p= 0.58], one or more comorbid personality disorders [$\chi^2_{(1)}$= 1.73, p= 0.18], current cannabis use [$\chi^2_{(1)}$= 0.89, p= 0.34]. The two groups did not differ for the number of participants on antidepressants [$\chi^2_{(1)}$= 0.27, p= 0.59] and anxiolytics [$\chi^2_{(1)}$= 1.61, p= 0.20], for the number of those having BLIPs [$\chi^2_{(1)=}$ 0.34, p= 0.55], belonging to the CAARMS vulnerability group [$\chi^2_{(1)}$= .058, p= 0.44]. The CBT and the control group did not significantly differ for intensity of subclinical positive symptoms assessed by the CAARMS [$F_{(1, 56)}$= 0.04, p=0.84] and frequency [$F_{(1, 56)}$= 0.68, p= 0.41]. An overview of baseline clinical characteristics is provided in Table 5.3.

5.3.4. Differences across gender and age on subclinical psychotic symptoms

No significant difference across gender was found on intensity and frequency of subclinical positive symptoms. Regarding types of subclinical symptoms, a significant difference was found only between males and females on disorganised speech [$F_{(1, 56)}$= 6.05, p<0.05], with males having more severe subclinical levels than females. No difference was found for unusual content thought, non-bizarre ideas and perceptual abnormalities.

Bivariate correlations between age and intensity and frequency of subclinical positive symptoms did not result significant [range of Pearson's r= 0.21-0.24, p= 0.07-0.11]. Correlations between age and types of subclinical symptoms were not significant for unusual content of thoughts, non-bizarre ideas and perceptual abnormalities [range of Pearson's r= -0.17-0.17, p= 0.18-0.19]. A moderate positive correlation was found between age and disorganised speech [Pearson's r= 0.32, p<0.05], suggesting that older participants reported higher subclinical symptoms of disorganised speech.

Table 5.3. Baseline clinical characteristics.

	Total group (*n*= 58)	**CBT condition (*n*= 29)**	**Control condition (*n*= 29)**	$\chi^2_{(df)}$ / $t_{(df)}$
	n (%)	*n (%)*	*n (%)*	
Any of non-psychotic Axis I disorders	45 (77.60)	21 (72.40)	24 (82.80)	$0.89_{(1)}$
Type of non-psychotic Axis I disorders				
Generalized anxiety disorder	6 (10.30)	4 (13.80)	2 (6.90)	
Dysthymia	18 (31)	11 (37.90)	7 (24.10)	
Obsessive compulsive disorder	12 (20.70)	7 (24.10)	5 (17.20)	
Panic disorder	7 (12.10)	4 (13.80)	3 (10.30)	
Agoraphobia	5 (8.60)	1 (3.40)	4 (13.80)	
Social phobia	5 (8.60)	4 (13.80)	4 (3.40)	
Major depressive disorder	8 (13.80)	4 (13.80)	4 (13.80)	
Eating disorders	2 (3.40)	0	2 (6.90)	
Specific phobias	2 (3.40)	0	2 (6.90)	
Hypocondriasis	2 (3.40)	0	2 (6.90)	
Alcol abuse	1 (1.70)	0	1 (3.40)	
Gambling	1 (1.70)	0	1 (3.40)	
Number of personality disorders				$1.73_{(1)}$
None of personality disorders	32 (55.20)	19 (65.50)	13 (44.80)	
One personality disorder	21 (36.20)	9 (31)	12 (41.40)	
More than one personality disorder	5 (8.60)	1 (3.40)	4 (13.80)	
Type of personality disorders				
Schizoid/schizotypal	14 (24.10)	5 (17.20)	9 (31)	
Avoidant	6 (10.30)	4 (13.80)	2 (6.90)	
Dependent	5 (8.60)	2 (6.90)	3 (10.30)	
Borderline	4 (6.90)	1 (3.40)	3 (10.30)	
Obsessive compulsive	3 (5.20)	1 (3.40)	2 (6.90)	
Paranoid	1 (1.70)	0	1 (3.40)	
Cannabis use	13 (22.40)	5 (17.20)	8 (27.60)	$0.89_{(1)}$
CAARMS groups				
APS intensity	58 (100)	29 (100)	29 (100)	$0_{(1)}$
APS frequency	58 (100)	29 (100)	29 (100)	$0_{(1)}$
BLIPs	3 (5.20)	2 (6.90)	1 (3.40)	$0.35_{(1)}$
Vulnerability group	8 (13.80)	3 (10.30)	5 (17.20)	$0.58_{(1)}$
Antidepressants	32 (55.20)			$0.27_{(1)}$
Sertraline	9 (15.50)	7 (24.10)	2 (6.90)	
Paroxetine	5 (8.60)	3 (10.30)	2 (6.90)	
Fluoxetine	2 (3.40)	2 (6.90)	0	
Fluvoxamine	3 (5.20)	1 (3.40)	2 (6.90)	
Citalopram	4 (6.90)	2 (6.90)	2 (6.90)	
Escitalopram	7 (12.10)	2 (6.90)	5 (17.20)	
Venlafaxine	1 (1.70)	0	1 (3.40)	
Mirtazapine	1 (1.70)	0	1 (3.40)	
Duloxetine	1 (1.70)	0	1 (3.40)	
Anxiolytic benzodiazepines	10 (17.20)	3 (10.30)	7 (24.10)	$1.61_{(1)}$

5.3.5. Relation between comorbidity and subclinical psychotic symptoms in the total group

In the total study group, the group with personality disorders had higher intensity of subclinical positive symptoms measured by the CAARMS [$F_{(1, 56)}$= 10.32, p<0.01], negative symptoms measured by the PANSS [$F_{(1, 56)}$= 17.37, p<0.001], and at a trend level higher frequency of subclinical positive symptoms measured by the CAARMS [$F_{(1, 56)}$= 3.69, p= 0.06] but not the positive symptoms measured by the PANSS [$F_{(1, 56)}$= 0.62, p= 0.43]. Specifically regarding subclinical symptoms, those with at least one of personality disorders had higher non-bizarre ideas [$F_{(1, 56)}$= 9.79, p<0.01] and disorganized speech measured by the CAARMS [$F_{(1, 56)}$= 11.51, p<0.01], and at a trend level usual thought content [$F_{(1, 56)}$= 3.08, p= 0.08] but not perceptual abnormalities [$F_{(1, 56)}$= 0.0, p= 0.98].

The group with any of non-psychotic Axis I disorders had higher disorganised speech [$F_{(1, 56)}$= 5.84, p< 0.05] but not the other subclinical positive symptoms measured by the CAARMS, neither intensity nor frequency of positive subclinical symptoms.

The group with any of unipolar mood disorders had higher general psychopathology measured by the PANSS [$F_{(1, 56)}$= 7.33, p<0.01], and at a trend level frequency of positive subclinical symptoms [$F_{(1, 56)}$= 3.36, p= 0.07]. The group with and that without any of anxiety disorders did not differ on any positive and negative symptoms measured.

5.3.6. Rates and characteristics of drop-outs in the total study group

In the total group, 13 participants (22.40%) left early the study before completing post-treatment assessments and were considered as drop-outs. Among drop-outs, the mean number of attended sessions was 4.92 (SD= 2.53; range= 2-11). The number of completed sessions and reasons for drop out are presented in Table 5.4.

The number of females in the drop-out group was significantly higher than in the group of those who completed all treatment sessions and post-treatment assessments [$\chi^2_{(1)}$= 10.11, p<0.001]. Drop-outs and completers were not significantly different for age [Mann Whitney U= 270, p= 0.67], having a non-psychotic Axis I disorder [$\chi^2_{(1)}$= 0.04, p= 0.94], having any of anxiety disorders [$\chi^2_{(1)}$= 0.10, p= 0.75], any of unipolar mood disorders [$\chi^2_{(1)}$= 0.44, p= 0.50], having a personality disorder [$\chi^2_{(1)}$= 0.01, p= 0.97] or current cannabis use [$\chi^2_{(1)}$= 0.67, p=0.41], intensity of subclinical positive symptoms on the CAARMS [$F_{(1, 56)}$= 0.07, p=0.79] or frequency [$F_{(1, 56)}$= 0.28, p=0.59], global functioning [$F_{(1, 56)}$= 1.29, p= 0.26].

5.3.7. Rates and characteristics of drop-outs in the CBT group

Three participants (10.30%) were drop outs in the CBT condition, while 10 (34.50%) were in the control group. The number of drop-outs in the CBT condition was significantly lower than in the control condition [$\chi^2_{(1)}= 4.85$, $p<0.05$].

In the CBT group, age was not significantly different between completers and drop-outs (Mann-Whitney U= 20, p= 0.17). A significant difference did not emerge also for gender [$\chi^2_{(1)}= 1.53$, p= 0.21], having a non-psychotic Axis I disorder [$\chi^2_{(1)}= 2.55$, p= 0.11], having any of anxiety disorders [$\chi^2_{(1)}= 0.03$, p= 0.86], any of unipolar mood disorders [$\chi^2_{(1)}= 0.45$, p= 0.50], having a personality disorder [$\chi^2_{(1)}= 0.03$, p= 0.86] or current cannabis use [$\chi^2_{(1)}= 0.69$, p=0.40], intensity of subclinical positive symptoms [Mann Whitney U= 28, p= 0.42], frequency [Mann Whitney U= 37.50, p= 0.91], global functioning [Mann Whitney U= 37.50, p= 0.91].

Table 5.4. Participants who left the study before post-treatment with completed sessions and reasons for drop out.

Participant	Assessments completed	Completed sessions	Reasons for stop attending sessions
20	Baseline	4	She said that felt better, returned to attending high school lessons and did not need continue treatment
23	Baseline	4	She said that attending sessions was unhelpful
29	Baseline	2	She said that she did not need a psychological treatment
21	Baseline	5	She said that did not need a psychological treatment, only needed medications
25	Baseline	3	She stopped coming, then was unable be contacted
28	Baseline	4	She stopped coming, then was unable be contacted
26	Baseline	11	She said that did not need any treatment
27	Baseline	2	He said that did not need a psychological treatment, only needed medications
24	Baseline	8	He said that the distance attending the centre was too long. He stopped coming, then was unable to be contacted.
58	Baseline	7	His parents were able to bring him only sporadically, then they refused continuing course
56	Baseline	6	She said that sessions were too demanding
57	Baseline	4	She stopped coming, then was unable be contacted
22	Baseline	4	He moved to other places

5.3.8. Primary outcomes

In the CBT group, mean survival time was 445.46 days (95% CI: 407.37-483.55), in the control condition it was 410.24 (95% CI: 350.39-470.09). The odds ratio was 0.30 (95% CI: 0.07-1.28). Overall, in the total study group, 7 participants (12.10%) at post-treatment and 11 (19%) at 14-month follow-up cumulatively made the conversion to psychosis. In the CBT group, 1 participant (3.40%) at post-treatment and 3 (10.30%) at 14-month follow-up cumulatively made the conversion to psychosis. In the control group, 6 (20.70%) participants at post-treatment and 8 (27.60%) at 14-month follow-up cumulatively made the conversion to psychosis. In the survival analyses, those who were lost to follow-up were conservatively classified as non-converters. The Kaplan-Meier curves showed a difference between individuals assigned to CBT and those in the control condition (Log rank test $\chi 2_{(1)}= 3.66$, $p= 0.05$), despite this difference was at a borderline significance level. Kaplan-Meier survival curves are presented in Figure 5.2. The number needed to treat (NTT) to prevent cumulatively transition to psychosis at 14-month follow-up was 5.88, suggesting that on average about 6 participants were necessary to be treated with CBT (instead of being assigned to the control condition) to prevent a transition event in one additional participant.

After conversion to psychosis, the DSM-IV-TR diagnoses were brief psychotic disorder (n= 5, 8.60%), schizoaffective disorder (n= 2, 3.40%), psychotic disorder not otherwise specified (n= 1, 1.70%), schizophrenia, disorganised type (n= 1, 1.70%), manic episode (n= 1, 1.70%). All patients who transitioned at post-treatment or follow-up fulfilled the criteria on the PANSS for psychosis.

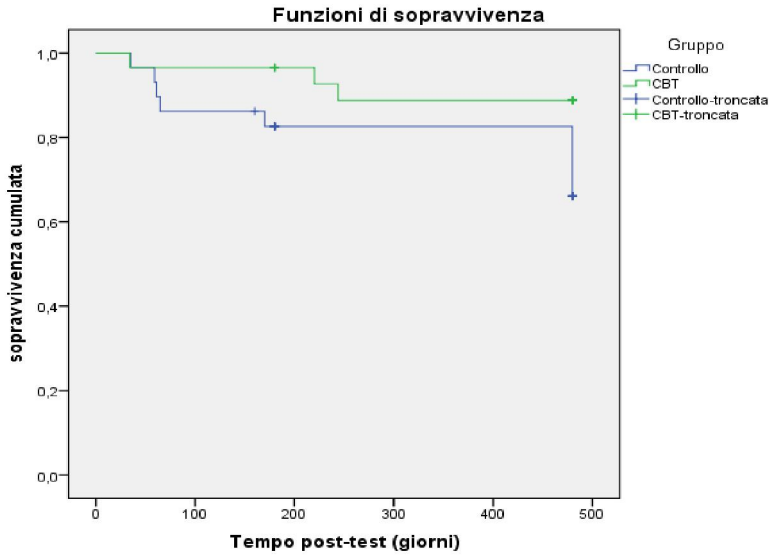


Figure 5.2. Cumulative survival CBT and control curves of psychosis transitions at 14-month follow-up.

5.3.9. Comparison between CBT and control on subclinical psychotic symptoms at 6-month post-treatment

In the total study group, at post-treatment 55% of participants achieved recovery on ARMS status, while 45% still reported subthreshold psychotic symptoms. The number of participants who recovered from ARMS was significantly higher in the CBT (80%) than in the control group (13.30%) [$\chi^2_{(1)}$= 16.83, p<0.001].

Subsequently, a series of ANCOVA was conducted entering group allocation as random factor, baseline CAARMS scores on each subclinical psychotic symptom as covariates and CAARMS scores on each subclinical psychotic symptom at post-treatment. Main and interaction effects of ANCOVAs are displayed in Table 5.5.

An interaction effect of baseline unusual content of thoughts and group allocation was found on unusual content of thoughts at post-treatment [F= 7.51, η^2= 0.14, p<0.01]: individuals with higher baseline unusual content of thoughts assigned to control group had significantly higher unusual content of thoughts at post-treatment [β= 0.71, t= 2.74, η^2= 0.14, p< 0.01].

An interaction effect of baseline non-bizarre ideas and group was found on non-bizarre ideas at post-treatment [F= 4.81, η^2= 0.09, p<0.05]: individuals with higher baseline non-bizarre ideas assigned to control group had significantly higher non-bizarre ideas at post-treatment [β= 0.68, t= 2.19, η^2= 0.09, p< 0.05].

A significant interaction effect between baseline perceptual abnormalities and group allocation was found on perceptual abnormalities at post-treatment [F= 6.40, η^2= 0.12, p<0.05]: individuals with

higher baseline perceptual abnormalities assigned to control group, had higher perceptual abnormalities at post-treatment [B= 0.66, t= 2.53, η^2, p< 0.05]. In addition, a main effect of baseline perceptual abnormalities was found [F= 12.61, η^2= 0.21, p<0.001]: individuals with higher baseline perceptual abnormalities had higher perceptual abnormalities at post-treatment.

Finally, a main effect of baseline disorganized speech on disorganized speech at post-treatment was found [F= 21.36, η^2= 0.31, p<0.001]. A baseline x group interaction effect did not emerge.

Table 5.5. Between-subject tests of group and baseline CAARMS subclinical psychotic symptoms effects on post-treatment subclinical psychotic symptoms.

	F	p-value	η^2
Group	0.42	0.51	0.01
CAARMS Unusual content of thoughts main effect	4.56	<0.05	0.09
Group x CAARMS Unusual content of thoughts	7.51	0.14	0.01
Group	0.47	0.49	0.01
CAARMS Non-bizarre ideas	3.12	0.08	0.06
Group x * CAARMS Non-bizarre ideas	4.81	<0.05	0.09
Group	0.15	0.69	0.01
Perceptual abnormalities	12.61	<0.001	0.21
Group x CAARMS Perceptual abnormalities	6.40	<0.05	0.12
Group	2.04	0.15	0.04
CAARMS Disorganised speech	21.36	<0.001	0.31
Group x CAARMS Disorganised speech	0.01	0.98	0.01

Note. CAARMS= Comprehensive Assessment of At-Risk-Mental States

5.3.10. Comparison between CBT and control on subclinical psychotic symptoms at 14-month follow-up

In the total study group, 54.30% achieved recovery on the ARMS status, while 45.70% still reported subclinical psychotic symptoms at follow-up. The number of participants recovered on ARMS was significantly higher in the CBT group (69.60%) than in the control group (25%) [χ^2= 6.31, p<0.05]. Subsequently, a series of ANCOVAs was conducted entering group allocation as random factor, baseline CAARMS scores on each subclinical psychotic symptom as covariates and CAARMS scores

on each subclinical psychotic symptom at follow-up. Main and interaction effects are displayed in Table 5.6.

A significant main effect of baseline unusual content of thoughts on unusual content of thoughts at follow-up was found [F= 7.65, η^2= 0.15, p<0.05]: individuals with higher baseline unusual content of thoughts had higher scores on this subclinical psychotic symptom after 14 months irrespective of group allocation.

No significant main effect or interaction between group and baseline scores were found on non-bizarre ideas at follow-up.

A significant main effect of baseline perceptual abnormalities was found on perceptual abnormalities at follow-up [F= 11.62, η^2= 0.21, p<0.01]. No interaction effect emerged between baseline perceptual abnormalities and group allocation.

A significant interaction effect between baseline disorganized speech and group allocation on disorganized speech was found [F= 7.10, η^2= 0.14, p<0.05]: individuals with higher baseline disorganized speech allocated to CBT group had lower disorganized speech after 14 months. A main effect of disorganized speech also was found.

5.6. Between-subject tests of group and baseline CAARMS subclinical psychotic symptoms effects on follow-up subclinical psychotic symptoms.

	F	p-value	η^2
Group	0.01	0.93	0.01
CAARMS Unusual content of thoughts main effect	7.65	<0.01	0.15
Group x CAARMS Unusual content of thoughts	1.74	0.19	0.04
Group	0.32	0.57	0.01
CAARMS Non-bizarre ideas	2.68	0.10	0.06
Group x * CAARMS Non-bizarre ideas	2.66	0.11	0.06
Group	0.26	0.61	0.01
Perceptual abnormalities	11.62	<0.01	0.21
Group x CAARMS Perceptual abnormalities	1.58	0.21	0.04
Group	0.53	0.47	0.01
Disorganised speech	28.81	<0.001	0.41
Group x CAARMS Disorganised speech	7.10	<0.05	0.14

Note. CAARMS= Comprehensive Assessment of At-Risk-Mental States

5.3.11. Secondary outcomes

No significant difference was found between the CBT and the control groups on BDI-II scores at post-treatment. A significant main effect of BDI-II baseline scores emerged [F= 96.92, p<0.001], indicating that individuals with higher baseline scores on the BDI-II had higher post-treatment scores

on the BDI-II irrespective of group allocation. In addition, an interaction effect was found between BDI-II baseline scores and group: individuals with higher baseline scores on the BDI-II in the control condition had significantly higher scores on the BDI-II at post-treatment than those in the CBT group. No significant difference was found between the CBT and the control groups on BAI scores at post-treatment. A significant main effect of BAI baseline scores emerged [F= 78.24, p<0.001]: individuals with higher baseline scores on the BAI had higher post-treatment scores on the BAI (β= 0.47, t= 4.12, p<0.001). In addition, an interaction effect was found between BAI baseline scores and group: individuals with higher baseline scores on the BAI in the control condition had significantly higher scores on the BAI at post-treatment than those in the CBT group (β= 0.47, t= 2.94, p<0.01).

No significant difference was found between the CBT and the control groups on PSWQ scores at post-treatment. A significant main effect of PSWQ baseline scores emerged [F= 40.53, p<0.001]: individuals with higher baseline scores on the PSWQ had higher post-treatment scores on the PSWQ. In addition, an interaction effect was found between PSWQ baseline scores and group: individuals with higher baseline scores on the PSWQ in the control condition had significantly higher scores on the PSWQ at post-treatment than those in the CBT group (β= 0.82, t= 5.54, p<0.01).

A significant main effect of baseline GAF scores was found on scores at post-treatment [β= 0.75, t= 2.93, p<0.01]. No interaction effect between baseline scores and group was found on scores at post-treatment.

Baseline, post-treatment and follow-up means on secondary outcomes in all the study groups are presented in Table 5.7.

5.3.12. Remission on secondary outcomes at 6-month post-treatment

In the total study group, 57.80% had a scores lower than the cut-off (20) on the BDI-II at post-treatment, while 42.20% had still a score equal to 20 or higher. In the CBT group, the number of participants who achieved remission (75%), measured by a BDI-II score lower than cut-off, was significantly higher than that (38.10%) in the control group [$\chi^2_{(1)}$= 6.25, p< 0.05]. Regarding anxiety, in the total study group, 57.80% had a scores lower than the cut-off (20) on the BAI at post-treatment, while 42.20% had still a score equal to 20 or higher. In the CBT group, the number of participants who achieved remission (75%), measured by a BAI score lower than cut-off, was significantly higher than that (38.10%) in the control group [$\chi^2_{(1)}$= 6.25, p< 0.05].

5.3.13. Remission on secondary outcomes at 14-month follow-up

In the total study group, 68.90% had a BDI-II score lower than the cut-off at follow-up, while 31.10% had a score equal or higher than 20. The number of participants who achieved remission on depression symptoms in the CBT group (87%) was significantly higher than that in the control group (50%) [$\chi^2_{(1)}$= 7.16, p<0.01]. Regarding anxiety, 61.40% of the total study group had a score lower than the cut-off at follow-up. The number of participants who achieved remission in the CBT group was significantly higher (79.20%) than in the control group (40%) [$\chi^2_{(1)}$= 7.05, p<0.01].

Table 5.7. Baseline, post-treatment and follow-up means (standard deviations) on secondary outcomes.

	Total study group (n= 58)			CBT (n= 29)			Control condition (n= 29)		
	Baseline	Post-treatment	Follow-up	Baseline	Post-treatment	Follow-up	Baseline	Post-treatment	Follow-up
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
BDI-II	21.37 (10.95)	15.34 (11.01)	14.23 (11.19)	21.54 (11.54)	11.08 (8.34)	10.43 (8.28)	21.20 (10.59)	20.18 (11.83)	18.38 (12.61)
BAI	24.20 (13.60)	18 (13.50)	17.04 (12.23)	25.59 (12.56)	13.78 (9.39)	13.13 (8.75)	22.81 (14.67)	22.75 (15.88)	21.52 (14.17)
PSWQ	51.94 (14.31)	47.21 (10.62)	45.77 (11.84)	53.84 (13.32	45.55 (9.33)	46.47 (12.45)	49.36 (15.68)	50.25 (12.51)	43.40 (10.33)
GAF	52.97 (9.55)	68.15 (14.24)	77.74 (12.45)	54.83 (8.01)	75.03 (11.88)	79.72 (12.18)	51.10 (10.69)	59.83 (12.43)	70.60 (11.86)

Note. BAI= Beck Anxiety Inventory, BDI-II= Beck Depression Inventory-II, CBT= cognitive behavioural therapy, GAF= Global Assessment of Functioning, PSWQ= Penn State Worry Questionnaire

5.3.14. Satisfaction with CBT

About half of individuals in the CBT group responded as “much” or “completely” (42.90% and 28.60%, respectively) on item 1, that asked whether his/her problems were understood during the psychotherapeutic path. The majority responded as “much” or “completely” (78.60% and 14.30%, respectively) on item 2 asking whether the psychotherapeutic path improved awareness of their problems.

Half of individuals (14.30% and 50%, respectively) responded as “a little” or “some” on item 7, asking whether the path provided useful tools and skills to manage on their own the period after the end of psychotherapy. About half (7.10% and 42.90%, respectively) responded as “a little” or “some” on item 8 asking whether the goals set for the psychotherapeutic path were achieved.

A detailed description of frequencies of responses on each item of the satisfaction questionnaire is provided in Table 5.8.

Table 5.8. Percentages of responses on each item of the satisfaction questionnaire in the CBT group.

	Not at all	A little	Some	Much	Completely
Item 1. Were your problems understood during the psychotherapeutic path?			28.60%	42.90%	28.60%
Item 2. Did the psychotherapeutic path allow you to become more aware of your problems?			7.10%	78.60%	14.30%
Item 3. Were your care needs met by the psychotherapeutic path?			42.90%	28.60%	28.60%
Item 4. Were your treatment expectations met by the psychotherapeutic path?			42.90%	28.60%	28.60%
Item 5. Did the psychotherapeutic path provide effective tools to deal with your problems?			28.60%	50.00%	21.40%
Item 6. Did the psychotherapeutic path strengthen your resources?		7.10%	7.10%	78.10%	7.10%
Item 7. Did the path provide useful tools and skills to be able to manage on your own the period after the end of psychotherapy?		14.30%	50.00%	14.30%	21.40%
Item 8. Were the goals of the psychotherapeutic path achieved?		7.10%	42.90%	35.70%	14.30%
Item 9. Did the psychotherapeutic path help you to manage the problems/symptoms which you suffered from?			35.70%	42.90%	21.40%
Item 10. Did the psychotherapeutic path improve your psychological well-being?			50%	35.70%	14.30%
Item 11. Overall, how much did you feel satisfied with the psychotherapeutic path?			28.60%	42.90%	28.60%

5.4. Discussion

5.4.1. Summary of findings on primary objectives

The current study investigated the efficacy of a CBT modular protocol for individuals at UHR of psychosis with the primary aim of prevention or postponement of a first episode of psychosis. As compared as previous research (Addington et al., 2011; Morrison et al., 2012; Stain et al., 2016; Yung et al., 2011), additional outcomes were considered to test secondary objectives, such as the effects of CBT on depression, anxiety, worry and functioning. Prevention of psychosis was assessed after 6 months since baseline (post-treatment) and 14 months at follow-up.

Fifty-eight individuals were randomised to CBT or a control condition that included supportive therapy as treatment as usual. Overall, in the current study mean age resulted higher than in the previous study by van der Gaag and colleagues (2012), where it was 22.9 years (SD= 5.60), and in the study by Stain and colleagues (2016), where it was 16.47 years (SD= 3.16).

All the participants (n= 58, 100%) reported having APS at baseline, while two smaller groups had also BLIPS (n= 3, 5.20%) and family history of psychosis or schizotypal personality disorder (n= 8, 13.80%). This result appeared consistent with recent data of the RCTs of Stain and colleagues (2016), where 46 (81%) had APS, 4 (7%) BLIPS and 19 (33%) a family history or schizotypal personality.

Overall, the number of drop-outs (n= 13, 22.40%) was lower than in the study by Stain and colleagues (n= 27, 53%), but it was higher than in the study by van der Gaag and colleagues (2012), where drop-outs were 27 (13.77%). A potential explanation for this could be that in the study of Stain and colleagues (2016), a much younger cohort was included; the study by van der Gaag and colleagues (2012) compared a generic CBT versus CBT for UHR states; thus, it could be hypothesized that just the use of CBT components has reduced drop-out rates as compared with the current study, where CBT was compared with a control condition not involving any of CBT principles.

In the total study group, the mean number of attended sessions among drop-outs was relatively small (4.92, SD= 2.53; range= 2-11). This could suggest that early drop out is a more typical phenomenon among UHR individuals; thus, more therapeutic efforts should be focused on the initial phase of treatment, including building motivation and engagement, defining goals.

Overall, female gender was associated with a higher probability of drop out. This finding was somewhat surprising and in contrast with previous research, given that females at CHR typically showed better functioning and more help-seeking behaviours than males (Barajas et al., 2015; Willhite et al., 2008).

On the other hand, other clinical variables potentially related to drop out, did not result significantly associated to early interruption of therapy, such as comorbid personality disorders, cannabis use, functioning and subclinical psychotic symptoms.

The number of drop-outs in the CBT condition (n= 3, 10.30%) was significantly lower than in control condition (n= 10, 34.50%). This result could suggest that a modular CBT protocol can significantly reduce attrition and increase feasibility of the treatment in a population difficult to be engaged in therapy due to intermittent loss of symptom insight or subclinical negative symptoms which frequently limit attending sessions. Drop out is a relevant phenomenon in psychosis treatment (van der Gaag et al., 2013). Some strategies were adopted in the protocol in order to minimize early drop out, such as conducting all the sessions in the mental health centre, where the participant had been recruited or at his/her home when he/she had difficulties going out due to panic attacks or agoraphobia. Additional engagement strategies were conducting "real-life" exposure sessions out of office, in order to increase motivation, willingness of the young individuals to expose themselves and also help them to generalize skills learnt during in-office sessions by confronting with the modelling behaviour of the therapist.

In contrast with findings in the total study group, no clinical variables were found to be significantly associated with drop out in the CBT group. Additional analyses were prevented in the current study due to the low number of drop-outs in the CBT group. Thus, further research should investigate other potential predictors of drop out during CBT course.

Overall, the transition rate in the current study was 19%, which resulted higher than that observed in recent trials, where it was ranging from 5 to 9% (Addington et al., 2011; Morrison et al., 2012; Stain et al., 2016; Yung et al., 2011), and also than that reported in the EDIE-NL trial by van der Gaag and colleagues (2012), who found a 16% of transition rate. Some differences across the studies could account for this inconsistency, as in the study of Stain and colleagues (2016) follow-up length was 12 months, while in the EDIE-NL trial it was 18 months (van der Gaag et al., 2012). In addition, the study of Stain and colleagues (2016) included a much younger cohort (mean age= 16.47, SD= 2.73, range= 16-30) and also in the study of van der Gaag and colleagues (2012) mean age was slightly lower (22.9, SD= 5.60). Moreover, an explanation of this finding was that in the current study participants were recruited through referrals from mental health professionals while in the EDIE-NL trial van der Gaag and colleagues (2012) used a two-step procedure screening help-seeking youth through the PQ, then identifying UHR individuals by the CAARMS administration. Indeed, previous research showed that differences in recruitment procedures are associated with different transition estimates with the group recruited through screening being much more prone to conversion than that recruited by referrals (Riedijk et al., 2012). On the other hand, current transition rate appeared

substantially in line with the rates reported in other trials (6-20%; Bechdolf et al., 2012; 10-21%; McGorry et al., 2013). Transition rate in the current study was, however, lower than that observed by Morrison and colleagues (2012), who reported a value of 22%.

In the current study, survival analyses indicated that the CBT protocol was associated with a reduced risk of transition to psychosis although the difference between the curves was found at a borderline significance level. In addition, the estimated number needed to treat suggested that on average about 6 participants should be treated with the CBT modular protocol, instead of being assigned to the control condition, to prevent a transition to psychosis in one additional participant.

Overall, 55% and 54% of participants reported remission on the ARMS status at post-treatment and follow-up, respectively. This suggested that remission remained stable over time in both CBT and control groups. In the CBT group, the number of participants who achieved remission on the ARMS at post-treatment was significantly higher (80% vs 13.30%) and also at follow-up (69.60% vs 25%), suggesting that CBT was effective on subclinical psychotic symptoms and that therapeutic gains were maintained after 14 months.

5.4.2. Summary of findings on secondary objectives

Results of ANOVAs showed interaction effects of baseline subclinical symptoms and group allocation on subclinical psychotic symptoms at post-treatment and follow-up. Specifically, analyses indicated that individuals with higher unusual content of thoughts, non-bizarre ideas and perceptual abnormalities reported lower scores on these types of subclinical symptoms when assigned to CBT condition than to control condition. This could suggest that CBT could add benefit on specific types of subclinical symptoms for those individuals having more severe subclinical symptoms at intake.

A higher number of individuals receiving CBT achieved remission on depression and anxiety (75% vs 38% for both depression and anxiety symptoms) at post-treatment and follow-up (87% vs 50% for depression, 79% vs 40% for anxiety). This finding was in contrast with most previous trials (Addington et al., 2011; Morrison et al., 2004, 2012; van der Gaag et al., 2012; Yung et al., 2011), which reported no significant difference between individuals assigned to CBT and those in the control conditions. This finding could be explained by the fact that the CBT protocol in the current study was a modular treatment, that included several additional techniques to target anxiety, mood, and worry problems. However, some differences in the control conditions between the previous trials could also account for this outcome. In effect, the study by van der Gaag (2012) assigned participants to evidenced-based psychological treatments for non-psychotic disorders + CBT for PLEs or evidenced-based psychological treatments alone; thus, different from the current study, where participants in the

control condition did not receive any ingredients of CBT, in the EDIE-NL trial (van der Gaag et al., 2012) participants also in the control conditions receive some components targeting anxiety and depression.

Main effects of group were not observed on secondary outcomes. However, interaction effects between group and baseline scores showed that individuals with higher baseline depression, anxiety and worry had significantly lower scores on secondary outcomes. Therefore, these results indicated that CBT did not add greater benefit than a control condition on secondary outcomes when such symptoms are considered as a continuous outcome. Thus, CBT could target the reduction of depression, anxiety and worry symptoms when they are present at a clinically significant level.

No interaction effect or main effect of group on functioning was found, suggesting that CBT did not produce a significantly higher improvement than control condition. This finding was consistent with that observed by van der Gaag and colleagues (2012), who reported no significantly greater effect of CBT for UHR on functioning and also quality of life.

Finally, current findings from a satisfaction scale indicated that about 70% of participants who completed all CBT sessions were much or completely satisfied with the treatment path overall. Specifically, about 90% were much or completely satisfied with the treatment path as it allowed them to become more aware of their problems or symptoms. About 70% of participants were much or completely satisfied with CBT as it provided effective tools to manage their symptoms, as during the path their problems were much or completely understood, and for over 85% of participants it strengthened their personal resources.

About 50% responded that CBT improved their well-being much or very, while another 50% responded that it did at some degree. Another point was that about 60% responded that CBT provided effective skills to self-manage their symptoms/problems at the end of the psychotherapy, while only about 35% responded as much or completely. In addition, only 50% stated that the therapeutic goals were achieved at the end of the CBT course, while another 50% responded that they were reached a little or at some degree.

Thus, data on satisfaction indicated that the CBT modular protocol was perceived by participants as a useful goal-oriented, problem-focused path able to increase their awareness of their symptoms/problems, to improve their strengths and personal resources and provide effective skills to manage symptoms. However, responses from a relevant part of the group highlighted that there is room for further improvement of the intervention. For example, additional strategies could be introduced to further perceived well-being but also self-management skills to be used when the psychotherapy course has finished; adding more booster sessions could improve this satisfaction

outcome. Moreover, further strategies targeting relapse prevention could be integrated. In effect, in the current protocol only a final session was dedicated to relapse prevention.

5.4.3. Limitations and future directions

Some important limitations should be noted. A potential bias in the recruitment strategies was the lack of a broad screening procedure, used for all the population of help-seeking individuals. Thus, this limitation could have influenced the identification of cases since hep-seeking individuals were only identified and recruited by referrals. Future research in Italy should use a wide screening strategy in order to optimize recruitment of suspected cases. In addition, the small number of recruited participants require additional studies with larger samples in Italy.

Another important limitation concerned the time window considered for follow-up assessments, which could be viewed as relatively short. Future research should use longer follow-up assessments with several years (2 years or longer), given that longer time windows are associated with increased risk of developing a fist episode of psychosis moving from a transition risk 21.7 to 35.8 (Fusar-Poli et al., 2012).

Another aspect that needs for further improvement regarded the use of a functioning measure. Some research has indicated differences between the functioning construct and quality of life dimensions (Muldoon et al., 1998). Thus, further research should use quality of life measures to assess the effects of CBT for UHR people. An additional outcome which should be investigate is subjective well-being.

Another limitation regarded the use of a monocentre design, which could prevent generalization to other mental health sites. In addition, the recruited individuals were from mental health centres; future studies in Italy should introduce recruitment strategies also from primary care settings in order to improve early detection.

The CBT protocol appeared to be more effective on reducing subclinical psychotic symptoms than the control condition. However, as participants assigned to control did not receive all the other therapeutic components included in CBT, this effect cannot be attributed to the module targeting distress related to psychotic experiences. Future process research should investigate which component could be associated to a better outcome on ARMS status.

5.5. Conclusions

In conclusion, the current study seemed to expand evidence on early detection and intervention on psychosis, highlighting also directions of future research. The present data provided further knowledge on the efficacy and feasibility of CBT for UHR groups, as in the current literature there is a small number of studies on this topic. CBT appeared to be a useful strategy to prevent or delay first episode of psychosis and also to produce remission on ARMS status. However, present data showed that transition conversion was reduced only at a trend level as compared with supportive therapy as control condition (treatment as usual). Current study considered a broad set of clinical and functional outcomes, that were not sufficiently assessed in the literature, including anxiety, depression, worry and global functioning. However, from the current analyses CBT did not seem to sufficiently improve functioning and worry. One of the future challenges in UHR research is the development of effective strategies to target worry and improve functioning in this population of young people.

Acknowledgements

I wish to gratefully thank the following colleagues for their kind participation in this study:

Prof. Davide Dèttore, PsyD, University of Florence

Dr. Sandro Domenichetti, MD, Azienda USL Toscana Centro

Dr. Andrea Cicogni, MD Azienda USL Toscana Centro

Dr. Nicoletta Giaquinta, PsyD Centre for Cognitive and Behavioural Therapy (CTTC)

Dr. Elisabetta Ruggieri, PsyD Azienda USL Toscana Centro

Dr. Andrea Bencini, MD Azienda USL Toscana Centro

Dr. Cinzia Di Matteo, MD Azienda USL Toscana Centro

Dr. Andrea Tanini, MD Azienda USL Toscana Centro

Dr. Stefano Calamandrei, MD Azienda USL Toscana Centro

Dr. Stefano Berrettini, MD Azienda USL Toscana Centro

Dr. Stefania Bianchini, nurse manager Azienda USL Toscana Centro

Dr. Riccardo Lo Parrino, MD Azienda USL Toscana Centro

Dr. Vanna Vocino, PsyD Azienda USL Toscana Centro

Dr. Daniela Falchini, PsyD Azienda USL Toscana Centro

Dr. Alberto Santelli, PsyD Cooperativa di Vittorio

Finally, I warmly, kindly thank all the participants of the study.

Ringraziamenti

Ringrazio il Professor Davide Dèttore, in tutti questi anni mio supervisore tanto nella pratica clinica quanto nell'attività scientifica universitaria, per avermi trasmesso la passione per questo delicato e avvincente lavoro, per tutti gli incoraggiamenti che mi ha dato, per avermi trasmesso l'attenzione al rigore metodologico, a essere consapevole dei miei obiettivi, alla ricerca delle fonti di ciò che citiamo ed al tempo stesso della semplicità in quello che facciamo.

Ringrazio il Dott. Sandro Domenichetti per avermi trasmesso quanto a volte sia importante nel nostro lavoro avere un atteggiamento di leggerezza, di ironia ma soprattutto di autoironia, per avermi insegnato che "l'ansia può essere la porta di accesso di qualcosa di più grande".

Ringrazio la Dott.ssa Anna Meneghelli, perché durante questo cammino, in momenti di fervore del lavoro, mi ha offerto l'opportunità di osservarmi dall'esterno in quello che stavo facendo, per l'entusiasmo che mi ha infuso, per l'interesse "ai casi clinici poco chiari".

Ringrazio tutti i membri della mia famiglia per avermi permesso di portare avanti questo percorso, per aver ascoltato i miei bisogni, per il loro affetto costante, per tutte le volte in cui si sono presi cura di me nei momenti difficili.

Ringrazio la mia compagna, Nicoletta, per tutte le volte in cui mi ha fatto sentire capito ed accettato nelle mie fragilità e per la forza che mi ha dato e mi dà ogni giorno nel fare certe scelte.

Ringrazio i miei amici, Alessandro, Giovanni e Gabriele, per tutti i sorrisi che ci siamo scambiati in questi anni.

Ringrazio infine, tutte le persone che in questi anni hanno deciso di partecipare a questo studio, per le fortissime emozioni che mi hanno permesso di condividere con loro.

.

References

Abel, K. M., Drake, R., & Goldstein, J. M. (2010). Sex differences in schizophrenia. *International Review of Psychiatry, 22*(5)*,* 417-428.

Addington, J., Cadenhead, K. S., Cannon, T. D., Cornblatt, B., McGlashan, T. H., Perkins, D. O., ... & Heinssen, R. (2007). North American Prodrome Longitudinal Study: a collaborative multisite approach to prodromal schizophrenia research. *Schizophrenia Bulletin, 33*(3), 665-672.

Addington, J., Case, N., Saleem, M. M., Auther, A. M., Cornblatt, B. A., & Cadenhead, K. S. (2014). Substance use in clinical high risk for psychosis: a review of the literature. *Early Intervention in Psychiatry, 8*(2), 104-112.

Addington, J., Case, N., Saleem, M. M., Auther, A. M., Cornblatt, B. A., & Cadenhead, K. S. (2014). Substance use in clinical high risk for psychosis: a review of the literature. *Early Intervention in Psychiatry*, *8*(2), 104-112.

Addington, J., Cornblatt, B. A., Cadenhead, K. S., Cannon, T. D., McGlashan, T. H., Perkins, D. O., ... & Heinssen, R. (2011). At clinical high risk for psychosis: outcome for nonconverters. *American Journal of Psychiatry, 168*(8)*,* 800-805.

Addington, J., Epstein, I., Liu, L., French, P., Boydell, K. M., & Zipursky, R. B. (2011). A randomized controlled trial of cognitive behavioral therapy for individuals at clinical high risk of psychosis. *Schizophrenia Research, 125*(1), 54-61.

Addington, J., Heinssen, R. K., Robinson, D. G., Schooler, N. R., Marcy, P., Brunette, M. F., ... & Robinson, J. A. (2015). Duration of untreated psychosis in community treatment settings in the United States. *Psychiatric Services, 66*(7), 753–756.

Addington, J., Penn, D., Woods, S. W., Addington, D., & Perkins, D. O. (2008). Social functioning in individuals at clinical high risk for psychosis. *Schizophrenia Research, 99*(1), 119-124.

Allen, P., Aleman, A., & Mcguire, P. K. (2007). Inner speech models of auditory verbal hallucinations: evidence from behavioural and neuroimaging studies. *International Review of Psychiatry, 19*(4), 407-415.

Allen, P., Chaddock, C. A., Howes, O. D., Egerton, A., Seal, M. L., Fusar-Poli, P., ... & McGuire, P. K. (2012). Abnormal relationship between medial temporal lobe and subcortical dopamine function in people with an ultra-high risk for psychosis. *Schizophrenia Bulletin, 38*(5), 1040-1049.

Álvarez-Jiménez, M., Parker, A. G., Hetrick, S. E., McGorry, P. D., & Gleeson, J. F. (2011). Preventing the second episode: a systematic review and meta-analysis of psychosocial and pharmacological trials in first-episode psychosis. *Schizophrenia Bulletin*, *37*(3), 619-630.

American Psychiatric Association (1987). *Diagnostic and Statistical Manual of Mental Disorders (3rd ed. Revised)*. Washington, DC: American Psychiatric Association Publishing.

American Psychiatric Association (2000). *Diagnostic and statistical manual of mental disorders (4th ed.)*. Washington, DC: American Psychiatric Association Publishing.

American Psychiatric Association (2013). *Diagnostic and Statistical Manual of Mental Disorders (DSM5), 5th ed*. Washington, DC: American Psychiatric Association Publishing.

Amminger, G. P., Berger, G. E., Schäfer, M. R., Klier, C., Friedrich, M. H., & Feucht, M. (2007). Omega-3 fatty acids supplementation in children with autism: a double-blind randomized, placebo-controlled pilot study. *Biological Psychiatry, 61*(4), 551-553.

Amminger, G. P., Leicester, S., Yung, A. R., Phillips, L. J., Berger, G. E., Francey, S. M., ... & McGorry, P. D. (2006). Early-onset of symptoms predicts conversion to non-affective psychosis in ultra-high risk individuals. *Schizophrenia Research, 84*(1), 67-76.

Amminger, G. P., & McGorry, P. D., (2012). Update on omega-3 polyunsaturated fatty acids in early-stage psychotic disorders. *Neuropsychopharmacology, 37*(1) 309-310.

Amminger, G. P., Schäfer, M. R., Klier, C. M., Schlögelhofer, M., Mossaheb, N., Thompson, A., ... & Nelson, B. (2012). Facial and vocal affect perception in people at ultra-high risk of psychosis, first-episode schizophrenia and healthy controls. *Early Intervention in Psychiatry, 6*(4), 450-454.

Amminger,G. P., Schafer, M. R., Papageorgiou, K., Klier, C. M., Cotton, S. M., Harrigan, S. M., Mackinnon, A., McGorry, P. D., Berger, G. E., (2010). Long-chain omega-3 fatty acids for indicated prevention of psychotic disorders: a randomized, placebo-controlled trial. *Archives of General Psychiatry, 67*(2), 146–154.

Amminger, G. P., Schäfer, M. R., Papageorgiou, K., Klier, C. M., Schlögelhofer, M., Mossaheb, N., ... & McGorry, P. D. (2012). Emotion recognition in individuals at clinical high-risk for schizophrenia. *Schizophrenia Bulletin, 38*(5), 1030-1039.

An, S. K., Kang, J. I., Park, J. Y., Kim, K. R., Lee, S. Y., & Lee, E. (2010). Attribution bias in ultra-high risk for psychosis and first-episode schizophrenia. *Schizophrenia Research, 118*(1), 54-61.

Auther, A. M., McLaughlin, D., Carrión, R. E., Nagachandran, P., Correll, C. U., & Cornblatt, B. A. (2012). Prospective study of cannabis use in adolescents at clinical high risk for psychosis: impact on conversion to psychosis and functional outcome. *Psychological Medicine, 42*(12), 2485-2497.

Barajas, A., Ochoa, S., Obiols, J. E., & Lalucat-Jo, L. (2015). Gender differences in individuals at high-risk of psychosis: a comprehensive literature review. *The Scientific World Journal, 1*(1), 1-13.

Barbato, M., Liu, L., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A., McGlashan, T. H., ... & Woods, S. W. (2015). Theory of mind, emotion recognition and social perception in individuals at clinical high risk for psychosis: Findings from the NAPLS-2 cohort. *Schizophrenia Research, 2*(3), 133-139.

Bechdolf, A., Wagner, M., Ruhrmann, S., Harrigan, S., Putzfeld, V., Pukrop, R., ... & Bottlender, R. (2012). Preventing progression to first-episode psychosis in early initial prodromal states. *The British Journal of Psychiatry, 200*(1), 22-29.

Beck, A. T. (1976) *Cognitive Therapy and the Emotional Disorders*. New York, NY: International Universities Press.

Beck, A. T. (1979) *Cognitive Therapy of Depression*. New York, NY: Guilford Press.

Beck, A. T., & Steer, R. A. (1990). *Beck anxiety inventory: BAI. Manual*. San Antonio, TX: The Psychological Corporation Harcourt Brace & Company.

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Beck Depression Inventory-Second Edition Manual.* San Antonio, TX: The Psychological Corporation Harcourt Brace & Company.

Bell, V., Halligan, P. W., & Ellis, H. D. (2006). Explaining delusions: a cognitive perspective. *Trends in Cognitive Sciences, 10*(5), 219-226.

Berger, G., Dell'Olio, M., Amminger, P., Cornblatt, B., Phillips, L., Yung, A., ... & McGorry, P. (2007). Neuroprotection in emerging psychotic disorders. *Early Intervention in Psychiatry, 1*(2), 114-127.

Bernstein, D. P., Stein, J. A., Newcomb, M. D., Walker, E., Pogge, D., Ahluvalia, T., ... & Zule, W. (2003). Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child Abuse & Neglect, 27*(2), 169-190.

Blazer, D. G., Kessler, R. C., & McGonagle, K. A. (1994). The prevalence and distribution of major depression in a national community sample: the National Comorbidity Survey. *Age (years), 15*(24), 24-7.

Blechert, J., & Meyer, T. D. (2005). Are measures of hypomanic personality, impulsive nonconformity and rigidity predictors of bipolar symptoms? *British Journal of Clinical Psychology, 44*(1), 15-27.

Bleuler, E. (1950). *Dementia Praecox or the group of Schizophrenias*. Oxford, UK: International Universities Press.

Bodatsch, M., Ruhrmann, S., Wagner, M., Müller, R., Schultze-Lutter, F., Frommann, I., ... & Brockhaus-Dumke, A. (2011). Prediction of psychosis by mismatch negativity. *Biological Psychiatry, 69*(10), 959-966.

Boonstra, N., Klaassen, R., Sytema, S., Marshall, M., De Haan, L., Wunderink, L., & Wiersma, D. (2012). Duration of untreated psychosis and negative symptoms—a systematic review and meta-analysis of individual patient data. *Schizophrenia Research, 142*(1), 12-19.

Boonstra, N., Sterk, B., Wunderink, L., Sytema, S., De Haan, L., & Wiersma, D. (2012). Association of treatment delay, migration and urbanicity in psychosis. *European Psychiatry, 27*(7), 500-505.

Borkovec, T. D., & Roemer, L. (1995). Perceived functions of worry among generalized anxiety disorder subjects: distraction from more emotionally distressing topics? *Journal of Behavior Therapy and Experimental Psychiatry, 26*(1), 25-30.

Broome, M. R., Johns, L. C., Valli, I., Woolley, J. B., Tabraham, P., Brett, C., ... & McGuire, P. K. (2007). Delusion formation and reasoning biases in those at clinical high risk for psychosis. *The British Journal of Psychiatry, 191*(51), 38-42.

Broussard, B., Kelley, M. E., Wan, C. R., Cristofaro, S. L., Crisafio, A., Haggard, P. J., ... & Compton, M. T. (2013). Demographic, socio-environmental, and substance-related predictors of duration of untreated psychosis (DUP). *Schizophrenia Research, 148*(1), 93-98.

Brüne, M. (2005). Emotion recognition, "theory of mind", and social behavior in schizophrenia. *Psychiatry Research*, *133*(2), 135-147.

Brüne, M., Özgürdal, S., Ansorge, N., von Reventlow, H. G., Peters, S., Nicolas, V., ... & Lissek, S. (2011). An fMRI study of "theory of mind" in at-risk states of psychosis: comparison with manifest schizophrenia and healthy controls. *Neuroimage, 55*(1), 329-337.

Buchanan, R. W., Kreyenbuhl, J., Kelly, D. L., Noel, J. M., Boggs, D. L., Fischer, B. A., ... & Keller, W. (2010). The 2009 schizophrenia PORT psychopharmacological treatment recommendations and summary statements. *Schizophrenia Bulletin, 36*(1), 71-93.

Buchy, L., Perkins, D., Woods, S. W., Liu, L., & Addington, J. (2014). Impact of substance use on conversion to psychosis in youth at clinical high risk of psychosis. *Schizophrenia Research*, *156*(2), 277-280.

Buckley, P. F., Miller, B. J., Lehrer, D. S., & Castle, D. J. (2009). Psychiatric comorbidities and schizophrenia. *Schizophrenia bulletin, 35(2)*, 383-402.

Burns, K. J. (2012). Cannabis use and duration of untreated psychosis: a systematic review and meta-analysis. *Current Pharmaceutical Design, 18*(32), 5093-5104.

Carpenter, W. T., & van Os, J. (2011). Should attenuated psychosis syndrome be a DSM-5 diagnosis? *American Journal of Psychiatry*, *168*(5), 460-463.

Carter, J. W., Parnas, J., Cannon, T. D., Schulsinger, F., & Mednick, S. A. (1999). MMPI variables predictive of schizophrenia in the Copenhagen High-Risk Project: a 25-year follow-up. *Acta Psychiatrica Scandinavica, 99*(6), 432-440.

Chan, A. W., Tetzlaff, J. M., Altman, D. G., Laupacis, A., Gøtzsche, P. C., Krleža-Jerić, K., & Moher, D. (2013). SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Annals of Internal Medicine, 158*(3), 200-207.

Chapman, L. J., & Chapman, J. P. (1980). Scales for rating psychotic and psychotic-like experiences as continua. *Schizophrenia Bulletin, 6*(3), 476.

Clark, D. M., & Wells, A. (1995). A cognitive model of social phobia. *Social phobia: Diagnosis, assessment, and treatment*, *41*(68), 22-23.

Cocchi, A., Lora, A., Meneghelli, A., La Greca, E., Pisano, A., Cascio, M. T., & Preti, A. (2014). Sex differences in first-episode psychosis and in people at ultra-high risk. *Psychiatry Research*, *215*(2), 314-322.

Cohen, J. (1977). *Statistical power analysis for the behavioral sciences*. Hillsdale, NJ, England: Lawrence Erlbaum Associates.

Comparelli, A., Corigliano, V., De Carolis, A., Mancinelli, I., Trovini, G., Ottavi, G., ... & Girardi, P. (2013). Emotion recognition impairment is present early and is stable throughout the course of schizophrenia. *Schizophrenia Research*, *143*(1), 65-69.

Compton, M. T., & Broussard, B. (2011). Conceptualizing the multifaceted determinants of the duration of untreated psychosis. *Current Psychiatry Reviews*, *7*(1), 1-11.

Compton, M. T., Chien, V. H., Leiner, A. S., Goulding, S. M., & Weiss, P. S. (2008). Mode of onset of psychosis and family involvement in help-seeking as determinants of duration of untreated psychosis. *Social Psychiatry and Psychiatric Epidemiology*, *43*(12), 975-982.

Compton, M. T., Gordon, T. L., Goulding, S. M., Esterberg, M. L., Carter, T., Leiner, A. S., ... & Kaslow, N. J. (2011). Patient-Level Predictors and Clinical Correlates of Duration of Untreated Psychosis Among Hospitalized First-Episode Patients [CME]. *The Journal of Clinical Psychiatry*, *72*(2), 225-232.

Corcoran, C. M., Kimhy, D., Stanford, A., Khan, S., Walsh, J., Thompson, J., ... & Cressman, V. (2008). Temporal association of cannabis use with symptoms in individuals at clinical high risk for psychosis. *Schizophrenia Research, 106*(2), 286-293.

Cornblatt, B. A., Carrión, R. E., Addington, J., Seidman, L., Walker, E. F., Cannon, T. D., ... & Woods, S. W. (2011). Risk factors for psychosis: impaired social and role functioning. *Schizophrenia Bulletin, 38*(6), 1247-1257.

Cornblatt, B. A., Carrión, R. E., Auther, A., McLaughlin, D., Olsen, R. H., John, M., & Correll, C. U. (2015). Psychosis prevention: a modified clinical high risk perspective from the Recognition and Prevention (RAP) Program. *American Journal of Psychiatry*, *172*(10), 986-994.

Cotton, S. M., Lambert, M., Schimmelmann, B. G., Foley, D. L., Morley, K. I., McGorry, P. D., & Conus, P. (2009). Gender differences in premorbid, entry, treatment, and outcome characteristics in a treated epidemiological sample of 661 patients with first episode psychosis. *Schizophrenia Research*, *114*(1), 17-24.

Couture, S. M., Penn, D. L., Addington, J., Woods, S. W., & Perkins, D. O. (2008). Assessment of social judgments and complex mental states in the early phases of psychosis. *Schizophrenia Research*, *100*(1), 237-241.

Crow, T. J. (1980). Molecular pathology of schizophrenia: more than one disease process? *British Medical Journal, 280*(6207) 66-68.

Crum, W. R., Griffin, L. D., Hill, D. L., & Hawkes, D. J. (2003). Zen and the art of medical image registration: Correspondence, homology, and quality. *Neuroimage, 20*(3), 1425–1437

Debbané, M., & Barrantes-Vidal, N. (2015). Schizotypy from a developmental perspective. *Schizophrenia Bulletin, 41*(Suppl. 2), S386-S395.

DeVylder, J. E., Ben-David, S., Kimhy, D., & Corcoran, C. M. (2013). Attributional style among youth at clinical risk for psychosis. *Early Intervention in Psychiatry*, *7*(1), 84-88.

DeVylder, J. E., Muchomba, F. M., Gill, K. E., Ben-David, S., Walder, D. J., Malaspina, D., & Corcoran, C. M. (2014). Symptom trajectories and psychosis onset in a clinical high-risk cohort: the relevance of subthreshold thought disorder. *Schizophrenia Research*, *159*(2), 278-283.

Dickinson, D., Ramsey, M. E., & Gold, J. M. (2007). Overlooking the obvious: a meta-analytic comparison of digit symbol coding tasks and other cognitive measures in schizophrenia. *Archives of General Psychiatry, 64*(5), 532-542.

Dragt, S., Nieman, D. H., Becker, H. E., van de Fliert, R., Dingemans, P. M., de Haan, L., ... & Linszen, D. H. (2010). Age of onset of cannabis use is associated with age of onset of high-risk symptoms for psychosis. *The Canadian Journal of Psychiatry*, *55*(3), 165-171.

Dragt, S., Nieman, D. H., Schultze-Lutter, F., Van Der Meer, F., Becker, H., De Haan, L., ... & Heinimaa, M. (2012). Cannabis use and age at onset of symptoms in subjects at clinical high risk for psychosis. *Acta Psychiatrica Scandinavica*, *125*(1), 45-53.

Drury, V., Birchwood, M., Cochrane, R., & MacMillan, F. (1996). Cognitive therapy and recovery from acute psychosis: a controlled trial. I. Impact on psychotic symptoms. *The British Journal of Psychiatry*, *169*(5), 593-601.

Eisenberg, D., Downs, M. F., Golberstein, E., & Zivin, K. (2009). Stigma and help seeking for mental health among college students. *Medical Care Research and Review*, *66*(5), 522-541.

Erlenmeyer-Kimling, L., Cornblatt, B. A., Rock, D., Roberts, S., Bell, M., & West, A. (1993). The New York High-Risk Project: anhedonia, attentional deviance, and psychopathology. *Schizophrenia Bulletin*, *19*(1), 141-153.

Farrer, C., & Franck, N. (2007). Self-monitoring in schizophrenia. *Current Psychiatry Reviews*, *3*(4), 243-251.

Fine, C., Gardner, M., Craigie, J., & Gold, I. (2007). Hopping, skipping or jumping to conclusions? Clarifying the role of the JTC bias in delusions. *Cognitive Neuropsychiatry*, *12*(1), 46-77.

Fisher, H. L., Major, B., Chisholm, B., Rahaman, N., Joyce, J., Woolley, J., ... & Johnson, S. (2013). Duration of untreated psychosis in adolescents: Ethnic differences and clinical profiles. *Schizophrenia Research*, *150*(2), 526-532.

Freeman, D., Garety, P., Kuipers, E., Colbert, S., Jolley, S., Fowler, D., ... & Bebbington, P. (2006). Delusions and decision-making style: use of the Need for Closure Scale. *Behaviour Research and Therapy, 44*(8), 1147-1158.

French, P., & Morrison, A. P. (2004). *Early detection and cognitive therapy for people at high risk of developing psychosis: A treatment approach*. New York, NY: John Wiley & Sons.

Fusar-Poli, P. (2012). Voxel-wise meta-analysis of fMRI studies in patients at clinical high risk for psychosis. *Journal of Psychiatry and Neuroscience*, *37*(2), 106-112.

Fusar-Poli, P., Borgwardt, S., Bechdolf, A., Addington, J., Riecher-Rössler, A., Schultze-Lutter, F., ... & Valmaggia, L. (2013). The psychosis high-risk state: a comprehensive state-of-the-art review. *JAMA Psychiatry*, *70*(1), 107-120.

Fusar-Poli, P., Broome, M. R., Matthiasson, P., Woolley, J. B., Mechelli, A., Johns, L. C., ... & McGuire, P. (2011). Prefrontal function at presentation directly related to clinical outcome in people at ultrahigh risk of psychosis. *Schizophrenia Bulletin*, *37*(1), 189-198.

Fusar-Poli, P., Cappucciati, M., Rutigliano, G., Schultze-Lutter, F., Bonoldi, I., Borgwardt, S., ... & McGlashan, T. H. (2015). At risk or not at risk? A meta-analysis of the prognostic accuracy of psychometric interviews for psychosis prediction. *World Psychiatry*, *14*(3), 322-332.

Fusar-Poli, P., Carpenter, W. T., Woods, S. W., & McGlashan, T. H. (2014). Attenuated psychosis syndrome: ready for DSM-5.1? *Annual Review of Clinical Psychology*, *10*(1), 155-192.

Fusar-Poli, P., Nelson, B., Valmaggia, L., Yung, A. R., & McGuire, P. K. (2014). Comorbid depressive and anxiety disorders in 509 individuals with an at-risk mental state: impact on psychopathology and transition to psychosis. *Schizophrenia Bulletin*, *40*(1), 120-131.

Fusar-Poli, P., Perez, J., Broome, M., Borgwardt, S., Placentino, A., Caverzasi, E., ... & McGuire, P. (2007). Neurofunctional correlates of vulnerability to psychosis: a systematic review and meta-analysis. *Neuroscience & Biobehavioral Reviews*, *31*(4), 465-484.

Fusar-Poli, P., Radua, J., McGuire, P., & Borgwardt, S. (2011). Neuroanatomical maps of psychosis onset: voxel-wise meta-analysis of antipsychotic-naive VBM studies. *Schizophrenia Bulletin, 38*(6), 1297-1307.

Galdas, P. M., Cheater, F., & Marshall, P. (2005). Men and health help-seeking behaviour: literature review. *Journal of Advanced Nursing*, *49*(6), 616-623.

Garety, P. A., Bebbington, P., Fowler, D., Freeman, D., & Kuipers, E. (2007). Implications for neurobiological research of cognitive models of psychosis: a theoretical paper. *Psychological Medicine*, *37*(10), 1377-1391.

Garner, B., Pariante, C. M., Wood, S. J., Velakoulis, D., Phillips, L., Soulsby, B., ... & Yung, A. R. (2005). Pituitary volume predicts future transition to psychosis in individuals at ultra-high risk of developing psychosis. *Biological Psychiatry*, *58*(5), 417-423.

Garner, B., Phassouliotis, C., Phillips, L. J., Markulev, C., Butselaar, F., Bendall, S., ... & McGorry, P. D. (2011). Cortisol and dehydroepiandrosterone-sulphate levels correlate with symptom severity in first-episode psychosis. *Journal of Psychiatric Research*, *45*(2), 249-255.

Gee, D. G., Karlsgodt, K. H., van Erp, T. G., Bearden, C. E., Lieberman, M. D., Belger, A., ... & Woods, S. W. (2012). Altered age-related trajectories of amygdala-prefrontal circuitry in adolescents at clinical high risk for psychosis: a preliminary study. *Schizophrenia Research*, *134*(1), 1-9.

Gerstenberg, M., Theodoridou, A., Traber-Walker, N., Franscini, M., Wotruba, D., Metzler, S., ... & Rössler, W. (2016). Adolescents and adults at clinical high-risk for psychosis: age-related differences in attenuated positive symptoms syndrome prevalence and entanglement with basic symptoms. *Psychological Medicine*, *46*(5), 1069-1078.

Goldberg, D. P., & Hillier, V. F. (1979). A scaled version of the General Health Questionnaire. *Psychological Medicine*, *9*(1), 139-145.

Goldstein, J. M., Cherkerzian, S., Seidman, L. J., Petryshen, T. L., Fitzmaurice, G., Tsuang, M. T., & Buka, S. L. (2011). Sex-specific rates of transmission of psychosis in the New England high-risk family study. *Schizophrenia Research*, *128*(1), 150-155.

Grant, P. M., & Beck, A. T. (2009). Defeatist beliefs as a mediator of cognitive impairment, negative symptoms, and functioning in schizophrenia. *Schizophrenia Bulletin*, *35*(4), 798-806.

Grant Steen, R., Mull, C., McCure, R., Hamer, R. M., & Lieberman, J. A. (2006). Brain volume in first-episode schizophrenia: Systematic review and meta-analysis of magnetic resonance imaging studies. *British Journal of Psychiatry*, *188*(6), 510-518.

Green, M. F., Bearden, C. E., Cannon, T. D., Fiske, A. P., Hellemann, G. S., Horan, W. P., ... & Subotnik, K. L. (2011). Social cognition in schizophrenia, part 1: performance across phase of illness. *Schizophrenia Bulletin*, *38*(4), 854-864.

Green, C. E. L., McGuire, P. K., Ashworth, M., & Valmaggia, L. R. (2011). Outreach and Support in South London (OASIS). Outcomes of non-attenders to a service for people at high risk of psychosis: the case for a more assertive approach to assessment. *Psychological Medicine*, *41*(2), 243-250.

Gross, G. (1987). The Bonn Scale for the Assessment of Basic Symptoms (BSABS). *International Journal of Neuroscience, 32*(1-2), 739-740.

Gross, G. (1989). The" basic" symptoms of schizophrenia. *The British Journal of Psychiatry*, *155*(7), 21-25.

Gumley, A., O' Grady, M., McNay, L., Reilly, J., Power, K., & Norrie, J. (2003). Early intervention for relapse in schizophrenia: results of a 12-month randomized controlled trial of cognitive behavioural therapy. *Psychological Medicine*, *33*(3), 419-431.

Haahr, U. H., Larsen, T. K., Simonsen, E., Rund, B. R., Joa, I., Rossberg, J. I., ... & Vaglum, P. (2016). Relation between premorbid adjustment, duration of untreated psychosis and close interpersonal trauma in first-episode psychosis. *Early Intervention in Psychiatry, 12*(1), 1-9.

Häfner, H., Maurer, K., Löffler, W., an der Heiden, W., Hambrecht, M., & Schultze-Lutter, F. (2003). Modeling the early course of schizophrenia. *Schizophrenia Bulletin*, *29*(2), 325-340.

Hanssen, M., Bak, M., Bijl, R., Vollebergh, W., & van Os, J. (2005). The incidence and outcome of subclinical psychotic experiences in the general population. *British Journal of Clinical Psychology*, *44*(2), 181-191.

Haroun, N., Dunn, L., Haroun, A., & Cadenhead, K. S. (2006). Risk and protection in prodromal schizophrenia: ethical implications for clinical practice and future research. *Schizophrenia Bulletin*, *32*(1), 166-178.

Harrison, G., Hopper, K. I. M., Craig, T., Laska, E., Siegel, C., Wanderling, J., ... & Holmberg, S. K. (2001). Recovery from psychotic illness: a 15-and 25-year international follow-up study. *The British Journal of Psychiatry*, *178*(6), 506-517.

Hasselbalch, H. C. (1993). Idiopathic myelofibrosis—an update with particular reference to clinical aspects and prognosis. *International Journal of Clinical and Laboratory Research*, *23*(1-4), 124-138.

Healey, K. M., Penn, D. L., Perkins, D., Woods, S. W., & Addington, J. (2013). Theory of mind and social judgments in people at clinical high risk of psychosis. *Schizophrenia Research*, *150*(2), 498-504.

Heckers, S. (2001). Neuroimaging studies of the hippocampus in Schizophrenia. *Hippocampus*, *11*(5), 520-528.

Heinimaa, M., Salokangas, R. K. R., Ristkari, T., Plathin, M., Huttunen, J., Ilonen, T., ... & McGlashan, T. H. (2003). PROD-screen – a screen for prodromal symptoms of psychosis. *International Journal of Methods in Psychiatric Research*, *12*(2), 92-104.

Hooker, C. I., Carol, E. E., Eisenstein, T. J., Yin, H., Lincoln, S. H., Tully, L. M., ... & Seidman, L. J. (2014). A pilot study of cognitive training in clinical high risk for psychosis: initial evidence of cognitive benefit. *Schizophrenia Research*, *157*(1), 314-316.

Howes, O. D., & Kapur, S. (2009). The dopamine hypothesis of schizophrenia: version III — the final common pathway. *Schizophrenia Bulletin*, *35*(3), 549-562.

Huber, G., & Gross, G. (1989). The concept of basic symptoms in schizophrenic and schizoaffective psychoses. *Recenti Progressi in Medicina*, *80*(12), 646-652.

Hui, C., Morcillo, C., Russo, D. A., Stochl, J., Shelley, G. F., Painter, M., ... & Perez, J. (2013). Psychiatric morbidity, functioning and quality of life in young people at clinical high risk for psychosis. *Schizophrenia Research*, *148*(1), 175-180.

Hur, J. W., Byun, M. S., Shin, N. Y., Shin, Y. S., Kim, S. N., Jang, J. H., & Kwon, J. S. (2013). General intellectual functioning as a buffer against theory-of-mind deficits in individuals at ultra-high risk for psychosis. *Schizophrenia Research*, *149*(1), 83-87.

Ising, H. K., Veling, W., Loewy, R. L., Rietveld, M. W., Rietdijk, J., Dragt, S., ... & van der Gaag, M. (2012). The validity of the 16-item version of the Prodromal Questionnaire (PQ-16) to screen for ultra-high risk of developing psychosis in the general help-seeking population. *Schizophrenia Bulletin*, *38*(6), 1288-1296.

Job, D. E., Whalley, H. C., Johnstone, E. C., & Lawrie, S. M. (2005). Grey matter changes over time in high risk subjects developing schizophrenia. *Neuroimage*, *25*(4), 1023-1030.

Johns, L. C., Allen, P., Valli, I., Winton-Brown, T., Broome, M., Woolley, J., ... & McGuire, P. (2010). Impaired verbal self-monitoring in individuals at high risk of psychosis. *Psychological Medicine*, *40*(9), 1433-1442.

Johns, L. C., Gregg, L., Allen, P., & McGuire, P. K. (2006). Impaired verbal self-monitoring in psychosis: effects of state, trait and diagnosis. *Psychological Medicine*, *36*(4), 465-474.

Johns, L. C., & McGuire, P. K. (1999). Verbal self-monitoring and auditory hallucinations in schizophrenia. *The Lancet*, *353*(9151), 469-470.

Johnstone, E. C., Ebmeier, K. P., Miller, P., Owens, D. G., & Lawrie, S. M. (2005). Predicting schizophrenia: findings from the Edinburgh high-risk study. *The British Journal of Psychiatry*, *186*(1), 18-25.

Kapur, S. (2003). Psychosis as a state of aberrant salience: a framework linking biology, phenomenology, and pharmacology in schizophrenia. *American Journal of Psychiatry, 160*(1), 13-23.

Katsura, M., Ohmuro, N., Obara, C., Kikuchi, T., Ito, F., Miyakoshi, T., ... & Matsumoto, K. (2014). A naturalistic longitudinal study of at-risk mental state with a 2.4 year follow-up at a specialized clinic setting in Japan. *Schizophrenia Research*, *158*(1), 32-38.

Kaymaz, N., van Os, J., de Graaf, R., ten Have, M., Nolen, W., & Krabbendam, L. (2007). The impact of subclinical psychosis on the transition from subclinicial mania to bipolar disorder. *Journal of Affective Disorders*, *98*(1), 55-64.

Keefe, R. S., Arnold, M. C., Bayen, U. J., & Harvey, P. D. (1999). Source monitoring deficits in patients with schizophrenia; a multinomial modelling analysis. *Psychological Medicine*, *29*(4), 903-914.

Kelleher, I., & Cannon, M. (2011). Psychotic-like experiences in the general population: characterizing a high-risk group for psychosis. *Psychological Medicine*, *41*(1), 1-6.

Kempton, M. J., Bonoldi, I., Valmaggia, L., McGuire, P., & Fusar-Poli, P. (2015). Speed of psychosis progression in people at ultra-high clinical risk: a complementary meta-analysis. *JAMA Psychiatry*, *72*(6), 622-623.

Kendler, K. S., Gallagher, T. J., Abelson, J. M., & Kessler, R. C. (1996). Lifetime prevalence, demographic risk factors, and diagnostic validity of nonaffective psychosis as assessed in a US community sample: the National Comorbidity Survey. *Archives of General Psychiatry*, *53*(11), 1022-1031.

Kirkbride, J. B., Errazuriz, A., Croudace, T. J., Morgan, C., Jackson, D., Boydell, J., ... & Jones, P. B. (2012). Incidence of schizophrenia and other psychoses in England, 1950–2009: a systematic review and meta-analyses. *PloS One*, *7*(3), e31660.

Kirkbride, J. B., Fearon, P., Morgan, C., Dazzan, P., Morgan, K., Tarrant, J., ... & Mallett, R. M. (2006). Heterogeneity in incidence rates of schizophrenia and other psychotic syndromes: findings from the 3-center AeSOP study. *Archives of general psychiatry*, *63*(3), 250-258.

Kline, E., & Schiffman, J. (2014). Psychosis risk screening: a systematic review. *Schizophrenia Research*, *158*(1), 11-18.

Kline, E., Wilson, C., Ereshefsky, S., Denenny, D., Thompson, E., Pitts, S. C., ... & Schiffman, J. (2012). Psychosis risk screening in youth: a validation study of three self-report measures of attenuated psychosis symptoms. *Schizophrenia Research*, *141*(1), 72-77.

Klosterkötter, J., Hellmich, M., Steinmeyer, E. M., & Schultze-Lutter, F. (2001). Diagnosing schizophrenia in the initial prodromal phase. *Archives of General Psychiatry*, *58*(2), 158-164.

Kobayashi, H., Nemoto, T., Koshikawa, H., Osono, Y., Yamazawa, R., Murakami, M., ... & Mizuno, M. (2008). A self-reported instrument for prodromal symptoms of psychosis: testing the clinical validity of the PRIME Screen—Revised (PS-R) in a Japanese population. *Schizophrenia Research*, *106*(2), 356-362.

Kohler, C. G., Richard, J. A., Brensinger, C. M., Borgmann-Winter, K. E., Conroy, C. G., Moberg, P. J., ... & Calkins, M. E. (2014). Facial emotion perception differs in young persons at genetic and clinical high-risk for psychosis. *Psychiatry Research*, *216*(2), 206-212.

Konings, M., Bak, M., Hanssen, M., Van Os, J., & Krabbendam, L. (2006). Validity and reliability of the CAPE: a self-report instrument for the measurement of psychotic experiences in the general population. *Acta Psychiatrica Scandinavica*, *114*(1), 55-61.

Korver, N., Nieman, D. H., Becker, H. E., van de Fliert, J. R., Dingemans, P. H., de Haan, L., ... & Linszen, D. H. (2010). Symptomatology and neuropsychological functioning in cannabis using subjects at ultra-high risk for developing psychosis and healthy controls. *Australian and New Zealand Journal of Psychiatry*, *44*(3), 230-236.

Koutsouleris, N., Riecher-Rössler, A., Meisenzahl, E. M., Smieskova, R., Studerus, E., Kambeitz-Ilankovic, L., ... & Borgwardt, S. (2014). Detecting the psychosis prodrome across high-risk populations using neuroanatomical biomarkers. *Schizophrenia Bulletin, 41*(2), 471-482.

Køster, A., Lajer, M., Lindhardt, A., & Rosenbaum, B. (2008). Gender differences in first episode psychosis. *Social Psychiatry and Psychiatric Epidemiology*, *43*(12), 940-946.

Kraan, T., Velthorst, E., Koenders, L., Zwaart, K., Ising, H. K., van den Berg, D., ... & van der Gaag, M. (2016). Cannabis use and transition to psychosis in individuals at ultra-high risk: review and meta-analysis. *Psychological Medicine*, *46*(4), 673-681.

Kraan, T., Velthorst, E., Smit, F., de Haan, L., & van der Gaag, M. (2015). Trauma and recent life events in individuals at ultra high risk for psychosis: review and meta-analysis. *Schizophrenia Research*, *161*(2), 143-149.

Kuepper, R., van Os, J., Lieb, R., Wittchen, H. U., Höfler, M., & Henquet, C. (2011). Continued cannabis use and risk of incidence and persistence of psychotic symptoms: 10-year follow-up cohort study. *British Medical Journal*, *342*(1), 731-738.

Kwapil, T. R., Miller, M. B., Zinser, M. C., Chapman, L. J., Chapman, J., & Eckblad, M. (2000). A longitudinal study of high scorers on the hypomanic personality scale. *Journal of Abnormal Psychology*, *109*(2), 222.

Kwon, J. S., Byun, M. S., Lee, T. Y., & An, S. K. (2012). Early intervention in psychosis: insights from Korea. *Asian Journal of Psychiatry*, *5*(1), 98-105.

Lam, M. M., Hung, S. F., & Chen, E. Y. (2006). Transition to psychosis: 6-month follow-up of a Chinese high-risk group in Hong Kong. *Australian and New Zealand Journal of Psychiatry*, *40*(5), 414-420.

Landa, Y., Mueser, K., Wyka, K., Shreck, E., Jespersen, R., Jacobs, M., ... & Silbersweig, D. (2015). Development of a group and family-based cognitive behavioral therapy program for youth at risk for psychosis. *Early Intervention in Psychiatry, 10*(6) 511-521.

Larsson, S., Andreassen, O. A., Aas, M., Røssberg, J. I., Mork, E., Steen, N. E., ... & Melle, I. (2013). High prevalence of childhood trauma in patients with schizophrenia spectrum and affective disorder. *Comprehensive Psychiatry*, *54*(2), 123-127.

Laruelle, M., Kegeles, L. S., & Abi-Dargham, A. (2003). Glutamate, dopamine, and schizophrenia. *Annals of the New York Academy of Sciences*, *1003*(1), 138-158.

Lemos-Giráldez, S., Vallina-Fernández, O., Fernández-Iglesias, P., Vallejo-Seco, G., Fonseca-Pedrero, E., Paíno-Piñeiro, M., ... & Gutiérrez-Pérez, A. (2009). Symptomatic and functional outcome in youth at ultra-high risk for psychosis: a longitudinal study. *Schizophrenia Research*, *115*(2), 121-129.

Lencz, T., Smith, C. W., Auther, A. M., Correll, C. U., & Cornblatt, B. A. (2003). The assessment of" prodromal schizophrenia": unresolved issues and future directions. *Schizophrenia Bulletin*, *29*(4), 717.

Lieberman, J. A., Tollefson, G. D., Charles, C., Zipursky, R., Sharma, T., Kahn, R. S., ... & Perkins, D. (2005). Antipsychotic drug effects on brain morphology in first-episode psychosis. *Archives of General Psychiatry*, *62*(4), 361-370.

Lin, A., Wigman, J. T. W., Nelson, B., Vollebergh, W. A. M., Van Os, J., Baksheev, G., ... & Yung, A. R. (2011). The relationship between coping and subclinical psychotic experiences in adolescents from the general population–a longitudinal study. *Psychological Medicine*, *41*(12), 2535-2546.

Lin, A., Wood, S. J., Nelson, B., Beavan, A., McGorry, P., & Yung, A. R. (2015). Outcomes of nontransitioned cases in a sample at ultra-high risk for psychosis. *American Journal of Psychiatry*, *172*(3), 249-258.

Loewy, R. L., Bearden, C. E., Johnson, J. K., Raine, A., & Cannon, T. D. (2005). The prodromal questionnaire (PQ): preliminary validation of a self-report screening measure for prodromal and psychotic syndromes. *Schizophrenia Research*, *79*(1), 117-125.

Loewy, R. L., Therman, S., Manninen, M., Huttunen, M. O., & Cannon, T. D. (2012). Prodromal psychosis screening in adolescent psychiatry clinics. *Early intervention in psychiatry*, *6*(1), 69-75.

Luzón, O., Harrop, C., & Nolan, F. (2009). Cognitive Processes during Acute Psychosis: The Role of Heightened Responsibility and Catastrophic Misinterpretations. *Behavioural and Cognitive Psychotherapy, 37*(4), 357-371.

Maric, N., Krabbendam, L., Vollebergh, W., de Graaf, R., & van Os, J. (2003). Sex differences in symptoms of psychosis in a non-selected, general population sample. *Schizophrenia Research*, *63*(1), 89-95.

Marshall, M., Lewis, S., Lockwood, A., Drake, R., Jones, P., & Croudace, T. (2005). Association between duration of untreated psychosis and outcome in cohorts of first-episode patients: a systematic review. *Archives of General Psychiatry*, *62*(9), 975-983.

Marshall, M., & Rathbone, J. (2011). Early intervention for psychosis. *Schizophrenia Bulletin*, *37*(6), 1111-1114.

Mason, O., Startup, M., Halpin, S., Schall, U., Conrad, A., & Carr, V. (2004). Risk factors for transition to first episode psychosis among individuals with ‘at-risk mental states’. *Schizophrenia Research*, *71*(2), 227-237.

Maurer, K., Hörrmann, F., Trendler, G., Schmidt, M., & Häfner, H. (2006). Früherkennung des Psychoserisikos mit dem Early Recognition Inventory (ERIraos) Beschreibung des Verfahrens und erste Ergebnisse zur Reliabilität und Validität der Checkliste. *Nervenheilkunde*, *25*(1), 11-16.

Mayer, J. D. (2002). *Mayer-Salovey-Caruso emotional intelligence test*. Toronto: Multi-Health Systems.

Mayer, J. D., Caruso, D. R., & Salovey, P. (1999). Emotional intelligence meets traditional standards for an intelligence. *Intelligence*, *27*(4), 267-298.

McGlashan, T. H. (1984). The Chestnut Lodge follow-up study: I. Follow-up methodology and study sample. *Archives of General Psychiatry*, *41*(6), 573-585.

McGlashan, T.H., Miller, T. J., Woods, S. W., Hofman, R. E., & Davidson, R. (2001). A scale for the assessment of prodromal symptoms and states. In T. J. Miller, S. A. Mednick, T. H. McGlashan, J. Libeger & J. O. Johannessen (Eds.), *Early Intervention in Psychotic Disorders* (pp. 135-149). Dordrecht: Kluwer Academic Publisher.

McGlashan, T., Walsh, B., & Woods, S. (2010). *The psychosis-risk syndrome: handbook for diagnosis and follow-up*. Oxford, UK: Oxford University Press.

McGlashan, T. H., Zipursky, R. B., Perkins, D., Addington, J., Miller, T., Woods, S. W., ... & Addington, D. (2006). Randomized, double-blind trial of olanzapine versus placebo in patients prodromally symptomatic for psychosis. *American Journal of Psychiatry, 163*(5), 790-799.

McGorry, P. D., Hickie, I. B., Yung, A. R., Pantelis, C., & Jackson, H. J. (2006). Clinical staging of psychiatric disorders: a heuristic framework for choosing earlier, safer and more effective interventions. *Australian and New Zealand Journal of Psychiatry*, *40*(8), 616-622.

McGorry, P. D., Killackey, E., & Yung, A. (2008). Early intervention in psychosis: concepts, evidence and future directions. *World Psychiatry*, *7*(3), 148-156.

McGorry, P. D., Nelson, B., Amminger, G. P., Bechdolf, A., Francey, S. M., Berger, G., ... & Schultze-Lutter, F. (2009). Intervention in individuals at ultra-high risk for psychosis: a review and future directions. *The Journal of Clinical Psychiatry*, *70*(9), 1206-1212.

McGorry, P. D., Nelson, B., Phillips, L. J., Yuen, H. P., Francey, S. M., Thampi, A., ... & Dip, G. (2013). Randomized controlled trial of interventions for young people at ultra-high risk of psychosis: twelve-month outcome. *The Journal of Clinical Psychiatry*, *74*(4), 349-356.

McGorry, P. D., Purcell, R., Hickie, I. B., Yung, A. R., Pantelis, C., & Jackson, H. J. (2007). Clinical staging: a heuristic model for psychiatry and youth mental health. *Medical Journal of Australia*, *187*(Suppl.7), S40-S42.

McGorry, P. D., Yung, A. R., Phillips, L. J., Yuen, H. P., Francey, S., Cosgrave, E. M., ... & Adlard, S. (2002). Randomized controlled trial of interventions designed to reduce the risk of progression to first-episode psychosis in a clinical sample with subthreshold symptoms. *Archives of General Psychiatry*, *59*(10), 921-928.

Meehl, P. E. (1962). Schizotaxia, schizotypy, schizophrenia. *American Psychologist*, *17*(12), 827-838.

Meneghelli, A., Meliante, M., Amato, L., Pozza, A., & Dettore, D. (2016). "I fear going crazy"... could Cognitive Concerns be early warning signs of Psychosis? Evidence from the Anxiety Sensitivity in the first stages of Psychosis study (ASP study). *Early intervention in psychiatry*, *10*(Suppl. 1), 229-229.

Meyer, T. J., Miller, M. L., Metzger, R. L., & Borkovec, T. D. (1990). Development and validation of the penn state worry questionnaire. *Behaviour Research and Therapy, 28*(6), 487-495.

Miklowitz, D. J., O'Brien, M. P., Schlosser, D. A., Addington, J., Candan, K. A., Marshall, C., ... & Friedman-Yakoobian, M. (2014). Family-focused treatment for adolescents and young adults at high risk for psychosis: results of a randomized trial. *Journal of the American Academy of Child & Adolescent Psychiatry*, *53*(8), 848-858.

Miller, T. J., Cicchetti, D., Markovich, P. J., McGlashan, T. H., & Woods, S. W. (2004). The SIPS screen: a brief self-report screen to detect the schizophrenia prodrome. *Schizophrenia Research*, 70 (1), 78-78.

Miller, T. J., McGlashan, T. H., Rosen, J. L., Somjee, L., Markovich, P. J., Stein, K., & Woods, S. W. (2002). Prospective diagnosis of the initial prodrome for schizophrenia based on the Structured Interview for Prodromal Syndromes: preliminary evidence of interrater reliability and predictive validity. *American Journal of Psychiatry*, *159*(5), 863-865.

Mittal, V. A., Dean, D. J., Mittal, J., & Saks, E. R. (2015). Ethical, Legal, and Clinical Considerations when Disclosing a High-Risk Syndrome for Psychosis. *Bioethics*, *29*(8), 543-556.

Mizrahi, R., Addington, J., Rusjan, P. M., Suridjan, I., Ng, A., Boileau, I., ... & Wilson, A. A. (2012). Increased stress-induced dopamine release in psychosis. *Biological Psychiatry*, *71*(6), 561-567.

Mondelli, V., Dazzan, P., Hepgul, N., Di Forti, M., Aas, M., D'Albenzio, A., ... & Morgan, C. (2010). Abnormal cortisol levels during the day and cortisol awakening response in first-episode psychosis: the role of stress and of antipsychotic treatment. *Schizophrenia Research*, *116*(2), 234-242.

Moore, T. H., Zammit, S., Lingford-Hughes, A., Barnes, T. R., Jones, P. B., Burke, M., & Lewis, G. (2007). Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *The Lancet*, *370*(9584), 319-328.

Morani, S., Pricci, D., & Sanavio, E. (1999). Penn State Worry Questionnaire e Worry Domains Questionnaire. Presentazione delle versioni italiane ed analisi della fedeltà. *Psicoterapia Cognitiva e Comportamentale, 5*(3), 13-34.

Morgan, V. A., Castle, D. J., & Jablensky, A. V. (2008). Do women express and experience psychosis differently from men? Epidemiological evidence from the Australian National Study of Low Prevalence (Psychotic) Disorders. *Australian and New Zealand Journal of Psychiatry*, *42*(1), 74-82.

Moritz, S., & Woodward, T. S. (2005). Jumping to conclusions in delusional and non-delusional schizophrenic patients. *British Journal of Clinical Psychology*, *44*(2), 193-207.

Moritz, S., & Woodward, T. S. (2007). Metacognitive training in schizophrenia: from basic research to knowledge translation and intervention. *Current Opinion in Psychiatry, 20*(6), 619-625.

Morosini, P. L., Magliano, L., Brambilla, L., Ugolini, S., & Pioli, R. (2000). Development, reliability and acceptability of a new version of the DSM-IV Social and Occupational Functioning Assessment Scale (SOFAS) to assess routine social funtioning. *Acta Psychiatrica Scandinavica*, *101*(4), 323-329.

Morrison, A. P. (2001). The interpretation of intrusions in psychosis: an integrative cognitive approach to hallucinations and delusions. *Behavioural and Cognitive Psychotherapy*, *29*(3), 257-276.

Morrison, A. P., Bentall, R. P., French, P., Walford, L., Kilcommons, A., Knight, A., ... & Lewis, S. W. (2002). Randomised controlled trial of early detection and cognitive therapy for preventing transition to psychosis in high-risk individuals. *The British Journal of Psychiatry*, *181*(43), s78-s84.

Morrison, A. P., French, P., Stewart, S. L., Birchwood, M., Fowler, D., Gumley, A. I., ... & Patterson, P. (2012). Early detection and intervention evaluation for people at risk of psychosis: multisite randomised controlled trial. *British Medical Journal, 344*, 2233.

Morrison, A. P., French, P., & Wells, A. (2007). Metacognitive beliefs across the continuum of psychosis: Comparisons between patients with psychotic disorders, patients at ultra-high risk and non-patients. *Behaviour Research and Therapy*, *45*(9), 2241-2246.

Mossaheb, N., Becker, J., Schaefer, M. R., Klier, C. M., Schloegelhofer, M., Papageorgiou, K., & Amminger, G. P. (2012). The Community Assessment of Psychic Experience (CAPE) questionnaire as a screening-instrument in the detection of individuals at ultra-high risk for psychosis. *Schizophrenia Research*, *141*(2), 210-214.

Nelson, M. T., Seal, M. L., Pantelis, C., & Phillips, L. J. (2013). Evidence of a dimensional relationship between schizotypy and schizophrenia: a systematic review. *Neuroscience & Biobehavioral Reviews*, *37*(3), 317-327.

Nelson, B., Thompson, A., & Yung, A. R. (2012). Basic self-disturbance predicts psychosis onset in the ultra high risk for psychosis "prodromal" population. *Schizophrenia Bulletin*, *38*(6), 1277-1287.

Nelson, B., Yuen, H. P., Wood, S. J., Lin, A., Spiliotacopoulos, D., Bruxner, A., ... & Francey, S. M. (2013). Long-term follow-up of a group at ultra high risk ("prodromal") for psychosis: the PACE 400 study. *JAMA Psychiatry*, *70*(8), 793-802.

Nelson, B., & Yung, A. R. (2009). Psychotic-like experiences as overdetermined phenomena: when do they increase risk for psychotic disorder? *Schizophrenia Research*, *108*(1), 303-304.

Newell, D. J. (1992). Intention-to-treat analysis: implications for quantitative and qualitative research. *International Journal of Epidemiology, 21*, 837-841.

Nieman, D. H., Rike, W. H., Becker, H. E., Dingemans, P. M., van Amelsvoort, T. A., de Haan, L., ... & Linszen, D. H. (2009). Prescription of antipsychotic medication to patients at ultra high risk of developing psychosis. *International Clinical Psychopharmacology*, *24*(4), 223-228.

Nordentoft, M., Thorup, A., Petersen, L., Øhlenschlæger, J., Melau, M., Christensen, T. Ø., ... & Jeppesen, P. (2006). Transition rates from schizotypal disorder to psychotic disorder for first-contact patients included in the OPUS trial. A randomized clinical trial of integrated treatment and standard treatment. *Schizophrenia Research*, *83*(1), 29-40.

Norman, R. M., & Malla, A. K. (2001). Duration of untreated psychosis: a critical examination of the concept and its importance. *Psychological Medicine*, *31*(3), 381-400.

O' Brien, M. P., Miklowitz, D. J., Candan, K. A., Marshall, C., Domingues, I., Walsh, B. C., ... & Cannon, T. D. (2014). A randomized trial of family focused therapy with populations at clinical high risk for psychosis: Effects on interactional behavior. *Journal of Consulting and Clinical Psychology*, *82*(1), 90.

O' Brien, M. P., Zinberg, J. L., Bearden, C. E., Daley, M., Niendam, T. A., Kopelowicz, A., & Cannon, T. D. (2007). Psychoeducational multi-family group treatment with adolescents at high risk for developing psychosis. *Early Intervention in Psychiatry*, *1*(4), 325-332.

O' Donoghue, B., Lyne, J. P., Renwick, L., Lane, A., Madigan, K., Staines, A., ... & Clarke, M. (2016). Neighbourhood characteristics and the incidence of first-episode psychosis and duration of untreated psychosis. *Psychological Medicine*, *46*(7), 1367-1378.

Ohayon, M. M. (2000). Prevalence of hallucinations and their pathological associations in the general population. *Psychiatry Research*, *97*(2), 153-164.

Olesen, J., Gustavsson, A., Svensson, M., Wittchen, H. U., & Jönsson, B. (2012). The economic cost of brain disorders in Europe. *European Journal of Neurology*, *19*(1), 155-162.

Overall, J. E., & Gorham, D. R. (1962). The brief psychiatric rating scale. *Psychological Reports, 10*(3), 799–812.

Palaniyappan, L., Mallikarjun, P., Joseph, V., White, T. P., & Liddle, P. F. (2011). Reality distortion is related to the structure of the salience network in schizophrenia. *Psychological Medicine*, *41*(8), 1701-1708.

Palaniyappan, L., Simmonite, M., White, T. P., Liddle, E. B., & Liddle, P. F. (2013). Neural primacy of the salience processing system in schizophrenia. *Neuron*, *79*(4), 814-828.

Palmier-Claus, J. E., Dunn, G., Taylor, H., Morrison, A. P., & Lewis, S. W. (2013). Cognitive-self-consciousness and metacognitive beliefs: Stress sensitization in individuals at ultra-high risk of developing psychosis. *British Journal of Clinical Psychology, 52*(1), 26-41.

Pantelis, C., Velakoulis, D., McGorry, P. D., Wood, S. J., Suckling, J., Phillips, L. J., ... & Desmond, P. (2003). Neuroanatomical abnormalities before and after onset of psychosis: a cross-sectional and longitudinal MRI comparison. *The Lancet*, *361*(9354), 281-288.

Pantelis, C., Yücel, M., Wood, S. J., Velakoulis, D., Sun, D., Berger, G., ... & McGorry, P. D. (2005). Structural brain imaging evidence for multiple pathological processes at different stages of brain development in schizophrenia. *Schizophrenia Bulletin*, *31*(3), 672-696.

Parnas, J., Handest, P., Jansson, L., & Sæbye, D. (2005). Anomalous subjective experience among first-admitted schizophrenia spectrum patients: empirical investigation. *Psychopathology*, *38*(5), 259-267.

Penttilä, M., Jääskeläinen, E., Hirvonen, N., Isohanni, M., & Miettunen, J. (2014). Duration of untreated psychosis as predictor of long-term outcome in schizophrenia: systematic review and meta-analysis. *The British Journal of Psychiatry*, *205*(2), 88-94.

Perivoliotis, D., Morrison, A. P., Grant, P. M., French, P., & Beck, A. T. (2009). Negative performance beliefs and negative symptoms in individuals at ultra-high risk of psychosis: a preliminary study. *Psychopathology*, *42*(6), 375-379.

Perkins, D. O., Gu, H., Boteva, K., & Lieberman, J. A. (2005). Relationship between duration of untreated psychosis and outcome in first-episode schizophrenia: a critical review and meta-analysis. *American Journal of Psychiatry*, *162*(10), 1785-1804.

Phillips, J. (2013). Conceptual issues in the classification of psychosis. *Current Opinion in Psychiatry*, *26*(2), 214-218.

Phillips, L. J., Curry, C., Yung, A. R., Pan Yuen, H., Adlard, S., & Mcgorry, P. D. (2002). Cannabis use is not associated with the development of psychosis in an ultra high-risk group. *Australian and New Zealand Journal of Psychiatry*, *36*(6), 800-806.

Phillips, L. J., Nelson, B., Yuen, H. P., Francey, S. M., Simmons, M., Stanford, C., ... & Amminger, P. (2009). Randomized controlled trial of interventions for young people at ultra-high risk of psychosis: study design and baseline characteristics. *Australian and New Zealand Journal of Psychiatry*, *43*(9), 818-829.

Phillips, L. J., Velakoulis, D., Pantelis, C., Wood, S., Yuen, H. P., Yung, A. R., ... & McGorry, P. D. (2002). Non-reduction in hippocampal volume is associated with higher risk of psychosis. *Schizophrenia Research*, *58*(2), 145-158.

Preti, A., & Cella, M. (2010). Randomized-controlled trials in people at ultra high risk of psychosis: a review of treatment effectiveness. *Schizophrenia Research*, *123*(1), 30-36.

Raine, A., & Benishay, D. (1995). The SPQ-B: A brief screening instrument for schizotypal personality disorder. *Journal of Personality Disorders*, *9*(4), 346-355.

Raine, A., Lencz, T., & Mednick, S. A. (1995). *Schizotypal personality*. Cambridge: Cambridge University Press.

Regier, D. A., Kuhl, E. A., Kupfer, D. J., & McNulty, J. P. (2010). Patient involvement in the development of DSM-V. *Psychiatry*, *73*(4), 308-310.

Riecher-Rössler, A., Aston, J., Ventura, J., Merlo, M., Borgwardt, S., Gschwandtner, U., & Stieglitz, R. D. (2008). [The Basel Screening Instrument for Psychosis (BSIP): development, structure, reliability and validity]. *Fortschritte der Neurologie-Psychiatrie*, *76*(4), 207-216.

Riecher-Rössler, A., Gschwandtner, U., Aston, J., Borgwardt, S., Drewe, M., Fuhr, P., ... & Stieglitz, R. D. (2007). The Basel early-detection-of-psychosis (FEPSY)-study–design and preliminary results. *Acta Psychiatrica Scandinavica*, *115*(2), 114-125.

Riecher-Rössler, A., Pflueger, M. O., Aston, J., Borgwardt, S. J., Brewer, W. J., Gschwandtner, U., & Stieglitz, R. D. (2009). Efficacy of using cognitive status in predicting psychosis: a 7-year follow-up. *Biological Psychiatry*, *66*(11), 1023-1030.

Rietdijk, J., Dragt, S., Klaassen, R., Ising, H., Nieman, D., Wunderink, L., ... & van der Gaag, M. (2010). A single blind randomized controlled trial of cognitive behavioural therapy in a help-seeking

population with an At Risk Mental State for psychosis: the Dutch Early Detection and Intervention Evaluation (EDIE-NL) trial. *Trials*, *11*(1), 1-9.

Rietdijk, J., Fokkema, M., Stahl, D., Valmaggia, L., Ising, H. K., Dragt, S., ... & Delespaul, P. (2014). The distribution of self-reported psychotic-like experiences in non-psychotic help-seeking mental health patients in the general population; a factor mixture analysis. *Social Psychiatry and Psychiatric Epidemiology*, *49*(3), 349-358.

Rietdijk, J., Hogerzeil, S. J., van Hemert, A. M., Cuijpers, P., Linszen, D. H., & van der Gaag, M. (2011). Pathways to psychosis: help-seeking behavior in the prodromal phase. *Schizophrenia Research*, *132*(2), 213-219.

Rubio, J. M., Sanjuán, J., Flórez-Salamanca, L., & Cuesta, M. J. (2012). Examining the course of hallucinatory experiences in children and adolescents: a systematic review. *Schizophrenia Research*, *138*(2), 248-254.

Ruhrmann, S., Bechdolf, A., KÜHN, K. U., Wagner, M., Schultze-Lutter, F., Janssen, B., ... & Maier, W. (2007). Acute effects of treatment for prodromal symptoms for people putatively in a late initial prodromal state of psychosis. *The British Journal of Psychiatry*, *191*(51), s88-s95.

Ruhrmann, S., Schultze-Lutter, F., & Klosterkötter, J. (2003). Early detection and intervention in the initial prodromal phase of schizophrenia. *Pharmacopsychiatry*, *36*(3), 162-167.

Ruhrmann, S., Schultze-Lutter, F., Salokangas, R. K., Heinimaa, M., Linszen, D., Dingemans, P., ... & Morrison, A. (2010). Prediction of psychosis in adolescents and young adults at high risk: results from the prospective European prediction of psychosis study. *Archives of General Psychiatry*, *67*(3), 241-251.

Russo, D. A., Stochl, J., Painter, M., Dobler, V., Jackson, E., Jones, P. B., & Perez, J. (2014). Trauma history characteristics associated with mental states at clinical high risk for psychosis. *Psychiatry Research*, *220*(1), 237-244.

Sadler, J. Z. (2013). *Making the DSM-5*. New York, NY: Springer.

Şahin, S., Yüksel, Ç., Güler, J., Karadayı, G., Akturan, E., Göde, E., ... & Üçok, A. (2013). The history of childhood trauma among individuals with ultra high risk for psychosis is as common as among patients with first-episode schizophrenia. *Early Intervention in Psychiatry*, *7*(4), 414-420.

Saleem, M. M., Stowkowy, J., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A., McGlashan, T. H., ... & Woods, S. W. (2014). Perceived discrimination in those at clinical high risk for psychosis. *Early Intervention in Psychiatry*, *8*(1), 77-81.

Salokangas, R. K. R., Dingemans, P., Heinimaa, M., Svirskis, T., Luutonen, S., Hietala, J., ... & Birchwood, M. (2013). Prediction of psychosis in clinical high-risk patients by the Schizotypal Personality Questionnaire. Results of the EPOS project. *European Psychiatry*, *28*(8), 469-475.

Salokangas, R. K., Ruhrmann, S., von Reventlow, H. G., Heinimaa, M., Svirskis, T., From, T., ... & Birchwood, M. (2012). Axis I diagnoses and transition to psychosis in clinical high-risk patients EPOS project: prospective follow-up of 245 clinical high-risk outpatients in four countries. *Schizophrenia Research*, *138*(2), 192-197.

Schlosser, D. A., Zinberg, J. L., Loewy, R. L., Casey-Cannon, S., O' Brien, M. P., Bearden, C. E., ... & Cannon, T. D. (2010). Predicting the longitudinal effects of the family environment on prodromal symptoms and functioning in patients at-risk for psychosis. *Schizophrenia Research*, *118*(1), 69-75.

Schmidt, A., Smieskova, R., Aston, J., Simon, A., Allen, P., Fusar-Poli, P., ... & Borgwardt, S. (2013). Brain connectivity abnormalities predating the onset of psychosis: correlation with the effect of medication. *JAMA Psychiatry*, *70*(9), 903-912.

Schmidt, S. J., Schultze-Lutter, F., Schimmelmann, B. G., Maric, N. P., Salokangas, R. K. R., Riecher-Rössler, A., ... & Morrison, A. (2015). EPA guidance on the early intervention in clinical high risk states of psychoses. *European Psychiatry*, *30*(3), 388-404.

Schultze-Lutter, F. (2009). Subjective symptoms of schizophrenia in research and the clinic: the basic symptom concept. *Schizophrenia Bulletin*, *35*(1), 5-8.

Schultze-Lutter, F., & Klosterkötter, J. (2002). *Bonn Scale for the Assessment of Basic Symptoms-Prediction list (BSABS-P)*. Cologne: University of Cologne.

Schultze-Lutter, F., Ruhrmann, S., Berning, J., Maier, W., & Klosterkötter, J. (2010). Basic symptoms and ultrahigh risk criteria: symptom development in the initial prodromal state. *Schizophrenia Bulletin*, *36*(1), 182-191.

Schwartz, R. C. (2007). Concurrent validity of the Global Assessment of Functioning Scale for clients with schizophrenia. *Psychological Reports*, *100*(2), 571-574.

Seeber, K., & Cadenhead, K. S. (2005). How does studying schizotypal personality disorder inform us about the prodrome of schizophrenia? *Current Psychiatry Reports*, *7*(1), 41-50.

Seidman, L. J., & Nordentoft, M. (2015). New targets for prevention of schizophrenia: is it time for interventions in the premorbid phase? *Schizophrenia Bulletin*, *41*(4), 795-800.

Seiferth, N. Y., Pauly, K., Habel, U., Kellermann, T., Shah, N. J., Ruhrmann, S., ... & Kircher, T. (2008). Increased neural response related to neutral faces in individuals at risk for psychosis. *Neuroimage*, *40*(1), 289-297.

Sensky, T., Turkington, D., Kingdon, D., Scott, J. L., Scott, J., Siddle, R., ... & Barnes, T. R. (2000). A randomized controlled trial of cognitive-behavioral therapy for persistent symptoms in schizophrenia resistant to medication. *Archives of General Psychiatry*, *57*(2), 165-172.

Shah, J., Eack, S. M., Montrose, D. M., Tandon, N., Miewald, J. M., Prasad, K. M., & Keshavan, M. S. (2012). Multivariate prediction of emerging psychosis in adolescents at high risk for schizophrenia. *Schizophrenia Research*, *141*(2), 189-196.

Sica, C., Ghisi, M., & Lange, M. A. (2007). *Leading-edge psychological tests and testing research*. New York, NY: Nova Publisher.

Simon, A. E., & Umbricht, D. (2010). High remission rates from an initial ultra-high risk state for psychosis. *Schizophrenia Research*, *116*(2), 168-172.

Smieskova, R., Fusar-Poli, P., Allen, P., Bendfeldt, K., Stieglitz, R. D., Drewe, J., ... & Borgwardt, S. J. (2010). Neuroimaging predictors of transition to psychosis—a systematic review and meta-analysis. *Neuroscience & Biobehavioral Reviews*, *34*(8), 1207-1222.

Smith, S. (2010). Gender differences in antipsychotic prescribing. *International Review of Psychiatry*, *22*(5), 472-484.

Spauwen, J., Krabbendam, L., Lieb, R., Wittchen, H. U., & van Os, J. (2003). Sex differences in psychosis: normal or pathological? *Schizophrenia Research*, *62*(1), 45-49.

Stain, H. J., Bucci, S., Baker, A. L., Carr, V., Emsley, R., Halpin, S., ... & Startup, M. (2016). A randomised controlled trial of cognitive behaviour therapy versus non-directive reflective listening for young people at ultra high risk of developing psychosis: The detection and evaluation of psychological therapy (DEPTh) trial. *Schizophrenia Research, 176*(2), 212-219.

Stanford, A. D., Messinger, J., Malaspina, D., & Corcoran, C. M. (2011). Theory of Mind in patients at clinical high risk for psychosis. *Schizophrenia Research*, *131*(1), 11-17.

Startup, H., Freeman, D., & Garety, P. A. (2007). Persecutory delusions and catastrophic worry in psychosis. Developing the understanding of delusion distress and persistence. *Behaviour Research and Therapy, 45*(3), 523-537.

Startup, M., Jackson, M. C., & Bendix, S. (2002). The concurrent validity of the Global Assessment of Functioning (GAF). *British Journal of Clinical Psychology*, *41*(4), 417-422.

Steen, N. E., Tesli, M., Kähler, A. K., Methlie, P., Hope, S., Barrett, E. A., ... & Agartz, I. (2010). SRD5A2 is associated with increased cortisol metabolism in schizophrenia spectrum disorders. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *34*(8), 1500-1506.

Tarrier, N., Kinney, C., McCarthy, E., Humphreys, L., Wittkowski, A., & Morris, J. (2000). Two–year follow–up of cognitive–behavioral therapy and supportive counseling in the treatment of persistent symptoms in chronic schizophrenia. *Journal of Consulting and Clinical Psychology*, *68*(5), 917-922.

Tarrier, N., Yusupoff, L., Kinney, C., McCarthy, E., Gledhill, A., Haddock, G., & Morris, J. (1998). Randomised controlled trial of intensive cognitive behaviour therapy for patients with chronic schizophrenia. *British Medical Journal*, *317*(7154), 303-307.

Thomas, S. P., & Nandhra, H. S. (2009). Early intervention in psychosis: a retrospective analysis of clinical and social factors influencing duration of untreated psychosis. *Primary care companion to the Journal of clinical psychiatry*, *11*(5), 212-214.

Thompson, K. N., Berger, G., Phillips, L. J., Komesaroff, P., Purcell, R., & McGorry, P. D. (2007). HPA axis functioning associated with transition to psychosis: combined DEX/CRH test. *Journal of Psychiatric Research*, *41*(5), 446-450.

Thompson, A., Papas, A., Bartholomeusz, C., Allott, K., Amminger, G. P., Nelson, B., ... & Yung, A. (2012). Social cognition in clinical "at risk" for psychosis and first episode psychosis populations. *Schizophrenia Research*, *141*(2), 204-209.

Thompson, A., Papas, A., Bartholomeusz, C., Nelson, B., & Yung, A. (2013). Externalized attributional bias in the Ultra High Risk (UHR) for psychosis population. *Psychiatry Research*, *206*(2), 200-205.

Thompson, K. N., Phillips, L. J., Komesaroff, P., Yuen, H. P., Wood, S. J., Pantelis, C., ... & McGorry, P. D. (2007). Stress and HPA-axis functioning in young people at ultra high risk for psychosis. *Journal of Psychiatric Research*, *41*(7), 561-569.

Thorup, A., Petersen, L., Jeppesen, P., Ohlenschlæger, J., Christensen, T., Krarup, G., ... & Nordentoft, M. (2007). Gender differences in young adults with first-episode schizophrenia spectrum disorders at baseline in the Danish OPUS study. *The Journal of Nervous and Mental Disease*, *195*(5), 396-405.

Tikka, M., Luutonen, S., Ilonen, T., Tuominen, L., Kotimäki, M., Hankala, J., & Salokangas, R. K. (2013). Childhood trauma and premorbid adjustment among individuals at clinical high risk for psychosis and normal control subjects. *Early Intervention in Psychiatry*, *7*(1), 51-57.

Tsujino, N., Nemoto, T., Morita, K., Katagiri, N., Ito, S., & Mizuno, M. (2013). Long-term efficacy and tolerability of perospirone for young help-seeking people at clinical high risk: a preliminary open trial. *Clinical Psychopharmacology and Neuroscience*, *11*(3), 132-136.

Usall, J., Ochoa, S., Araya, S., & Marquez, M. (2003). Gender differences and outcome in schizophrenia: a 2-year follow-up study in a large community sample. *European Psychiatry*, *18*(6), 282-284.

Van Dael, F., Versmissen, D., Janssen, I., Myin-Germeys, I., Van Os, J., & Krabbendam, L. (2006). Data gathering: biased in psychosis? *Schizophrenia Bulletin*, *32*(2), 341-351.

van der Gaag, M. (2006). A neuropsychiatric model of biological and psychological processes in the remission of delusions and auditory hallucinations. *Schizophrenia Bulletin*, *32*(Suppl 1), S113-S122.

van der Gaag, M., Nieman, D. H., Rietdijk, J., Dragt, S., Ising, H. K., Klaassen, R. M., ... & Linszen, D. H. (2012). Cognitive behavioral therapy for subjects at ultrahigh risk for developing psychosis: a randomized controlled clinical trial. *Schizophrenia Bulletin, 38*(6) 1180-1188.

Van der Gaag, M., Nieman, D., & Van den Berg, D. (2013). *CBT for Those at Risk of a First Episode Psychosis: Evidence-based Psychotherapy for People with an "at Risk Mental State"*. New York, NY: Routledge.

van der Gaag, M., Smit, F., Bechdolf, A., French, P., Linszen, D. H., Yung, A. R., ... & Cuijpers, P. (2013). Preventing a first episode of psychosis: meta-analysis of randomized controlled prevention trials of 12month and longer-term follow-ups. *Schizophrenia Research, 149*(1), 56-62.

van Os, J., Hanssen, M., Bijl, R. V., & Vollebergh, W. (2001). Prevalence of psychotic disorder and community level of psychotic symptoms: an urban-rural comparison. *Archives of General Psychiatry*, *58*(7), 663-668.

van Os, J., & Linscott, R. J. (2012). Introduction: the extended psychosis phenotype—relationship with schizophrenia and with ultrahigh risk status for psychosis. *Schizophrenia Bulletin*, *38*(2), 227-230.

Van Os, J., Linscott, R. J., Myin-Germeys, I., Delespaul, P., & Krabbendam, L. (2009). A systematic review and meta-analysis of the psychosis continuum: evidence for a psychosis proneness–persistence–impairment model of psychotic disorder. *Psychological Medicine*, *39*(2), 179-195.

van Rijn, S., Schothorst, P., van't Wout, M., Sprong, M., Ziermans, T., van Engeland, H., ... & Swaab, H. (2011). Affective dysfunctions in adolescents at risk for psychosis: emotion awareness and social functioning. *Psychiatry Research*, *187*(1), 100-105.

Velakoulis, D., Wood, S. J., Smith, D. J., Soulsby, B., Brewer, W., Leeton, L., ... & Pantelis, C. (2002). Increased duration of illness is associated with reduced volume in right medial temporal/anterior cingulate grey matter in patients with chronic schizophrenia. *Schizophrenia Research*, *57*(1), 43-49.

Velakoulis, D., Wood, S. J., Wong, M. T., McGorry, P. D., Yung, A., Phillips, L., ... & Pantelis, C. (2006). Hippocampal and amygdala volumes according to psychosis stage and diagnosis: A magnetic resonance imaging study of chronic schizophrenia, first-episode psychosis, and ultra–high-risk individuals. *Archives of General Psychiatry*, *63*(2), 139-149.

Velthorst, E., Nelson, B., O'Connor, K., Mossaheb, N., de Haan, L., Bruxner, A., ... & Thompson, A. (2013). History of trauma and the association with baseline symptoms in an ultra-high risk for psychosis cohort. *Psychiatry Research*, *210*(1), 75-81.

Velthorst, E., Nieman, D. H., Becker, H. E., van de Fliert, R., Dingemans, P. M., Klaassen, R., ... & Linszen, D. H. (2009). Baseline differences in clinical symptomatology between ultra high risk subjects with and without a transition to psychosis. *Schizophrenia Research*, *109*(1), 60-65.

Velthorst, E., Nieman, D. H., Klaassen, R. M. C., Becker, H. E., Dingemans, P. M., Linszen, D. H., & De Haan, L. (2011). Three-year course of clinical symptomatology in young people at ultra high risk for transition to psychosis. *Acta Psychiatrica Scandinavica*, *123*(1), 36-42.

Versmissen, D., Janssen, I., Johns, L., McGUIRE, P. H. I. L. I. P., Drukker, M., Campo, J. A., ... & Krabbendam, L. (2007). Verbal self-monitoring in psychosis: a non-replication. *Psychological Medicine*, *37*(04), 569-576.

Versmissen, D., Myin-Germeys, I., Janssen, I., Franck, N., Georgieff, N., Campo, J., ... & Krabbendam, L. (2007). Impairment of self-monitoring: part of the endophenotypic risk for psychosis. *The British Journal of Psychiatry*, *191*(51), s58-s62.

Walder, D. J., Holtzman, C. W., Addington, J., Cadenhead, K., Tsuang, M., Cornblatt, B., ... & Seidman, L. J. (2013). Sexual dimorphisms and prediction of conversion in the NAPLS psychosis prodrome. *Schizophrenia Research*, *144*(1), 43-50.

Walker, E. F., Brennan, P. A., Esterberg, M., Brasfield, J., Pearce, B., & Compton, M. T. (2010). Longitudinal changes in cortisol secretion and conversion to psychosis in at-risk youth. *Journal of Abnormal Psychology*, *119*(2), 401.

Weinberger, D. R., & Marenco, S. (2003). Schizophrenia as a neurodevelomental disorder. In S. R. Hirsch & D. R. Weinberger (Eds.), *Schizophrenia*. Oxford, UK: Blackwell Science Ltd.

Weinstein, D. D., Diforio, D., Schiffman, J., Walker, E., & Bonsall, R. (1999). Minor physical anomalies, dermatoglyphic asymmetries, and cortisol levels in adolescents with schizotypal personality disorder. *American Journal of Psychiatry, 156*(4), 617–623.

Wells, A. (1995). Meta-cognition and worry: A cognitive model of generalized anxiety disorder. *Behavioural and Cognitive Psychotherapy*, *23*(3), 301-320.

Wells, A., & Cartwright-Hatton, S. (2004). A short form of the metacognitions questionnaire: properties of the MCQ-30. *Behaviour Research and Therapy*, *42*(4), 385-396.

Welsh, P., & Tiffin, P. A. (2014). The "at-risk mental state" for psychosis in adolescents: clinical presentation, transition and remission. *Child Psychiatry & Human Development*, *45*(1), 90-98.

Wigman, J. T. W., Lin, A., Vollebergh, W. A. M., van Os, J., Raaijmakers, Q. A. W., Nelson, B., ... & Yung, A. R. (2011). Subclinical psychosis and depression: co-occurring phenomena that do not predict each other over time. *Schizophrenia Research*, *130*(1), 277-281.

Wigman, J. T., van Nierop, M., Vollebergh, W. A., Lieb, R., Beesdo-Baum, K., Wittchen, H. U., & van Os, J. (2012). Evidence that psychotic symptoms are prevalent in disorders of anxiety and depression, impacting on illness onset, risk, and severity—implications for diagnosis and ultra–high risk research. *Schizophrenia Bulletin, 38*(2)247-257.

Willhite, R. K., Niendam, T. A., Bearden, C. E., Zinberg, J., O'Brien, M. P., & Cannon, T. D. (2008). Gender differences in symptoms, functioning and social support in patients at ultra-high risk for developing a psychotic disorder. *Schizophrenia Research*, *104*(1), 237-245.

Wilson, J. M. G., & Jungner, G. (1968). Principles and practice of screening for disease. *World Health Organization. Public Health Paper, 34*(1) 1-163.

Wiltink, S., Velthorst, E., Nelson, B., McGorry, P. M., & Yung, A. R. (2015). Declining transition rates to psychosis: the contribution of potential changes in referral pathways to an ultra–high-risk service. *Early Intervention in Psychiatry*, *9*(3), 200-206.

Winton-Brown, T. T., Broome, M. R., Allen, P., Valli, I., Howes, O., Garety, P. A., ... & McGuire, P. (2015). Misattributing speech and jumping to conclusions: a longitudinal study in people at high risk of psychosis. *European Psychiatry*, *30*(1), 32-37.

Wolff, S., Townshend, R., McGuire, R. J., & Weeks, D. J. (1991). "Schizoid" personality in childhood and adult life. II: Adult adjustment and the continuity with schizotypal personality disorder. *The British Journal of Psychiatry*, *159*(5), 620-629.

Wölwer, W., Brinkmeyer, J., Stroth, S., Streit, M., Bechdolf, A., Ruhrmann, S., ... & Gaebel, W. (2012). Neurophysiological correlates of impaired facial affect recognition in individuals at risk for schizophrenia. *Schizophrenia Bulletin*, *38*(5), 1021-1029.

Woods, S. W., Addington, J., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A., Heinssen, R., ... & McGlashan, T. H. (2009). Validity of the prodromal risk syndrome for first psychosis: findings from the North American Prodrome Longitudinal Study. *Schizophrenia Bulletin*, *35*(5), 894-908.

Wood, S. J., Berger, G., Velakoulis, D., Phillips, L. J., McGorry, P. D., Yung, A. R., ... & Pantelis, C. (2003). Proton magnetic resonance spectroscopy in first episode psychosis and ultra high-risk individuals. *Schizophrenia Bulletin*, *29*(4), 831.

Woods, S. W., Tully, E. M., Walsh, B. C., Hawkins, K. A., Callahan, J. L., Cohen, S. J., ... & McGlashan, T. H. (2007). Aripiprazole in the treatment of the psychosis prodrome. *The British Journal of Psychiatry*, *191*(51), 96-101.

World Health Organization. (1994). *The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research*. Geneva, Switzerland: The World Health Organization.

Yıldırım, O., Dogan, O., Semiz, M., & Kilicli, F. (2011). Serum cortisol and dehydroepiandrosterone-sulfate levels in schizophrenic patients and their first-degree relatives. *Psychiatry and Clinical Neurosciences*, *65*(6), 584-591.

Yung, A. R., Cotter, J., Wood, S. J., McGorry, P., Thompson, A. D., Nelson, B., & Lin, A. (2015). Childhood maltreatment and transition to psychotic disorder independently predict long-term functioning in young people at ultra-high risk for psychosis. *Psychological Medicine*, *45*(16), 3453-3465.

Yung, A. R. (2003). Commentary: The schizophrenia prodrome: a high-risk concept. *Schizophrenia Bulletin, 29*(4) 859-865.

Yung, A. R., & McGorry, P. D. (1996). The initial prodrome in psychosis: descriptive and qualitative aspects. *Australian and New Zealand Journal of Psychiatry*, *30*(5), 587-599.

Yung, A. R., McGorry, P. D., McFarlane, C. A., Jackson, H. J., Patton, G. C., & Rakkar, A. (2004). Monitoring and care of young people at incipient risk of psychosis. *Focus, 2*(1) 158-174.

Yung, A. R., & Nelson, B. (2011). Young people at ultra high risk for psychosis: a research update. *Early Intervention in Psychiatry*, *5*(1)52-57.

Yung, A. R., Nelson, B., Baker, K., Buckby, J. A., Baksheev, G., & Cosgrave, E. M. (2009). Psychotic-like experiences in a community sample of adolescents: implications for the continuum model of psychosis and prediction of schizophrenia. *Australian and New Zealand Journal of Psychiatry*, *43*(2), 118-128.

Yung, A. R., Nelson, B., Thompson, A. D., & Wood, S. J. (2010). Should a "Risk Syndrome for Psychosis" be included in the DSMV? *Schizophrenia Research*, *120*(1), 7-15.

Yung, A. R., Phillips, L. J., Yuen, H. P., Francey, S. M., McFarlane, C. A., Hallgren, M., & McGorry, P. D. (2003). Psychosis prediction: 12-month follow up of a high-risk ("prodromal") group. *Schizophrenia Research*, *60*(1), 21-32.

Yung, A. R., Woods, S. W., Ruhrmann, S., Addington, J., Schultze-Lutter, F., Cornblatt, B. A., ... & Cannon, T. D. (2012). Whither the attenuated psychosis syndrome? *Schizophrenia Bulletin*, *38*(6), 1130-1134.

Yung, A. R., Yuen, H. P., Berger, G., Francey, S., Hung, T. C., Nelson, B., ... & McGorry, P. (2007). Declining transition rate in ultra high risk (prodromal) services: dilution or reduction of risk? *Schizophrenia Bulletin*, *33*(3), 673-681.

Ziermans, T. B., Schothorst, P. F., Sprong, M., & van Engeland, H. (2011). Transition and remission in adolescents at ultra-high risk for psychosis. *Schizophrenia Research*, *126*(1), 58-64.

Zimmermann, G., Favrod, J., Trieu, V. H., & Pomini, V. (2005). The effect of cognitive behavioral treatment on the positive symptoms of schizophrenia spectrum disorders: a meta-analysis. *Schizophrenia Research*, *77*(1), 1-9.

APPENDIX

COGNITIVE BEHAVIOURAL THERAPY MANUAL

AND

THERAPEUTIC MATERIALS AND WORKSHEETS

Challenging High Risk of psychosis

MANUALE DI TERAPIA COGNITIVO COMPORTAMENTALE E MATERIALI TERAPEUTICI

MODULO “INTRODUZIONE”

SEDUTE 1-4

INTRODUZIONE DEL PERCORSO
ASSESSMENT
DEFINIZIONE DEGLI OBIETTIVI TERAPEUTICI
INGAGGIO

SCHEDA. INTRODUZIONE DEL PERCORSO

- ✓ Discussione dei risultati alle interviste e scale di valutazione
- ✓ Descrizione dei problemi/sintomi emersi dalle scale
- ✓ Presentazione generale del percorso

SCHEDA: OBIETTIVI DEL PERCORSO PSICOTERAPEUTICO

Lista dei problemi attuali

1) .....
.....
.....
.....
2) .....
.....
.....
.....
3) .....
.....
.....
.....
4) .....
.....
.....
.....
5) .....
.....
.....
.....

Obiettivi a medio-breve termine

1) .....
.....
.....
2) .....
.....
.....
3) .....
.....
.....

Obiettivi a lungo termine

1) .....
.....
.....
2) .....
.....
.....

SCHEDA: PENSIERI, EMOZIONI, COMPORTAMENTI SONO COLLEGATI TRA LORO…

IL MODELLO ABC

Secondo il modello ABC e emozioni e i comportamenti delle persone sono influenzati dalla loro percezione ed interpretazione degli eventi. Non è la situazione di per sé a determinare ciò che le persone sentono, ma è piuttosto il modo in cui queste interpretano tale situazione (Beck, 1964; Ellis, 1962). Immagina, per esempio, una situazione nella quale un gruppo di studenti sta leggendo in classe lo stesso libro di narrativa. Ciascuno di loro ha risposte emotive a questa situazione piuttosto differenti, a seconda di quello che sta passando loro nella sua mente mentre legge.

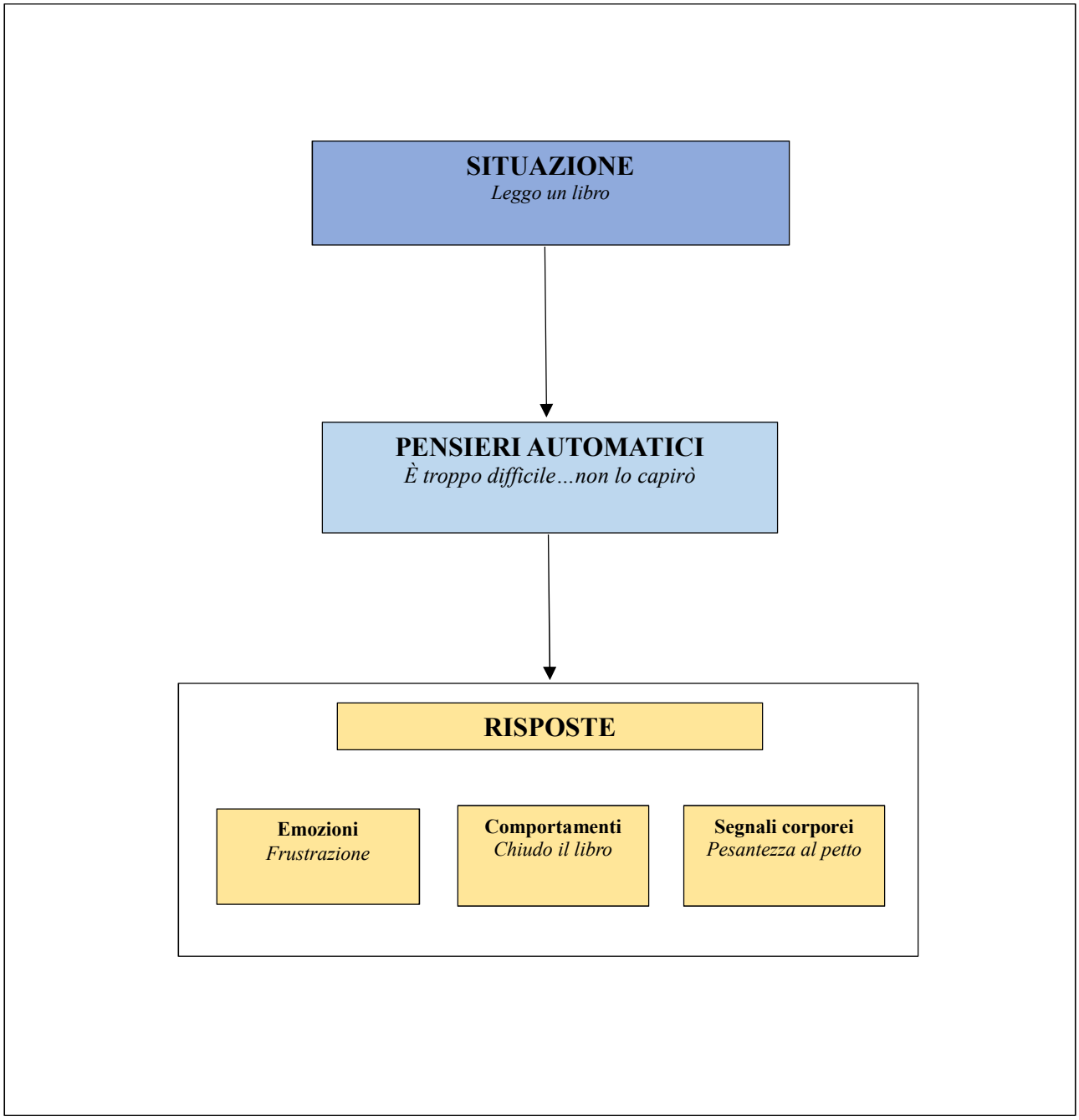
- *Maria pensa: "Quello che sto leggendo è davvero affascinante, questo racconto è avvincente", e si sente eccitata.*
- *Riccardo, invece, pensa: "Questa roba è inutile, una perdita di tempo, vorrei fare altro", e si sente scontento.*
- *Silvia ha i seguenti pensieri: "Questo libro non è quello che mi aspettavo. Che spreco di soldi", e si sente delusa, frustrata.*
- *Roberto pensa: "È troppo difficile…. e se all'interrogazione non ricordassi quello che ho letto?", e si sente ansioso.*

Così, il modo in cui le persone si sentono è associato al modo in cui interpretano e quello che passa per la loro mente in una situazione. La situazione in sé stessa non determina direttamente il modo in cui si sentono: il modo in cui ci sentiamo dipende dalla percezione della situazione.

MESSAGGI PUBBLICITARI CHE ARRIVANO ALLA NOSTRA MENTE….

I PENSIERI AUTOMATICI

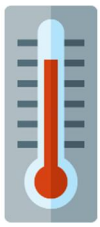
Mentre leggi questo testo potresti notare vari pensieri che ti passano per la mente. Ci sono diversi livelli di nel tuo pensiero. Parte della mente è focalizzata sulle informazioni contenute nel testo: ciò significa che stai cercando di capire e integrare alcune informazioni. Ad un altro livello, tuttavia, potresti avere alcuni pensieri veloci, di tipo valutativo. Questi ultimi sono chiamati pensieri automatici e non sono il risultato della riflessione o del ragionamento. Piuttosto, questi pensieri sembrano comparire improvvisamente e sono spesso piuttosto veloci e concisi. Potresti esserne appena consapevole, ma, più probabilmente, sei consapevole delle emozioni che ad essi seguono. Come risultato, con più probabilità accetti acriticamente come veri i tuoi pensieri automatici. Tuttavia, è possibile imparare ad identificare i propri pensieri automatici prestando attenzione ai cambiamenti dell'umore. Avendo identificato i tuoi pensieri automatici, puoi valutarne la validità, e probabilmente in qualche misura lo fai già. Se ti accorgi che la tua interpretazione è erronea e la correggi, probabilmente scoprirai che il tuo umore migliora. In termini cognitivi, quando i pensieri disfunzionali sono soggetti alla riflessione razionale, le emozioni generalmente cambiano.


SITUAZIONE
Leggo un libro
PENSIERI AUTOMATICI
È troppo difficile…non lo capirò
RISPOSTE
Emozioni
Frustrazione
Comportamenti
Chiudo il libro
Segnali corporei
Pesantezza al petto

SCHEDA DI AUTO-OSSERVAZIONE ABC: "PENSIERI, EMOZIONI E COMPORTAMENTI"

Data	**Situazioni stimolo** *(Dove ero, quando è successo, cosa facevo)*	**Pensieri automatici** *(Cosa mi passa per la mente?)*	**Emozioni** *(Intensità 0-100)*	**Segnali corporei**	**Comportamenti** *(Cosa faccio in risposta a pensieri e emozioni?)*

SCHEDA: TERMOMETRO DELL'INTENSITÀ DELLE EMOZIONI



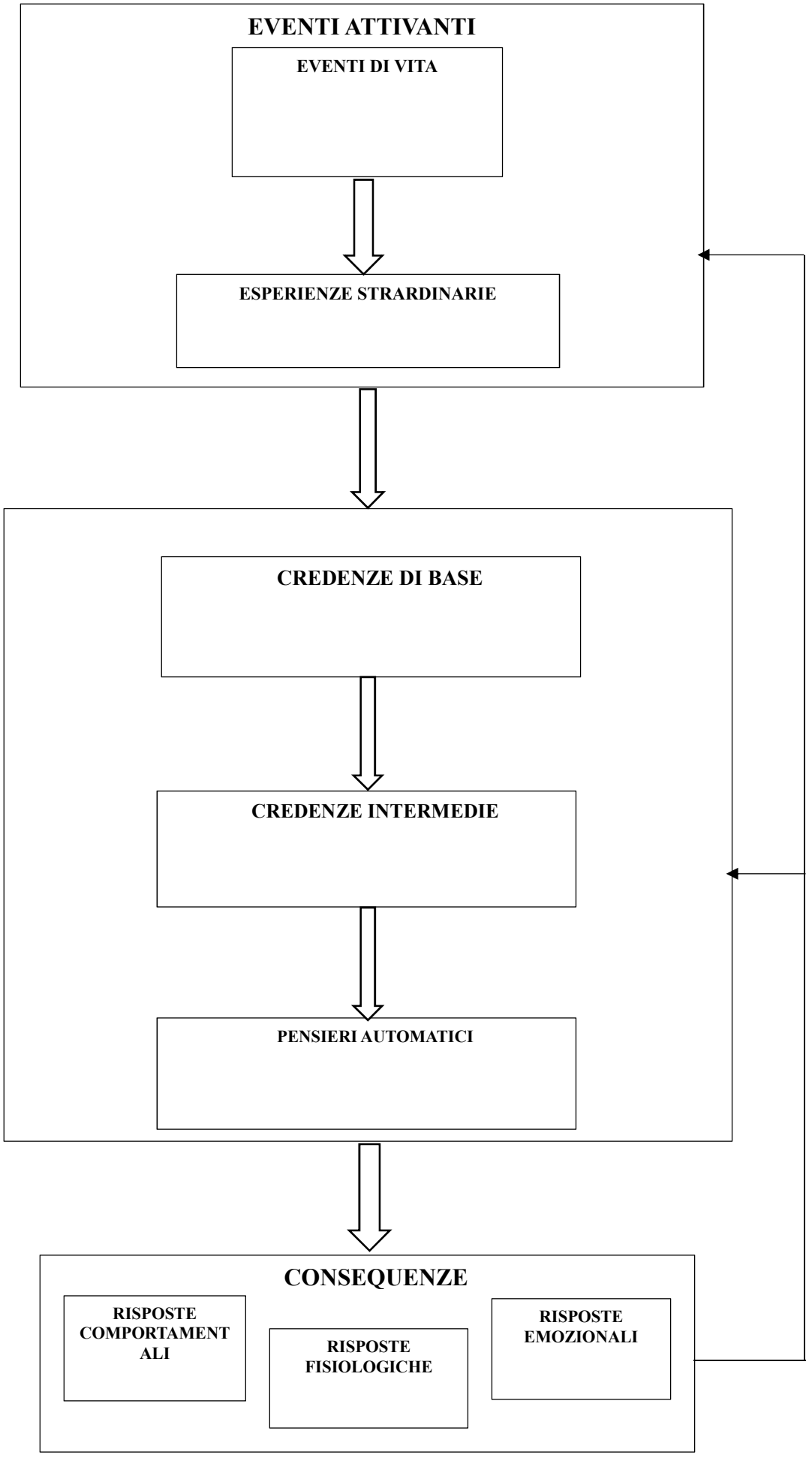
Le emozioni non sono un'esperienza tutto o nulla. Esiste una varietà di sfumature di intensità che noi sentiamo. Ciascuno di noi possiede un personale termometro delle emozioni che prova, ovvero la nostra percezione di quanto intense le avvertiamo nel nostro corpo, siano esse emozioni positive o negative.

ANSIA

/_____/_____/_____/_____/_____/_____/_____/_____/_____/_____/

0 10 20 30 40 50 60 70 80 90 100

Per niente ansioso | Un po' ansioso | Moderatamente ansioso | Molto ansioso | Estremamente ansioso


EVENTI ATTIVANTI
EVENTI DI VITA
ESPERIENZE STRARDINARIE
CREDENZE DI BASE
CREDENZE INTERMEDIE
PENSIERI AUTOMATICI
CONSEQUENZE
RISPOSTE COMPORTAMENTALI
RISPOSTE FISIOLOGICHE
RISPOSTE EMOZIONALI

SCHEDA: SINTESI DELLA SEDUTA E HOMEWORK PER LA SETTIMANA

DATA: _____

MESSAGGI CHIAVE DA PORTARE CON ME A CASA:

IMPEGNI ED ESERCIZI DA SVOLGERE DURANTE LA SETTIMANA:

SCHEDA: AVVIO DELLA SEDUTA

Introdurre la seduta terapeutica riprendendo la seduta precedente:

- ✓ *Ricordi i punti/gli argomenti che abbiamo affrontato la scorsa seduta?*
- ✓ *Hai delle domande?*
- ✓ *Hai dei dubbi che sono emersi durante la settimana e vorresti chiarire?*
- ✓ *Hai trovato qualcosa di spiacevole o poco chiaro tra i temi che abbiamo affrontato?*
- ✓ *Quali problemi/eventi/aspetti della tua quotidianità vorresti che affrontassimo oggi?*
- ✓ *Quali sono le cose per te essenziali/importanti che vorresti affrontare oggi?*
- ✓ *Cosa ti piacerebbe cambiare per prima?*

SCHEDA: CONCETTUALIZZAZIONE DEL PROBLEMA

Riassumi con parole tue lo schema di concettualizzazione del problema: .....

.....

.....

.....

.....

.....

.....

.....

.....

.....

.....

.....

.....

.....

.....

.....

.....

.....

.....

.....

.....

.....

.....

.....

MODULO "ESPERIENZE STRAORDINARIE"

SEDUTE 5-7

PSICOEDUCAZIONE E
NORMALIZZAZIONE
DELLE ESPERIENZE PSICOTICHE

Le esperienze straordinarie e l'ipersensibilità della dopamina

Periodi di stress prolungato possono favorire uno squilibrio di alcune sostanze normalmente presenti nel nostro cervello, i cosiddetti neurotrasmettitori. Nel caso della depressione lo squilibrio riguarda il livello di serotonina. Se invece ad alterarsi è il livello di dopamina, un'altra sostanza simile alla serotonina, questo può favorire le esperienze straordinarie, come sentire delle voci o avvertire la sensazione che qualcosa di importante stia per accadere oppure avere certi pensieri strani che invece sembrano appartenere a altre persone. Inoltre, alcuni dettagli specifici dell'ambiente che ci circonda possono diventare il fuoco su cui concentriamo tutta la nostra attenzione e darci la sensazione che abbiano un significato o un messaggio per noi molto importante. Tutto questo, accompagnato talvolta da sensazioni di eccitamento o di forte ansia, può darci la sensazione terrificante che qualcosa di molto brutto stia per accaderci.
La dopamina regola anche il nostro livello di motivazione, le nostre iniziative e la nostra capacità di iniziare le attività quotidiane. Un'alterazione dei suoi normali livelli di concentrazione può portarci anche a perdere i nostri abituali interessi per le attività piacevoli, per i nostri hobby, sport, relazioni sociali e per la sessualità.
Abitualmente, la dopamina viene rilasciata nel nostro cervello appena facciamo esperienza di una nuova situazione nel nostro campo di attenzione. Ad esempio, se per strada mi succede di incontrare l'auto della polizia che le sirene spiegate, le terminazioni nervose nel mio cervello potranno rilasciare dopamina nello spazio sinaptico tra una fibra nervosa e l'altra. Di conseguenza, la mia esperienza potrà essere più o meno la seguente:

- *Smetto di fare ciò che stavo facendo per un attimo*
- *Focalizzo la mia attenzione sulle sirene e sull'auto*
- *Provo a capire quello che sta accadendo*
- *Mi preparo a scappare (nel caso in cui io abbia la "coscienza sporca" oppure dopo poco riprendo a fare ciò che stavo facendo*

Non appena hai capito quello che puoi fare in questa situazione, i livelli di dopamina tenderanno a calare e conseguentemente tornerai a fare le tue cose.
Gli studiosi del comportamento umano ritengono che nelle persone che hanno esperienze straordinarie, la dopamina sia rilasciata nel cervello senza un vero e proprio motivo. Dato che il rilascio di questa sostanza avviene di solito quando facciamo esperienza di eventi nuovi e che per noi sono importanti, queste persone possono avere reazioni simili anche in situazioni più neutre o casuali. Se per esempio stai guardando il telegiornale, ed il tuo cervello improvvisamente inizia a rilasciare dopamina, potrai avere la sensazione che quello che stai dicendo il cronista abbia un significato di vitale importanza per te, sia un messaggio personalmente diretto a te. Dal momento che la sensazione in quel preciso momento è estremamente forte e reale, la maggior parte delle persone che fanno questa esperienza non avrà dei dubbi sul fatto che sia solo un'interpretazione. Ad esempio, se il cronista parla del fatto che ci sono stati dei brogli elettorali alle ultime elezioni, potrai pensare che ti stia dando avvertendo del fatto che c'è qualcuno che ti sta ingannando.

Il rilascio di dopamina può portarci ad interpretazioni distorte degli eventi…

Situazioni inaspettate possono capitare e potrai avere la sensazione che qualcosa o qualcuno abbia preso il controllo dei tuoi pensieri e delle tue emozioni.

Cosa favorisce l'ipersensibilità della dopamina

Una specifica popolazione di persone può avere una vulnerabilità in parte ereditaria sulla disfunzione del sistema che regola nel cervello la dopamina. In questo gruppo di persone, durante periodi di stress prolungati le persone possono non riuscire ad abituarsi. Questo significa che i problemi quotidiani possono diventare fonte di forte disagio.

La dopamina è anche responsabile del nostro livello di motivazione nelle attività, come si è detto. Questo significa che è possibile che tu abbia delle difficoltà negli impegni scolastici o a lavoro.

La maggior parte delle persone che hanno esperienze straordinarie semplicemente ne fanno esperienza di volta in volta che esse si presentano – così queste esperienze spesso vanno e vengono oppure "rimangono sullo sfondo", non prendono grande importanza per la persona, quindi non hanno grande influenza sul loro comportamento nella vita quotidiana.

Tuttavia, un sottogruppo di persone, una proporzione molto piccola, può sviluppare una particolare ipersensibilità della dopamina che viene chiamata psicosi. Alcune di queste persone possono avvertire uno stato di forte malessere a causa delle esperienze straordinarie e quindi passare da una normale sospettosità a pensieri di tipo paranoico che via via vengono confermati da piccoli eventi quotidiani.

La cannabis influenza il sistema della dopamina ed aumenta la probabilità che si sviluppi l'ipersensibilità della dopamina. Questo può accadere anche con altre droghe come la cocaina, le amfetamine. Allo stesso modo, fare esperienza di un trauma come un abuso fisico o sessuale oppure l'esperienza di essere bullizzato o discriminato possono aumentare la probabilità di ipersensibilità della dopamina.

Le esperienze straordinarie sono normali

Ti sarà qualche volta accaduto di sentirti chiamare mentre sei solo nella tua stanza e questo ti può preoccupare. Esperienze strane, insolite, inspiegabili sono relativamente frequenti nella popolazione generale e il più delle volte innocue. Da varie ricerche che gli studiosi hanno fatto su grandi campioni di persone sappiamo oggi che circa metà della popolazione generale tende a credere in un certo modo alla telepatia e che molti effettivamente ne hanno fatto esperienza. Ad esempio, quando ti capita di pensare a qualcosa, può succedere in quel momento che squilli il telefono e per l'appunto è proprio la persona a cui stavi pensando. Oppure pensi al nome di qualcuno e proprio in quel momento lo senti pronunciare alla radio. Queste esperienze ci accadono certe volte durante la settimana e questo non che sembrare altro che una mera coincidenza.

La maggior parte della gente tende ad essere sospettosa verso gli altri e questo non è necessariamente una cosa negativa…le persone che sono troppo inclini alla fiducia incondizionata possono subire prevaricazioni…

Una sana sospettosità ci protegge dai pericoli quotidiani

Nei gruppi è molto comune che ci sia qualcuno che ha il ruolo della cosiddetta "pecora nera" – esperienze di bullismo e prevaricazione sono purtroppo comuni a scuola o sul lavoro.

Sentire, vedere, avvertire suoni, cose, odori che gli altri non notano, e senza che vi sia una fonte ben precisa nell'ambiente circostante, sono sensazioni che vengono chiamata "esperienze straordinarie" – allucinazione e talvolta, visioni.

Circa una persona su sei nel corso della propria vita può attraversare un periodo in cui tende a avvertire voci o suoni che non sono presenti in quel momento attorno

Da diverse ricerche sappiamo che circa il due per cento del nostro Paese nelle ultime due settimane ha avvertito voci o suoni non presenti nell'ambiente. È un'esperienza molto comune, sono sensazioni familiari a molti di noi e che spesso tendono a scomparire spontaneamente con il passare dei giorni.

Tuttavia, un piccolo gruppo di persone può iniziare ad attribuire estrema importanza a questi fenomeni che avverte, sentirsi preoccupato da queste percezioni – queste esperienze possono iniziare a interferire con il funzionamento quotidiano. Qualcuno può iniziare a sviluppare sospettosità sempre più forte da chiudersi in casa gran parte del giorno. Altri possono iniziare a portare l'attenzione continuamente sulle voci che sentono ed iniziare a credere che abbia dei poteri soprannaturali o provengano da creature molto potenti, quindi sentirsi intimoriti da queste esperienze e talvolta obbedire ciò che chiedono loro di fare. Altri possono iniziare a ritirarsi dalla vita sociale quotidiana, ogni piccola cosa costa un enorme fatica, troppa energie e provocare sensazioni molto negative di ansia. Altri ancora possono iniziare a trascorrere molto tempo a riflette sulle proprie esperienze straordinarie, immergersi in un vero e proprio rimuginio mentale e preoccuparsene.

Diverse ricerche hanno mostrato come la possibilità che normali esperienze straordinarie diventino fonte di forte disagio e si sviluppino in un vero e proprio disturbo psicologico dipende, almeno in parte, dal modo in cui inizialmente interpretiamo e ci spieghiamo queste stesse esperienze.

Vari tipi di esperienze straordinarie

Esperienze alienanti
✓ *L'ambiente circostante mi appare strano, come se fosse nuovo o non familiare*
✓ *Il tempo sembra passare più velocemente, in altri momenti poi più lentamente*
✓ *Ti sembra di perdere il contatto con te stesso, come se non fossi nella realtà*
Esperienze legate al sentirsi influenzati
✓ *Emozioni e pensieri non sembrano sotto il controllo della tua volontà*
✓ *Emozioni e pensieri sembrano come se fossero inseriti dall'esterno o sottratti alla mia mente*
✓ *Il pensiero che ti vengano inviati dei messaggi speciali con un significato personale diretto a te, inviato da altre persone tramite radio, internet, TV, giornali*
Esperienze di danno personale
✓ *La sensazione che gli altri si riferiscano a te*
✓ *La sensazione che gli altri stiano cospirando contro di te*
Esperienze percettive che solo te avverti
✓ *L'esperienza di suoni, voci, bisbigli, dentro o fuori la tua testa*
✓ *L'esperienza di sentire i tuoi pensieri pronunciati da altri*
✓ *Visioni strane*
✓ *Sensazioni corporee insolite, inspiegabili, senza un motivo ben definito*
Sensazioni di confusione e difficoltà di concentrazione
✓ *Avvertire la difficoltà a organizzare i pensieri e scegliere le parole giuste*
✓ *Sentire che gli altri fanno spesso fatica a comprender quello che vogliamo dire*
Cambiamenti nelle esperienze a contatto con le persone
✓ *Avvertire spesso poco interesse o piacere a stare in compagnia degli altri*
✓ *Avvertire un senso di nervosismo a stare a contatto con le persone, in luoghi affollati*
✓ *Gli altri tendono spesso a dirti che hai delle abitudini, dei modi di fare strani o che non esprimi abbastanza le tue emozioni*
✓ *Gli impegni, i cambiamenti stressanti della vita quotidiana diventano spesso difficili, pesanti da sostenere*

Esperienze dispercettive straordinarie: le voci

Le voci sono produzioni linguistiche che provengono da aree della nostra mente di cui siamo in genere poco consapevoli. Dato che esse si presentano con le caratteristiche vocali della voce di qualcun altro e dato che il messaggio che portano è un tema ricorrente, l'impressione che possono dare è che siano create da qualcun altro diverso da noi stessi. Talvolta le voci possono suggerirci di sapere delle cose che noi non conosciamo, tuttavia, se proviamo a metterle alla prova scopriremo in realtà che non è mai così… .ad esempio, prova chiedere alle voci se conoscono i titoli del giornale di domani senza che tu li sappia. Non sapranno risponderti. In realtà, le voci sanno solo quello che tu già sai.
Quando noi facciamo una scansione del cervello con i macchinari computerizzati di cui oggi disponiamo, quello che possiamo vedere è che si attivano le stesse identiche aree che si attivano quando pensiamo e parliamo.

I discorsi che sentiamo nell'ambiente esterno arrivano all'orecchio da cui si dirigono all'area di Wernicke, l'area della comprensione del linguaggio, che si trova proprio dietro l'orecchio. Se percepiamo i nostri pensieri come un nostro dialogo interno, questi dall'area della corteccia prefrontale dall'area di produzione del linguaggio (area di Broca) successivamente si dirigono all'area di Wernicke.
La corteccia cingolata anteriore ha il compito di avvertirci se il discorso che stiamo avvertendo in quel momento è un dialogo interno nostro oppure un suono proveniente dall'esterno. Quindi la corteccia cingolata anteriore ha il compito di monitor in grado di etichettare i pensieri come prodotti nostri oppure come rumori esterni. Durante le esperienze dispercettive, questa corteccia tende a essere meno attiva, quindi questo può far sì che pensieri che provengono dalla nostra mente vengano da noi erroneamente etichettati come rumori esterni, appunto le voci.

Quando udiamo le voci, qualsiasi cosa esse stiano dicendo in quel momento, noi non siamo responsabili del loro contenuto

Quello che le voci dicono in quel momento non fa parte della nostra personalità. Quello che le crea quindi è solo un meccanismo temporaneamente bloccato nella nostra mente.

Esperienze straordinarie percettive…come funzionano

Il nostro cervello è una macchina molto complessa. Negli ultimi anni abbiamo imparato molto sul suo funzionamento, ma rimangono ancora diverse cose da conoscere meglio. Alcune teorie che spiegano il modo in cui si sviluppano le dispercezioni e diventano poi allucinazioni assumono che alcune nostre informazioni personali, come pensieri, ricordi, immagini mentali - provenienti dalla nostra memoria o dalle parti di noi di cui siamo meno consapevoli - vengono da noi etichettate sul momento come informazioni provenienti dall'esterno, appunto voci o rumori presenti nell'ambiente ma che in realtà sono da attribuire alla nostra mente.

Quando ci troviamo in certe particolari condizioni, tutti noi tendiamo a avere allucinazioni

- ✓ *Quando siamo stanchi*
- ✓ *Quando assumiamo certe sostanze*
- ✓ *Quando stiamo a lungo deprivati da un punto di vista sensoriale*
- ✓ *Mentre stiamo per addormentarci o subito dopo il risveglio*

In mancanza di input sensoriali il nostro cervello può crearne di propri per tenersi stimolato. Ad esempio, si è visto che alcuni detenuti in carcere per anni spesso tendono a riferire esperienze sensoriali come le voci. Analogamente, gli scalatori delle montagne che trascorrono lunghi periodi in isolamento e in deprivazione di ossigeno possono sviluppare queste esperienze.
Tecniche moderne di visualizzazione del cervello in funzione hanno mostrato come le voci sono prodotte dal cervello stesso. Si è notato un aumento del livello di attività nelle aree cerebrali deputate alla produzione del linguaggio quando la persona avverte in quel momento le allucinazioni verbali. Allo stesso modo, si è visto che la tensione delle corde vocali tende ad aumentare quando la persona avverte le voci, in modo simile a quando pensiamo ad alta voce.

Le allucinazioni sono quindi innocui, normali fenomeni interni prodotti dal nostro cervello che vengono percepiti come provenienti dall'esterno

SCHEDA. QUANDO MI SENTO FUORI DI ME… LA DEPERSONALIZZAZIONE

È la sensazione di perdere il contatto con noi stessi. Spesso si presenta associata alla derealizzazione – la sensazione che il mondo che mi circonda non sia reale. È come sentirmi in un sogno e guardare la realtà da dietro un vetro.

Questo tipo di esperienze è di per sé innocuo e comune tra le persone – circa il 50% della popolazione generale ne ha sperimentate in qualche momento nel corso della sua vita.

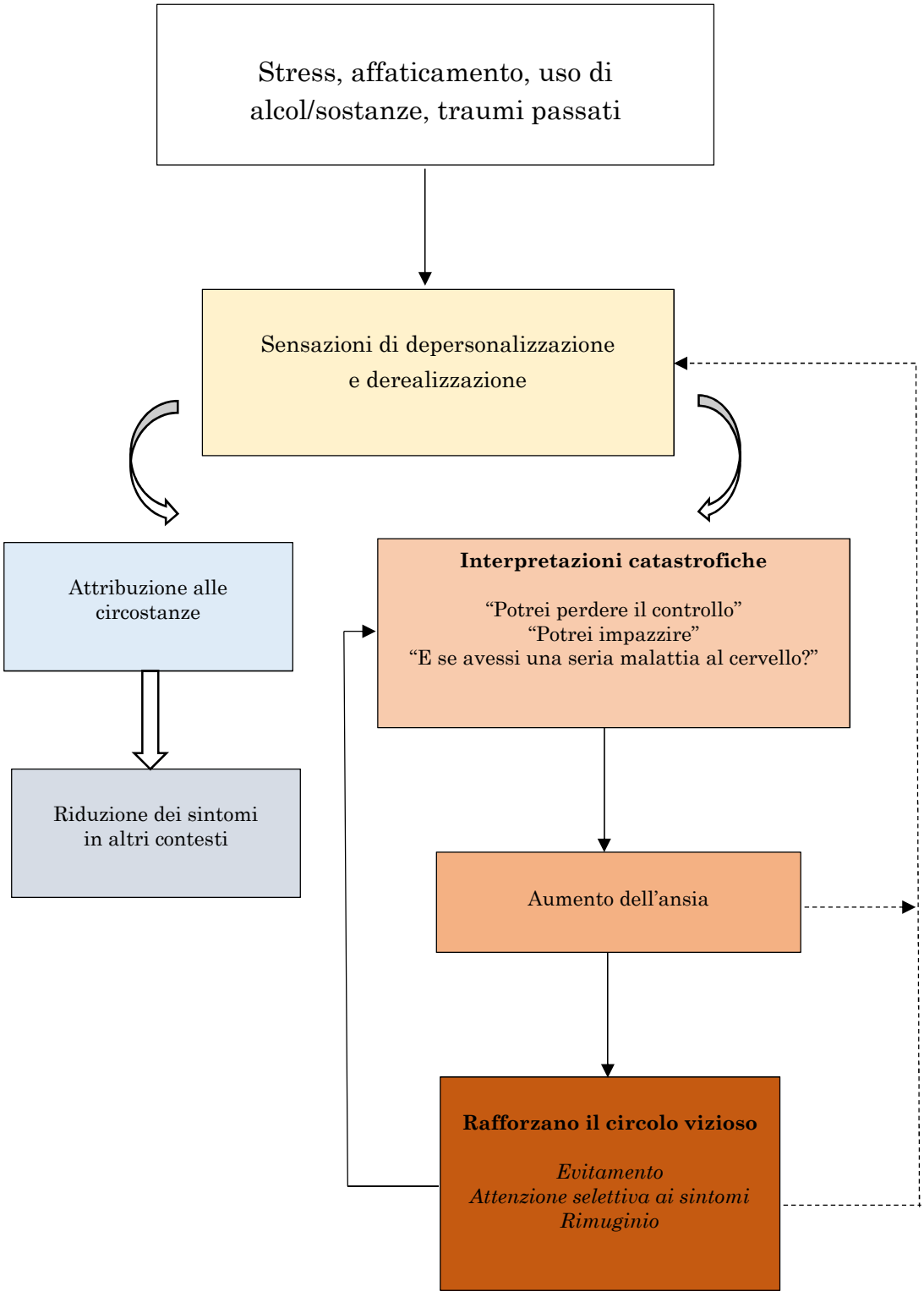
Spesso tende a presentarsi in persone che sono state traumatizzate nel corso dell'infanzia o che hanno un disturbo di ansia o depressivo. Anche stati prolungati di stress, abuso di alcol o droghe possono ricreare questa esperienza.

Se attribuiamo queste esperienze alle circostanze e le tolleriamo come una sensazione passeggera, in genere il problema tende a scomparire in modo naturale e avere un effetto limitato sulla nostra vita.

Se però interpretiamo queste sensazioni in modo catastrofico, può essere più problematico – ad esempio come segno di stare per perdere il controllo, di poter impazzire, di poter avere una malattia neurologica o mentale, di poter divenire invisibili. In casi come questi la nostra reazione può essere di ansia, di paura.

Può sembrare strano ma le ricerche hanno mostrato che in realtà durante la depersonalizzazione non c'è un aumento dell'attività del sistema nervoso autonomo – ovvero quel sistema che regola la frequenza cardiaca, la pressione arteriosa, la sudorazione, la respirazione, l'afflusso di sangue ai tessuti. Al contrario, avviene una diminuzione dell'attività autonoma e questo è responsabile della sensazione di non essere coinvolti nelle ose che ci circondano.

Evitando certe situazioni che possono ricreare la depersonalizzazione (le lezioni a scuola, il lavoro, le uscite con gli amici, i viaggi in treno/bus) manteniamo il nostro stato di preoccupazione che possa riverificarsi questa sensazione. A lungo termine, l'ansia tende a aumentare. Allo stesso tempo la trappola dell'attenzione selettiva ci porta a monitorare continuamente il più piccolo segnale di depersonalizzazione durante il giorno ma portare l'attenzione su noi stesso così intensamente aumenta l'ansia di fronte a ogni cambiamento, ansia che a volte diventa panico e quindi paradossalmente fa scattare un nuovo episodio di depersonalizzazione.


Stress, affaticamento, uso di alcol/sostanze, traumi passati
Sensazioni di depersonalizzazione e derealizzazione
Attribuzione alle circostanze
Riduzione dei sintomi in altri contesti
Interpretazioni catastrofiche
"Potrei perdere il controllo"
"Potrei impazzire"
"E se avessi una seria malattia al cervello?"
Aumento dell'ansia
Rafforzano il circolo vizioso
Evitamento
Attenzione selettiva ai sintomi
Rimuginio

FLASHCARD. ACCOGLI LA DEPERSONALIZZAZIONE

- ✓ *Quando noti le sensazioni di depersonalizzazione o derealizzazione, è importante che tu rimanga calmo fino a quando non calano da sole*
- ✓ *Sono esperienza comuni a molti di noi, innocue, possono essere un modo con cui la nostra mente ci avverte che siamo stressati, stanchi*
- ✓ *Interpretarle in modo catastrofico – segnali di una malattia al cervello – può solo aumentare la tua apprensione e così facendo amplifica la depersonalizzazione stessa*
- ✓ *Focalizzare la tua attenzione sul tuo corpo aumenta l'ansia che la depersonalizzazione possa peggiorare*
- ✓ *Porta la tua attenzione su quello che avverti con i 5 sensi nell'ambiente che ti circonda, tocca qualcosa e nota le sensazioni tattili, ascolta qualcosa e nota i suoni…*

AFFRONTARE LE ESPERIENZE STRAORDINARIE

Non è l'esperienza straordinaria di per sé...
è la nostra interpretazione

L'interpretazione che noi tendiamo a dare alle nostre esperienze straordinarie è di grande importanza e può determinare il fatto che noi riusciamo a conviverci oppure iniziamo a soffrirne in modo intenso. Un'esperienza straordinaria può diventare nociva per noi il nostro tempo inizia a essere troppo occupato da essa e ci impedisce dal partecipare alle attività per noi significative e dallo stare in contatto con gli altri. La maggior parte delle esperienze straordinarie sono innocue, normali per molti di noi. È importante non prestare più di tanto ascolto ed attenzione. È molto utile imparare a prendere in considerazione spiegazioni alternative alle interpretazioni che ci verrebbero immediatamente di un fatto

Francesco
Occasionalmente sente il proprio nome pronunciato mentre è per strada, anche se nota che nessuno lo avverte. A volte sente che i propri pensieri sono ripetuti da una voce – altre volte una voce nella sua testa gli sussurra cosa deve fare: "non fidarti dei vicini".
Una persona su 50 può sentire una voce mentre nessuno in realtà sta parlando. Il modo migliore più efficace per affrontare questa esperienza è non prendere questa voce sul serio e cercare di continuare a fare ciò che stiamo facendo. A volte la mente gioca degli scherzi, soprattutto prima di andare a letto.
In alternativa, Francesco potrebbe iniziare a interpretare la voce come un suono che proviene da qualcuno molto potente, come i servizi segreti, una setta satanica, il diavolo o altro. Se Francesco interpreta quella voce in questo modo, allora è più probabile che poi si senta ansioso, spaventato o anche sopraffatto ed umiliato, senta che non c'è via di fuga da questa voce. Di conseguenza, inizia a dormire male la notte, a rimuginare spesso durante la giornata, evita le uscite, progressivamente si ritira in casa – può cercare di tenere la voce segreta, cercare di resistere alle sue pressioni o anche accondiscendere.

MODULO "CREDENZE DISFUNZIONALI"

SEDUTE 8-15

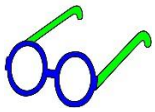
RISTRUTTURAZIONE COGNITIVA
INTERVENTO METACOGNITIVO
ESPERIMENTI COMPORTAMENTALI

SCHEDA DIARIO ABC DELLE ESPERIENZE STRAORDINARIE

Esperienza straordinaria	*Interpretazione*	*Risposta emotiva*

QUANDO LA SOLUZIONE È IL PROBLEMA: LA TRAPPOLA DELL'EVITAMENTO

Il meccanismo che può favorire la sospettosità è proprio l'evitamento. Chiunque abbia vissuto un incidente in auto, è molto probabile che sperimenti disagio e tensione appena riprende a guidare. Chi si propone di riprendere l'auto nonostante questo, riesce più facilmente a superare questa paura. Chi invece decide di smettere di guidare appena avverte la paura impara a evitare le auto e i loro rischi però con il risultato che ogni volta prova a salirvi sentirà il cuore che batte forte e gli altri segnali della tensione. È come quando si sviluppa la paura per i cani dopo che si è stati morsi. L'evitamento crea un circolo vizioso che mantiene la paura. Nello stesso modo funziona anche la sospettosità. La paranoia aumenta dopo l'evitamento ripetuto di una data situazione. Il modo migliore per ridurre la sospettosità e l'ansia che crea è esporsi alle situazioni, affrontarle per permetterci di metter in discussione in pensieri automatici e le interpretazioni che abbiamo.



SCHEDA: LE DISTORSIONI COGNITIVE

Tutti noi tendiamo a fare continui errori di pensiero. Quando abbiamo un pensiero automatico, possiamo provare ad identificare mentalmente, verbalmente o per iscritto il tipo di errore che stiamo facendo. Gli errori di pensiero più comuni sono riportati di seguito.

PENSIERO "TUTTO O NULLA" (chiamato anche pensiero in bianco/nero o dicotomico)
Vediamo una situazione in soli due modi contrapposti, in due categorie, invece che in un continuum. Gli eventi vengono visti come tutti bianchi o tutti neri, buoni o cattivi. Si ha un'insistenza su scelte e valutazioni estreme. Ci possiamo sentire perfetti o completamente imperfetti. Non esiste una via di mezzo. Quando usiamo il pensiero "tutto o nulla" seguiamo binari prestabiliti e rigidi. Siamo nella logica del "o...o".
Esempi:
a. "O fai quello che dico, o non ci vedremo mai più"
b. "Se non mi realizzo nel lavoro, la mia vita sarà un completo fallimento"
c. "Siete con me o contro di me?"
d. ……

PENSIERO CATASTROFICO (chiamato anche predizione del futuro)
Prediciamo il futuro in maniera negativa senza considerare altri possibili esiti o sviluppi. Ci si aspetta in continuazione che avvenga un disastro. Siamo sempre all'erta perché ci aspettiamo che arrivi da un momento all'altro la temuta tragedia. "Che ne sarà di noi?". Pensando in questo modo al futuro, si creano intense reazioni di ansia.
Esempi:
a. "Ho un neo, si trasformerà sicuramente in un tumore..."
b. "Se all'ora di pranzo non è tornata a casa è perché sicuramente ha avuto un incidente"
c. "Sarò così agitato che non sarò in grado di agire adeguatamente"
d.……

LETTURA DEL PENSIERO
Crediamo di sapere quello che gli altri pensano e provano, o il motivo per cui agiscono in un certo modo evitando di considerare, più probabili, possibilità. In particolare diventiamo abili a prevedere quello che una persona pensa di noi (effetto "palla di vetro").
Esempi:
a. "Anche se lei mi sorride, io so che non le piaccio"
b. "Non mi ha salutato perché non mi ritiene un suo amico"

FILTRO MENTALE (chiamato anche astrazione selettiva)
Prestiamo un'attenzione ingiustificata ad un unico dettaglio negativo invece di considerare e valutare appropriatamente tutto l'insieme.
Esempi:
a. “Ho un solo voto basso nella mia valutazione (in cui ci sono però numerosi voti alti), divento triste perché penso di aver fatto un pessimo lavoro”
b. “Tutti mi hanno fatto i complimenti per le scarpe nuove, ma a Marta non sono piaciute. Quel solo giudizio negativo cancella tutti gli altri, rendendomi insoddisfatta”
c.……

PERSONALIZZAZIONE
Crediamo che gli altri si comportino negativamente a causa nostra, senza prendere in considerazione spiegazioni più plausibili per il loro comportamento.
Esempi:
a. “Il tecnico riparatore è stato sgarbato con me perché ho fatto qualcosa di sbagliato”
b. “Papà beve perché sono cattivo”
c. “Mi tratta male perché non valgo nulla”
d.……

IPERGENERALIZZAZIONE
Tendiamo ad arrivare a conclusioni di carattere generale in maniera affrettata, allontanandoci dalla situazione concreta e attuale.
Esempi:
a. “Siccome non mi sono sentito a mio agio al party penso: Non ho ciò che ci vuole per fare amicizia”
b. “Mi tratta sempre male”
c. “Non mi ascolta mai”
d.……

RAGIONAMENTO EMOTIVO
Pensiamo che qualcosa sia vera solo per il fatto che "sentiamo" (in realtà crediamo) fortemente che è così, ignorando, svalutando o minimizzando tutto ciò che prova il contrario.
Esempi:
a. “Mi sento stupido e insignificante”. Il fatto di sentire "qualcosa" non significa affatto che sia vero.
b. “Lo sentivo che alla fine mi avrebbe abbandonato”
c. “So di far bene molte cose al lavoro ma mi 'sento' lo stesso un fallimento”
d.……

VISIONE TUNNEL

Vediamo solo gli aspetti negativi di una situazione. Ad esempio, le persone con visione tunnel vedono soltanto ciò che collima con il loro atteggiamento o stato mentale. Altri aspetti importanti sono cancellati, censurati o minimizzati.

Esempio:

a. "Non abbiamo fatto altro che litigare per tutto il viaggio" (in realtà quando valutiamo obiettivamente il tempo del litigio ci rendiamo conto che era durato non più di 5 minuti).

b. "Nessuno mi ha mai amato"

c.……

AFFERMAZIONI "DOVREI" E "DEVO" (chiamate anche Doverizzazioni)

Abbiamo un'idea fissa, precisa, rigida di come noi o gli altri dovremmo comportarci e diamo una valutazione eccessivamente negativa alle possibilità che queste aspettative non vengano soddisfatte. L'errore sta nel considerare un'esigenza assoluta ciò che nella maggior parte dei casi sarebbe obiettivamente solo preferibile. Chi infrange tali regole provoca in noi una collera intollerabile; se siamo noi stessi a farlo, ci colpevolizziamo.

Esempi:

a. "È terribile che io abbia fatto un errore. Devo sempre essere irreprensibile"

b. "Non devi mai fare domande personali alla gente"

c.……

ETICHETTAMENTO

Tendiamo ad attribuire a noi stessi e agli altri etichette globali, rigide senza considerare che l'evidenza potrebbe condurre più ragionevolmente a conclusioni meno drastiche o disastrose. Diamo, infatti, giudizi definitivi ad un evento o a una persona basandoci su una o poche caratteristiche che li riguardano.

Esempi:

a. "Paola è stata una perdente dal primo giorno che l'ho conosciuta"

b. "Io sono un buono a nulla"

c.……

SQUALIFICARE O SVALUTARE IL POSITIVO

Irragionevolmente ci diciamo che le nostre esperienze, azioni o qualità positive non contano, non hanno valore o, nello stesso modo rifiutiamo o svalutiamo il nostro fisico o parti di esso, non attribuendogli alcun valore.

Esempi:

a. "Ho realizzato bene quel progetto, ma questo non vuol dire che sono competente; ho semplicemente fortuna"

b. "Ho eseguito bene questo compito, ma tutti ne sarebbero capaci"

c. "Tutti mi dicono che ho dei begli occhi ma per me non è così"

d.……

ESAGERAZIONE / MINIMIZZAZIONE

Quando valutiamo noi stessi, un'altra persona o una situazione, esageriamo irragionevolmente il negativo e/o minimizziamo il positivo.

Esempi:

a. "Se ottengo una valutazione mediocre, questo prova quanto io sia inadeguato"

b. "Se ottengo un voto alto, non significa che sono brillante"

c.……

SCHEDA: LA TRAPPOLA DELL'ATTENZIONE SELETTIVA

Se provi a prestare tutta la attenzione a una situazione, a un dettaglio dell'ambiente che apparentemente non porta con sé pericolo o aspetti negativi, è molto probabile che poi tenderai a notare pericoli, minacce o aspetti negativi in molte altre situazioni.
Facciamo un esercizio che può aiutarci a capire come funziona la trappola dell'attenzione selettiva.

La prossima settimana dovrai prestare tutta la tua attenzione possibile a un elemento specifico ogni giorno:

1. Il primo giorno devi appuntarti quante macchine blu hai visto, le scriverai nella nostra scheda di appunti. Ogni ora della giornata devi segnare quante macchine blu vedi, mentre sei a casa, mentre fuori per strada, mentre sei in bus o in treno, mentre sei a scuola, a lavoro o all'università. Poi devi sommare quante macchine blu hai visto quel giorno; oltre a questo devi annotare le sensazioni che provavi in quel momento mentre facevi l'esercizio.
2. Il secondo giorno devi annotare tutti i rumori, i suoni che puoi percepire mentre sei in una stanza e che provengono da fuori quella stanza, quando sei in camera tua, in altre camere di casa, in aula a scuola, in stanza a lavoro etc. devi poi somare i rumori che hai notato e appuntare anche le tue sensazioni mentre facevi l'esercizio.
3. Il terzo giorno appunta tutte le persone che vedi che portano gli occhiali, poi sommale e annota anche le tue sensazioni durante l'esercizio.
4. Il quarto giorno è di riposo. Dopo cena, prediti del tempo per annotare le sensazioni che hai avuto oggi e confrontale con quelle dei tre giorni precedenti.
5. Il quinto giorno presta la tua attenzione e segna tutte le persone che durante la giornata ti creano sensazioni spiacevoli (ansia, rabbia, tristezza etc). Potranno essere persone che hai avuto la sensazione ti abbiano guardato in un modo strano, che si vestono in un modo completamente diverso da te, che sono più alti di te, che sembrano criminali, che sembrano atteggiarsi con supponenza etc. metti insieme tutte queste situazioni annotate e riporta le sensazioni che hai provato durante l'esercizio.

SCHEDA: L'ESERCIZIO DELL'ATTENZIONE SELETTIVA

Tempo	Giorno 1 *Macchine blu*	Giorno 2 *Rumori/suoni fuori la stanza*	Giorno 3 *Persone con occhiali*	Giorno 4 *Riposo*	Giorno 5 *Persone spiacevoli*
8.00					
9.00					
10.00					
11.00					
12.00					
13.00					
14.00					
15.00					
16.00					
17.00					
18.00					
19.00					
20.00					
21.00					
22.00					

Giorno 1	*Sensazioni provate e considerazioni:*
Giorno 2	*Sensazioni provate e considerazioni:*
Giorno 3	*Sensazioni provate e considerazioni:*
Giorno 4	*Sensazioni provate e considerazioni:*
Giorno 5	*Sensazioni provate e considerazioni:*

SCHEDA

LE VOCI - NOSTRI PENSIERI AUTOMATICI CHE ATTRIBUIAMO AD ALTRI

La distorsione "Attribuzione di pensieri a altri"

È un tipo di distorsione che più frequentemente accade a chi ha una tendenza a sperimentare voci. È molto importante essere consapevoli se stiamo seguendo questa distorsione.

Il nostro cervello è in grado di etichettare il contenuto della memoria in modo tale da aiutarci a capire se un certo evento è avvenuto dentro di noi (es un pensiero) oppure fuori (un rumore esterno). Talvolta per alcuni è possibile che questo processo non funzioni correttamente in dei momenti, quindi un evento interno può essere etichettato come esterno erroneamente. Questo meccanismo di etichettamento scorretto è quello che accade durante le allucinazioni, quando pensieri interni vengono percepiti e considerati esterni. La voce appare come una cosa diversa da te e sembra dire qualcosa che qualcun altro potrebbe dire.

Esistono varie sfumature di esperienze. Alcune persone possono sentire i propri pensieri detti ad alta voce. In tal caso sono pensieri ma si differenziano dai normali pensieri per il fatto che li sente all'esterno. Altri tipi di esperienze sono pensieri ripetitivi che improvvisamente diventano udibili, come una voce.

I pensieri ossessivi sono pensieri percepiti come involontari ed automatici, spesso arrivano veloci alla mente, sono percepiti come indesiderabili perché spesso hanno un contenuto aggressivo o sessuale, morale. Da questo punto di vista, pensieri ossessivi e voci sono simili. Entrambi sono intrusivi, la persona cerca di controllarli ma con scarso successo. Ciò che li differenzia i primi sono pensieri riconosciuti dal soggetto come pensieri mentre le seconde sono gli stessi pensieri prodotti dalla nostra mente senza che però sembrino pensieri, piuttosto frasi pronunciate all'esterno da altri.

FLASHCARD. MESSAGGI DA PORTARE CON TE

- ✓ *Le esperienze straordinarie sono normali, sono reali esperienze*
- ✓ *Sono favorite da lievi squilibri in alcune sostanze nel tuo cervello, la conseguenza del rilascio di dopamina in situazioni improvvise*
- ✓ *Con il tempo, in alcune persone possono scomparire da sole, in altre rimanere ma non in modo invadente*
- ✓ *Le distorsioni cognitive e l'evitamento mantengono le emozioni di ansia che possono provocarti*
- ✓ *Il problema è se pensi che dipendano da qualcun altro fuori di te*
- ✓ *Abbiamo poco controllo su queste esperienze, quindi la prima spiegazione logica che uno potrebbe avere è che sia coinvolto qualcun altro….ma non è così*

SCHEDA. CERCARE UNA SPIEGAZIONE ALLE COINCIDENZE

Può succedere che le coincidenze non ci sembrino coincidenze. Ti concentri a lungo guardando il dado e ti ripeti a bassa voce: "Un sei, un sei, un sei". Lanci il dado ed esce un sei. Allora lo puoi fare!
Nel Medioevo alcune popolazioni iniziarono a pensare che la peste fosse provocata da dai gas pericolosi nelle città. Allora alcuni gruppi si ritirarono a vivere nelle montagne. Nessuno si ammalò nelle montagne: l'aria era salutare – il collegamento fu ovvio….
Successivamente, si scoprì che la qualità dell'aria non aveva niente a che vedere con la peste, che invece si capì era provocata da batteri trasferiti all'uomo dai ratti.

Una coincidenza a volte non sembra una coincidenza

Se lanci un dado sei volte di fila, la serie 6-6-6-6-6-6 è tanto probabile quanto la serie 3-4-2-1-5-3. Eppure la prima serie può sembrarci una coincidenza ma lo di fatto lo è….a ogni lancio la probabilità di avere un 6, un 3, un 2 o un 5 è sempre 1 su 6!
Non sempre teniamo sufficientemente a mente l'effetto del caso...spesso confondiamo la sincronicità con la causa.

FLASHCARD. MESSAGGI DA PORTARE CON TE

Se due eventi ci capitano contemporaneamente, potrebbe esserci un legame di causa ed effetto

…. ma in genere è solo una coincidenza

SCHEDA

LA DISTORSIONE DELLE ASPETTATIVI PESSIMISTICHE

Dopo alcuni insuccessi può succedere di iniziare a pensare che non dobbiamo aspettarci niente di positivo dalle situazioni. Possiamo iniziare ad avere una visione pessimista del futuro: niente di positivo ci aspetta, qualsiasi sforzo per raggiungere determinati obiettivi non servirà. L'estremo pessimismo può talvolta essere una "profezia che si auto-avvera": se non mi aspetto niente di buono, evito di impegnarmi in comportamenti positivi e quindi sarà più probabile che non raggiunga nessuno dei miei obiettivi.

Sappiamo che le interpretazioni che diamo delle cose influenzano il nostro modo di sentire le emozioni e comportarci. Le interpretazioni vanno oltre i fatti. I fatti sono eventi distinti, registrabili, misurabili. Il nostro linguaggio influenza molto le nostre interpretazioni. Pensiamo adesso a un uomo che sta sotto la pioggia con un lungo cappotto. Il linguaggio potrebbe affermare questo evento così: "Quell'uomo sta sotto la pioggia con un lungo cappotto". Però, potrebbe anche portare ad un'interpretazione: "Quell'uomo sotto la pioggia è stato appena lasciato dalla sua ragazza" oppure un'altra interpretazione potrebbe essere "Quell'uomo sotto la pioggia con un lungo cappotto è in attesa della sua ragazza". Ma potrebbe essere anche essere che gli piace la pioggia ed è sceso per una passeggiata. C'è quindi una differenza tra un fatto ed un'interpretazione. La prima interpretazione che abbiamo dato è un'interpretazione pessimistica.

SCHEDA

DIARIO DELLE INTERPRETAZIONI PESSIMISTICHE

Prova a notare la settimana che segue le situazioni nelle quali tendi a dare un'interpretazione pessimistica. In fondo alla giornata, prova a riesaminare quello che è successo e ad appuntare gli eventi in cui hai dato un'interpretazione pessimistica del risultato e come quest'ultima ha influenzato il tuo comportamento, il tuo modo di sentire. È molto importante provare a tenere a mente possibili interpretazioni alternative.

Situazioni della giornata	***Interpretazione pessimistica e conseguenze sul mio modo di sentire e comportarmi***	***Interpretazione alternativa***

SCHEDA

COME AIUTARMI A METTERE IN DISCUSSIONE I MIEI PENSIERI AUTOMATICI

Quando sei troppo lontano da ciò che puoi percepire con i tuoi cinque sensi, è facile entrare nel mondo della fantasia e dell'irrazionale. Quando ti aggrappi a ciò che percepisci con i 5 sensi sei di solito su un terreno più sicuro. Questa lista di domande può aiutarti a creare pensieri alternativi e comportamenti più assertivi. Provando a considerare domande come queste puoi aiutarti a mettere in discussione i pensieri automatici che talvolta creano emozioni troppo intense, come rabbia o ansia:

1. *Da cosa lo vedo che le cose stanno come dice questo pensiero automatico?*
2. *C'è una spiegazione alternativa? Quali sono le prove contro questa idea?*
3. *Qual è la cosa peggiore che potrebbe accadere?*
4. *Qual è la cosa migliore che potrebbe accadere?*
5. *Cosa può succedere a me se credo a questo pensiero automatico?*
6. *Quale potrebbe essere l'effetto del cambiare il mio pensiero?*
7. *Che cosa direi a un amico se lui si trovasse nella stessa situazione?*
8. *Questo mio pensiero è basato su fatti reali?*
9. *Posso provare in base alle distorsioni cognitive che conosco che la mia convinzione è falsa?*
10. *Mantenendo questo pensiero potrò raggiungere dei buoni risultati?*
11. *Le mie interpretazioni delle situazioni sono troppo lontano dalla realtà per essere vere?*
12. *Sto confondendo la mia versione dei fatti?*
13. *Sto pensando in termini di tutto o niente?*
14. *Sto usando parole o frasi che sono estreme o esagerate? (Parole come sempre, mai, devo, non posso, ogni volta, raramente corrispondono alla realtà)*
15. *Sto portando esempi scelti al di fuori dal contesto?*
16. *È attendibile la mia fonte di informazione?*
17. *Sto pensando in termini di certezza invece che di probabilità?*
18. *Sto confondendo una bassa probabilità con un'alta probabilità?*
19. *I miei giudizi sono basati su sensazioni piuttosto che su fatti o eventi?*
20. *Mi sto concentrando su fattori irrilevanti?*

COSTRUIRE UNA GERARCHIA DI SITUAZIONI ATTIVANTI

SITUAZIONI	**TERMOMETRO INTENSITÀ EMOZIONI NEGATIVE (0-100%)**
	10
	20
	30
	40
	50
	60
	70
	80
	90
	100

ESPERIMENTO COMPORTAMENTALE

Data _____

Descrizione esercizio

_____
_____
_____

Cosa prevedo che accadrà? Quali conseguenze su di me/sugli altri?

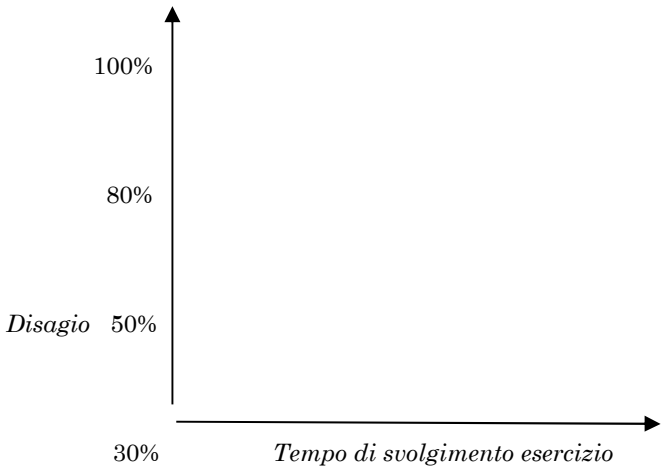
_____
_____

Quanto disagio/ansia/tensione prevedo di provare? (valuta 0-100%)_____

Cosa è realmente successo?

_____
_____

Quanto disagio ho provato? (0-100%) _____



Cosa ho imparato?

_____
_____

Grado di successo dell'esercizio (0-100%) _____

SCHEDA: METTERE IN DISCUSSIONE I PENSIERI AUTOMATICI

Pensiero Automatico _____

Prove a favore	*Prove contrarie*

SCHEDA: VALUTA L'UTILITÀ DEI PENSIERI AUTOMATICI

Pensiero Automatico _____

Vantaggi nel seguire/credere quel pensiero (a breve e lungo termine)	*Svantaggi nel seguire/credere quel pensiero (a breve e lungo termine)*

SCHEDA: CREA PENSIERI ALTERNATIVI

La prima interpretazione che abbiamo di un evento potrebbe non essere la migliore. Impulsivamente possiamo intuire il significato di una data situazione e aderire a questa iniziale interpretazione, pensando che debba essere corretta. I giudizi successivi, spesso più razionali, solo raramente sembrano confermarsi così solidi come quelli iniziali. Di conseguenza, alcune persone continuano a pensare che, ad esempio, una tensione ai muscoli pettorali possa indicare un attacco cardiaco, semplicemente perché questo è stato il pensiero iniziale oppure si convincono di essere antipatici a qualcuno, solo perché quella persona non li ha salutati in un'occasione.

1. Pensa alle emozioni spiacevoli che hai sperimentato durante la settimana (come rabbia, tristezza, paura, etc.) e annotale sul diario dei pensieri automatici.
2. Scrivi l'evento (situazione) legato all'emozione che hai provato e la tua prima interpretazione di questo evento/pensiero.
3. Rileggi la tua prima interpretazione e valuta, in base a ciò che hai appreso, se è corretta. Se ti accorgi che non lo è, trova almeno altre quattro interpretazioni alternative.

Prendi l'abitudine di discutere e sostituire i tuoi pensieri irrazionali in questo modo, per più tempo possibile. Ricordati che ci sono voluti anni ad apprendere ad essere come sei, ci vorrà molta forza ed energia per poter cambiare il tuo modo di pensare. È molto importante che le interpretazioni alternative che provi a creare siano realistiche; non è utile sostituire un pensiero automatico negativo con una falsa credenza positiva.

SCHEDA:

STILE DI VITA E STRATEGIE PER METTERE IN DISCUSSIONE I PENSIERI AUTOMATICI

- ✓ Concediti di discutere alcune delle esperienze straordinarie che ti accadono con persone che conosci: scegli uno o più amici o parenti con i quali parlarne e di cui hai fiducia, che sai essere persone comprensive. È molto utile. Può aiutarti a comprendere anche che spesso i pensieri automatici che arrivano alla nostra mente sono realistici in un certo modo.

- ✓ Porta la tua attenzione sull'effetto che credere a un certo pensiero automatici ha sulle tue sensazioni corporee, sulle emozioni che provi e sul tuo comportamento. Prima di agire prova a notare l'effetto che avrebbe credere a quel pensiero automatico, prova a notare cosa stai pensando in quel momento particolare.

- ✓ Considera che anche le esperienze sensoriali straordinarie sono semplicemente esperienze, in genere favorite un meccanismo temporaneamente alterato nei neurotrasmettitori. Questo passeggero cambiamento nella nostra mente può risolversi da solo e scomparire in modo naturale dopo un po' con il passare del tempo.

- ✓ Cerca di impegnarti in attività sociali, come incontrare amici, frequentare la scuola/università o lavoro.

- ✓ Riduci il tempo durante la giornata che dedichi ad attività di pensiero su questioni esistenziali e prova ad individuare piccoli obiettivi giornalieri da programmare e poi svolgere, come passeggiate, attività sportive e sociali, la cura del tuo corpo, la cura della tua casa e della tua camera.

- ✓ Fissa degli obiettivi:
  - Specifici: definire esattamente cosa si vuole
  - Misurabili: quali saranno i criteri per valutare il successo
  - Appropriati: assicurati che siano appropriati per te
  - Realistici e realizzabili
  - Limitati: al momento in cui li stai attuando

- ✓ Impegnati a trattenerti dal fare uso di sostanze e cannabis, soprattutto quando noti che amplificano le esperienze straordinarie.

SCHEDA TRAINING ATTENTIVO

Adesso che ti sei esercitato con il training attentivo insieme al tuo terapeuta, è molto importante che tu possa fare pratica anche a casa. Affinché sia efficace, deve essere un vero e proprio allenamento per l'attenzione. Questa scheda è pensata per aiutarti a tener traccia degli esercizi.

1. Individua un posto dove esercitarti, in cui potrai introdurre – o identificare – diversi suoni (almeno tre, ma più sono meglio è). È utile che i suoni provengano da punti diversi dell'ambiente che ti circonda. Ad esempio, la radio nella stanza accanto (cucina), la TV in salotto, i rumori che vengono dalla finestra aperta sulla strada, il ticchettio dell'orologio nella tua camera Alcuni possono essere anche soltanto punti dello spazio verso cui dirigere la tua attenzione al di là che vi siano effettivamente rumori nelle vicinanze
I suoni che potrei introdurre sono:
a……..
b……...
c. suoni che posso udire nelle vicinanze
d. suoni che posso udire in lontananza
e. suoni che possono provenire da destra
f. suoni che possono provenire da sinistra

2. Esercitati per circa 10-15 minuti, dividendo il tempo come segue: approssimativamente 5 minuti in cui focalizzi la tua attenzione su singoli suoni differenti; 5 minuti in cui la sposti rapidamente tra i vari suoni; 2 minuti di attenzione divisa.

3. Annota i giorni in cui ti sei esercitato contrassegnando una X nelle caselle sottostanti

Lunedì	Martedì	Mercoledì	Giovedì	Venerdì	Sabato	Domenica

-6 -5 -4 -3 -2 -1 0 +1 +2 +3 +4 +5 +6
/_____/_____/_____/_____/_____/_____/_____/_____/_____/_____/_____/____/

Attenzione completamente sui pensieri automatici **Attenzione equamente divisa** **Attenzione completamente sull'ambiente esterno**

MODULO “EMOZIONI”

SEDUTE 16-17

CONSAPEVOLEZZA E

STRUMENTI DI GESTIONE DELLE EMOZIONI

PSICOEDUCAZIONE SULLE EMOZIONI

TECNICHE DI RILASSAMENTO

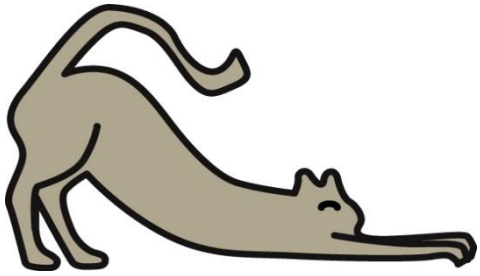
SCHEDA: DIARIO DEI SEGNALI CORPOREI

Giorni e orario	***Segnali corporei (0-100)***	***Disagio (0-100)***	***Pensieri automatici*** *(quanto sono convinto da questi pensieri? 0-100)*	***Quanto sento la necessità di controllare? (0-100)***

SCHEDA: GESTIONE DELL'ANSIA E METODI DI RILASSAMENTO

AUDIO SU ESERCIZIO DI RESPIRAZIONE DIAFRAMMATICA
15 MINUTI DI ASCOLTO

AUDIO SU RILASSAMENTO MUSCOLARE PROGRESSIVO
15 MINUTI DI ASCOLTO



SCHEDA: DAI UN NOME ALLE TUE EMOZIONI

Emozioni	Parole che esprimono l'emozione	Alcuni segnali corporei che le accompagnano
Rabbia	*Pazzo, inquietato, adirato, risentito, irritato, esasperato, arrabbiato, furioso, turbato, incazzato, alterato*	***Testa*** *Calda, pesante, mi scoppia, come se salisse il sangue al cervello, tesa* ***Viso*** *Rosso, pesante, brucia, teso, contratto* ***Gambe*** *Rigide, tese, irrequiete, muscoli tesi*
Ansia	*Preoccupato, timoroso, terrorizzato, preso dal panico, pauroso, spaventato, nervoso, apprensivo, inquietato, agitato, sopraffatto, sotto pressione, teso, soffocato*	***Respiro*** *corto, veloce, affannoso, superficiale, pesante, interrotto* ***Testa*** *leggera, confusa, vuota, come se non funzionasse* ***Petto*** *pesante, rigido, come se ci fosse un macigno o un peso che lo porta giù* ***Addome*** *peso, fastidio* ***Gola*** *sensazione che si stringa, che ci sia un nodo, sensazione amara* ***Gambe*** *Rigide, tese, irrequiete, muscoli tesi* ***Cuore*** *Batte più forte, veloce*
Imbarazzo	*Stupido, impacciato, confuso, inadeguato*	***Viso*** *Caldo, rosso* ***Mani, gambe*** *Vacillanti, mi mancano le forze, tremanti*
Senso di colpa	*Pieno di vergogna, sentirsi in colpa, cattivo*	***Petto*** *pesante, rigido, come se ci fosse un macigno o un peso che lo porta giù* ***Gola*** *si stringe, manca l'aria*
Senza speranza	*Senza speranza Scoraggiato, pessimista, disperato, impotente, sfiduciato*	***Petto*** *pesante, rigido, come se ci fosse un macigno o un peso che lo porta giù* ***Gola*** *si stringe, manca l'aria*
Tristezza	*Dispiaciuto, giù, infelice, triste, melanconico, ferito, deluso, depresso, Abbandonato, solo, isolato, rifiutato, indesiderato, respinto*	***Petto*** *pesante, rigido, come se ci fosse un macigno o un peso che lo porta giù* ***Gola*** *si stringe, manca l'aria* *Testa* *leggera, confusa, vuota, come se non funzionasse* ***Petto*** *pesante, rigido, come se ci fosse un macigno o un peso che lo porta giù* ***Addome*** *peso, fastidio* ***Gola*** *sensazione che si stringa, che ci sia un nodo, sensazione amara* ***Gambe:*** *Rigide, tese, irrequiete, muscoli tesi*

SCHEDA: L'IPERVENTILAZIONE E LA RESPIRAZIONE DIAFRAMMATICA

Per imparare a gestire l'ansia può essere utile conoscere il particolare fenomeno dell'iperventilazione. Il corpo ha bisogno di ossigeno per sopravvivere: quando inspiriamo, l'ossigeno viene trasportato ai polmoni è raccolto dall'emoglobina che lo trasporta alle cellule che poi lo utilizzano per produrre energia necessaria tutte le nostre funzioni. Come sotto prodotto si forma l'anidride carbonica che attraverso la circolazione viene trasportata ai polmoni per essere espirata. L'efficienza delle nostre funzioni dipende dall'equilibrio tra consumo di ossigeno e produzione di anidride carbonica dipende: questo equilibrio è garantito da una adeguata frequenza e profondità respiratoria. L'iperventilazione, che può essere definita come l'aumento della frequenza e profondità respiratoria proporzionata alle esigenze energetiche delle nostre cellule, può provocare una riduzione dei livelli di anidride carbonica; l'ipoventilazione ha invece, l'effetto opposto.

Naturalmente, se la richiesta di ossigeno e la produzione di anidride carbonica aumentano entrambi (come durante l'attività fisica), anche la frequenza e la profondità respiratoria devono aumentare in funzione delle maggiori richieste energetiche. Al contrario, se come durante il rilassamento il bisogno di ossigeno e la produzione di anidride carbonica diminuiscono, la frequenza e la profondità del respiro devono diminuire.

La funzione respiratoria è regolata da sistemi chimici e fisici "automatici" ma anche sotto il controllo della nostra volontà. Infatti è abbastanza facile trattenere il respiro (es. nuotare sott'acqua), oppure soffiare (ad es. per gonfiare un palloncino); perciò numerosi meccanismi volontari e tra questi anche l'emozione, lo stress o l'abitudine possono indurre l'iperventilazione. Questi meccanismi possono essere particolarmente importanti per le persone che soffrono di ansia. L'iperventilazione è responsabile della vasocostrizione e ciò riduce l'apporto di sangue ai vari organi. Quindi si verifica che meno sangue raggiunge i vari tessuti ma anche meno ossigeno viene rilasciato alle cellule. Paradossalmente mentre, con l'iperventilazione catturiamo più ossigeno, in pratica meno ossigeno raggiunge le zone periferiche del nostro corpo. Queste conseguenze dell'iperventilazione spiegano i sintomi che possiamo avvertire durante gli attacchi di panico: vertigini, capogiri, visione confusa, confusione mentale e sensazioni di irrealtà, palpitazione, dispnea, tensione muscolare, estremità fredde, sudate ed intorbidite sono dovute al ridotto apporto di ossigeno agli organi dell'organismo. Spasmi e crampi muscolare possono essere causati dal protrarsi dell'iperventilazione. Importante sottolineare, però che il diminuito apporto di ossigeno alla periferia è trascurabile e del tutto innocuo. Inoltre l'iperventilazione è responsabile dell'aumento del lavoro fisico: l'aumento della frequenza della profondità respiratoria per periodi prolungati di tempo causano stanchezza ed esaurimento, il soggetto si sente accaldato, arrossato e sudato e può avvertire dolore o costrizione toracica. Quando iperventiliamo, tendiamo a respirare con il torace, piuttosto che con il diaframma, il muscolo che separa i polmoni dall'addome. Esistono due tipi respirazione:

- ✓ *toracica (di petto)*
- ✓ *diaframmatica.*

La respirazione toracica comprende i muscoli intercostali esterni, che alza la gabbia toracica in alto ed in fuori ad ogni inspirazione, mentre quella diaframmatica coinvolge l'uso del diaframma ed è caratterizzata dal movimento dello stomaco verso l'interno e l'esterno durante la stessa. La maggior parte delle persone utilizza la respirazione addominale, infatti utilizza di più l'uso del diaframma piuttosto che quella toracica.

Riconoscere e controllare l'iperventilazione

Il primo passo per evitare e/o controllare l'iperventilazione è riconoscerla. Provate a fare un monitoraggio della vostra frequenza respiratoria.

Respirate molto velocemente?
In media necessitiamo solo di 10-12 respiri al minuto quando siamo a riposo. Se la vostra frequenza respiratoria è maggiore, è utile ridurla.

Respirate troppo profondamente? Qualche volta il vostro petto vi sembra sovraespanso?
È utile respirare con il diaframma e attraverso il naso.

Respirate dall'addome?
Sedetevi con le braccia incrociate leggermente sulla pancia, e mentre respirate naturalmente, osservate le braccia, il petto e le spalle. Mentre si muovono tutti e tre, il movimento principale dovrebbe essere quello della pancia, se respirate correttamente dal diaframma.

Ansimate o inspirate fortemente quando qualcuno nomina quello che temete?
Fare un respiro profondo può fare scattare un ciclo di iperventilazione in molte persone.

Respirate attraverso la bocca?
È più probabile che iperventiliate se respirate attraverso la bocca, tutte le volte che vi accorgete di questo, dovreste ritornare consciamente a respirare attraverso il naso. La respirazione cadenzata a bocca chiusa può essere sufficiente, se effettuata prima di un vero forte attacco.

Cosa fare se siete in iperventilazione?
Tecnica del respiro lento
Questa tecnica va utilizzare ai primi segnali di ansia o quando si riconoscono i primi segnali di iperventilazione:

- *interrompere quello che si sta facendo*
- *trattenere il fiato (senza prima fare un respiro profondo) e contare fino a 10*
- *quando si arriva a 10 si lascia uscire fuori l'aria e si pensa "mi rilasso" in modo calmo e tranquillo*
- *inspirare ed espirare lentamente in cicli di 6 secondi: inspirare per tre secondi ed espirare per tre secondi. In questo modo si fanno circa 10 respiri completi al minuto, si pensa "mi rilasso" ogni volta che si espira*
- *Ogni minuto (dopo una serie di 10 respiri) si trattiene di nuovo il fiato per 10 secondi, poi si riprende a respirare in cicli di 6 secondi.*
- *Si continua così fino alla scomparsa di tutti i sintomi dell'iperventilazione*

Per quanto riguarda gli attacchi di panico, se invece siete già in iperventilazione non dovete usate la tecnica del respiro lento, ma i vostri sintomi cesseranno respirando una miscela di ossigeno CO2 al 30% o più semplicemente aria arricchita di CO2 per esempio riciclando l'aria espirando e respirando con un sacchetto di plastica sulla bocca.

MODULO “SINTOMI DEPRESSIVI”

SEDUTE 18-21

GRAFICO DELL’UMORE

DISTORSIONI COGNITIVE CHE MANTENGONO LA DEPRESSIONE

RISTRUTTURAZIONE COGNITIVA

ESPERIMENTI COMPORTAMENTALI

PROGRAMMAZIONE DI ATTIVITÀ

GESTIRE LA TENDENZA A PROCRASTINARE

SCHEDA: PROGRAMMAZIONE DELLE ATTIVITÀ GIORNALIERE

Orario	*Lunedì*	*Martedì*	*Mercoledì*	*Giovedì*	*Venerdì*	*Sabato*	*Domenica*
8-10							
10-12							
12-14							
14-16							
16-18							
18-20							
20-22							
22-24							

SCHEDA: TERMOMETRO DELL'UMORE

GIORNI _____-_____

0_____10_____20_____30_____40_____50_____60_____70_____80_____90_____100

SEGNALI	DEPRESSIONE	DISTIMIA	EUTIMIA	IPOMANIA	MANIA

SCHEDA: DIARIO DELLE EMOZIONI POSITIVE

ATTIVITA' PIACEVOLE *Cosa stavo facendo? Dove ero? Con chi?*	**EMOZIONI** *Come mi sentivo in quel momento? Quali sensazioni positive avevo?*	**SENSAZIONI CORPOREE** *Quali sensazioni nel corpo sentivo associate a quelle emozioni?*	**PENSIERI** *Cosa mi passava per la mente di positivo che mi faceva sentire quelle emozioni?*

Le attività piacevoli

Questo elenco è un insieme di attività costruttive e di rinforzo che possono esserti utili a regolare il tuo umore e contrastare uno stato depressivo. Ognuno di noi può individuare quali di queste possono, nel proprio caso, risultare piacevoli, dare distrazione, dare degli scopi giornalieri. Questa lista può stimolarti a riflettere sulle attività quotidiane da inserire nel tuo programma giornaliero.

1. *Fare una gita in campagna*
2. *Indossare abiti costosi o esclusivi*
3. *Offrire un contributo per una giusta causa*
4. *Conversare di sport*
5. *Fare una nuova conoscenza (stesso sesso)*
6. *Sostenere un esame ben preparati*
7. *Andare a un concerto pop*
8. *Giocare a pallone*
9. *Programmare escursioni o vacanze*
10. *Fare degli acquisti per se stessi*
11. *Stare sulla spiaggia*
12. *Fare attività creative (pittura, scultura, disegno, cinema,)*
13. *Fare alpinismo*
14. *Leggere la Bibbia o altri testi religiosi*
15. *Giocare a golf o a minigolf*
16. *Modificare la disposizione dei mobili della casa o della stanza*
17. *Correre in giro nudi*
18. *Andare a vedere un avvenimento sportivo*
19. *Andare alle corse (cavalli, automobili, barche)*
20. *Leggere consigli per la propria situazione*
21. *Leggere romanzi, racconti, pezzi teatrali, poesie*
22. *Andare in un locale*
23. *Andare a una conferenza*
24. *Guidare l'automobile*
25. *Scrivere una canzone o comporre un pezzo musicale*
26. *Giocare col computer*
27. *Esprimere un'opinione apertamente*
28. *Andare in barca a vela o in canoa*
29. *Fare una cosa gradita ai genitori*
30. *Restaurare pezzi antichi (mobili, ecc.)*
31. *Guardare la televisione*
32. *Parlare da solo*
33. *Andare in campeggio*
34. *Fare attività politica*
35. *Dedicarsi a semplici lavori di manutenzione (automobile, moto, bicicletta, elettrodomestici)*
36. *Fare progetti per il futuro*
37. *Giocare a carte*
38. *Svolgere bene un impegno difficile*
39. *Ridere*
40. *Fare parole crociate, puzzle, ecc.*
41. *Partecipare a matrimoni, battesimi, lauree,*
42. *Criticare qualcuno*
43. *Mangiare insieme a parenti o amici*
44. *Partecipare a corsi culturali*
45. *Giocare a tennis*
46. *Fare una doccia*
47. *Guidare per un lungo tratto*
48. *Fare lavori di intaglio o carpenteria*
49. *Scrivere romanzi, racconti, pezzi teatrali, poesie*
50. *Occuparsi di animali*
51. *Andare in aereo*
52. *Fare giri esplorativi (deviare dalle strade consuete, esplorare zone non conosciute,)*
53. *Intrattenere un discorso leale e aperto*
54. *Cantare in un coro*
55. *Riflettere su se stessi o sui propri problemi*
56. *Attivarsi professionalmente*
57. *Andare a un party*
58. *Parlare una lingua straniera*
59. *Andare a manifestazioni religiose (raccolte benefiche, conferenze)*
60. *Andare a riunioni di associazioni socialmente utili*
61. *Andare a un'inaugurazione*
62. *Guidare una macchina sportiva o di lusso*
63. *Suonare uno strumento musicale*
64. *Sciare*
65. *Ricevere aiuto*
66. *Essere vestiti leggeri*
67. *Pettinarsi o spazzolarsi i capelli*
68. *Fare attività di recitazione*
69. *Fare un pisolino*
70. *Stare insieme agli amici*
71. *Preparare alimenti, conservarli, congelarli*
72. *Guidare veloce*
73. *Risolvere un problema personale*
74. *Fare un bagno*
75. *Canticchiare*
76. *Giocare a biliardo*
77. *Stare insieme ai nipotini*
78. *Giocare a scacchi o a dama*
79. *Impegnarsi in lavori creativi (lavorare con creta, gioielli, pelle, perle, uncinetto, ecc.)*
80. *Andare allo zoo o al circo*
81. *Grattarsi*
82. *Truccarsi, pettinarsi, ecc.*
83. *Creare o disegnare qualcosa*
84. *Andare a trovare persone malate o in difficoltà*
85. *Essere contenti, trasmettere buonumore*
86. *Giocare a bowling*
87. *Osservare gli animali*
88. *Avere un'idea originale*
89. *Fare giardinaggio o lavori di campagna*
90. *Fare un buon affare*
91. *Leggere testi e manuali professionali specifici*

92. *Indossare degli abiti nuovi*
93. *Ballare*
94. *Stare seduti al sole*
95. *Andare in motocicletta*
96. *Starsene seduti a riflettere*
97. *Bere un bicchierino in compagnia*
98. *Partecipare a un avvenimento positivo per la famiglia o per un amico*
99. *Visitare un parco di divertimenti*
100. *Discutere di argomenti religiosi o filosofici*
101. *Giocare d'azzardo*
102. *Progettare o organizzare qualcosa*
103. *Andare al cimitero*
104. *Bere qualcosa da soli*
105. *Ascoltare i rumori della natura*
106. *Prendere appuntamento per amoreggiare con qualcuno dell'altro sesso*
107. *Sostenere un'accesa discussione*
108. *Fare gare di corsa*
109. *Ascoltare la radio*
110. *Ricevere la visita di amici*
111. *Partecipare a una gara sportiva*
112. *Presentare l'un l'altro delle persone che si presume possano intendersi bene*
113. *Fare regali*
114. *Assistere alle udienze*
115. *Essere massaggiati*
116. *Ricevere lettere*
117. *Osservare il cielo, le nuvole o una tempesta*
118. *Intrattenersi all'aperto (in un parco o in un giardino per un pic-nic, una grigliata, ecc.)*
119. *Giocare a pallacanestro o a pallavolo*
120. *Comprare qualcosa per la famiglia*
121. *Fotografare*
122. *Tenere un discorso o una conferenza*
123. *Studiare carte geografiche*
124. *Collezionare oggetti della natura (bacche selvatiche, pietre, ecc.)*
125. *Badare alle proprie faccende*
126. *Indossare abiti puliti*
127. *Fare un acquisto o un investimento (automobile, oggetti per la casa)*
128. *Aiutare qualcuno*
129. *Concorrere per un nuovo lavoro*
130. *Ascoltare barzellette*
131. *Vincere una scommessa*
132. *Parlare dei propri figli o nipoti*
133. *Fare una nuova conoscenza dell'altro sesso*
134. *Parlare della propria salute*
135. *Mangiare bene*
136. *Fare qualcosa per la salute (far mettere a posto i denti, comprare gli occhiali nuovi, cambiare alimentazione)*
137. *Farsi un giro per la città*
138. *Praticare lotta o boxe*
139. *Dedicarsi al tiro con la pistola*
140. *Suonare in una banda*
141. *Fare escursionismo*
142. *Visitare un museo o una esposizione*
143. *Tenere un diario*
144. *Svolgere bene un compito*
145. *Avere tempo libero*
146. *Andare a pescare*
147. *Prestare qualcosa*
148. *Essere notato come sessualmente attraente*
149. *Fare contento il datore di lavoro, l'insegnante*
150. *Consigliare qualcuno*
151. *Andare in una palestra o in una sauna*
152. *Imparare qualcosa di nuovo*
153. *Fare complimenti a qualcuno o lodarlo*
154. *Pensare a persone care*
155. *Vendicarsi di qualcuno*
156. *Stare insieme ai propri genitori*
157. *Cavalcare*
158. *Fare conversazioni telefoniche*
159. *Sognare a occhi aperti*
160. *Giocare con foglie, sabbia, pietrisco, ecc*
161. *Giocare a bocce*
162. *Andare a raduni di vecchi compagni di scuola*
163. *Vedere gente famosa*
164. *Andare al cinema*
165. *Baciarsi*
166. *Stare da soli*
167. *Cucinare*
168. *Riuscire a mettere nel sacco una persona ritenuta molto furba*
169. *Fare in casa dei lavori occasionali*
170. *Piangere*
171. *Sentirsi dire che si è utili*
172. *Partecipare a una festa o a un incontro con familiari*
173. *Organizzare un party o un incontro piacevole*
174. *Lavarsi i capelli*
175. *Dare disposizioni a qualcuno*
176. *Guardare o odorare un fiore o una pianta*
177. *Essere invitati a uscire*
178. *Mettersi un profumo o dell'acqua di colonia*
179. *Essere d'accordo con qualcuno*
180. *Rivivere ricordi, parlare di tempi passati*
181. *Alzarsi al mattino presto*
182. *Trovare pace*
183. *Fare esperimenti o ricerche scientifiche*
184. *Andare a trovare degli amici*
185. *Farsi consigliare, ricevere un consiglio*
186. *Pregare*
187. *Massaggiare qualcuno*
188. *Viaggiare in autostop*
189. *Praticare meditazione o yoga*
190. *Assistere a un combattimento*
191. *Parlare con i compagni di classe o di lavoro*
192. *Rilassarsi*
193. *Essere pregati per concedere un consiglio o un aiuto*
194. *Riflettere sui problemi di altre persone*
195. *Giocare a giochi di società*
196. *Dormire profondamente di notte*
197. *Fare lavori pesanti all'aperto (tagliare la legna, fare giardinaggio)*
198. *Leggere il giornale*
199. *Partecipare a gruppi di autoesperienza*
200. *Giocare a tennis da tavolo*
201. *Lavarsi i denti*
202. *Nuotare*
203. *Correre, fare jogging, ginnastica o altre attività all'aperto*
204. *Correre scalzi*
205. *Giocare ad acchiapparello o simili*
206. *Fare il bucato o le pulizie*
207. *Ascoltare musica*
208. *Avere piacere sessuale*
209. *Lavorare a maglia, uncinetto, cucire in maniera creativa*
210. *Flirtare*
211. *Fare divertire delle persone*
212. *Parlare di problemi sessuali*
213. *Andare dal parrucchiere o dall'estetista*
214. *Avere ospiti a casa*

215. *Stare insieme a qualcuno cui si vuol bene*
216. *Leggere delle riviste*
217. *Dormire fino a sentirsi completamente riposati*
218. *Iniziare una nuova attività*
219. *Essere ostinati*
220. *Discutere*
221. *Avere rapporti sessuali*
222. *Andare in biblioteca*
223. *Giocare a pallavolo*
224. *Preparare una pietanza nuova o speciale*
225. *Osservare gli uccelli*
226. *Uscire per compere*
227. *Osservare la gente*
228. *Accendere o osservare un fuoco*
229. *Superare con successo un confronto*
230. *Vendere o contrattare qualcosa*
231. *Portare a termine un impegno*
232. *Confessare o farsi perdonare*
233. *Acquistare degli oggetti*
234. *Andare in bicicletta*
235. *Dire alla gente cosa deve fare*
236. *Stare in compagnia di persone*
237. *Partecipare a giochi durante una festa*
238. *Scrivere lettere o cartoline*
239. *Parlare di politica o di questioni sociali*
240. *Chiedere aiuto o consigli*
241. *Parlare dei propri hobby o interessi specifici*
242. *Guardare uomini o donne*
243. *Sorridere alle persone*
244. *Giocare sulla sabbia, sull'erba, presso il fiume*
245. *Parlare di altre persone*
246. *Stare insieme al coniuge*
247. *Ricevere attenzione per le proprie opinioni da parte di altre persone*

248. *Fumare tabacco*
249. *Occuparsi delle piante di casa*
250. *Bere un caffè o un tè con gli amici*
251. *Fare una passeggiata*
252. *Collezionare diverse cose*
253. *Cucire*
254. *Ricordarsi di un amico morto*
255. *Fare qualcosa insieme a dei bambini*
256. *Ricevere complimenti o gratificazioni per qualcosa che si è compiuto*
257. *Sentirsi dire di essere amati*
258. *Fare uno spuntino*
259. *Rimanere alzati fino a tardi*
260. *Stare insieme ai figli*
261. *Andare a un'asta*
262. *Riflettere su una domanda interessante*
263. *Fare volontariato o partecipare a progetti sociali*
264. *Praticare sci d'acqua, surf, attività subacquea*
265. *Difendere o proteggere qualcuno; intervenire contro una truffa o un abuso*
266. *Dare un passaggio a un autostoppista*
267. *Vincere una lotteria*
268. *Parlare del lavoro o della scuola*
269. *Leggere giornali a fumetti*
270. *Farsi prestare qualcosa*
271. *Partecipare a un viaggio di gruppo*

SCHEDA: RINVIA LA TENDENZA A PROCRASTINARE

Sei costantemente in ritardo? Hai la sensazione di non aver raccolto molto alla fine della tua giornata? La lista delle "cose da fare" continua a crescere? Oppure ti succede di trascorrere molto tempo senza fare niente o sapere come gestirlo? Se la risposta a una o più di queste domande è sì, allora potresti avere alcuni problemi nella gestione del tempo. Alcune di queste strategie potrebbero esserti di aiuto per gestire in modo migliore il tuo tempo:

Fai una lista degli obiettivi.
Scrivi i lavori o i compiti che vuoi portare a termine nella settimana. Crea una lista delle "cose da fare". Questo aiuta e incoraggia a pianificare in anticipo.

Fissa le priorità.
Valuta le priorità di ogni compito: alto, medio o basso. Per quanto? Valuta la quantità di tempo necessaria per svolgere ogni compito

Fai un programma.
Utilizza un'agenda per programmare quando farai ogni cosa. Assegna scadenze realistiche

Accorda le cose da fare con il tuo livello di energia.
Per esempio, "sei una persona mattiniera?" se sì, allora programma i compiti più impegnativi al mattino. Non aspettare il pomeriggio o la sera quando potresti essere troppo stanco.

Hai troppe cose da fare?

- *Delega: assegna alcune delle tue cose ad altre persone*
- *Snellisci: c'è un modo per fare le cose in modo più efficiente? Le cose raramente devono essere perfette*
- *Scarta: alcune cose possono essere omesse*
- *Riduci le fonti di disturbo per migliorare la tua efficienza. Se hai bisogno di un certo periodo di tempo per portare a termine un compito importante, per esempio, chiudi la porta dell'ufficio e inoltra le tue telefonate*

Rimandare è un problema?

- *Esamina i tuoi pensieri. Stai dicendo a te stesso che il compito da affrontare è troppo difficile? Che deve essere perfetto? Che non sei abbastanza bravo per affrontarlo? Questi pensieri sono realistici? Le persone spesso rimandano perché sovrastimano la difficoltà di un compito e sottovalutano le proprie capacità*
- *Motivati. Pensa in modo da auto-motivarti come "Consideralo già fatto", "Fallo e basta!". Poi premiati per aver portato a termine ciò che avevi da fare.*
- *Appuntamento con il destino. Usando la tua agenda giornaliera metti da parte il giusto tempo per svolgere ciò che devi fare*
- *La regola dei 5 minuti. Dì a te stesso che lavorerai su di una cosa difficile per 5 minuti, dopodiché vedrai se avrai voglia di continuare. È probabile che una volta che hai iniziato, vorrai proseguire.*

MODULO “RIMUGINIO”

SEDUTE 22-25

GRAFICO DELL’UMORE

DISTORSIONI COGNITIVE CHE MANTENGONO LA DEPRESSIONE

RISTRUTTURAZIONE COGNITIVA

ESPERIMENTI COMPORTAMENTALI

PROGRAMMAZIONE DI ATTIVITÀ

GESTIRE LA TENDENZA A PROCRASTINARE

SCHEDA: UN FALSO COMPAGNO DI VIAGGIO: IL RIMUGINIO

- ✓ *Cosa è il rimuginio?*
- ✓ *Riguarda prevalentemente situazioni che devono accadere*
- ✓ *È fatto di pensieri automatici del tipo "E se…?"*
- ✓ *Porta con sé la distorsione della catastrofizzazione*
- ✓ *Vantaggi a breve termine: ci fa sentire più preparati ad affrontare le situazioni, ci fa sentire che possiamo controllare i problemi se dovessero presentarsi*
- ✓ *Svantaggi a lungo termine: mantiene la preoccupazione per gli eventi futuri, predita di tempo, predita di concentrazione ed energie, svaluto il presente*
- ✓ *Non è problem solving*
- ✓ *Sembra incontrollabile - se porti la tua attenzione, noterai che ci sono momenti della giornata non cui lo sospendi volontariamente (mentre rispondi al telefono, quando fai esercizi di rilassamento, quando programmi attività giornaliere…)*

SCHEDA. PRENDI UN APPUNTAMENTO CON IL RIMUGINIO

- ✓ *Fissa un appuntamento con il rimuginio nella tua giornata ad un orario prestabilito*
- ✓ *L'orario dovrà essere il più possibile sempre lo stesso*
- ✓ *L'appuntamento potrà durare un massimo di 20 minuti*
- ✓ *Nei 20 minuti potrai preoccuparti dei pensieri automatici della giornata*
- ✓ *Al di fuori di questo orario programma nella tua giornata attività piacevoli, interessanti, coinvolgenti, che attirino la tua attenzione e ti impegnino con obiettivi a breve termine nella quotidianità*
- ✓ *Mentre svolgi le attività presta la tua attenzione con i 5 sensi a quello che senti, odori, vedi, noti…*
- ✓ *Programma attività che ti impegnino dal rimuginio*

SCHEDA: DIARIO DELLE PREOCCUPAZIONI

DATA ORA	**PREOCCUPAZIONE** *Di cosa mi sono preoccupato?* *Che cosa mi ha dato apprensione?*	**INTENSITA' ANSIA** *Da 0=molto bassa* *a 100=molto alta*	**REAZIONE** *Cosa ho fatto per calmarmi? Cosa hanno fatto gli altri?* *Cosa mi sono detto? Cosa hanno detto gli altri?*

SCHEDA: TORTA DELLE PROBABILITÀ

*Pensiero automatico:*_____

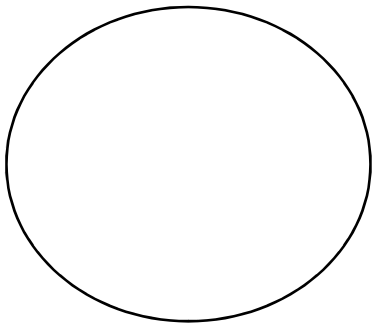
Probabilità prima dell'evento che ciò che viene predetto da quel pensiero si realizzi? _____%

Possibili esiti/conseguenze alternative:

_____

_____

Probabilità di quelle conseguenze? _____%

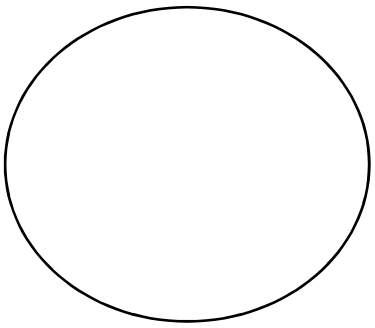


Nuova probabilità dopo l'evento che ciò che viene predetto da quel pensiero si realizzi? _____%

Nuova probabilità delle conseguenze alternative? _____%

Nuove conseguenze? _____

Pensieri alternativi più realistici: _____

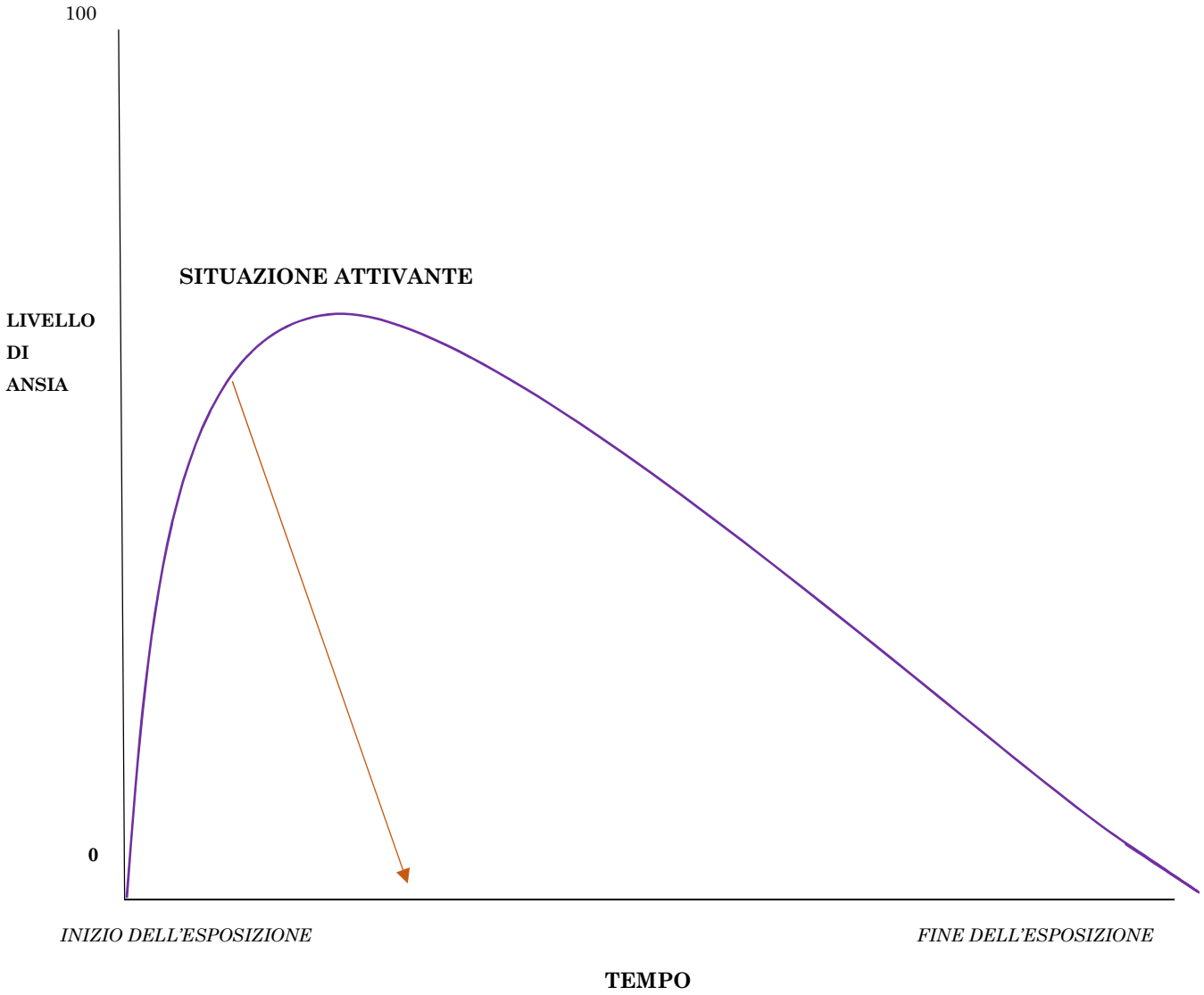


SCHEDA:

LA BILANCIA DELL'EVITAMENTO DI SITUAZIONI FONTE DI ANSIA PER ME

VANTAGGI DELL'EVITAMENTO	SVANTAGGI DELL'EVITAMENTO
SVANTAGGI DI AFFRONTARLE	**VANTAGGI DI AFFRONTARLE**

SCHEDA: LA CURVA DEL'ANSIA



Se non ti sforzi di evitarla, l'ansia è come un'onda del mare quando ti passa addosso…

…cala da sola

SCHEDA: PASSI DEL PROBLEM SOLVING

Identifica la situazione
Individua il problema
Quali sono i tuoi scopi/obiettivi/bisogni in questa situazione?
Quali comportamenti hai adottato finora in risposta ai pensieri automatici?
Quali sono i vantaggi di questi comportamenti? Quali gli svantaggi?
Brainstorming: Quali potrebbero essere comportamenti assertivi o alternativi? Prova a scrivere di getto una lista di possibili comportamenti senza valutarli rispetto alla funzionalità
Quali sono i comportamenti maggiormente funzionali ed utili a perseguire i tuoi scopi/obiettivi/bisogni? Confronta vantaggi e svantaggi di ciascuno
Pesa ogni vantaggio/svantaggio
Confronta i vari comportamenti individuati
Scegli il/i comportamenti/i con maggiori vantaggi e minori svantaggi
[Dopo aver eseguito l'esercizio sull'assertività] Hai raggiunto i tuoi scopi?

MODULO “ANSIA SOCIALE”

SEDUTE 26-29

ASSERTIVITÀ E ABILITÀ SOCIALI

ROLE PLAYING

ESPOSIZIONI A SITUAZIONI SOCIALI

I COMPORTAMENTI ASSERTIVI

Il comportamento passivo

- ✓ *Restio ad esprimere le proprie opinioni e, in particolare, i propri sentimenti*
- ✓ *Spesso si sente usato dagli altri*
- ✓ *Non si ribella quando gli altri approfittano di lui*
- ✓ *Si trattiene dal lamentarsi quando i servizi o i prodotti non sono adeguati allo standard*
- ✓ *Trova difficoltà nel rifiutare le richieste altrui*
- ✓ *Dimostra acquiescenza verso le opinioni ed i desideri della maggioranza anche se essi sono in conflitto con le inclinazioni personali*
- ✓ *Giunge spesso a dei compromessi per mantenere l'armonia*
- ✓ *È riluttante a disturbare le persone per i propri bisogni*
- ✓ *Si sottomette in presenza di un comportamento aggressivo*
- ✓ *Preferisce mantenere privati i propri punti di vista*
- ✓ *Antepone i bisogni altrui ai propri*

Il comportamento aggressivo

- ✓ *Discute frequentemente con gli altri*
- ✓ *Si arrabbia frequentemente e pensa che gli altri abbiano bisogno di essere messi al loro posto*
- ✓ *Non ha difficoltà a protestare quando riceve prodotti o servizi di scarsa qualità*
- ✓ *Di solito agisce di testa sua*
- ✓ *Si aspetta che gli altri si adattino ai suoi tempi*
- ✓ *Ha delle forti convinzioni su molti argomenti e non ha difficoltà ad esprimerle*
- ✓ *Facilmente e frequentemente trova difetti negli altri*
- ✓ *Lavora in continuazione secondo il proprio ordine del giorno a spese degli altri*
- ✓ *Si preoccupa raramente dei bisogni o sentimenti altrui*
- ✓ *È in competizione con gli altri e si arrabbia se non ottiene successo*

Il comportamento assertivo

Quando si è assertivi, si bilanciano i bisogni degli altri coi propri. Si trattano gli altri come si desidererebbe essere trattati. Quando è necessario si può scegliere se dare la priorità alle necessità altrui o se considerare maggiormente le proprie necessità.

- ✓ *È capace ad esprimere agli altri desideri e sentimenti*
- ✓ *È capace a conversare e lavorare bene con gli altri a tutti i livelli*
- ✓ *È capace ad apprezzare i punti di vista degli altri e ad accettarli se appaiono più ragionevoli dei propri*
- ✓ *È anche capace di mostrarsi in disaccordo con gli altri pur mantenendo la loro amicizia ed il loro rispetto*
- ✓ *Si preoccupa dei desideri e bisogni altrui*
- ✓ *È in grado di fare concessioni agli altri senza sentimenti d'inadeguatezza*
- ✓ *È capace ad esprimere una preoccupazione o un bisogno col minimo imbarazzo per entrambe le parti*
- ✓ *È capace a controllare i sentimenti e le emozioni anche nelle situazioni difficoltose o emotivamente forti*
- ✓ *È capace a rifiutare una richiesta senza sentirsi colpevole o obbligato*
- ✓ *È capace a chiedere qualcosa che desidera e può insistere su ciò che gli compete di diritto senza emozionarsi*

VANTAGGI DELL'ASSERTIVITÀ

- ✓ *Essere più in contatto con i nostri bisogni*
- ✓ *Far valere i nostri diritti e raggiungere più efficacemente i nostri obiettivi nel rispetto altrui*
- ✓ *Si può porre un limite al proprio ed all'altrui comportamento*
- ✓ *Si può avere una visione realistica di cosa è nelle proprie possibilità e cosa non lo è*
- ✓ *Non si è influenzati negativamente da chi è sgarbato o scortese*
- ✓ *Si è capaci di rallegrarsi dei propri successi e di accettare i propri fallimenti*
- ✓ *Si può mantenere sempre il controllo del proprio comportamento, e non farsi istigare all'ira o forzare alla sottomissione*
- ✓ *Sentirsi capiti dagli altri*

HOMEWORK: FARE COMPLIMENTI

Individua cinque amici o colleghi; per ognuno elenca tre o quattro qualità positive che ti piacciono di loro e pensa a degli esempi di quando loro dimostrano queste qualità o comportamenti, soprattutto nei tuoi confronti.

- ✓ *Scrivi cosa dirai loro la prossima volta che si comporteranno così; usa l'affermazione in prima persona ("Io penso/sento/vorrei che tu sapessi" invece di "Sei così bravo a…"), sii specifico, menzionando nel tuo apprezzamento il comportamento che stanno mettendo in atto.*
- ✓ *Stai a vedere come reagiscono e osserva se aumentano o meno quella caratteristica del loro comportamento in tua presenza.*
- ✓ *Per una settimana prendi la decisione di complimentarti con almeno tre persone per il loro lavoro, comportamento o aiuto che ti danno; annotati sul diario gli specifici "apprezzamenti" per ricordarti di averli effettivamente fatti*

SCHEDA: RINFORZA L'AUTOSTIMA

Assertività ed autostima sono collegate tra loro. Si può migliorare significativamente la propria autostima psicologica occupandoci di noi stessi. Alcune strategie per farlo possono includere:

1. Fai regolarmente esercizio fisico per tenerti in forma.
2. Pianifica il "tempo dedicato a me", in modo da ricavarti dei momenti in ogni settimana per avere tempo per te stesso.
3. Rimpiazza la televisione con un interesse che impegni in qualche modo (fisicamente, socialmente, intellettualmente o emotivamente).
4. Pianifica momenti di qualità con la famiglia e con chi è sentimentalmente importante per te
5. Premiati per i tuoi successi, con piccoli premi per le piccole cose e significative ricompense per i traguardi maggiori.

Flashcards 1. Saper dire di no				
"Sono costretto a rifiutare, ma grazie di aver pensato a me"	*"Stavolta non posso proprio"*	*"In questo momento non ho proprio tempo per fare quello che mi chiedi"*	*"Sono molto impegnato in questo periodo"*	*"So troppo indaffarato per fare questa cosa"*
"Non mi sento di fare questa cosa"	*"In questo momento non posso, magari più avanti"*	*"Sembra interessante ma non ho tempo di farla"*	*"No, non posso aiutarti"*	*"Vorrei poterti aiutare ma non ho tempo"*
Flashcards 2. Affermare il mio punto di vista				
"Non sono d'accordo con questo"	*"Io invece penso/credo che…."*	*"Le cose stanno così, però stanno anche in questo modo…"*	*"Ci sono rimasto male del fatto che tu…"*	*"Sono rimasto stupito da te che…"*
"Non lo condivido"	*"Capisco il tuo punto di vista ma io penso…"*	*"Quello che dici è vero, ma è anche vero che …"*	*"Non mi aspettavo che tu…"*	*"Le cose non stanno proprio come dici te"*
Flashcards 3. Motivare me stesso				
"Posso farcela"	*"Continua così!"*	*"Non arrenderti!"*	*"Mi sto impegnando!"*	*"Altre volte ce l'ho fatta!"*
"Ce la puoi fare!"	*"Non mollare!"*	*"Posso cambiare!"*	*"In altre situazioni ci sono riuscito!"*	*"E' meglio fare qualcosa, anche piccola, che non fare niente"*
Flashcards 4. Essere più in contatto con i miei bisogni				
"Qual è il mio obiettivo in questa situazione?"	*"Quali sono i miei bisogni in questa situazione?"*	*"Cosa vorrei ottenere con il mio comportamento?"*	*"E' davvero fondamentale che io raggiunga il mio obiettivo alla perfezione?"*	*"Come mi sento in questa situazione? Quale emozione sto provando?"*
"Se penso così, riesco a raggiungere veramente i miei obiettivi?"	*"Quali sono le conseguenze su me stesso se credo a questo pensiero?*	*"Quali sono le conseguenze su me stesso se <u>non</u> do importanza a questo pensiero?"*	*"Ci sono delle cose positive che ho fatto in questa situazione? Posso provare a vedere le cose positive che ho fatto?"*	*"In quali altri contesti ho avuto questo pensiero?"*

SCHEDA: ESPERIMENTI ED ESPOSIZIONI A SITUAZIONI SOCIALI

Provare prima con role playing in studio o con il terapeuta. Prima di iniziare prova ad appuntare i pensieri automatici negativi che arrivano alla mente sulla situazione da affrontare, individua la probabilità con cui stai temendo certe possibili conseguenze negative. Dopo l'esperimento rivaluta la probabilità, formula pensieri alternativi.

1. Per strada impegnati a guardare le persone fisso negli occhi e prova a non smettere finché loro distolgono lo sguardo, poi fai un leggero sorriso in modo tranquillo ed amichevole dicendo "Buongiorno"
2. Recati ad una bancarella e mercanteggia sul prezzo: a. Facendo delle offerte, b. Chiedendo se si può abbassarlo
3. Entra dal parrucchiere, chiedi un appuntamento, prenota, dopo 15 minuti, torna, disdici ed esci salutando cordialmente
4. In un bar chiede acqua del rubinetto, bevi ed esci senza pagare
5. Inizia una conversazione sul tempo, sui mezzi pubblici etc con persone alla fermata del bus
6. Chiedi informazioni stradali in un negozio
7. Entra in un negozio, chiedi alla commessa di farti mostrare varie tipologie di capi, chiedile dei consigli, prezzo, caratteristiche, provali, poi esci senza acquistare niente.
8. Paga un caffè con una banconota da 50 euro

MODULO “PREVENZIONE DELLE RICADUTE”

SEDUTA 30

SCHEDA: I SEGNALI DI ALLARME

Come possiamo sapere se sta per venire un temporale? Forse possiamo metterci in ascolto dei tuoni, rimanere ad osservare per un po' il cielo, notare se è scuro o ci sono nuvole grigie. Se non vogliamo farci cogliere impreparati da un temporale, allora possiamo decidere di rientrare a casa, chiudere le finestre, mettere al riparo i panni…

In un modo molto simile, se acquisisco più consapevolezza dei primi segnali di allarme, posso prevenire momenti di più forte ansia, stress, depressione e quindi evitare ricadute. Ciascuno di noi ha i propri segnali specifici, anche se alcuni posso risultare comuni a molti. Una volta che sono diventato più consapevole dei miei segnali di allarme, il secondo passo e controllarli regolarmente. Non è molto utile che tu sia consapevole dei segnali ma non li monitori con regolarità e continui a vivere le giornate senza prestarvi attenzione.

SCHEDA: RICONOSCI I SEGNALI DI ALLARME

Compila un elenco dei segnali di allarme che più ti riguardano e porta questa scheda con te. Controlla questo elenco ogni cinque giorni durante la settimana. Chiedi alle persone che vivono con te e in cui ha fiducia di informarti quando notano nei tuoi comportamenti dei possibili segnali di allarme.

I MIEI COMPORTAMENTI DI ALLARME, COSA FACCIO, COME AGISCO	**I PENSIERI CHE MI PASSANO PER LA MENTE**
LE EMOZIONI CHE PROVO, COME MI SENTO	**COME AGISCO, MI COMPORTO CON LE ALTRE PERSONE**
COSA POSSONO NOTARE LE PERSONE CHE MI STANNO VICINO (PARENTI, AMICI)	**SITUAZIONI CHE FANNO SCATTARE IN ME EMOZIONI NEGATIVE E STRESS**