

1 ***Self-evaluation of negative symptoms in adolescent and young adult first***
2 ***psychiatric episodes***

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25 **Words count. 3957**

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27 **Abstract (295 words)**

28 *Background:* Negative Symptoms (blunted affect, alogia, anhedonia, avolition, and
29 asociality) are usually described in schizophrenia but they are also present in other
30 psychiatric disorders. The diagnosis and prognosis relevance of negative symptoms
31 (NS) self-assessment during a first psychiatric episode is still unknown.

32 *Aims:* To determine (i) the rate of self-assessed NS in a first psychiatric episode among
33 adolescents and young adults compared to control subjects; and (ii), whether there is a
34 difference in the prevalence of NS between schizophrenia and major depressive
35 disorder first episodes.

36 *Methods:* The population included patients aged 15-25 years, with no psychiatric history
37 and no history of medication. A dimensional evaluation was assessed during
38 hospitalization, including depressive (Hamilton Depression Scale), psychotic symptoms
39 (Prodromal Questionnaire, 16 items) and the self-evaluation of negative symptoms (SNS
40 scale). Prospective categorical diagnoses were updated 6 months after hospitalization.
41 The population included 117 individuals (58 patients and 59 healthy controls).

42 *Results:* Among healthy individuals, 47.5% reported at least one NS, the most reported
43 being amotivation. After binary logistic regression, Negative Symptoms (SNS score)
44 were associated with a diagnostic of psychiatric disorder at the 6-months follow-up (OR
45 = 1.163, $p=.001$), whereas depressive symptoms and psychotic experiences were not. A
46 SNS threshold allowed to screen first episode patients and SZ patients in the general
47 population (assessed with ROC curve). A high prevalence of self-reported NS was
48 observed across diagnostic boundaries in first psychiatric episodes, with a mean SNS
49 score of 19.3 ± 7.1 for schizophrenic disorders and 20.7 ± 8.6 for depressive disorders.

50 The prevalence of NS was not significantly different between depressive disorders as in
51 schizophrenic disorders ($p>.05$).

52 *Conclusion:* NS are an important transnosographic dimension during first psychiatric
53 episodes among adolescents and young adults. Negative symptoms self-assessment
54 with the SNS scale is relevant during a first psychiatric episode.

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56 **Keywords.** negative symptoms, first episode, schizophrenia, depression,
57 transdiagnostic, dimensional

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59 **Declarations of interest.** None.

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67 **Highlights.**

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- Negative symptoms are transdiagnostic in first psychiatric episodes
- Negative symptoms self-assessment is pertinent during first psychiatric episodes
- There is a high negative symptoms prevalence during first psychiatric episodes
- Negative symptoms were as frequent in depression as in schizophrenia in our sample
- Negative symptoms differentiate patients from the general population in our study, better than depressive symptoms and psychotic experiences do

78 **1. Introduction**

79 Negative symptoms (NS) encompass five symptoms: alogia, blunted affect,
80 anhedonia, avolition, and asociality. At the beginning of the 20th century, Bleuler and
81 Kraepelin considered NS as major symptoms of schizophrenia (Tandon et al. 2013;
82 Mach and Dollfus 2016). During the second part of the 20th century, Schneider's first-
83 rank symptoms, which are mostly positive symptoms, prevailed over NS (Tandon et al.
84 2013). This omission of NS could be explained by their subtle symptomatology, their
85 difficult clinical evaluation (differential diagnosis of depression, extrapyramidal
86 symptomatology, social withdrawal secondary to delusions, disorganization,
87 environmental hypostimulation), the low inter-judge reliability, and the low efficacy of
88 medications and psychosocial interventions (Mach and Dollfus 2016).

89 NS have long been considered as associated with several-years long and
90 gradually deteriorating schizophrenia (Bleuler et al. 1983), whereas they are also
91 observed at early stages (Quattrone et al. 2018). NS are transnosographic symptoms
92 that are observed in schizophrenia and mood disorders (Guessoum et al. 2020), and
93 have also been described in other disorders such as borderline personality disorder
94 (Marissen, Arnold, and Franken 2012), substance use disorders (Garfield, Lubman et al.
95 2014; Cook et al. 2015), neurological diseases (Winograd-Gurvich et al. 2006) or even in
96 the general population (Stefanis et al. 2002; van Os and Reininghaus 2016; Werbeloff et
97 al. 2015). Identifying NS at an early stage of the disorders is an important prognosis
98 challenge. An early and active management is associated with a decrease incidence of
99 NS (Lutgens et al. 2018). Conceptual borders between symptoms of schizophrenia and
100 depressive disorders can be unclear and NS are overlapping symptoms across
101 diagnostic categories (Moritz et al. 2018; Guessoum et al. 2020).

102 NS are an important factor of disability and a public health burden. More than
103 50% of patients with schizophrenia have at least one NS (Sicras-Mainar et al. 2014), and
104 more than 40% have at least two NS, which are associated with more and longer
105 hospitalizations (Patel et al. 2015). In depressive disorders, anhedonia leads to poorer
106 recovery among depressed patients (McMakin et al. 2012) and it is a strong predictor of
107 psychosocial functioning (Vinckier, Gourion, and Mouchabac 2017).

108 At the early stage of psychiatric disorders, psychiatric assessment of NS is
109 however limited. The Prodromal Questionnaire (PQ-16), that aims at detecting
110 psychosis prodromes, is composed of 16 items, only 2 of which are related to NS (Ising
111 et al. 2012). Yet, early assessment and management of NS is a challenge for patients
112 with schizophrenia and mood disorders. The Self-evaluation of Negative Symptoms
113 Scale (SNS) has been recently developed to fill the need of a reliable and acceptable tool
114 to assess NS. The SNS has a good correlation with the Scale for the Assessment of
115 Negative Symptoms (SANS) and presents good psychometric properties (Dollfus, Mach,
116 and Morello 2016).

117 To date, the diagnosis and prognosis relevance of NS self-assessment during a
118 first psychiatric episode is unclear. No study has yet examined the prevalence of NS in
119 the general population compared to patients during a first psychiatric episode. The
120 objectives of this prospective observational study are:

- 121 1) to evaluate the rate of self-reported NS in a population of adolescents and young
122 adults with first psychiatric episodes versus the general population,
- 123 2) to evaluate the difference in NS self-assessment across diagnostic categories,
124 especially between schizophrenia and depressive disorder first episodes.

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127 **2. Methods**

128 **Population:** Adolescents and young adults hospitalized for the first time in the
129 Adolescents Unit or the Young Adults Unit of the Psychiatry Department of Louis
130 Mourier University Hospital in Colombes (a suburb of Paris), France. The inclusion
131 criteria were: age 15 to 25 years, no personal history of psychiatric disorder, no lifetime
132 psychiatric medication. Inclusions were conducted from July 2016 to November 2018.
133 The study was carried out in accordance with ethical principles for medical research
134 involving humans (WMA, Declaration of Helsinki). All data were collected anonymously.
135 Each patient agreed to participate and gave an oral consent. The control subjects were
136 aged 15 to 25 years and had no psychiatric history or lifetime psychiatric medication
137 (inclusion criteria). Subjects were recruited among the friends of relatives from the
138 entourage of the staff. The study was approved by the local ethics committee (Comité
139 d'Evaluation de l'Ethique des projets de Recherche Biomédicale (CEERB) Paris Nord :
140 N°2019-032) .

141 **Assessment:** Patients were assessed at their arrival in the unity. The diagnoses
142 were established at the end of hospitalizations and updated 6 months later. The NS
143 were assessed using the SNS scale (Dollfus, Mach, et al. 2016), a 20-item Likert scale
144 evaluating the five dimensions of NS. For each of the five NS dimensions, patients
145 answer "Strongly agree" (2 points), "Somewhat agree" (1 point) or "Strongly disagree"
146 (0 points), to 4 items such as: "1: I prefer to be alone in my corner" or " 6: There are
147 many happy or sad things in life but I don't feel concerned by them". The total score is a
148 continuous score from 0 to 40. For each NS dimension, we calculated a continuous
149 subscore from 0 to 8.

150 The psychiatric diagnosis was discussed by two different senior psychiatrists
151 and recorded at the end of hospitalization (diagnoses of the International Classification

152 of Diseases 10 (World Health Organization and WHO 1992)). The prospective diagnosis
153 was updated 6 months later by contacting each patient's psychiatrist. The prospective
154 diagnosis was used to determine the subgroups of patients: schizophrenia disorder (SZ)
155 and depressive disorder (DEP).

156 Psychotic symptoms were assessed with the Prodromal Questionnaire (PQ16), a
157 16-item self-assessment questionnaire (Ising et al. 2012). As no French validation of the
158 PQ16 was available at the time of inclusion, we translated and retrotranslated this
159 questionnaire with the help of a bilingual speaker. It was initially designed to identify
160 young patients at risk of psychosis. A score with positive responses to 6 or more items is
161 assumed to identify patients at a higher risk of psychosis. Depressive symptoms were
162 assessed with a hetero-evaluation, using the Hamilton Depression Scale (HAMD17)
163 (Hamilton 1960).

164 In the control population, depression was assessed with the Beck Depression
165 Inventory (Beck, Steer, et al. 1996; Beck, Steer, et al. 1988) and maniac symptoms with
166 the Mood Disorder Questionnaire (Hirschfeld et al. 2000; Weber Rouget et al. 2005).

167 Other parameters were included: family psychiatric history, treatment at the end
168 of hospitalization, substance use, place of residence, and school or academic level.

169 **Statistics:** Sociodemographic and clinical characteristics are presented using
170 means and standard deviations for continuous data and distribution frequencies for
171 categorical variables. The normality of the distributions was verified with Shapiro-Wilk
172 tests. In Tables 1 and 2, univariate associations between demographic and clinical
173 characteristics across subject groups were made using a Chi-2 test for categorical
174 variables, and continuous variables were analyzed with Student t-tests for data with a
175 normal distribution. Non-parametric tests were used when necessary. For the total

176 population, a binary logistic regression was performed using Odds Ratio and their 95%
177 confidence intervals.

178 The prevalence of individuals with at least one NS was calculated, according cut-offs
179 within the SNS subscores that rate from 0 to 8 for each NS dimension (alogia, blunted
180 affect, anhedonia, avolition, and asociality). To determine the discriminant
181 performances of the SNS, Area Under Receiver Operating Characteristic Curve (AUROC)
182 analysis were performed. Sensitivity (Se) and specificity (Sp) of SNS thresholds for
183 discriminating patients with psychiatric disorders and with SZ were calculated
184 (Supplementary material). All p-values were two sided and $p < 0.05$ was considered
185 statistically significant. Statistics were conducted using the Statistical Pack for Social
186 Sciences Software (SPSS-22).

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190 **3. Results**

191 **3.1 Socio-demographic and clinical characteristics**

192 The total population of 117 subjects was composed of 58 patients and 59 control
193 subjects. The patients' group included 19 subjects with schizophrenia disorder (SZ), 22
194 with depressive disorder (DEP), 3 with bipolar disorder (BD) and 15 with other
195 psychiatric disorders (personality disorder, adjustment disorder or anxiety disorder).
196 Socio-demographic and clinical characteristics of patients and control subjects are
197 presented in **Table 1**. NS differed significantly between patients and control subjects,
198 for the total SNS score as well as for each of the five subscores that assess alogia,
199 blunted affect, anhedonia, amotivation and asociality ($p < .001$). The Pearson correlation
200 coefficient of the SNS score with the PQ-16 score was 0.521 ($p < .001$). A binary logistic

201 regression showed that NS measured with SNS score was significantly associated with
202 any psychiatric disorder in the total population, whereas depressive symptoms
203 (HAMD17) and psychotic experiences (PQ-16) were not (**Table 2**). Age was also
204 associated with any psychiatric disorder, as expected in the univariate analyse.

205 In patients group, due to small numbers in subgroups, patients with a diagnosis
206 of BD, personality disorder and adjustment disorder were excluded from the analysis of
207 the population of patients. SZ (N= 19) and DEP (N= 22) patients were compared in
208 **Table 3**. SNS, HAMD17 and PQ16 scores were normally distributed for SZ and DEP
209 patients. No significant difference in NS was observed between SZ and DEP patients,
210 including analyses of the five subscores for the five dimensions of NS (all $p > .05$). There
211 was no significant difference between SZ and DEP patients for the PQ-16 score. There
212 was no correlation between the SNS and HAMD17 scores (Pearson's coefficient = 0.180,
213 $p = 0.261$) and between the SNS and PQ16 scores (Pearson's coefficient = 0.110, $p =$
214 0.493). There was a high correlation ($p < 0.001$) between total SNS score and the
215 negative item of the PQ16 (item 1), as expected.

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Table 1. Socio-demographic and clinical characteristics of the total population (n = 117)

	Controls (n = 59)	Patients (n = 58)	Statistics	p
Ratio Female/Male	37/22	33/25	$\chi^2 = 0.41$.521
Age (mean \pm SD)	20.4 \pm 2,8	18.1 \pm 2.6	t = -4.73	<.001
Educational level (mean \pm SD)	14.5 \pm 2.2	11.7 \pm 1.7	t = -7.71	<.001
1st degree psychiatric history (%)	10 (17)	24 (41)	$\chi^2 = 8.47$.004
2nd degree psychiatric history (%)	9 (15)	10 (17)	$\chi^2 = 0.09$.771
Cannabis use (%)	16 (27)	20 (34)	$\chi^2 = 0.745$.388
Negative symptoms (mean \pm SD)				
Total SNS score	8.9 \pm 5.5	19.3 \pm 8.1	t = 8.186	<.001
Alogia	1.6 \pm 1.8	4.2 \pm 2.4	t = 6.509	<.001
Blunted Affect	1.8 \pm 1.7	3.8 \pm 2.2	t = 5.531	<.001
Avolition	3.3 \pm 2.2	4.7 \pm 2.4	t = 3.198	.002
Anhedonia	0.7 \pm 1.1	3.2 \pm 2.2	t = 7,685	<.001
Asociality	1.5 \pm 1.4	3.5 \pm 2.1	t = 6,061	<.001
Positive symptoms				
PQ16 number of positive items (mean \pm SD)	3.8 \pm 2.8	7.3 \pm 3.8	t = 5.73	<.001
Depressive symptoms				
Moderate or severe depression (%)	8 (14)	34 (59)	$\chi^2 = 25.809$	<.001

220 AUDIT: Alcohol Use Disorders Identification Test, CUDIT: Cannabis Use Disorders Identification Test, SNS:
221 Self-Evaluation of Negative Symptoms scale, PQ16: Prodromal Questionnaire 16 items, χ^2 : Chi2 test, t: t-
222 test, SD: standard deviation, p<0.05 in **bold**
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225 **Table 2. Binary logistic regression showing odd ratios for the dimensions of symptoms comparing**
226 **the patients and the controls groups (n = 117)**

	Coefficient	SD	Wald	p value	OR	IC 95%
Age	-.298	.096	9.557	0.002	0.742	0.615-0.897
Negative symptoms <i>SNS score</i>	0.151	.044	11.632	0.001	1.163	1.066-1.268
Positive symptoms <i>Number PQ16 positive items</i>	0.136	.089	2.336	0.126	1.146	0.962-1.364
Depressive symptoms <i>Moderate or severe depression</i>	-1.127	.628	3.221	0.073	0.324	0.095-1.109
Constant	3.607	2.043	3.119	0.077	36.871	

227 SNS: Self-evaluation of Negative Symptoms scale, PQ16: Prodromal questionnaire, Wald: wald statistic,
228 SD: standard deviation, OR: odd ratio, IC 95%: confidence interval 95 %, Significant value (p<0.05) in bold
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232 **Table 3. Socio-demographic and clinical characteristics of patients with schizophrenia (SZ),**
233 **depressive disorder (DEP)**

	SZ (= 19)	DEP (n = 22)	Statistics	p value
Ratio Female/Male	7/12	13/9	$\chi^2 = 2.020$.155

Age (mean ± SD)	19.4 ± 3.0	18.0 ± 2.0	t = 2.21	.033
Educational level(mean ± SD)	12.1 ± 2.0	11.4 ± 1.5	t = 1.27	.214
1st degree psychiatric history (n, %)	9 (47)	9 (41)	χ ² = 0.173	.678
2nd degree psychiatric history (n, %)	4 (21)	4 (18)	χ ² = 0.054	.817
Cannabis use (n, %)	8 (42)	6 (27)	χ ² = 0.997	.318
Negative symptoms (mean ± SD)				
Total SNS score	19.3 ± 7.1	20.7 ± 8.6	t = - 0.566	.575
Alogia	4.4 ± 2.2	4.5 ± 2.8	t = - 0.10	.921
Blunted Affect	3.8 ± 2.1	3.7 ± 2.4	t = 0.15	.881
Avolition	4.7 ± 2.5	4.9 ± 2.2	t = -0.23	.817
Anhedonia	2.9 ± 1.7	3.5 ± 2.4	t = - 0.84	.404
Asociality	3.5 ± 2.0	4.2 ± 2.3	t = - 1.05	.302
Positive symptoms				
PQ16 number of positive items (mean ± SD)	8.5 ± 4.1	7.5 ± 3.3	t = 0.879	.385
Depressive symptoms				
Hamilton Depression Scale				
Hamilton score (mean ± SD)	13.2 ± 6.7	19.0 ± 6.6	t = -2.797	.008

234 Significant value (p<0.05) in **bold**; AUDIT: Alcohol Use Disorders Identification Test, CUDIT: Cannabis Use
235 Disorders Identification Test, SNS: Self-Evaluation of Negative Symptoms scale, PQ16: Prodromal
236 Questionnaire 16 items, χ²: Chi² test, t: t-test, SD: standard deviation
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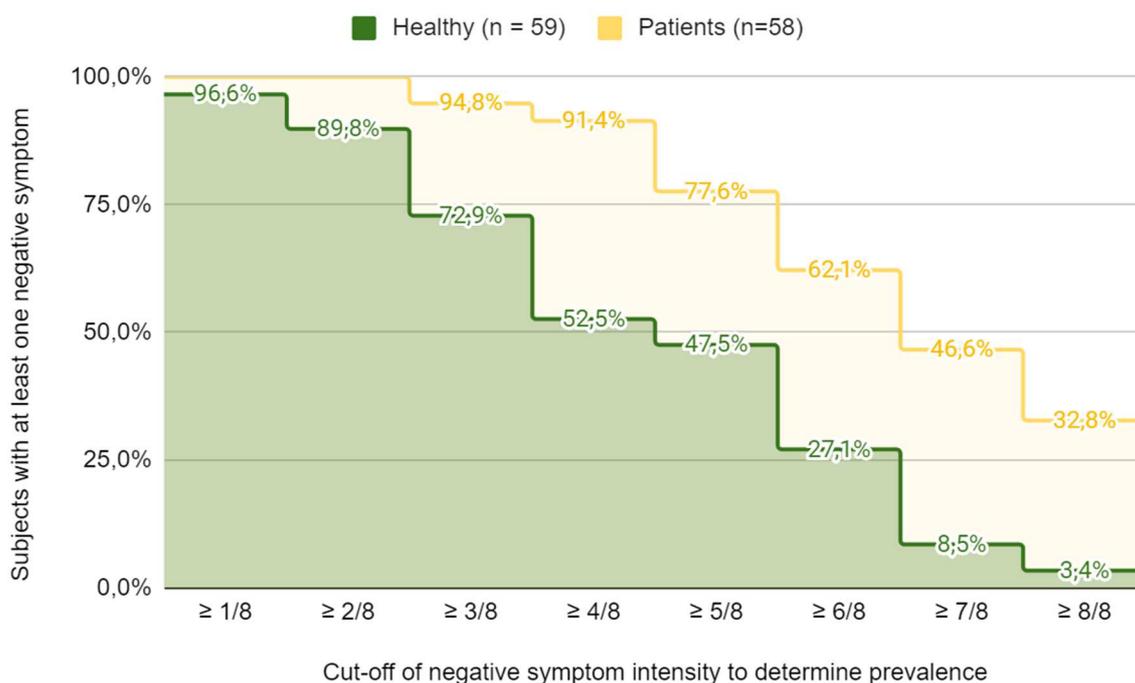
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240 **3.2 Prevalence of Negative Symptoms**

241 The prevalence of individuals with at least one NS, depending on various cut-off
242 scores within the continuous NS subscores of the SNS, are presented in **Figures 1a and**
243 **1b**. A cut-off score > 4/8 was proposed to establish NS prevalence, as it seemed
244 clinically relevant (**Table 4**). Indeed, for each NS dimension, a NS 4-item subscore > 4/8
245 can be achieved answering at least: (i) “somewhat agree” to 3 items and “strongly
246 agree” to 1 item, or (ii) “strongly agree” to 2 items and “somewhat agree” to 1 item. In
247 patient population, 77.8% present at least one NS in comparison to 47.5% in the healthy
248 controls (HC) group. According to this cut-off score, NS prevalences are relatively
249 similar in the two groups of patients (84.2% in the SZ group versus 81.8% in the DEP
250 group).

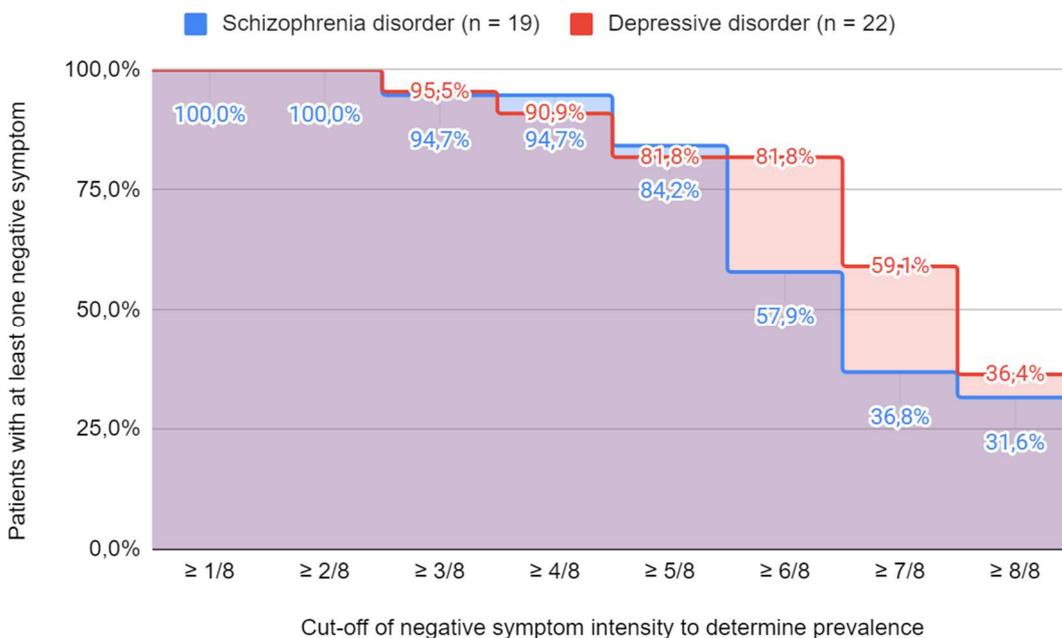
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252 **Figure 1a. Prevalence of individuals with at least one negative symptom in the total population**



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 254 The Self-Evaluation of Negative Symptoms scale is a 20-item scale with a continuous score (0-40), with 4 items for each of the 5
 255 Negative Symptom dimension, thus a continuous score from 0 to 8. This figure presents the percentage of patients with at least 1
 256 Negative Symptom, depending on the cut-off, from 1 to 8, chosen to determine the existence of a Negative Symptom.

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 259 **Figure 1b. Prevalence of individuals with at least one negative symptom within the patients' population**
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 262 The Self-Evaluation of Negative Symptoms scale is a 20-item scale with a continuous score (0-40), with 4 items for each of the 5
 263 Negative Symptom dimension, thus a continuous score from 0 to 8. This figure presents the percentage of patients with at least 1
 264 Negative Symptom, depending on the cut-off, from 1 to 8, chosen to determine the existence of a Negative Symptom.
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Table 4. Prevalence of negative symptoms according to the SNS (score > 4/8 for at least one negative symptom)

Negative symptom (%)	Total population		Patients	
	Healthy (n = 59)	Patients (n=58)	Schizophrenia disorder (n = 19)	Depressive disorder (n = 22)
Alogia	10.2	48.3	52.6	59.1
Blunted affect	10.2	37.9	36.8	40.9
Anhedonia	0	24.1	15.8	31.8
Avolition	32.2	50.0	52.6	50.0
Asociality	5.1	37.9	36.8	54.5
Individuals with at least one NS (%)	47.5	77.6	84.2	81.8

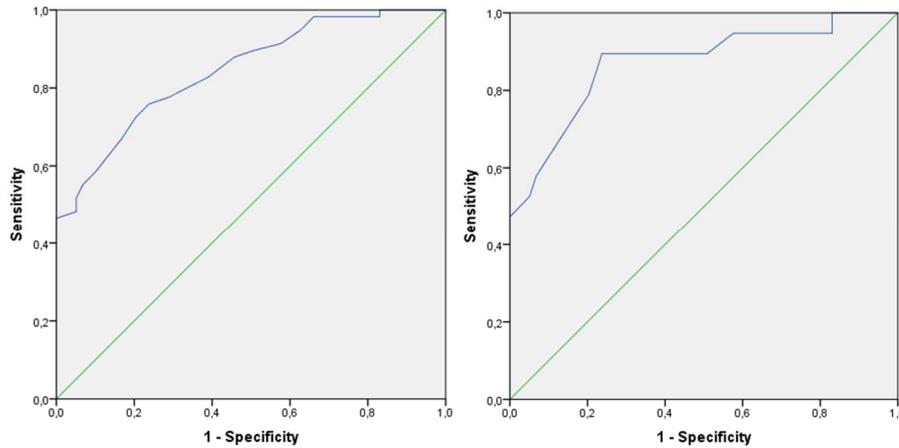
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3.2 Screening performances of the SNS

275 An AUROC analysis was performed to assess the discriminant performance of the SNS
276 scale for screening first psychiatric episodes or SZ patients in the general population
277 (figure 2 and 3).The SNS seems to be an appropriate screening tool for distinguishing
278 first episode patients and HC at a threshold value of 11 (>11 versus < or =11), with an
279 AUROC=0.845 (SE= 0.035), CI 95%= (0.776-0.914), p<.001. The sensitivity and
280 specificity were 77.6% and 71.2% (Table S1, supplementary material). The results were
281 similar when using a graphic method (where the threshold corresponds to the point lies
282 at the intersection of the ROC curve and the line perpendicular to the diagonal of no
283 discrimination). Concerning the performances to discriminate SZ patients and HC, the
284 performances were also good (AUROC=0.872, SE=0.052, 95%CI=0.769-0.974, p<0.001).
285 The threshold was comparable (respectively >11 versus < or = 11) with a sensitivity of
286 89.5% and a specificity of 77.2%.

287

288 **Figure 2. Performances of SNS scale to screen patients with (a) psychiatric first episode and (b)**
289 **schizophrenic disorder in the general population (ROC curve)**



290
291 (a) Psychiatric disorder

(b) Schizophrenic disorder

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295 **3. Discussion**

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297 This study suggests (i) that NS can discriminate first psychiatric episode
298 adolescents from healthy ones and (ii) that within the patients' group, NS are as
299 prevalent in early SZ as in the first depressive disorder episode in adolescence. This is
300 an important finding because the easy self-assessment of NS with the SNS scale could
301 specifically identify young patients with psychiatric disorders in the general population.
302 NS self-assessment would also be useful in young patients with psychiatric disorders at
303 an early stage of the disorders, regardless of the diagnosis. Thus, whereas under-
304 evaluated, NS are an important transdiagnostic dimension of the clinical profiles of
305 adolescents and young adults during a first psychiatric episode. This study also suggests
306 a threshold to screen first episode adolescents using the SNS.

307

308 **3.1 Negative symptoms from the general population to first psychiatric episode**

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310 Studies evaluating NS in the general population using a self-assessment tool are
311 scarce, in comparison to studies evaluating psychotic-like experiences and their
312 correlates. Our results suggest that the self-assessment of NS with the SNS could
313 identify adolescents with psychiatric disorders in the general population, which PQ16
314 and depressive symptoms did not in binary logistic regression in this study (Table 2).
315 This is intriguing, as positive and depressive symptoms may seem noisier and clinically
316 relevant. These results are based on a self-assessment, which can more easily highlight
317 NS (compared to hetero-evaluation, when NS are evaluated, which is rare). NS could
318 also be considered as sub-threshold and non-clinical forms of mental illness processes,
319 as psychotic-like experiences are, in a continuum approach between healthy individuals
320 and clinical populations.

321 This study reported that 47.5 % of the young healthy group had at least one NS
322 (Figure 1, Table 4). This is relevant for dimensional studies. However, for targeting
323 individuals with significant psychiatric disorders, it highlights the pertinence of a
324 syndromic approach encompassing both the number and the intensity of the NS, which
325 the SNS does, rather than a one-symptom-approach.

326 A study among 4,914 individuals from general population, aged 25-34 years,
327 reported that 20.2% had at least one NS, but no specific tool for the evaluation of NS
328 was used (Werbeloff et al. 2015). Another recent large general population study among
329 adolescents aged 11 to 18 years old in Spain provided results close to ours, with a total
330 mean SNS score of 10.57 ± 6.27 , especially a high avolition score (3.23 ± 2.12), when our
331 study reports a mean SNS score of 8.9 ± 5.5 in healthy controls and a also a high
332 avolition score (3.3 ± 2.2)(Rodríguez-Testal et al. 2019). Interestingly, in a population of
333 99 healthy subjects aged 28.8 ± 13.2 , a lower mean SNS score was observed ($3.47 \pm$
334 3.58) and the avolition score was low (0.86 ± 1.10) (Dollfus et al. 2019). It suggests that
335 healthy adolescents report more NS, in particular more amotivation. One explication
336 might be the amotivational effects of chronic cannabis use, which is relatively high in
337 young samples (27% in this study).

338 Concerning the psychometric properties of the SNS scale, a threshold of 7 was
339 proposed as a screening tool for distinguishing between SZ and HC among adult
340 populations (Dollfus et al. 2019). However, the mean score of HC seems higher in
341 adolescent population, as shown by our results and Rodriguez-Testal et al. (Rodríguez-
342 Testal et al. 2019). The mean SNS score in Rodriguez-Testal's study is 10,57 (SD = 6.27)
343 among 4521 adolescents aged 14.32 (SD = 1.66, range 11–18 years). In our study and
344 Rodriguez-Testal's study, we found higher scores than in the study of Dollfus et al., in
345 which the 99 HC have an SNS mean score of 3.47 (SD = 3.58). This difference suggests
346 that healthy adolescents report more NS than healthy adults. These results are
347 consistent with a dimensional approach of NS, with symptoms from the normal to the
348 pathological, but it also supports a longitudinal reflexion on NS throughout the
349 development from adolescence to adult age. For psychiatric disorders, the screening
350 threshold in an adolescent population may be higher, as our result suggest (threshold of
351 11). In our study, a threshold of 7 would lead to a sensitivity of 94.7% with a low
352 specificity (57.6%), which is not far from chance (50%). In Dollfus's study, the 109 SZ
353 patients have an SNS score of 16.39 (SD = 7.87) whereas we found SNS scores around
354 20 for SZ and DEP first episode adolescent patients. This suggests different SNS score
355 interpretations depending on the population. Adolescents may report higher scores of
356 NS, and patients may report higher scores during acute episodes. The age may be an
357 important variable to detect NS.

358 In a community sample of 777 adolescents (mean age: 14.4 years), various
359 avolition-related experiences were reported by 31 to 83% of adolescents but the
360 prevalence decreased to 0.9 to 5.0 % regarding adolescents who reported these
361 experiences "nearly always" (Barragan et al. 2011), similarly to our healthy sample
362 wherein only 3.4% report at least one NS dimension of maximal intensity (all 4 items,
363 each rated "Strongly agree"), which highlights the utility of a continuous scores to
364 identify intense symptoms (Figure 1a).

365

366 **3.2 Negative symptoms across diagnostic categories**

367 Identifying NS during a first psychiatric episode is an important issue for both
368 dimensional diagnosis and treatment. In the patient population, we observed high levels
369 of NS in both schizophrenia and depressive disorders. NS being transnosographic, our
370 results suggest that the SNS may be useful across diagnostic boundaries, and not only in
371 SZ. Patients with DEP or SZ showed significant difference on Hamilton's score but not
372 SNS's score. In schizophrenia spectrum disorders, a study among 1452 outpatients
373 (mean age: 40.7 years old) reported the most frequent NS are social withdrawal
374 (45.8%), emotional withdrawal (39.1%), poor rapport (35.8%) and blunted affect
375 (33.1%) (Bobes et al. 2010). However, these patients were treated with antipsychotic
376 drugs. In our study, first episode patients had no history of drug medication, which
377 avoids confusion bias with secondary NS caused by antipsychotic drugs.

378 The prevalence of NS in the SZ sample is relatively high (88%), in comparison to
379 a recent study by Mucci et al (2019), who found prevalences around 55% with the BNSS
380 (Brief Negative Symptom Scale) and the PANSS (Positive and Negative Syndrome Scale).
381 However, this discrepancy may be due to the difference of assessment (the SNS is a self-
382 evaluation), and to the samples differences (Mucci et al provide prevalence in chronic
383 and stabilized patients). Among first psychiatric episodes, Lyne et al. reported that
384 items from the Scale for the Assessment of Negative Symptoms) were more prevalent in
385 schizophrenia spectrum disorder (87% with a score ≥ 3 on any SANS item) (mean age of
386 patients: 30.2 ± 10.4) but frequently presented major depressive disorders (68%)
387 (mean age of patients: 37.7 ± 14.4) and other psychiatric disorders (bipolar disorders,
388 acute psychotic disorders, delusional disorders) (Lyne et al. 2012).

389 Our study shows that NS are important dimensions of first psychiatric episodes,
390 whether it is a psychotic or a mood disorder. Our results highlight that more than 80%
391 of the patients with schizophrenic and mood disorders reported at least one NS during

392 the first episode. NS were particularly studied in schizophrenia whereas there is scarce
393 data on NS in early depressive disorders. NS may even precede a first psychotic episode
394 (Schmidt et al. 2017). In particular, social withdrawal and anhedonia may be factors of
395 vulnerability to schizophrenic disorders (Matheson et al. 2013; Tarbox and Pogue-Geile
396 2008; Kwapil 1998). NS would predict the functioning of patients with "Ultra High Risk"
397 of psychosis (Mechelli et al. 2017) and they would be present at a very early stage of
398 the disorders (Matheson et al. 2013; Tarbox and Pogue-Geile 2008; Schmidt et al. 2017).
399 Transdiagnostic studies examining the prognosis value of NS would be relevant.

400

401 The results of studies comparing NS in patients with schizophrenic disorders and
402 patients with other disorders are heterogeneous. In our study, there is no significant
403 difference in NS between SZ and DEP groups. Some studies report more NS in
404 schizophrenic disorders compared to mood disorders (Strauss et al. 2016; Herbener
405 and Harrow 2001; Lewine 1990), while others do not find any difference (Gerbaldo et
406 al. 1994; Klosterkötter et al. 1995). However, studies rarely take into account the
407 duration or sequence of NS setup during the disorder. The results may also depend on
408 whether or not the studies differentiate between primary and secondary NS and
409 transient and persistent NS. In a transdiagnostic study among 76 patients, there was no
410 difference in NS between patients with SZ and those with DEP, hospitalized for an acute
411 episode. However, the duration of persistent NS assessed by patients and their relatives
412 distinguished the two groups (Bottlender, Sato, et al. 2003). A transdiagnostic study
413 among 96 outpatients (46 BD, 50 SZ, 27 control subjects) did not report any difference
414 between the BD et SZ groups regarding anhedonia, avolition, and asociality items, but a
415 difference regarding items related to blunted affect and alogia (Strauss et al. 2016).

416 However, this study hetero-evaluated NS in older patients with BD and SZ while our
417 study regards first episode young patients with SZ and DEP.

418

419

420 **3.3 Perspectives**

421 Each dimension of NS could have specific pathophysiological correlates that are
422 partly common to schizophrenia and depressive disorders (Guessoum et al. 2020) and
423 the pathophysiology of persistent NS during first psychotic episodes may be specific
424 (Makowski et al. 2017). A study on a patient population during a first psychotic episode
425 showed an association between low metacognitive abilities and NS (Trauelsen et al.
426 2016). The genetic risk for schizophrenia (according polygenic risk scores) appears to
427 be manifest as anxiety and NS during adolescence (Jones et al 2016). SZ patients with
428 more NS would also represent a specific subgroup with more neurodevelopmental and
429 cognitive impairment (Mallet et al. 2017). A greater focus on these phenotypes rather
430 than on psychotic experiences might be required for prediction of transition in at-risk
431 samples. In a recent work (Bourgin et al. 2020), we found that the negative dimension of
432 psychotic-like experiences was associated with various mental disorders and
433 personality disorders (e.g adjusted Odd Ratio=2,88 IC95% (2,70–3,07) for Major
434 Depressive Disorder). Further prospective studies are needed. If NS are associated with
435 later risk of psychotic disorders, it raises important question about the consequences of
436 NS themselves, even in healthy populations.

437 There are neurodevelopmental hypotheses suggesting interactions between
438 neurodevelopmental cognitive deficits and neuroplasticity changes leading to NS and
439 functional decline (Bora 2015). Adding cognitive assessments of patients with NS would
440 help identify cognitive correlates of negative symptoms.

441 NS may also have an important role in the functional prognosis of patients. The
442 early assessment of NS at an early stage of psychiatric disorders is, therefore, an
443 important issue. After the first psychotic episode, the NS remission at 24 months follow-
444 up would depend on the prior baseline intensity of NS in adolescents and adults (Veru
445 et al. 2016). Significant NS during the first psychotic episode may be a predictive factor
446 for poor social functioning recovery, whether patients are in remission or not (Gee et al.
447 2016). A recent study showed that NS trajectories were associated with long-term
448 prognosis (Chang et al. 2018). In depressive disorders, anhedonia may also be a
449 prognostic factor in resistant depressions in adolescents (McMakin et al. 2012). In a
450 study of 178 young adults (22.4 ± 4.4 years), NS improved significantly during the first 2
451 years after a first psychotic episode (Lutgens et al. 2018). In this study, management
452 included low-dose antipsychotic medication, psychological and psychosocial
453 interventions aimed at recovery, including cognitive-behavioral therapy and family
454 interventions. Therefore, NS should be evaluated and studied to explore early
455 therapeutic strategies.

456

457 **3.4 Limitations**

458 First, while being the first one to provide a comparison in both general sample and in
459 first psychiatric episode patients, the whole sample is relatively small. Second, this
460 study does not specify the duration of the NS, nor their persistence. Transient NS are
461 different from persistent NS. Persistent NS are defined by a duration of 6 months or
462 more. Persistent NS are reported to be more specific to schizophrenia (Bottlender, Sato,
463 et al. 2003). In a 10-year longitudinal transdiagnostic study of 150 patients, more
464 persistent NS were observed in individuals with schizophrenia or schizoaffective
465 disorders, compared to patients with DEP (Herbener and Harrow 2001). However the

466 present study focuses on acute-stage NS during a first psychiatric episode and provides
467 a good inventory. Third, the self-assessment of NS has not been completed by a hetero-
468 assessment scale, which would have been complementary. Nevertheless, the SNS is a
469 validated self-assessment scale, whose scores correlate with the SANS (Scale for the
470 Assessment of Negative Symptoms) and are not correlated with the patients' insight
471 level (Dollfus, Mach, and Morello 2016). Self-assessment of NS allows the patient to
472 evaluate its own experience and it can provide information that is not provided by
473 standard interviews (Dollfus, Mach, et al. 2016). On the contrary, hetero-evaluation of
474 NS can be influenced by the assumed or suggested diagnosis to the evaluator. Indeed,
475 psychiatrists use different semiological terms for the same NS depending on the
476 suggested diagnosis of depression or schizophrenia (Moritz et al. 2018). Fourth, The HC
477 sample is older than patients sample. It is a limit but also a strength of our study, as the
478 subjects did not develop a psychiatric disorder during this 1.7 years difference. Finally,
479 the follow-up was limited to 6-months to decrease drop-out. A more extended follow-up
480 may have had an impact on categorical diagnoses (as an example, some DEP patients
481 may correspond to BD who have not yet experienced any manic or hypomanic episode).

482

483 **4. Conclusions**

484 NS are transdiagnostic and dimensional symptoms, observed in the general
485 population and in several psychiatric disorders. This study shows that the self-
486 assessment of NS with the SNS scale can help to identify patients during a first
487 psychiatric episode, regardless of diagnosis, compared to healthy controls. In our study,
488 there was no transdiagnostic difference for the NS of adolescents and young adults
489 during a first psychiatric episode progressing to schizophrenic or depressive disorder.

490 Using the SNS during first psychiatric episodes could help to measure specific
491 symptoms that categorical diagnoses do not clearly point out. SNS threshold of 11 could
492 identify adolescents with psychiatric disorders with good psychometric properties. This
493 threshold is higher than the previous threshold mentioned in an adult population to
494 distinguish SZ and HC.

495 These results show that NS are important transdiagnostic clinical symptoms
496 during first psychiatric episodes among adolescent and young adult patients.
497 Longitudinal transnosographic studies could clarify the prognostic value and the
498 correlates of effective management of NS at early stages of psychiatric disorders.

499

500

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504

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506 The authors declare no conflict of interest

507

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514

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