The *p* Factor Outweighs the Specific Internalizing Factor in Predicting Recurrences of Adolescent Depression

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Abstract

Background: The early prediction of adolescent depression recurrence poses a

significant challenge in the field. This study aims to investigate and compare the

abilities of two psychopathology factors, namely the general psychopathology factor

(p) and the specific internalizing factor, in predicting depression recurrence over a

2-year course, as well as identifying remitted depressed adolescents from healthy

adolescents. Longitudinal changes of these two factors in different trajectory groups

were also tracked to examine their sensitivity to sustained remission and relapse.

Methods: We included 255 baseline-remitted depressed adolescents and a healthy

control group (n=255) matched in age, sex, and race, sourced from the Adolescent

Brain Cognitive Development Study. The Linear Mixed Model was employed to

differentiate between healthy controls and remitted depressed adolescents, predict

depression recurrence, and track longitudinal changes over a subsequent 2-year course

using the p factor and the specific internalizing factor respectively.

Results: The p factor not only effectively discriminated between remitted depressed

adolescents and healthy controls, but also robustly predicted the depression recurrence

over a subsequent 2-year course. The specific internalizing factor could only differentiate remitted depressed adolescents from healthy controls. Additionally, a noteworthy longitudinal decline of the p factor in the sustained-remission group was observed.

Conclusions: Psychopathology factors serve as the inherent and enduring measurement of long-term mental health aberrations. Longitudinal results indicate that the p factor is more sensitive to respond to sustained remission than the internalizing factor. The ability of the overall p factor to anticipate depression relapse, unlike the specific internalizing factor, suggests clinical interventions should monitor and mitigate the coincident symptoms across all dimensions to preempt relapse of adolescent depression, rather than an exclusive focus on internalizing symptoms.

Key words: depression, recurrence, p factor, psychopathology factor, adolescence

Introduction

Depressive disorders, as an umbrella term, ranging from major depression to atypical depression to dysthymia, is one of the most serious mental health concerns and leading contributors of the global health-related burden [1–4]. Depression is more common in adolescents compared to prepubertal children [5]. Adolescents are particularly at risk for developing depression, with estimates of major depressive disorder ranging from 8% to 20% occurring before the age of 18 [5–9]. In addition, depression frequently co-occurs with anxiety in adolescents, occurring both simultaneously and sequentially, and the emergence of depression often heightens the risk of developing anxiety over the course of time [10].

Notably, depression that begins in adolescence often presents as a recurring condition, with a higher risk of recurrence linked to an older onset age [11]. The recurrence rate ranges from 20% to 54%, and this form of depression tends to be associated with more severe outcomes when compared to depression that begins in adulthood [12–15]. This recurrent pattern can lead to substantial impairments across crucial psychosocial domains, with effects that may persist into adulthood [16–19]. However, there is no permanent treatment solution for depressive disorders due to their relapsing-remitting nature. Individuals experience a relapse after the treatment of their first episode of depression may tend to recur with greater severity and with lessening responsivity to conventional treatments [20]. Therefore, there is a pressing need for a deeper

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understanding of early-stage markers that can predict the later development of depression recurrence [18,21–23]. Monitoring changes in markers can help individuals and healthcare professionals become aware of early warning signs of a potential relapse. This awareness allows them to implement tailored interventions, enhancing the effectiveness of relapse prevention and even circumventing the onset of initial treatment resistance. In another word, this approach may heighten the prospect of sustained recovery and prevent the intensification of depression during the later stages of adulthood [24].

Prior research has identified various risk factors for depression recurrence in remitted patients, including a higher number of preceding episodes, higher levels of residual symptoms, lower levels of positive refocusing [25], presence of anxiety [26], longer symptom duration, higher symptom severity, and earlier age of onset [27]. While previous studies have made valuable contributions to our understanding of predictors for depression recurrence, a shared limitation is their focus on syndrome-specific indicators such as the Patient Health Questionnaire-9 (PHQ-9) or the Hamilton Depression Rating Scale (HAMD), designed to detect specific signs or symptoms of depression. However, considering the latent intricate etiology of depression, which encompasses interplays of a broader spectrum of symptoms across multiple dimensions and a high degree of comorbidity with other disorders like externalizing disorders that can significantly impact the trajectory of depression and increase the

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risk of further recurrence [28], the incorporation of multi-dimensional psychopathology becomes a necessity. Therefore, using the indicators that encompasses information from symptoms across multiple dimensions could potentially yield a more accurate prediction of depression recurrence. Recent advancements in psychopathology studies have indicated an overall latent factor, the general psychopathology factor, that may further provide an explanation for these pathways [29].

The general psychopathology factor, commonly referred to as p factor, accounts for common variance across a wide range of symptoms spanning multiple diagnostic domains [30]. It embodies shared aspects among various mental disorders [31], and directly impacts symptoms across distinct dimensions [32]. Previous research has identified the presence of the p factor in adolescents and suggested that investigating this factor could enhance our understanding of the etiology, risk, and correlates of psychopathology in this age group [31,33,34]. For instance, Moore et al. [35] identified the overall p factor through a bifactor model using Child Behavior Checklist (CBCL) from the Adolescent Brain Cognitive Development (ABCD) Study. In this bifactor model, three lower-level factors in distinct domains (Internalizing, Attention Deficit Hyperactivity Disorder (ADHD), and Conduct Problems) have also been identified, that accounts for shared variance within a specific dimension, from which the overall variance (p) across all dimensions has been subtracted.

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Indeed, compared to previously identified predictors such as diagnostic comorbidity at baseline, a recent study suggested that p at baseline in adolescents with anxiety predicted long-term anxiety outcomes including more mental health disorders, poorer functioning, and greater impairment more effectively [36]. In addition, as compared to syndrome-specific psychopathology factors, another recent study has found that the p factor in adolescents may be more predictive of long-term adverse mental health outcomes, including diagnoses of depression and anxiety, psychological well-being, criminal activity, alcohol use, and educational attainment. This finding indicates that interventions should focus on addressing the co-occurrence of internalizing and externalizing symptoms to mitigate the long-term impact on individuals [33]. However, there is limited knowledge regarding the prognostic effect of the overall p factor or the specific lower-level internalizing factor to which depression is directly related, on the prediction of adolescent depression recurrences. Additionally, the comparative performance of these two factors in terms of their predictive ability in depression recurrence remains unknown. This information would be valuable in guiding interventions and improving the effectiveness of targeted treatments for depression in adolescents.

To fill this research gap, our study evaluated the capacity of the two factors—the p factor and the specific internalizing factor—all measured during a remitted state, to

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predict the recurrence of depression over a 2-year period, and to discriminate between depressed adolescents and their healthy counterparts. This was achieved by using two waves of clinical data collected at baseline and at a 2-year-follow-up from the ABCD Study. Simultaneously, we tracked the longitudinal change of each factor over 2 years to detect their sensitivity in response to either sustained remission or relapse. Our aim is to enhance our understanding of the underlying mechanisms involved in the recurrence of adolescent depression and provide valuable insights into effective intervention strategies for managing recurrent depression in adolescents.

Methods

Participants

Data for this study were derived from a large-scale, multi-site, and longitudinal study in the United States: the Adolescent Brain Cognitive Development (ABCD) Study® (Release 3.0, November 2020) [37]. This extensive dataset included comprehensive clinical, behavioral, cognitive, and multi-modal neuro-imaging data collected at four distinct timepoints (baseline, 1-year follow-up, 2-year follow-up, and 3-year follow-up). The current research focused on a portion of the baseline data (n=11,876, aged 9-10 years) and the 2-year-follow-up data (n=10,404, aged 11-12 years) within the ABCD Study, given that Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS) depressive diagnostic information was collected biennially.

Depressive disorder diagnoses were determined using parent or guardian ratings in the computerized KSADS based on Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) criteria [38]. Our study included 255 subjects who met our selection criteria (Fig. 1): (i) presence of a diagnosed past Major Depressive Disorder (MDD), Dysthymia, or unspecified depressive disorder at baseline; (ii) exclusion of a diagnosed bipolar disorder, psychosis, or substance use at either baseline or 2-year-follow-up. It should be noted that our study concentrated on subjects who received KSADS diagnoses of past (in a remitted state at the moment of baseline measurement) depressive disorders at the baseline. This was due to the limited number of subjects diagnosed with present depressive disorders at both timepoints.

The current study also involved a control group of 255 healthy individuals (HC, M_{age} = 118.41 months, SD = 7.20; 53.73% were girls, and 50.98% were non-Hispanic White) who showed none of any KSADS diagnoses at both the baseline and the 2-year follow-up. These control subjects were matched with the 255 depressed adolescents on age, sex, and race. We have also tested all subsequent statistical analyses utilizing the unmatched healthy control sample (n = 1597), and the outcomes were consistent with those derived from the matched healthy controls (Supplementary Table 2, Supplementary Figure 1).

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Definition of diagnosis trajectory groups

We defined the diagnosis trajectory groups according to the absence (G1, n=178; M_{age} =119.23 months, SD = 7.24; 44.38% were girls and 51.69% were non-Hispanic White) or presence (G2, n=77; M_{age} =121.38 months, SD = 7.74; 49.35% were girls and 61.04% were non-Hispanic White) of 2-year-follow-up parent-report KSADS diagnosed MDD, Dysthymia, or unspecified depressive disorder that was present (in the recent two weeks, n=4), in partial remission (n=4), or past (since baseline assessment, n=75) (Fig. 1). According to the defined criteria, G1 represented a remission group with participants who experienced no recurrence of depression for a minimum of 2 years; while G2 represented a recurrence group, consisting of individuals who were in remission at the baseline measurement but experienced a recurrence over the subsequent two-year period. Thus, G1 represented a more favorable trajectory, tending towards stable remission, while G2 represented a recurrence trajectory within the 2-year course.

Demographic information

Age, sex, race, site was included as covariates (Supplementary Table 1).

Measure of psychopathology

Psychopathology was measured from parent-reported Child Behavior Checklist (CBCL) which was used to assess emotional and behavioral problems in school-aged children [39]. All 119 items were scored using a 3-point Likert scale, ranging from 0 ("not true") to 2 ("very true"). In a prior study [35], Exploratory Factor Analyses (EFA) of the CBCL data were initially conducted using a random half of the ABCD Study sample (N = 5932). Among various models, the bi-factor model identified four distinct psychopathology factors—comprising the general psychopathology factor (p factor) and three subordinate factors: internalizing, ADHD, and conduct problems. These factors exhibited significant associations with external criterion measures. In our current study, we followed the exact same methods as stated in the prior study [35], but constructed bi-factor confirmatory models based on the confirmed exploratory model derived from the entire sample at both baseline (N=11866) and the 2-year-follow-up (N=10353). Our models demonstrated a good fit, meeting conventional fit thresholds (Baseline model: $\chi2$ = 17611.842, df = 2013, p < 0.001; RMSEA = 0.026; CFI = 0.936; TLI = 0.931; SRMR = 0.060; Follow-up model: $\chi2$ = 14928.909, df = 2013, p < 0.001; RMSEA = 0.025; CFI = 0.930; TLI = 0.926; SRMR = 0.064).

Statistical Analysis

In our present statistical analysis, we intentionally concentrated solely on the overall p factor and the internalizing factor, omitting the lower-level psychopathology factors

associated with ADHD and Conduct Problems dimensions. This deliberate exclusion aligns with the study's primary aim, which centers on discerning the differences in predicting depression trajectories between the overall p factor and the specific lower-level factor encompassing depression.

Predict depression trajectories

Generalized Linear Mixed Model (GLMM) were applied to predict depression trajectory groups utilizing R lmeTest packages [40]. For the two trajectory groups (G1, G2), the ability of the baseline p factor and baseline specific internalizing factor respectively in predicting trajectory groups were examined. In the GLMM formula, the p factor and the specific internalizing factor served as the independent variable respectively, the group was the dependent variable, and age, sex, and race were employed as fixed-effects covariates, while site was utilized as a random-effects covariate [41].

In addition, we have also examined the predictive effects of the p factor and the internalizing factor on depression recurrences while controlling for each other, in order to further elucidate the distinct information contributed by each in predicting depression recurrences when the other is controlled. To accomplish this, both the p factor and the internalizing factor were concurrently incorporated into the GLMM

formula to forecast the dependent variable "group." Fixed-effects covariates included age, sex, and race, while site served as a random-effects covariate.

All the continuous variables were standardized, including the p factor, the specific internalizing factor, and age. Other categorical variables were dummy coded before being put into the model, including group, sex, race, and site [42]. False Discovery Rate (FDR) was applied for multiple comparisons to avoid the type I errors.

Distinguish remitted depressed adolescents from healthy controls

The same GLMM model was used to distinguish between depressed adolescents and healthy controls, only differing in that the dependent variable "group" was either HC and G1 or HC and G2. FDR was applied for multiple comparisons.

Longitudinal analysis

The longitudinal alterations of the p factor and the specific internalizing factor in each group were investigated by employing Linear Mixed Model (LMM). For each group, the p factor and the specific internalizing factor functioned as the dependent variable respectively, the time variable (baseline defined as 0, 2-year follow-up defined as 1) served as the independent variable, and sex and race were used as fixed-effects covariates, with site as a random-effects covariate. Additionally, the participant was

incorporated as a random-effects covariate to eliminate individual differences. FDR was applied for multiple comparisons.

Results

Psychopathology Factors Distinguish Remitted depressed adolescents from Healthy Controls

Both the *p* factor and the internalizing factor were capable of distinguishing depressed adolescents from healthy controls, as both G1 and G2 exhibited significantly higher *p* factor than HC at both baseline (G1 vs. HC: $p_{FDR} < 0.0001$, $\beta = 2.12$; G2 vs. HC: $p_{FDR} < 0.0001$, $\beta = 2.71$) and 2-year-follow-up (G1 vs. HC: $p_{FDR} < 0.0001$, $\beta = 1.69$; G2 vs. HC: $p_{FDR} < 0.0001$, $\beta = 2.48$) (Fig. 2 A) as well as higher internalizing factor than HC at both baseline (G1 vs. HC: $p_{FDR} < 0.0001$, $\beta = 0.69$; G2 vs. HC: $p_{FDR} < 0.0001$, $\beta = 0.85$) and 2-year-follow-up (G1 vs. HC: $p_{FDR} < 0.0001$, $\beta = 0.58$; G2 vs. HC: $p_{FDR} < 0.0001$, $\beta = 1.14$). The boxplots of the *p* factor and the internalizing factor in each subgroup at baseline and 2-year-follow-up were presented in Fig. 2 B. Detailed modelling results are shown in Table 1.

The *p* Factor Predicts Depression Trajectories

Of the two factors examined, only the baseline *p* factor was found to be capable of predicting depression trajectories over the subsequent 2-year period (G1 vs. G2: $p_{FDR} < 0.01$, $\beta = 0.44$), with a higher *p* factor being indicative of depression recurrence

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(Fig. 3 A). However, the baseline internalizing factor failed to exhibit predictive ability in predicting depression trajectories over the next 2 years (G1 vs. G2: $p_{FDR} > 0.05$, $\beta = 0.19$). Detailed modelling results were showed in the Table 1.

Furthermore, it was observed that the baseline p factor consistently and significantly predicted depression recurrences ($\beta = 0.44$, $p < 0.01$), even when accounting for the baseline internalizing factor. In contrast, the baseline internalizing factor exhibited a weak and non-significant association with depression recurrences ($\beta = 0.18$, $p > 0.05$).

Longitudinal Decrease of the *p* Factor in the Remission Group

Among the three groups, only G1 exhibited a significant decrease in *p* factor from baseline to 2-year-follow-up ($p_{FDR} < 0.01$, $\beta = 0.22$) (Fig. 3 B). And no significant changes of the specific internalizing factor were found in any of the three groups. Detailed modelling results were showed in the Table 2.

Discussion

This study aims to examine and compare the impact of the specific internalizing factor and the *p* factor on the prediction of depression recurrence, as well as their ability to differentiate between currently remitted depressed adolescents and healthy individuals. Our research findings reveal that latent psychopathology factors may

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serve as inherent and enduring indicators for long-term mental health aberrations, while the p factor, rather than the internalizing factor, exhibits sensitivity to both relapse and sustained remission of depression. Therefore, it is crucial to emphasize the importance of monitoring and intervening in the co-occurrence of symptoms across all dimensions, represented by the p factor, as an effective tool to prevent the recurrence of adolescent depression.

We firstly assessed the ability of the specific internalizing factor and p factor respectively in distinguishing currently remitted depressed adolescents from their healthy counterparts. Our results revealed that both the specific internalizing factor and p factor were found to be significantly higher in depressed adolescents compared to healthy controls even if measured at a remitted state. This observation indicates that both the overall the specific internalizing factor and p factor are capable of capturing residual symptoms in remitted depressed adolescents, therefore, greatly equipped to identifying remitted depressed adolescents. And this finding is also consistent with views common in the antidepressant field that the depressive disorder is merely suppressed at a remitted state and the underlying disturbance continues until spontaneous remission occurs [43], which explains why the remitted patients exhibited higher specific internalizing factor and p factor than their healthy counterparts.

Subsequently, we examined the prognostic effect of the two factors on depression recurrence separately. Our study specifically found that an elevated baseline p factor (not the internalizing factor), measured during a remitted state, can effectively predict the recurrence of depression in the following two years, even with the information of the specific internalizing factor controlled. This observation aligns with a recent study that discovered patients with a high baseline p factor were more likely to experience poorer outcomes in terms of short-term psychotherapy response [44]. This observation reflects the relatively insensitive or insubstantial role of the specific internalizing factor in predicting depression recurrence. In contradistinction, the overarching p factor presents itself as a more sensitive predictor, aligning with prior research that indicates the p factor's greater relevance for long-term outcomes compared to specific factors [33].

It is important to note that our findings do not imply that internalizing symptoms have no association with future depression recurrence. In fact, our results suggest that once the shared variance across all dimensions (the p factor) is taken into account, the remaining unique variance (the specific internalizing factor) does not significantly relate to future depression recurrence [33]. This observation highlights the crucial role of symptoms in other dimensions of psychopathology, such as ADHD and Conduct Problems, in the development of future episodes. In line with the transdiagnostic approach, the findings lead us to consider recurrent depression as potentially arising

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from complex interactions among symptoms across all dimensions, rather than being strictly confined to the internalizing dimension[28,45]. By acknowledging the intricate interplay of symptoms across diverse dimensions, we gain a deeper understanding of the complex nature of recurrent depression and its underlying mechanisms. This realization prompts a shift in perspective, which highlighting the importance of monitoring and addressing comorbid symptoms across all dimensions[46]. In this process, the p factor emerges as a highly sensitive tool for detecting the risk of future depression recurrences [32]. Further research is warranted to delve deeper into the mechanisms underlying the influence of the specific psychopathology factors, especially given that the total variance of the p factor has been accounted for [29].

Furthermore, even after an extended period of remission (at least two years), both the specific internalizing factor and the p factor in the remission group remained considerably higher than that of the healthy controls at the 2-year-follow-up measurement. This observation suggests that individuals with a history of depression might continue to exhibit a higher specific internalizing factor and p factor compared to those without such a history, even during prolonged, stable recovery and when deemed healthy at the time of assessment. This observation indicates that latent psychopathology factors reflect inherent and enduring mental health deviations, which

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may serve as a straightforward and effective measurement for lifetime psychopathology evaluations.

Interesting, the longitudinal analysis over a 2-year period showed a significant decrease in the p factor within the remission group. However, no significant longitudinal changes were found in the specific internalizing factor. This observation aligns with a previous study which observed a diminishing pattern in the p factor during short-term psychotherapies, while the specific lower-level factors remained stable [44]. This finding suggests that the sustained depression remission may not necessarily induce significant changes in the specific characteristics of internalizing dimension when p's variance was accounted for. In contrast, the fluctuation of p factor is more sensitive to reflect sustained remission. Therefore, the significant decline in the p factor could be considered as a more sensitive and effective indicator for detecting the long-term remission of depression compared to the lower-level specific internalizing factor.

Several limitations inherent to our study should be acknowledged. Firstly, this study was only based on parent-reported KSADS diagnoses because of the lack of child-reported KSADS diagnosis data of depressive disorders in the ABCD release 3.0. Controversy exits in previous findings about the discrepancies between parent- and child-reports of depression. Some studies found significant but low agreement

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between parents and their children about depressive symptoms [47]. However, some studies suggested that discrepancies between informants were not clinically meaningful [48]. Future studies are needed to validate our findings using both child- and parent-reported diagnoses and examine the concordance of results from different informants. Secondly, the delineation of depression trajectories in our study was based on KSADS diagnoses at two timepoints. While informative, this approach may not capture the full nuance of depression trajectories. Future research should aim to explore more precisely defined depression trajectories. Thirdly, we were unable to consider factors such as first onset age, number of episodes, and antidepressant treatment due to the lack of available data from the ABCD cohort. It would be valuable for subsequent studies to explore the influence of these factors on predicting depression recurrence. Despite these limitations, our study provides valuable insights and lays the groundwork for further research in this area.

Conclusion

In conclusion, our study shed light on the critical role of the *p* factor, rather than the specific internalizing factor, in predicting future recurrence of adolescent depression and mirroring sustained remission. Moreover, our study suggested the importance of monitoring and intervening co-occurrence of symptoms across all dimensions in preventing adolescent depression recurrence, rather than solely focusing on the internalizing dimension. Further research examining the *p* factor in predicting

adolescent depression trajectories over an extended period and investigating novel interventions and treatments aimed at mitigating symptoms across all dimensions and reducing the p factor could be conducted.

Authors' Contributions

Yinuo Shu was responsible for the study conception and design, statistical analysis, first draft writing and revision. Na Ao was responsible for validating the results. Xue Wen was responsible for calculating the psychopathology factors. Zaixu Cui, Diyang Qu, and Runsen Chen were responsible for study conception, supervise the whole study and revising the manuscript. All authors read and approved the final manuscript.

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Conflict of Interest

All the authors declare that they have no conflict of interest.

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Table 1. Generalized Linear Mixed Modelling results for using psychopathology factors to distinguish depressed adolescents from HC and

predict future depression trajectories after controlling for age, sex, race, and site

| Factors | Use psychopathology factors to distinguish depressed adolescents from HC | | | | | | | | | | | | Use baseline psychopathology factors to predict future depression trajectories | | |
| | HC vs. G1 | | | | | | HC vs. G2 | | | | | | G1 vs. G2 | | |
| | Baseline | | | 2-year | | | Baseline | | | 2-year | | | Baseline | | |
	β	SE	p	β	SE	p	β	SE	p	β	SE	p	β	SE	p
p factor	2.12	0.21	$<2\times10^{-16}$	1.69	0.18	$<2\times10^{-16}$	2.71	0.34	3.67×10^{-15}	2.48	0.32	1.33×10^{-14}	0.44	0.15	0.003
Internalizing factor	0.69	0.11	8.86×10^{-10}	0.58	0.11	2.49×10^{-7}	0.85	0.15	6.37×10^{-9}	1.14	0.16	2.12×10^{-12}	0.19	0.14	0.20

Note: β = *Standardized Coefficient, SE = Standard Error, p values in this table are the original p values before FDR correction.*

Table 2. Linear Mixed Modelling results of longitudinal analysis after controlling for age, sex, race, and site

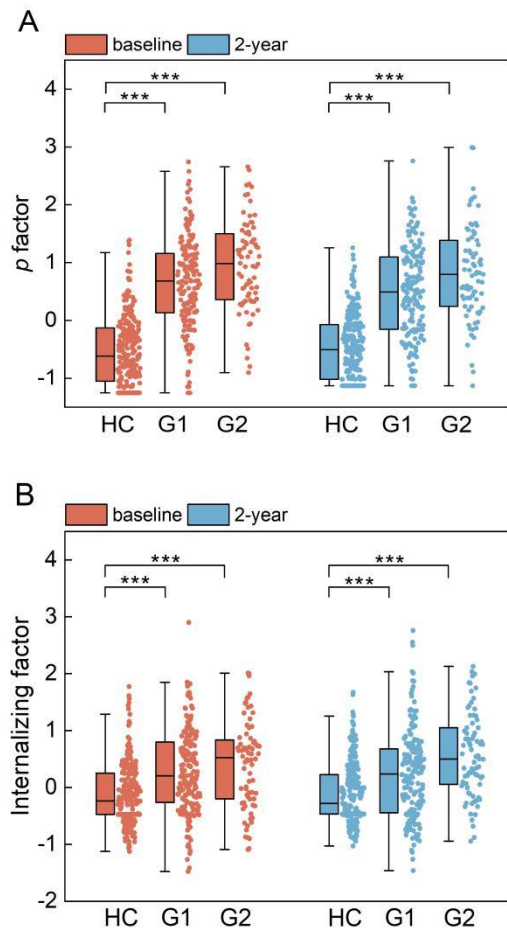| Group	p factor			Internalizing factor		
	β	SE	p	β	SE	p
HC	-0.098	0.058	0.092	-0.047	0.073	0.52
G1	0.22	0.067	0.001	0.056	0.070	0.42
G2	0.20	0.10	0.054	-0.20	0.10	0.047

Note: *β = Standardized Coefficient, SE = Standard Error, p values in this table are the original p values before FDR correction.*

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Figure 1. Flowchart of participant selection criteria and group allocation
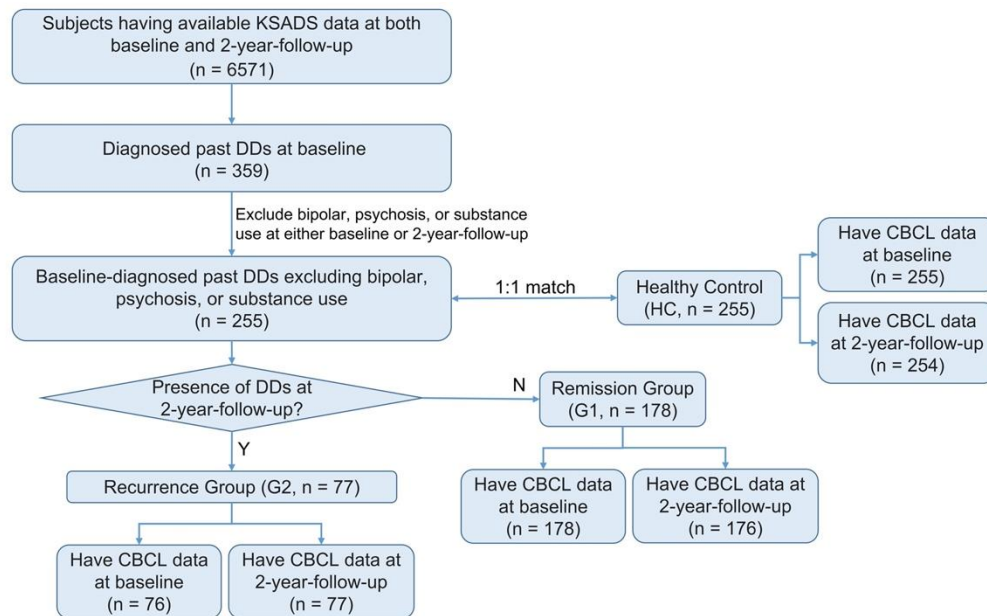
Note: *DDs = Depressive Disorders, including major depressive disorder, dysthymia,*

and unspecified depressive disorders. Y = Yes, N= No. n = the number of

participants.

Figure 2. Results of the *p* factor and internalizing factor distinguishing between remitted depressed adolescents and healthy controls at baseline and 2-year-follow-up

Note: (A) represents the distribution of the p factor in each subgroup at both baseline and 2-year-follow-up measurements. (B) represents the distribution of the specific internalizing factor in each subgroup at both baseline and 2-year-follow-up measurements. *** = p <.001, ** = p < .01. HC = healthy group. G1 = Remission group, G2 = Recurrence group.

Figure 3. Results of the *p* factor predicting depression trajectories and mirroring sustained remission over a 2-year course
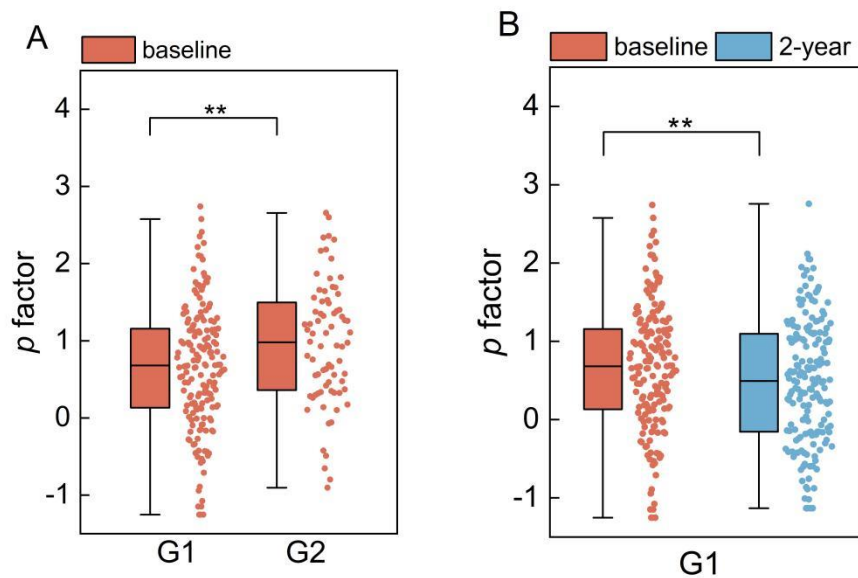
Note: (A) represents the results that baseline p factor in the recurrence group were significantly higher than baseline p factor in the remission group. (B) represents the longitudinal decrease of the p factor in the remission group from baseline to 2-year-follow-up. *** = p <.001, ** = p < .01. G1 = Remission group, G2 = Recurrence group.