

Anhedonia in adolescents at Ultra-High Risk (UHR) and its relation with suicidal ideation.

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Background - Anhedonia is traditionally defined as the inability to experience pleasure. Since the earliest psychopathological conceptualizations of Krapelin and Bleuler, it has been considered a core feature of schizophrenia and a marker of vulnerability integrated into the construct of schizotypy. The clinical feature of anhedonia in schizophrenia has been recently challenged by modern laboratory-based studies on hedonic response to pleasant/rewarding stimuli. Specifically, while the psychometric assessment of noncurrent hedonic experiences (based on self-reports) suggests that schizophrenic patients experience lower levels of pleasure in comparison with healthy individuals (Chapman et al., 1976), recent meta-analyses on current pleasant feelings in laboratory-based assessment found comparable valence and arousal in relation to pleasant stimuli between the two groups (Pelizza et al., 2009). Interestingly, another paradox was recently characterized in this field. This paradox is related to the emerging empirical evidence that, along the clinical staging of psychosis, the hedonic capacity is intact in patients with schizophrenia, while is reduced in prodromal individuals identified by ultra-high risk (UHR) criteria (Strauss et al., 2018). **Aim** – Aim of the study was: (1) to assess anhedonia levels in distinct help-seeking subgroups of adolescents (age ≤ 18 years) identified through the UHR criteria [i.e., non-UHR vs. UHR vs. First Episode Psychosis (FEP)]; (2) to explore any significant association between anhedonia and other psychopathological features (i.e., positive symptoms, negative symptoms, disorganized symptoms, depressive symptoms, general psychopathology, schizotypal personality dimensions) and functioning in the UHR group; and (3) to monitor longitudinally the stability of anhedonia in UHR individuals after a 1-year follow-up period.

Materials and Methods – 123 participants (13-18 years) completed the Comprehensive Assessment of At-Risk Mental States (CAARMS), the Beck Depression Inventory-II, the Schizotypal Personality Questionnaire-Brief version, the Brief-O-LIFE questionnaire (BOL), and the Brief version of the World Health Organization Quality of Life scale (WHOQOL-BREF). Two different indexes of anhedonia were used: CAARMS “Anhedonia” item 4.3 and BOL “Introvertive Anhedonia” subscale scores.

Results - At baseline, FEP and UHR+ adolescents showed higher CAARMS “Anhedonia” item 4.3 scores than UHR- individuals (Table 1). Notably, no differences in CAARMS item 4.3 subscores were found between UHR+ and FEP subgroups. Compared to UHR-, UHR+ subjects showed higher BOL “Introvertive Anhedonia” subscale scores (Table 1). No difference in BOL “Introvertive Anhedonia” subscale scores was found between UHR+ and FEP groups, as well as between FEP and UHR- subsamples. As of December 2017, 12 UHR+ participants had a follow-up period of < 1 year and did not achieve the 12-month assessment time. With respect to the stability of anhedonia levels in the UHR+ sample, while no significant difference was found between BOL “Introvertive Anhedonia” subscale scores at baseline and after a 1-year follow-up period, a statistically significant decrease in severity of CAARMS item 4.3 score after 12 months of follow-up was observed (Table 2).

Table 1 Demographic characteristics and anhedonia levels of the total sample and the three subgroups

| Variable | Total sample (n=123) | UHR- (n=47) | UHR+ (n=44) | FEP (n=32) | χ^2 | Post-hoc test |
|------------------------------|----------------------|---------------|---------------|----------------|--------------------|--------------------------------|
| Gender (females) | 63 (51.2%) | 23 (48.9%) | 26 (59.1%) | 14 (43.8%) | 1.90 | - |
| Ethnic group (Caucasian) | 103 (83.7%) | 39 (83.0%) | 38 (86.4%) | 26 (81.6%) | 0.39 | - |
| Mother tongue (Italian) | 114 (92.7%) | 45 (95.7%) | 42 (95.5%) | 27 (84.4%) | 2.12 | - |
| Age | 15.80 ± 1.68 | 15.83 ± 1.77 | 15.43 ± 1.58 | 16.28 ± 1.59 | 5.61 | - |
| Education (in years) | 10.45 ± 1.57 | 10.60 ± 1.61 | 10.20 ± 1.52 | 10.56 ± 1.58 | 1.65 | - |
| DUI (in weeks) | 85.86 ± 52.88 | 85.12 ± 54.63 | 65.82 ± 37.71 | 116.68 ± 56.63 | 10.63 ^b | FEP > UHR+ ^c |
| Anhedonia | | | | | | |
| CAARMS item 4.3 score | 0.52 ± 0.66 | 0.40 ± 0.61 | 0.75 ± 0.70 | 0.48 ± 0.63 | 31.57 ^a | FEP = UHR+ > UHR- ^d |
| BOL “Introvertive Anhedonia” | 1.43 ± 1.71 | 0.91 ± 1.46 | 1.78 ± 1.72 | 1.60 ± 1.79 | 7.85 ^c | UHR+ > UHR- ^f |

Table 2 Anhedonia levels across 1-years follow-up period in the total UHR+ group (n=32)

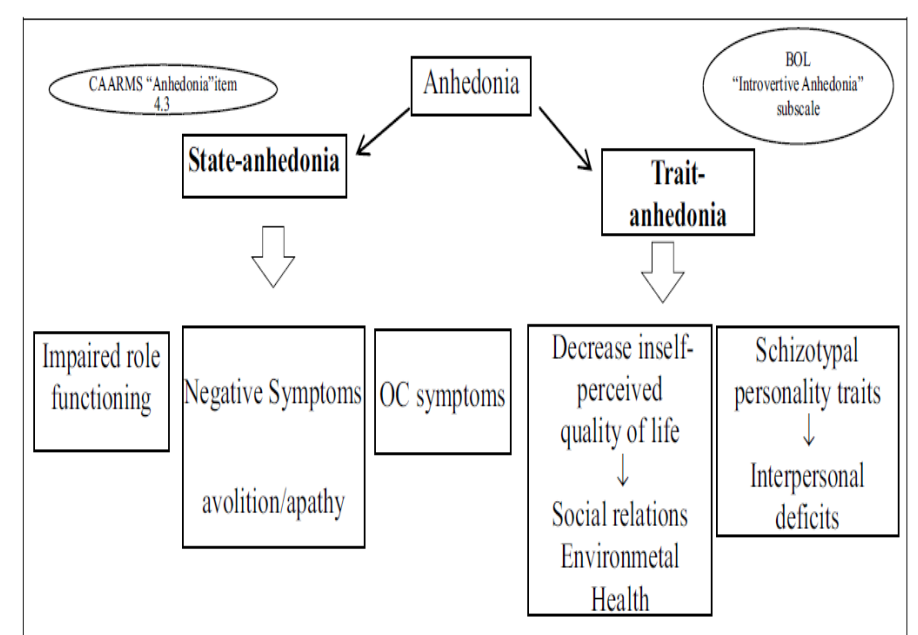
| Anhedonia | Baseline (T0) | 1 year (T1) follow-up assessment | Z |
|------------------------------------|---------------|----------------------------------|--------------------|
| CAARMS item 4.3 score | 3.05 ± 1.52 | 2.16 ± 1.87 | -2.58 ^a |
| BOL “Introvertive Anhedonia” score | 4.93 ± 2.09 | 5.03 ± 2.11 | -0.04 |

Within the total UHR+ sample, CAARMS “Anhedonia” item 4.3 score showed a significant positive correlation with CAARMS “Negative Symptoms” and “Behavioral Change” subscores (in particular with CAARMS “Avolition/Apathy” and “Impaired Role Functioning” item scores), as well as with CAARMS “Obsessive-Compulsive Symptoms” item subscore (Table 3). Even excluding CAARMS “Anhedonia” item 4.3 from “Negative Symptoms” subscore, Spearman’s correlation coefficient remained significant. However, CAARMS “Anhedonia” item 4.3 score showed no significant correlation with CAARMS “Positive Symptoms”, “Cognitive Change”, “Emotional Disturbance”, “Motor/Physical Changes”, and “General Psychopathology” subscores, as well as with BDI, WHOQOL, and SPQ-B scores. Differently, BOL “Introvertive Anhedonia” subscale score had significant negative correlations with WHOQOL “Social Relationships” and “Environmental Health” subscores, as well as significant positive correlations with SPQ-B “Interpersonal Deficit” dimension subscore (Table 3). BOL anhedonia levels showed no correlation with the other psychopathological parameters. As expected, no correlation between CAARMS “Anhedonia” item 4.3 and BOL “Introvertive Anhedonia” subscale scores was found. Furthermore, no significant correlations between baseline anhedonia measures (both CAARMS and BOL) and other functioning, quality of life, and psychopathological parameters at 1-year follow-up assessment were found.

| Psychopathological parameters | CAARMS item 4.3 (r) | BOL “Introvertive Anhedonia” (r) |
|--|---------------------|----------------------------------|
| SOFAS | -0.317 | 0.227 |
| CAARMS | | |
| Positive symptoms | -0.206 | 0.193 |
| Unusual thought content | -0.042 | 0.097 |
| Non bizarre ideas | -0.183 | -0.010 |
| Perceptual abnormalities | -0.240 | 0.065 |
| Disorganized speech | -0.059 | 0.132 |
| Cognitive change | -0.061 | 0.065 |
| Subjective cognitive change | 0.016 | -0.041 |
| Observed cognitive change | -0.049 | 0.034 |
| Emotional disturbance | 0.351 | 0.096 |
| Subjective emotional disturbance | 0.292 | 0.027 |
| Observed blunted affect | 0.407 | 0.032 |
| Observed inappropriate affect | -0.030 | 0.251 |
| Negative symptoms (without item 4.3) | 0.552 ^a | -0.141 |
| Alogia | 0.247 | -0.154 |
| Avolition/apathy | 0.714 ^a | -0.093 |
| Behavioral change | 0.476 ^b | 0.005 |
| Social isolation | 0.209 | -0.113 |
| Impaired role functioning | 0.546 ^a | -0.133 |
| Disorganizing/odd/stigmatizing behavior | 0.130 | 0.070 |
| Aggressive/dangerous behavior | 0.321 | 0.094 |
| Motor/physical change | 0.384 | 0.012 |
| Subjective impaired motor functioning | 0.279 | -0.226 |
| Objective impaired motor functioning | 0.236 | 0.046 |
| Subjective impaired bodily sensation | 0.214 | 0.145 |
| Subjective impaired autonomic functioning | 0.137 | -0.080 |
| General psychopathology | 0.327 | 0.066 |
| Mania | -0.053 | -0.111 |
| Depression | 0.294 | -0.039 |
| Suicidality/self-harm | 0.189 | -0.007 |
| Mood swings/lability | -0.127 | 0.054 |
| Anxiety | 0.263 | 0.011 |
| Obsessive-compulsive symptoms | 0.574 ^a | 0.046 |
| Dissociative symptoms | -0.046 | 0.244 |
| Subjective impaired tolerance to normal stress | 0.238 | -0.131 |
| BDI-II | | |
| Total score | 0.240 | -0.162 |
| Cognitive subscale | 0.296 | 0.139 |
| Somatic-affective subscale | 0.269 | -0.286 |
| Item 9 (“Suicidal ideation”) score | 0.238 | 0.064 |
| WHOQOL-BREF | | |
| Physical health | -0.051 | -0.293 |
| Psychological health | -0.138 | -0.340 |
| Social relationships | 0.146 | -0.386 ^c |
| Environmental health | 0.075 | -0.430 ^c |
| SPQ-B | | |
| Total score | -0.203 | 0.358 |
| Cognitive-perceptual deficits | -0.242 | 0.156 |
| Interpersonal deficits | -0.083 | 0.346 ^c |

Conclusion - Anhedonia is prominent in the psychosis prodrome, also in adolescence. Its severity is substantially indistinguishable from that of FEP adolescents with full-blown psychotic symptoms. Moreover, the inability to feel pleasure in UHR+ adolescents is related to a more severe functioning deterioration and a worse self-perceived quality of life.

As functioning impairment is a risk factor for transition to psychosis in high-risk cohort and persists beyond FEP in schizophrenia, anhedonia should be considered a risk factor for a psychosis outcome: therefore it should deserve clinical care in UHR individuals, especially in adolescents, together with other targets of interventions as attenuated positive and affective symptoms. No specific relation between anhedonia and suicidal thinking was found.



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