Development of executive functions as reflected in daily life behaviors in young adults at ultra-high risk for psychosis: associations with symptoms and functioning

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Abstract
There is a paucity of evidence on executive functions (EF) as reflected in daily life behaviors in individuals at ultra-high risk (UHR) for psychosis. This prospective follow-up study investigated the 1-year development in EF in UHR compared to healthy controls (HC) and how this change may relate to change in severity of clinical symptoms, social communication and functioning. UHR (N=132) and HC (N=66) were assessed with the Behaviour Rating Inventory of Executive Function–Adult version (BRIEF-A) self and informant report at baseline and 12-months follow-up comprising the Behavioral Regulation Index (BRI) and the Metacognition Index (MI). Additionally, data on depressive-, negative-, and attenuated psychotic symptoms and everyday social functioning was collected. The study found UHR to display large baseline impairments in EF in real life on both self-and informant reports. UHR and HC showed a significantly different development of EF over time with UHR displaying greater improvements in EF compared to HC. Change in clinical symptoms did not relate to improvements in EF, except for depressive symptoms negatively associating with the development of the MI. Improvements on the BRI and MI were significantly associated with improvements in social functioning. Findings suggest the potential of UHR individuals displaying a larger ongoing maturational development of daily life EF than HC that seems predominantly independent of development of clinical symptoms. If replicated, this supports a maturational trajectory of daily life EF in UHR that approaches, but do not reach, the level of HC and may indicate a window of opportunity for targeted remediation approaches.

Clinical-high risk; prodromal psychosis; at-risk mental state; executive function; BRIEF-A
1. Introduction

Individuals at ultra-high risk (UHR) for psychosis display substantial deficits in cognitive function\(^1\). Executive functions are central aspects of cognition that encompasses a top-down regulation of cognitive processes in the service of goal-directed, anticipated behavior\(^2,3\). Recent theories propose executive functions to consist of interrelated but distinct components, commonly described as the “unity and diversity” framework of executive functions\(^4\). Executive dysfunctions are proposed to be key cognitive deficits in patients with schizophrenia\(^5,6\), and they relate to functional outcome\(^7,8\). Regarding individuals at ultra-high risk for psychosis, the central role of executive functioning is reflected in the cross-sectional\(^9\) and longitudinal findings\(^10,11\) of executive dysfunction relating to social- and role impairments. While prominent in psychosis spectrum disorders, executive dysfunction has also been reported in other psychiatric disorders such as bipolar disorder\(^12,13\), borderline personality disorder\(^14\), attention deficit hyperactivity disorder\(^15\), and autism spectrum disorders\(^16\).

Research has identified the development of executive functions to begin as early as 12 months of age\(^17\) and exhibit a rapid development during childhood and adolescence. Additionally, different aspects of executive functions are found to display different developmental trajectories\(^17–19\): e.g., while inhibition and attentional control may emerge and develop in early childhood, goal-setting and flexibility may have a continued development into adolescence\(^20\). The neurotypical development of executive functions is supposedly a continued process up until the mid-twenties when brain development is considered to be complete\(^21\). Brain injury or psychopathology may, however, interfere with the typical developmental process.

Executive functions are primarily assessed using performance-based neuropsychological tests that provide a standardized, objective estimate of cognitive functions. While performance-based tests may tap executive functions in specific and explicit ways, they may however, be challenged by limited ecological relevance, as they do not capture how the cognitive deficits may present themselves in the individuals’ daily life\(^22–24\). Furthermore, it has been argued that performance- and questionnaire-based ratings may capture different aspects of executive functioning with questionnaires assessing executive dysfunction at a more behavioral than cognitive level\(^25\). This points to a need for supplementing the
performance-based cognitive tests with additional standardized measures elucidating on daily life difficulties related to executive dysfunction. The Behaviour Rating Inventory of Executive Function (BRIEF) is a commonly used informant- and self-report measure assessing activities of daily living implicating behaviors associated with executive dysfunction. Modest literature is available on the use of the BRIEF questionnaire in patients with schizophrenia, but the few studies conducted support the utility of the BRIEF to detect executive dysfunction in schizophrenia spectrum disorders. To the best of our knowledge, only one study has evaluated the use of the BRIEF in a UHR population, finding a substantial proportion of the children and adolescent-based UHR sample to display elevated scores on the BRIEF Global Executive Composite (GEC) overall index, Behavioural Regulation Index (BRI), Metacognition Index (MI), and all nine subscales, based on published norms. Additionally, the study found that the BRIEF Behavioral Regulation Index related to poor social- and role functioning, while the BRIEF BRI and MI scores were largely unrelated to severity of attenuated psychotic- and negative symptoms. This pilot study did, however, suffer the shortcomings of a small sample size (N=31), lacking a healthy control group, and being cross-sectional. Little is therefore known about daily life executive dysfunctions in young adults at UHR for psychosis, and whether their developmental trajectories of executive functions parallel those of healthy controls in a late maturational phase. To extend the current knowledge on daily life executive dysfunction in the UHR population, this study aimed to investigate the severity of everyday executive dysfunctions and in particular the developmental changes over time in executive dysfunctions in young adults at UHR for psychosis compared to healthy controls (HC). Additionally, the study aimed to elucidate on the relationship between the development of executive functioning, and baseline and change scores in clinical symptoms and self-report daily social functioning in UHR individuals.

1.1. Hypotheses

Based on previous literature, we hypothesized that UHR individuals would show more severe impairments of executive dysfunction on the index scores and subscales scores of the Behaviour Rating Inventory of Executive Function Adult version (BRIEF-A) compared to HC at baseline. Furthermore, we hypothesized that UHR individuals would show less improvements in executive functioning than HC over the course of 12-months, indicating a
developmental lag in this late maturation phase of executive function development in UHR. Lastly, we hypothesized that changes on the executive dysfunction indices would associate significantly with changes in social functioning but be unrelated to symptoms in UHR.

2. Method

The data was collected as part of a randomized clinical trial (RCT) examining the effect of cognitive remediation compared to treatment as usual (TAU) in individuals at UHR for psychosis; with this study comprising exploratory, secondary analyses to the RCT. The cognitive remediation in the RCT followed a 20-sessions protocol that targeted neuro- and social cognition. Participants underwent weekly, group-based cognitive training and were additionally instructed to do one-hour per week of home-based neurocognitive training. The neurocognitive training was tailored to target the primary areas of deficit for each participant. Assessments were carried out at baseline, prior to randomization, and at post-intervention (6-months) and at 12-months follow-up.

The RCT did not find any significant difference between the intervention and TAU groups on the BRIEF-A indices at baseline or follow-up (effect sizes in the range 0.2 – 0.3)\textsuperscript{31}. Additionally, we investigated potential between group differences in change scores (baseline to 12-months) on the BRIEF-A self- and informant report indices finding no significant differences between the groups (all p-values in the range .26 - .79, effect sizes in the range 0.1 – 0.2). Data from the total UHR sample was therefore used in the analyses. Participants were recruited from psychiatric in- and outpatient facilities in the greater Copenhagen area, Denmark from April 2014 to December 2017. The trial protocol was approved by the Committee on Health Research Ethics of the Capital Region Denmark (study: H-6-2013-015). Participants provided written informed consent prior to inclusion in the study.

2.1. Participants

The baseline sample consisted of 132 help-seeking individuals aged 18 to 40 years meeting one or more UHR criteria according to the Comprehensive Assessment of At-Risk Mental States\textsuperscript{32}: attenuated psychotic symptom group; brief limited intermittent psychotic symptoms group; and/or trait and vulnerability group along with a significant drop in functioning or sustained low functioning for the past year. Patients were excluded if they:
had a history of a psychotic episode of ≥ one week duration; experienced psychiatric symptoms explained by a physical illness with psychotropic effect (e.g. delirium) or acute intoxication (e.g. cannabis use); had a diagnosis of a serious developmental disorder (e.g., Asperger’s syndrome or mental retardation, i.e. IQ <70); or currently received methylphenidate.

A total of 66 matched HC’s were recruited from the community by advertising on a webpage, or via ads at local educational institutions. HC did not meet criteria for any DSM-IV disorder and did not have a first degree relative with a psychotic disorder currently or previously. The HC were matched to patients (2:1) on gender, age (+/- 2 years), ethnicity, and parental socioeconomic status.

2.2. Assessments

2.2.1. Cognitive assessment

The BRIEF-A\textsuperscript{33} is a 75-item questionnaire capturing executive functioning in daily life. Each of the 75 items can be rated in terms of frequency with the scores 1 (never), 2 (sometimes), and 3 (often). The BRIEF-A assesses the nine aspects of executive functions: Inhibit, Shift, Emotional Control, Self-Monitoring, Initiate, Working Memory, Plan/Organize, Task Monitoring, and Organization of Materials. Based on the nine subscale scores, two indices scores; the Behavioral Regulation Index (BRI) composed of Inhibition, Shift, Emotional Control, and Self-Monitoring subscale, and the Metacognition Index (MI) composed of Initiate, Working Memory, Plan/Organize, Task Monitoring, and Organization of Materials subscale be extracted, along with a Global Executive Composite (GEC) composed of the BRI and MI scores. The BRIEF-A has a self-report and an informant-report version that each take approximately 15 minutes to complete. T-scores can be extracted from the BRIEF-A raw scores based on comparison with an American normative sample. The BRIEF-A raw scores were, however, used in the current analyses due to the presence of a matched healthy control sample as there are no Danish norms available. Higher scores on the BRIEF-A reflect a greater degree of executive dysfunction. The BRIEF-A has proven good reliability with moderate inter-rater reliability correlations between self-report and informant ratings, moderate to high test-retest correlations for the self-report and informant ratings\textsuperscript{33}. Additionally, concurrent validity of the BRIEF-A has been established with the BRIEF-A
indexes correlating moderately to strongly with other measures of executive-/frontal lobe dysfunctions: the Frontal Systems Behavior Scale (FrSBe)\textsuperscript{34} and the Dysexecutive Index (DEX)\textsuperscript{33,35}.

Current IQ was estimated using the four subtests from the Third version of the Danish Weschler Adult Intelligence Scale (WAIS-III); Vocabulary, Similarities, Block Design, and Matrix reasoning\textsuperscript{36}.

2.2.2. Clinical and functional assessments
Level of attenuated psychotic symptoms was assessed with the Comprehensive Assessment of At-Risk Mental States (CAARMS)\textsuperscript{32} composite score; negative symptoms with the Scale for the Assessment of Negative Symptoms (SANS)\textsuperscript{37}; and depressive symptoms with the Montgomery-Åsberg Depression Rating Scale (MADRS)\textsuperscript{38}. Social functioning was indexed with the Social Responsiveness Scale, Adult version (SRS-A), total score\textsuperscript{39,40}. The SRS-A is a self-report measure of social impairments, detecting subclinical autistic social-communication traits. It contains 65 items rated on a Likert scale (0-3) generating a total score of a maximum of 195. The SRS was originally validated in autism spectrum disorders, but subsequently administered to subjects with non-autistic disorders including patients with psychosis and individuals at UHR for psychosis\textsuperscript{41–45}. The SRS has proven initial concurrent validity in UHR samples\textsuperscript{44,46}.

The clinical assessments were conducted by experienced psychologists or medical doctors with extensive training in using the assessment instruments.

2.3. Statistical analysis
All analyses were performed using SPSS version 25.0. Descriptive statistics were reported as means and standard deviations. Chi-square tests and analyses of variance (ANOervas) were used to compare the group attending 12-months follow-up assessment with those not attending 12-months assessment. ANOervas were computed to investigate potential group-differences on the BRIEF-A subscales and index scores at baseline between UHR and HC. Paired t-tests were conducted to compare BRIEF-A index scores at baseline and 12-months follow-up in the UHR and HC group, respectively. Linear mixed models with repeated measurements and an unstructured covariance matrix assessing the interaction term...
between time and intervention were run to investigate changes over time (12-months) on the BRIEF-A indices (GEC, BRI, and MI) between the UHR and HC groups. Univariate linear regression analyses were performed to investigate the potential associations between change on the BRIEF-A BRI, and MI as dependent variables and the change on the clinical and symptom variables of CAARMS, SANS, MADRS, and SRS-A (predictor variables). Furthermore, the regression analyses were conducted to investigate the associations between the sociodemographic variables of age, sex, and estimated IQ and the change scores on the BRIEF-A BRI and MI. Significance levels were set to \( p < .05 \).

3. Results

A total of 146 UHR participants were enrolled in the RCT and randomized to either cognitive remediation as an add on to treatment as usual (CR + TAU, \( N=73 \)) or TAU (\( N=73 \)). Of the 73 participants allocated to the experimental intervention group, 51 received the cognitive remediation intervention. Protocol adherence was low in the study, and participants in the intervention group had an average of 11.9 (SD=16.4) hours of neurocognitive training out of the target number of 40 training hours. The baseline sample included in this study consisted of 132 UHR participants that completed the BRIEF-A self-report, and 103 that completed the BRIEF-A informant report. At 12-months follow-up, 84 UHR individuals completed the BRIEF-A self-report, and 41 the BRIEF-A informant rating. Reasons for not attending follow-up were primarily participants being non-contactable or refused further contact with the study. Additionally, in some few cases, the patients moved away or developed psychosis as being the reasons for not attending 12-months follow-up. The UHR sample had a mean age of 24 (SD= 4.26), and 55% were females. Most of the participants (76%) fulfilled the CAARMS criteria of attenuated psychotic symptoms (APS). Attrition analyses found that participants completing the BRIEF-A at 12-months follow-up differed from those not completing follow-up by being older, having higher estimated IQ, and longer education, but they did not differ significantly on the baseline BRIEF-A indices or symptom ratings. At baseline, a total of 66 HC completed the BRIEF-A self-report, and 51 the BRIEF-A informant report. At 12-months follow-up, 66 HC completed the BRIEF-A self-report, and 60 the BRIEF-A informant report. The UHR and HCs differed significantly on the baseline variables of estimated IQ and years of education, with the HCs displaying higher IQ and having more years of education. Table 1 displays sample demographics and clinical characteristics.
3.1. Results

3.1.1. Between-group differences on the BRIEF-A
As displayed in figure 1 and 2, the UHR individuals showed elevated baseline raw scores on the three indexes GEC, BRI, and MI all of the nine BRIEF-A subscale items compared to the HC (all \( p \)-values <.001 with large effect sizes: Cohen’s \( d \) in the range .99 - 2.57 (table 2) on BRIEF-A self-report, and Cohens \( d \) in the range .70 - 1.84 on the BRIEF-A informant-report). ANCOVAS were run to with age and sex as covariates in the models. Including these covariates in the between-group analyses did, however, not change the finding of highly significant differences between UHR and HCs on the BRIEF-A subscale and index scores (all \( p \)-values <.001).

3.1.2. Changes on BRIEF-A indices over the course of 12-months in UHR and HC
The mixed models’ analyses (fig. 3) revealed significant time by group interaction between the UHR and HC group with the UHR group showing greater decrease over time on the BRIEF-A GEC, BRI, and MI self- and informant-reports (all \( p \)-values in the range <.001 – .014). Scores on the three BRIEF-A self-report indices significantly decreased over time in both groups (lower score reflects less executive dysfunction), but the decrease was greatest in the UHR group (table 3). To control for the findings reflecting an effect of the cognitive remediation in the RCT, we re-ran the mixed models’ analyses comparing only the treatment as usual (TAU) group with the healthy control group. These analyses still revealed significant time by group interaction between the UHR (TAU) and HC group (all \( p \)-values in the range<.001 – .04), with the UHR group showing greater decrease over time on all the BRIEF-A indices self- and informant-reports.

3.1.3. The relationship between change in BRIEF-A indexes and change in clinical and symptom variables in UHR
As depicted in table 4, regression analyses revealed change scores on the SRS-A to positively associate with change on the BRI and MI; greater change in severity of social functioning deficits associated with greater change in severity of executive dysfunction. Change scores on the MADRS was positively related to the MI, that is; improvements in depressive symptoms resulted in improvements on the metacognition index. Change scores on attenuated psychotic and negative symptoms did not relate to BRI or MI change scores.
Additional regression analyses were conducted to evaluate whether the baseline demographic variables of age and sex along with estimated IQ related to change scores on the BRI and MI self-report indices. We did not find these variables to be significantly associated with BRIEF-A change scores. Furthermore, we conducted regression analyses between the baseline measures of the BRIEF-A indices and the symptom measures. These analyses revealed significant baseline associations between the MADRS and the self-report measures of BRIEF-A GEC, BRI, and MI along with the SANS also associating significantly with the latter measure. CAARMS did not correlate with any of the BRIEF-A indices at baseline.

4. Discussion

As expected, we found the UHR individuals to display significant deficits on all self- and informant reports of the BRIEF-A executive functioning indices and subscales with large effect sizes. The substantial impairments on both self- and informant-reports were in the executive functions of shift, emotional control, and initiate (effect sizes in the range 1.62 – 2.57). This partly corroborates the preliminary findings of Niendam et al. that found shift and initiate to be among the mostly impaired domains of executive function in UHR adolescents, albeit the largest impairments were found on the working memory subscale. Likewise, Kumbahni et al. reported the largest impairments on the BRIEF-A subscales of shift and initiate in patients with schizophrenia. In general, these findings indicate that flexibility and initiation may be some of the primary areas of deficits in daily life executive function in patients with psychosis spectrum disorders. Additionally, our findings add weight to the potential utility of the BRIEF-A as a quick and easy administrable screening tool for daily life executive dysfunction in UHR individuals.

Furthermore, we investigated the 12-months change in daily life executive dysfunction in UHR individuals compared to HC. We hypothesized that UHR individuals would show less improvements in executive functioning than HC over the course of 12-months. We found that both groups displayed significant improvements in executive functions over time, indicating a continued maturation of daily life executive functions in both the patients and healthy controls in this rather late maturational phase (mean age 24 years). However, contrasting our hypothesis, the UHR group showed greater positive change over the course of 12-months. This suggest that the UHR group have a larger ongoing cognitive development
in this late maturational phase, which seem in line with the neurodevelopmental and not
the neurodegenerative model of psychosis spectrum disorders\(^\text{47,48}\). Speculating, contrasting
a deterioration trajectory, the findings may indicate UHR individuals to display a partial
catch-up of development of daily life executive functions during a late maturational phase.
This is, however, an incomplete developmental catch-up, as the UHR individuals do not
reach the same level of daily life executive functions as the HC. This brain plasticity
potential\(^\text{49}\) suggests a window of opportunity for targeted interventions such as cognitive
remediation in order to facilitate the development of cognitive functions in UHR. While this
represents one interpretation of the study findings, the UHR individuals observed
improvements in daily life executive functions over time could alternatively be interpreted
as reflecting a regression to the mean, with the low baseline performance of the UHR group
stressing this hypothesis. Additionally, we cannot exclude the possibility of the cognitive
remediation in the RCT having yielded subtle effects on executive functions, albeit such a
possible effect was not measurable in the RCT (no post-treatment effect was found on the
BRIEF-A indices). Finally, it could be argued that the findings of UHR individuals showing
greater improvements in executive functions than HC is caused by an ascertainment bias,
although the enrollment of trial participants was purely based on whether eligible
participants fulfilled CAARMS criteria or not with no additional selection based on level of
cognitive function. We therefore believe our study sample to be representative of the UHR
population.

We did not find any demographic variables predicting change on the BRIEF-A indices
indicating that improvement on the BRIEF-A is independent of age, gender, and IQ. Finally,
we hypothesized that change scores on the BRIEF-A indices would be unrelated to changes
in symptoms but related to change in social functioning. Partly corroborating our
hypothesis, we found the BRIEF-A indices to be unrelated to changes in attenuated
psychotic- and negative symptoms, while we did find change in depressive symptoms to be
related to change on the metacognition index; that is, greater change in level of depressive
symptoms associated with greater change in severity of executive dysfunctions. This
supports previous literature suggesting the BRIEF-A index scores in general being unrelated
to positive and negative symptoms in UHR\(^\text{30}\). While indicating that positive and negative
symptoms are unrelated to executive function development, this finding does, however,
suggest that aspects of cognitive maturation may associate with change in depressive symptoms. The suggested link between change in levels of depressive symptoms and levels of daily life executive dysfunction mirrors cross-sectional findings from patients with depression displaying substantial impairments in multiple aspects of executive function\textsuperscript{50}. Moreover, depressive ruminations have been linked to decreased mental flexibility\textsuperscript{51}. The reversed interpretation of the observed relationship may, however, be that improvements in executive functions influence improvements in depressive symptoms, which would imply the need for applying targeted remediation of executive dysfunctions when aiming at alleviating depressive symptoms in UHR. The associations between changes in negative and depressive symptoms and changes on the BRI were non-significant but approached a trend level. In theory, improvements in the behavioral aspects of executive functions such as e.g. inhibition and shifting may associate with improved depression and negative symptoms severity but difficult to observe, because differences, i.e. change scores, may have lower reliability as they are based on two measurements.

Finally, we found a highly significant relationship between change on the BRIEF-A indices and change in self-report social communication and functioning with the social functioning measure explaining 33 and 25\% of the variance on the Behavioural Regulation Index and Metacognition Index, respectively, or vice versa. This observed relationship between everyday executive dysfunctions and poorer functioning is in keeping with cross-sectional findings from patients with schizophrenia\textsuperscript{27}. Furthermore, in a previous study in UHR children and adolescents, Niendam et al. found the BRIEF behavioral regulation index to relate cross-sectionally to social- and role functioning\textsuperscript{30}. Our study extends this suggested link between aspects of daily life executive functions and social functioning in UHR by indicating a longitudinal link between improvement of executive dysfunction and that of social functioning in adults at UHR for psychosis. Hence, executive functions may be important to modulate daily social functioning, or alternatively social functioning may moderate executive functions as suggested in a previous study of adults with a serious mental illness, predominantly a schizophrenia spectrum disorder\textsuperscript{52}. This potential important relationship between executive dysfunction and functional impairments indicate daily life executive dysfunction to be a central target of remediation approaches, when aiming at improving the functional prognosis of UHR individuals.
Methodological considerations

Strengths of the study comprise the longitudinal study with the hitherto largest UHR sample to report on an ecological assessment measure of executive function including a matched healthy control sample. Limiting the study is that the 1-year follow-up may be regarded as a short follow-up period, which limits the sensitivity to detect age related cognitive development. Future studies on the subject are therefore warranted with a longer follow-up interval. Notwithstanding, this rather short-term follow-up, we did find significant developmental differences in executive dysfunction in the UHR group compared to HC. Additionally, while it is common to investigate the relationship between BRIEF scores and social functioning in diverse psychiatric disorders, it holds the potential of an item overlap on the BRIEF and social functioning scales that may inflate the association between these domains. Finally, the study participants were part of an RCT evaluating the effect of cognitive remediation. It therefore cannot be ruled out that the intervention in the RCT may have had a small influence on the study findings (effect sizes on change scores in the range 0.1 – 0.2 between the CR and TAU group), even though we did not find any significant differences between the intervention and TAU group at 6- and 12-months follow-up, nor any significant differences in change scores between the group (between baseline and 12-months follow-up). Furthermore, all participants were in receipt of supportive, out-patient treatment which leaves open the possibility of treatment per se having an influence on the findings. This stresses the need to conduct studies on development of executive functions in naturalistic follow-up study designs.

Conclusion

In conclusion, our findings suggest young adults at UHR for psychosis to show an ongoing maturational trajectory of daily life executive functions that seems largely independent of clinical symptoms at baseline. Development of metacognitive aspects of daily life executive functions may, however, be associated with improvements in depressive symptoms. Also, our study adds evidence of a distinct link between daily life executive dysfunction and social functioning in UHR. Lastly, our study reports utility of the BRIEF-A informant and self-report questionnaires to detect daily life executive dysfunctions in UHR individuals. In general, the findings indicate the existence of a window of opportunity for clinical interventions targeting daily life executive dysfunctions in the UHR population.
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Figure legends

Figure 1. Group differences on the BRIEF-A indices in Ultra-High Risk (UHR) individuals and Healthy Controls (HC) at baseline.

Note: GEC: Global Executive Composite; BRI: Behavioral Regulation Index; MI: Metacognition Index.

Figure 2. Group differences on the BRIEF-A subscales in Ultra-High Risk (UHR) individuals and Healthy Controls (HC) at baseline.

Figure 3. 12-months change on the BRIEF-A index scores between Ultra-High Risk (UHR) individuals and Healthy Controls (HC).

Note: GEC: Global Executive Composite; BRI: Behavioral Regulation Index; MI: Metacognition Index.

T0=baseline, T1=12-months follow-up.
Table 1. Clinical baseline characteristics of ultra-high risk participants (UHR) and healthy controls (HC).

| Variable                      | N (%)      |
|-------------------------------|------------|
|                               | UHR (N=132) | HC (N=66)   |
| Female                        | 73 (55.3%)  | 37 (56.1%)  |
| CAARMS status                 |            |            |
| - APS                         | 101 (76.5%) | -          |
| - BLIPS                       | 0 (0%)      | -          |
| - Trait/state                 | 1 (0.8%)    | -          |
| - APS + trait/state           | 27 (20.5%)  | -          |
| - APS + BLIPS                 | 3 (2.2%)    | -          |
| Medication*                   |            |            |
| - Antipsychotics              | 40 (30.3%)  | -          |
| - Antidepressant              | 43 (32.6%)  | -          |
| - Mood stabilizers            | 5 (3.8%)    | -          |
| - Benzodiazepines             | 9 (6.8%)    | -          |
| Mean (SD)                     |            |            |
| Age                           | 24.14 (4.26)| 24.47 (3.62)|
| Years of education            | 14.65 (2.71)| 16.16 (2.28)|
| Estimated IQ (WAIS III)       | 103.23 (12.28)| 111.89 (13.39)|
| CAARMS composite              | 49.29 (13.74) Range: 15-85 | - |
| SANS total                    | 1.53 (0.80) Range: 0-4 | - |
| MADRS total                   | 15.17 (6.90) Range: 3-34 | - |
| SRS-A                         | 74.05 (27.91) Range: 7-137 | - |

*Patients would be taking one or a combination of the listed compounds.

CAARMS: Comprehensive assessment of at-risk mental states; APS: Attenuated Psychotic Symptom; BLIPS: Brief Limited Intermittent Psychotic Symptom; CAARMS: Comprehensive Assessment of At-Risk Mental State; SANS: Scale for the Assessment of Negative Symptoms; MADRS: Montgomery-Åberg Depression Rating Scale; SRS-A: Social Responsiveness Scale Adult version.
Table 2. Effect sizes (Cohen’s d) on the differences between Ultra-High Risk (UHR) individuals and Healthy Controls (HC) on the self-report and informant ratings of the BRIEF-A indices and subscales at baseline. The between-group differences are illustrated in figure 1 and 2.

| Variable                  | Self-report Cohen’s d | Informant Ratings Cohen’s d |
|---------------------------|-----------------------|-----------------------------|
| GEC                       | 2.42                  | 1.84                        |
| BRI                       | 2.33                  | 1.82                        |
| MI                        | 2.06                  | 1.36                        |
| Inhibit                   | 1.29                  | 0.83                        |
| Shift                     | 2.57                  | 1.79                        |
| Emotional Control         | 2.33                  | 1.94                        |
| Self-monitoring           | 1.07                  | 0.76                        |
| Initiate                  | 2.16                  | 1.62                        |
| Working Memory            | 1.20                  | 1.38                        |
| Plan/Organize             | 1.89                  | 1.43                        |
| Task Monitoring           | 1.28                  | 0.88                        |
| Organization of Materials | 0.99                  | 0.70                        |

Note: GEC: Global Executive Composite BRI: Behavioral Regulation Index; MI: Metacognition Index
Table 3. Scores on BRIEF-A indices at baseline and 12-months in Ultra-High Risk (UHR) individuals and Healthy Controls (HC).

|                  | Possible score range | UHR (N=132 at baseline, N=84 at 12M) Mean (SD) | p-value | Observed score range | HC (N=66 at baseline and 12M) Mean (SD) | p-value | Observed score range |
|------------------|----------------------|-----------------------------------------------|---------|----------------------|----------------------------------------|---------|----------------------|
| **BRIEF-A**      |                      |                                               |         |                      |                                        |         |                      |
| **GEC**          | 70-210               | 137.45 (22.20) 123.92 (23.86)                  | <.001   | 93-187 78-186        | 93.79 (15.69) 88.53 (14.23)            | <.001   | 70-132 70-133        |
| **Baseline**     |                      |                                               |         |                      |                                        |         |                      |
| **12-months**    |                      |                                               |         |                      |                                        |         |                      |
| **BRIEF-A**      | 30-90                | 56.86 (10.96) 50.52 (11.21)                    | <.001   | 37-84 31-77          | 37.50 (6.10) 35.85 (6.00)              | .006    | 30-52 30-55          |
| **BRI**          |                      |                                               |         |                      |                                        |         |                      |
| **Baseline**     |                      |                                               |         |                      |                                        |         |                      |
| **12-months**    |                      |                                               |         |                      |                                        |         |                      |
| **BRIEF-A**      | 40-120               | 80.60 (14.17) 73.34 (14.94)                    | <.001   | 45-109 46-111        | 56.29 (10.49) 52.68 (9.26)             | <.001   | 40-81 40-79          |
| **MI**           |                      |                                               |         |                      |                                        |         |                      |
| **Baseline**     |                      |                                               |         |                      |                                        |         |                      |
| **12-months**    |                      |                                               |         |                      |                                        |         |                      |

* Paired t-tests were conducted to compare UHR and HC on the BRIEF-A indices at baseline and 12-months follow-up.

Note: BRIEF-A: Behaviour Rating Inventory of Executive Function Adult version; GEC: Global Executive Composite; BRI: Behavioral Regulation Index; MI: Metacognition Index.
Table 4. Linear regression analyses of change scores on symptoms and functioning variables predicting changes on the BRIEF-A self-report indices in UHR individuals.

|                  | Univariable |          |        |        |
|------------------|-------------|----------|--------|--------|
|                  | β [95% CI]  | t        | p      | R²     |
| **BRIEF-A BRI**  |             |          |        |        |
| Change CAARMS    | .061 [-.031 – .153] | 1.321   | .191   |        |
| Change SANS      | 2.709 [-.391 – 5.809] | 1.741   | .086   |        |
| Change MADRS     | .212 [-.028 – .451] | 1.761   | .082   |        |
| Change SRS-A     | .241 [.162 – .319] | 6.108   | <.001  | .326   |
| **BRIEF-A MI**   |             |          |        |        |
| Change CAARMS    | .103 [-.025 – .232] | 1.608   | .112   |        |
| Change SANS      | 3.564 [-.742 – 7.870] | 1.649   | .103   |        |
| Change MADRS     | .357 [.025 – .689] | 2.143   | .035   | .045   |
| Change SRS-A     | .297 [.179 – .415] | 5.014   | <.001  | .244   |

Predictors that are significant at the P≤.05 level are given in bold.

Note: BRI: Behavioral Regulation Index; MI: Metacognition Index; CAARMS: Comprehensive Assessment of At-Risk Mental States; SANS: Scale for the Assessment of Negative Symptoms; MADRS: Montgomery-Åsberg Depression Rating Scale; SRS-A: Social Responsiveness Scale Adult Version
