Supplementary Material to

Effects of age and sex on clinical high-risk for psychosis in the community

by

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Contents

Supplementary text 1: Studies of age effects on CHR symptoms and criteria

Almost all studies of the age effect on the prevalence, clinical relevance and psychosis-predictive value of CHR symptoms and criteria focused on UHR symptoms and criteria, in particular attenuated psychotic symptoms (APS) and the related risk syndrome (APSS; Table 1 in main text). APSS is the most frequently met UHR criterion [1,2]. APS resemble positive psychotic symptoms but with some insight still being maintained. While potential neurobiological correlates on UHR samples have been frequently studied, in particular in imaging studies, a recent meta-analysis concluded that, typically, cortical thickness alterations were not detected in UHR patients[3]. Contrary to this, the more limited findings on inflammation markers in UHR patients[4,5] seem to be more consistent and to link inflammatory processes to neurocognitive deficits. These were consistently reported for UHR samples in most domains and, with respect to working memory and visual learning, were linked to conversion to psychosis[6,7]. These findings might be seen in support of developmental and cognitive models of psychosis that assume that APS and positive psychotic symptoms would result from dysfunctional cognitive schemas and coping with first symptoms and stressors, when a vulnerable person's resilience and protective factors are overstrained[8, 9-13]. This might include the development of inadequate explanatory models[8,9,10].

For both APS and APSS, an effect of age on the prevalence and clinical significance was recently reported from clinical and community studies[14,15-19] with the exception of one study of patients with 22q11 deletion syndrome[20]. This negative finding in 22q11 deletion syndrome patients[49] was explained by the high genetic liability to develop schizotypal personality features and psychosis, respectively, and consequently, the lesser involvement of other age-related factors, e.g., development of cognitive abilities, on the occurrence of APS. Other studies on mixed-age samples[14,16-18], including one on a subsample of the present sample[14], indicate a higher prevalence of APS, in particular hallucinatory APS, in children and young adolescents, as well as less clinical significance in terms of a weaker association with functional impairments, mental disorder or BS criteria. In doing so, suggesting an age threshold of around 15/16 years of age, also for the psychosis-predictive value of APSS[14,15,16,19]. Interestingly, when age effects were studied in child and adolescent

samples only[18], older adolescents showed better functioning and lower depressive scores.

With regard to BS and BS criteria[21-24], age effects have so far been described on the dimensional structure of BS[25,26] and on their prevalence[8,18]. BS are subtle, subjectively experienced subclinical disturbances in all kinds of mental processes and can usually be assessed from age 8 onwards[26]. They have been conceptualized as the most immediate symptomatic expression of the neurobiological correlates of the illness and thus, the earliest subjectively experienced symptoms of psychosis[21-24]. Preliminary studies on potential neurobiological mechanisms underlying BS suggest that diverse anatomical, pharmacological and functional correlates may be involved in the manifestation of BS in psychotic and CHR patients[24]. For this proposed characteristic of BS as being "substrate-close"[21, p.646], it has been assumed that BS are influenced by neurodevelopment to an even greater degree than are APS. Within the BS concept[8,21-23], APS and positive psychotic symptoms are considered to arise from BS when everyday demands overstrain patients' already pathologically vulnerable information processing capacity. Thus, given favorable personal and environmental conditions (e.g., good social, problem solving, and coping skills; or high self-efficacy, a supportive social network), BS, of which many may also occur in other disorders[27], might be counterbalanced as long as their number and/or severity do not overextend protective factors and patients' resilience[21,22].

Studies on age effects on the 14 criteria-relevant cognitive and perceptual BS and the two BS criteria[28,29], Cognitive Disturbances (COGDIS) and Cognitive-Perceptive BS (COPER) (Table 1), are limited. A community study on a subsample of the present sample[8] demonstrated higher prevalence rates and lesser clinical relevance, in particular with regard to functional impairments, and of the 14 BS, especially cognitive BS, in children and adolescents compared to adults. In doing so, the age thresholds were higher than in the case of APS and were in the first half of the twenties for cognitive BS and, though less significantly, around age 17/18 for perceptual BS. No clear results were found for BS criteria due to their rare occurrence[8]; yet, in a clinical sample, fewer adolescents than adults reported BS criteria in addition to APSS[18].

Supplementary text 2: Studies of sex effects on CHR symptoms and criteria

Current literature mainly on clinical samples provides only few, inconsistent findings about sex-differences in psychopathology of CHR states [30], thereby rarely specifically focusing on CHR symptoms or including BS. Some studies described more negative symptoms at baseline or within the course of the CHR state[31-37], more disorganized communication[17,36] and more grandiosity[36] in males. For females, more severe APS[31], particularly more unusual perceptual experiences[34,38], and more cognitive, perceptual and coenesthetic BS[31] were reported. Furthermore, in a community sample of 6- to 14-year-olds, more females reported APS[39]. Other clinical studies[40-42], however, found no psychopathological sex-differences in UHR samples. Only two studies[36,43] examined sex differences in respect to conversion to psychosis. One study[43] indicated that, among females, childhood adjustment, baseline functioning, and baseline positive, negative and disorganized symptom dimensions could not predict conversion; while, among males, baseline positive symptoms (mostly APS) and baseline social functioning significantly predicted conversion. The other study[36] reported that, in converters, females experienced more pronounced perceptual abnormalities, bizarre thinking and odd behaviors at baseline, while males expressed and experienced emotions to a lower degree. Furthermore, sexes differed in psychosis-predictive symptoms: paranoid and speech-disorganization APS predicted psychosis in males, whereas attentional impairment did so in females[36].

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