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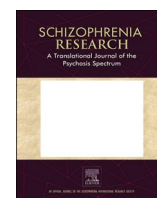
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## Impact of coping styles on substance use in persons with psychosis, siblings, and controls

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### ABSTRACT

**Background:** Substance use is overrepresented in patients with psychosis. Maladaptive coping has been proposed as one of the mechanisms which might underlie this high prevalence. Patients are known to apply more maladaptive coping compared to the healthy population. However, it is unknown whether coping is associated with the use of different substances across those with different vulnerability for psychosis, and whether coping mediates the possible association between life events and substance use.

**Methods:** In this multicenter, cohort study, 429 patients, 504 siblings, and 220 controls were included. We determined whether coping was associated with tobacco smoking, cannabis use, or alcohol consumption. Multivariable logistic regression models were applied whilst correcting for potential confounders. We performed post-hoc analyses to explore the association between negative life events, tobacco smoking, and the role of coping as a mediator in patients with psychosis.

**Results:** A positive association was found in patients between passive coping and tobacco smoking (fully adjusted OR 1.65, 95% CI 1.18–2.31). Tobacco smoking patients experienced more negative life events compared to non-smoking patients and passive coping mediated this association. In siblings and controls, none of the coping strategies were associated with substance use.

**Conclusions:** The coping style of patients with psychosis is associated with tobacco smoking and mediates the association between negative events and tobacco smoking. No significant associations were found in siblings, controls or concerning other substance use. Future research is required to examine whether enhancing healthy coping strategies decreases tobacco use in patients with psychosis.

### 1. Introduction

It is a well-known fact that the use of substances is overrepresented in people with psychotic disorders (Koskinen et al., 2010). Cannabis and alcohol are the most commonly used substances among patients with psychosis, followed by stimulants and opioids (Lähteenvuo et al., 2021), although substantially less frequent (Margoless et al., 2004). Rates of cannabis use were approximately twice as high among these than among the general population (Arseneault et al., 2004). Hazardous drinking, defined as alcohol use that places patients at risk for negative consequence (Reid et al., 1999) was found in 26.4% of patients with a first-

episode psychosis and in 21.0% of a matched controlled population (Archie et al., 2007). With respect to the use of nicotine, patients with psychosis have a three times higher prevalence of ever smoking tobacco compared to the general population (de Leon and Diaz, 2005). Interestingly, higher prevalence rates of substance use have also been found in unaffected siblings of patients with psychosis, compared to control subjects (van der Meer et al., 2015; Vermeulen et al., 2019). For example, a recent study showed that 38% of unaffected siblings smoked cigarettes, versus 25% of controls (Vermeulen et al., 2019).

Maladaptive coping (i.e. the use of coping which generally increase levels of psychological distress) is one of the proposed mechanisms that

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has been linked to the use of several substances in patients with psychosis (Marquez-Arrico et al., 2015). Patients with psychosis have a higher tendency to apply maladaptive coping strategies - such as passive reactions, palliative reactions, and avoidant coping - as compared to healthy individuals (Moritz et al., 2016b; van Dijk et al., 2019). In the general population, maladaptive coping was found to be more prevalent in smokers compared to non-smokers (Siqueira et al., 2000). Maladaptive or disengagement coping (e.g., avoidance or emotion-focused) were positively related to cannabis use (McConnell et al., 2014). Furthermore, avoidant coping styles were more common among patients using alcohol compared to healthy controls (Cerea et al., 2017). Relapse and cessation studies found that coping mechanisms play an important role in the prolongation of substance use. Relapse of tobacco smoking is best predicted by maladaptive coping strategies (Brodbeck et al., 2013) and studies suggested positive effects of interventions focused on improving coping skills on smoking cessation (Yalcin et al., 2014). Besides, emotion regulation (closely related to coping (Compas et al., 2014)) plays a mediating role between anxiety and problems with cannabis cessation (Buckner et al., 2017). Although it is well established that coping strategies are important predictors of substance use in the general population (Anderson et al., 2006), literature on this topic in psychosis is scarce. Considering the high prevalence of substance use in patients with psychosis and consistent evidence that maladaptive coping strategies are more prevalent in those patients compared to the general population (Moritz et al., 2016b; van Dijk et al., 2019), it is essential to gain insight into the interplay between these factors. Besides, in the few studies concerning this subject, substance use was operationalized as a disorder according to the DSM-5 (Marquez-Arrico et al., 2015; Marquez-Arrico et al., 2019). This approach may overlook associations between coping and substance use that are not severe enough to meet diagnostic criteria.

The current study aims to investigate the association between different coping strategies and the use of several substances in daily life. We hypothesized that maladaptive coping styles would be associated with the use of nicotine, cannabis, or alcohol in patients with psychosis, unaffected siblings, and in controls. Furthermore, we explored whether coping preferences might act as a mediator between the experience of life events and substance behaviour. Based on previous literature in the general population (Dariotis and Chen, 2020; Johnson et al., 2009), we hypothesized a positive association between negative life events and tobacco smoking and a mediating role of maladaptive coping.

## 2. Method

### 2.1. Study sample and design

This study was performed within the Genetic Risk and Outcome of Psychosis (GROUP) project, a multi-site, longitudinal, cohort study involving in- and outpatients with a non-affective psychotic disorder, unaffected siblings, and healthy controls. All patients ( $N = 429$ ) were diagnosed with a non-affective psychotic disorder according to the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders: DSM-IV-TR. Washington: American Psychiatric Publisher), of whom 320 (74.6%) had a diagnosis of a schizophrenia spectrum disorder (DSM-IV 295.1–4, 295.6, and 295.9), 46 (10.7%) had a schizoaffective disorder (DSM-IV 295.7), and 63 (14.7%) patients had a diagnosis of unspecified psychosis (298.8, 298.9, and other remaining categories). Patients were recruited in selected representative geographical areas of the Netherlands and (the Dutch-speaking part of) Belgium. Random mailings to addresses were used to recruit controls in the selected areas. Interviewers received extensive training to optimize the reliability of measurements (Korver et al., 2012b). Inclusion criteria were an age range from 16 to 50 years and mastery of the Dutch language. Patients had to meet the DSM-IV-TR criteria for a non-affective psychotic disorder, assessed with the Comprehensive Assessment of Symptoms and History (CASH) (Andreaesen et al., 1992) or the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) (Schutzwohl et al., 2007). Evaluation of coping styles in

patients, siblings, and controls was collected at wave 2 (3-year follow-up) in Utrecht and wave 3 (6-year follow-up) in Amsterdam and Groningen. We only included participants with corresponding coping and substances use data. Written informed consent was acquired from all participants before the first assessment. Further information about the study procedures is described by Korver et al. (2012a). The study was approved by the Medical Ethics Committee of the University Medical Center Utrecht.

### 2.2. Assessment instruments

#### 2.2.1. Coping strategies

Coping strategies were assessed with the 47-item Utrechtse Coping List (Schreurs et al., 1993), a self-rating questionnaire which evaluates how people generally react to problems or unpleasant situations. It has good internal consistency and test-retest reliability (Schreurs et al., 1993) and has been previously used in patients with psychosis (van Dijk et al., 2019). It distinguishes seven coping strategies:

- i. *Proactive action* (active approach, goal-oriented problem solving)
- ii. *Seeking social support* (looking for emotional support, sharing your problems with others)
- iii. *Calming thoughts* (reassurance with positive thoughts or putting things into perspective)
- iv. *Palliative reaction* (looking for distraction, e.g. by smoking, drinking, or relaxing)
- v. *Avoidance/await* (sit and wait, remove oneself from the difficult situation)
- vi. *Passive reaction* (being overwhelmed by negative feelings, having ruminative thoughts, feeling down or incapable of changing the situation)
- vii. *Expression of emotion* (showing anger, irritation, or taking problems out on others)

Each subscale consists of several items, rated on a 4-point Likert scale assessing the frequency varying from never/rarely to nearly always. Based on previous literature (Kronenberg et al., 2015), coping styles i-iii were defined as adaptive coping, in contrast with the more maladaptive coping styles iv-vii.

#### 2.2.2. Substances

To determine the degree of substance use, the Composite International Diagnostic Interview (CIDI) was used from wave 2 in Utrecht and wave 3 in Amsterdam and Groningen, corresponding with the available coping data. The CIDI allows evaluation of the quality and severity of substance use, as well as its course over time. The cross-cultural acceptability and reliability of the questions were found to be high in a field trial (Cottler et al., 1989). Participants were defined as “smokers” if they had used tobacco daily for at least one month in the past twelve months. Furthermore, tobacco smoking participants were asked how many cigarettes they smoked per day in the period of most severe smoking. Participants were defined as “cannabis users” if they had used cannabis in the last twelve months. In addition, cannabis-using participants were asked whether they smoked daily, weekly, or less in the period of most intensive use. Participants were asked about a period in the last year where they had consumed 12 alcohol units or more within two weeks. If responses were affirmative, participants were labelled as “alcohol users” and the average amount of alcohol units per week was noted.

#### 2.2.3. Life events

To explore experience of life events over the past three years, the Recent Life Event Scale (Paykel, 1997) was administrated at wave 3. This questionnaire includes 61 positive and negative life events in ten different categories (e.g., work, education, migration) and has been previously used in patients with psychosis (van Dijk et al., 2019).

Participants were asked to rate possible events on a 5-point scale from ‘very pleasant’ to ‘very disturbing’. A continuous exposure variable was calculated from all events scored 1 or 2 (unpleasant subjective appraisal), thus representing the number of negative life events. The same applied to all events scored 3–5 (pleasant subjective appraisal), thus creating a score representing the number of pleasant events.

### 2.3. Covariates

All participants provided information on sociodemographic features. Based on existing literature (Thornton et al., 2012; Vermeulen et al., 2019), age and sex were set as covariates as well as the educational level (Tan et al., 2019; Vermeulen et al., 2019). In siblings and controls, the severity of psychopathology was explored with the Community Assessment of Psychic Experiences (CAPE), a self-rated questionnaire to evaluate psychotic and depressive experiences (Mossaheb et al., 2012). The positive, negative, and depressive symptom subscales were included in the analyses. In patients, the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) was used, a 30-item structured clinical interview of which the positive and negative psychopathology subscales were included as covariates, based on previous literature supporting associations between coping, symptomatology (van Dijk et al., 2019), and substances (Ludwig et al., 2019; Mian et al., 2018; Vermeulen et al., 2019). Lastly, the use of antipsychotic medication (yes/no/unknown) was added as a covariate in the patient group (de Leon and Diaz, 2005; van Dijk et al., 2019).

### 2.4. Statistical analyses

IBM SPSS Statistics version 26.0 and release 7.00 of the GROUP database were used for the analyses in the current study. Comparisons of demographic characteristics and outcomes between substance-using and non-using participants were carried out with independent *t*-tests, Mann-Whitney-*U* tests, and Pearson chi-square tests, depending on the type of variable. Normality was assessed by visual inspection of histograms. In controls, deviations from normality were detected in the coping styles pro-active action, seeking social support, and calming thoughts. Multi-variable logistic regression models were applied to determine whether a specific coping style (independent variable) was associated with the use of nicotine, cannabis, or alcohol (binary dependent variables), whilst correcting for potential confounders. To avoid overlap between the independent and dependent variables, one item evaluating substance behaviour (“drive away tension by smoking, drinking, eating or exercising”) was excluded from the palliative subscale in the UCL. Assumptions surrounding multicollinearity were assessed and deemed to have been (mildly) violated based on the variance inflation factor (VIF) (Crane and Surlis, 2002). Hence, we chose to evaluate each coping style separately. To account for multiple testing, a Bonferroni correction was included to minimize the risk of type I errors. Thus, the two-tailed significance threshold was set at 0.007 (0.05 divided by 7) in the final model Hosmer–Lemeshow tests were conducted to test the goodness of fit of the logistic regression analyses. With the exception of one model which evaluated *passive reaction* and smoking status in controls, all tests yielded non-significant *p*-values which indicated a satisfactory model fit. In the first logistic model, age and gender were entered as covariates. If logistic models showed significant results, the following a priori defined covariates were included in the second model: educational level, psychopathology and antipsychotic medication in patients. To test significant findings in model 2 as sensitivity analysis, we replaced the substance use status by the numeric outcome variable number of cigarettes, whilst accounting for covariates. To explore prospective links between the experience of life events, coping, and tobacco smoking, we tested whether coping preferences might act as a mediator between the experiences of life events and tobacco smoking. We first tested a direct link between life events and tobacco smoking. Subsequently, a mediation model was performed using PROCESS (Hayes, 2012), a tool for

mediation and moderation analyses. Three pathways were calculated: *a*-pathway between predictor (negative life events) and mediator (coping strategies), *b*-pathway between mediator and outcome of interest (tobacco smoking), and *c*-pathway which represented the direct pathway between predictor and outcome. A bootstrapping approach was used to examine the indirect effects of negative life events on tobacco smoking through coping strategies (*ab*-pathways). We calculated the mean of 5.000 estimates of the *ab*-pathways and a 95% confidence interval.

## 3. Results

### 3.1. Sample characteristics

Table 1 presents the sociodemographic characteristics for patients, siblings, and controls. See supplement 1–4 for further detailed information.

#### 3.1.1. Smoking

There was data on coping styles and smoking status in 429 patients with psychosis, 501 siblings, and 220 controls. Of all patients, 239 (55.7%) were smokers, with an average of 19.6 (SD = 10.3) cigarettes smoked on a daily basis. 171 (34.1%) siblings used nicotine, consuming 11.9 (SD 6.9) cigarettes on average per day. In controls, 42 (19.1%) smoked 10.7 (SD = 7.3) cigarettes per day.

**Table 1**  
Demographic characteristics of patients, siblings and controls.

	PATIENTS <i>N</i> = 429	SIBLINGS <i>N</i> = 504	CONTROLS <i>N</i> = 220
Male	328 (76.5%)	217 (43.1%)	123 (55.9%)
Age	32.8 (7.1)	33.3 (7.9)	35.7 (10.6)
Education (in years)	12.7 (3.9) <i>N</i> = 407	13.8 (4.3) <i>N</i> = 487	14.8 (3.5) <i>N</i> = 209
Illness duration	10.2 (3.9)	n.a.	n.a.
Antipsychotics		n.a.	n.a.
Yes	295 (68.8%)		
No	10 (2.3%)		
Unknown	124 (28.9%)		
Smoking	239 (55.7%)	171 (34.1%) <i>N</i> = 501	42 (19.1%)
Cigarettes per day	19.6 (10.3)	11.9 (6.9)	10.7 (7.3)
Cannabis	94 (31.1%) <i>N</i> = 302	68 (13.5%)	30 (13.6%)
Daily cannabis	33 (35.1%)	12 (17.6%)	6 (20.0%)
Alcohol	94 (22.4%) <i>N</i> = 420	156 (31.3%) <i>N</i> = 499	72 (33.0%) <i>N</i> = 218
Alcohol units/ week	26.9 (28.7)	19.0 (18.9)	21.2 (18.3)
Comorbid substance use			
0 substances	59 (19.5%)	66 (13.2%)	20 (9.1%)
Single substance	77 (25.5%)	262 (52.4%)	144 (65.5%)
2 substances	93 (30.8%)	124 (25%)	43 (19.5%)
3 substances	73 (24.2%)	47 (9.4%)	13 (5.9%)
PANSS			
Positive subscale	11.7 (5.5) <i>N</i> = 413	n.a.	n.a.
Negative subscale	12.3 (5.4) <i>N</i> = 412	n.a.	n.a.
General subscale	23.7 (7.0) <i>N</i> = 419	n.a.	n.a.
CAPE			
Positive subscale	n.a.	0.09 (0.13) <i>N</i> = 498	0.09 (0.12) <i>N</i> = 218
Negative subscale	n.a.	0.49 (0.42) <i>N</i> = 498	0.41 (0.31) <i>N</i> = 217
Depressive subscales	n.a.	0.52 (0.42) <i>N</i> = 498	0.45 (0.38) <i>N</i> = 218

Data are *N* (%) or mean (SD). PANSS = Positive and Negative Syndrome Scale. CAPE = Community Assessment of Psychic Experience, frequency subscales.

3.1.2. Cannabis

In total 302 patients, 504 siblings, and 220 controls were included as they had complete data on coping and cannabis. Of all patients, 94 (31.1%) used cannabis, of whom 33 (35.1%) used cannabis on a daily basis. In siblings, 68 (13.5%) used cannabis, of whom 12 (17.6%) used cannabis daily. In controls, 30 (13.6%) used cannabis, of whom 6 (20.0%) on a daily basis.

3.1.3. Alcohol

In total, 420 patients, 499 siblings, and 218 controls were included as they had data for both coping style and alcohol consumption. 94 (22.4%) of the patients, 156 (31.3%) siblings and 72 (33.0%) controls were categorized as alcohol users (at least 12 alcohol units or more within two weeks). Patients consumed 26.9 (SD 28.7) alcohol units per week, siblings 19.0 (SD 18.9), and controls 21.2 (SD 18.3) alcohol units per week.

3.2. Associations between coping styles and substance use in patients

Results are listed in Table 2. More details are described in supplements 5–9.

3.2.1. Tobacco

In patients, the coping style *passive reaction* was associated with tobacco smoking after correcting for multiple testing (adjusted OR 1.65, 95% CI 1.18–2.31,  $p = 0.003$ ). Comparable findings were yielded when smoking status was replaced by the number of cigarettes (E 3.12, SE 0.95, 95% CI 1.26–4.99,  $p = 0.001$ ). The coping style *avoidance/await* lost significance when applying Bonferroni correction (adjusted OR 1.52, 95% CI 1.05–2.22,  $p = 0.028$ ). The remaining coping strategies (*social support, calming thoughts, palliative reaction, and expression emotion*) were not found to be significantly associated with tobacco smoking.

3.2.2. Cannabis

The association between *avoidance/await* and cannabis use lost significance when correcting for multiple testing (adjusted OR 1.72, 95% CI 1.03–2.90,  $p = 0.037$ ). Other coping strategies were not significantly associated with the use of cannabis in patients with psychosis.

3.2.3. Alcohol

No significant relations were found between any of the seven coping strategies and the use of alcohol in patients with psychosis.

3.3. Associations between coping styles and substance use in siblings and controls

In siblings and controls, no significant associations were found between any of the seven coping strategies and the use of tobacco, cannabis, or alcohol.

3.4. Mediating effects of coping styles on the association between negative life events and smoking

Smoking patients reported significantly more negative life events (supplement 10). As we found a significant association between *passive reacting* and tobacco smoking, post-hoc analyses were performed to explore whether this coping style might act as a potential mediator on negative life events and tobacco smoking. As shown in Table 3, mediation occurred through passive reaction (indirect effect: 0.021, 95% CI 0.001–0.048).

4. Discussion

4.1. Main findings

The current study examined associations between coping strategies and substance use, and explored direct and indirect relations with the appraisal of life events. In line with our hypothesis, the use of *passive*

**Table 2**  
Associations between coping style and substance use in patients, siblings and controls.

Smoking	Patients N = 429		Siblings N = 501		Controls N = 220				
	Adjusted OR	Model 1 OR [95% CI]	Model 2 OR <sup>2</sup> [95% CI]	Model 1 OR [95% CI]	Model 2 OR <sup>2</sup> [95% CI]	Model 1 OR [95% CI]	Model 2 OR <sup>2</sup> [95% CI]		
Proactive action	0.98	[0.72–1.33]	–	0.96	[0.70–1.31]	–	0.75	[0.41–1.36]	
Social support	0.89	[0.66–1.22]	–	0.82	[0.63–1.08]	–	1.12	[0.61–2.05]	
Calming thoughts	1.12	[0.83–1.51]	–	0.91	[0.67–1.23]	–	0.75	[0.43–1.32]	
Palliative reaction	1.33	[0.97–1.84]	–	1.19	[0.88–1.62]	–	1.10	[0.62–1.95]	
Avoidance/await	1.56	[1.11–2.19]*	1.52	[1.05–2.22]*	1.09	[0.78–1.51]	–	0.89	[0.51–1.58]
Passive reaction	1.66	[1.29–2.23]**	1.65	[1.18–2.31]**	1.23	[0.92–1.65]	–	1.47	[0.83–2.59]
Expression emotion	1.21	[0.90–1.64]	–	1.21	[0.91–1.60]	–	0.96	[0.56–1.64]	
CANNABIS	PATIENTS N = 302		SIBLINGS N = 504		CONTROLS N = 220				
Adjusted OR	Model 1 OR [95% CI]	Model 2 OR <sup>2</sup> [95% CI]	Model 1 OR [95% CI]	Model 2 OR <sup>2</sup> [95% CI]	Model 1 OR [95% CI]	Model 2 OR <sup>2</sup> [95% CI]			
Proactive action	1.41	[0.92–2.17]	–	0.71	[0.46–1.09]	–	0.82	[0.38–1.76]	
Social support	0.78	[0.51–1.18]	–	0.79	[0.55–1.16]	–	1.09	[0.54–2.20]	
Calming thoughts	1.48	[0.98–2.24]	–	0.88	[0.58–1.35]	–	0.78	[0.39–1.56]	
Palliative reaction	1.59	[1.03–2.45]*	1.38	[0.85–2.20]	1.37	[0.90–2.08]	–	1.90	[0.91–3.97]
Avoidance/await	1.77	[1.12–2.77]*	1.72	[1.03–2.87]*	1.35	[0.86–2.11]	–	1.59	[0.80–3.15]
Passive reaction	1.72	[1.19–2.47]**	1.45	[0.97–2.17]	1.34	[0.89–2.02]	–	2.18	[1.09–4.36]*
Expression emotion	1.12	[0.76–1.65]	–	1.10	[0.75–1.62]	–	1.20	[0.62–2.33]	
ALCOHOL	PATIENTS N = 420		SIBLINGS N = 499		CONTROLS N = 218				
Adjusted OR	Model 1 OR [95% CI]	Model 2 OR <sup>2</sup> [95% CI]	Model 1 OR [95% CI]	Model 2 OR <sup>2</sup> [95% CI]	Model 1 OR [95% CI]	Model 2 OR <sup>2</sup> [95% CI]			
Proactive action	1.14	[0.79–1.64]	–	1.21	[0.88–1.66]	–	1.09	[0.64–1.87]	
Social support	1.05	[0.73–1.51]	–	1.28	[0.97–1.68]	–	1.23	[0.73–2.10]	
Calming thoughts	1.01	[0.71–1.44]	–	1.26	[0.92–1.71]	–	0.77	[0.47–1.26]	
Palliative reaction	1.00	[0.69–1.45]	–	1.43	[1.05–1.96]*	1.35	[0.97–1.87]	0.83	[0.50–1.38]
Avoidance/await	0.87	[0.59–1.29]	–	1.17	[0.84–1.64]	–	0.77	[0.47–1.27]	
Passive reaction	0.89	[0.63–1.25]	–	1.11	[0.82–1.50]	–	0.89	[0.54–1.47]	
Expression emotion	1.11	[0.79–1.58]	–	1.27	[0.95–1.69]	–	1.02	[0.63–1.64]	

Abbreviations: OR = Odds Ratio. [95% CI] = 95% confidence interval. <sup>1</sup>Model 1: Age and gender. <sup>2</sup>Model 2: Age, gender, psychopathology, education and anti-psychotics (patients).

\*  $p < 0.05$ .

\*\*  $p < 0.007$ .

**Table 3**

Passive coping as mediator on the association between the appraisals of negative life events and smoking in patients.

X	M	Y	X to M pathway a	M to Y pathway b	X to Y (direct) pathway c	Indirect effect pathway ab
Appraisal of negative life events	Passive reaction	Smoking	0.044 [0.023–0.065]*	0.478 [0.025–0.931]*	0.054 [–0.027–0.136]	0.021 [0.001–0.048]

[95% CI] = 95% confidence interval.

\*  $p < 0.05$ .

*copying* was associated with an increased odds ratio of tobacco smoking in patients with psychosis. Interestingly, in siblings and controls, coping styles were not significantly related to tobacco smoking. Furthermore, we found that tobacco smoking patients reported significantly more negative life events, compared to their non-smoking counterparts. Lastly, *passive coping* played a modest but significant mediating role in the relationship between the appraisal of negative life events and tobacco smoking in patients with psychosis. In contrast with our hypotheses, none of the coping strategies were significantly associated with cannabis or alcohol use by patients, siblings, or controls.

#### 4.2. Previous literature

To date, studies investigating copings strategies and substance use in psychosis are scarce. To the best of our knowledge, we were the first to evaluate the association between coping strategies and the use of different substances in patients with psychosis, unaffected siblings, and controls. Coping strategies have been examined in patients with substance use disorders (SUD) and psychosis by Marquez-Arrico et al. (2015). They concluded that patients with psychosis and SUD were less likely to use *adaptive coping styles* compared to those without psychosis. Our finding that *passive coping* and tobacco smoking are associated is consistent with findings observed in the general population (Siqueira et al., 2000). The association between *avoidance/await* coping and smoking was no longer significant when correcting for multiple testing. Compared to previous literature, Adan et al. (2017) found that *avoidant coping* was a strong predictor for SUD in patients with depression (Adan et al., 2017). Also, a large longitudinal study (Bricker et al., 2011) in the general population ( $N = 3.305$ ) concluded that individuals who used *avoidant coping* at age 18 were 2.5 times more likely to be tobacco smokers by age 20. Interestingly, this coping style did not predict smoking at age 28. The authors suggested that *avoidant coping* may have mainly (relatively) short-term negative effects on the risk of smoking. Future studies with a longitudinal design are required to elucidate this hypothesis.

Consistent with previous literature, negative life events were positively associated with the risk of tobacco smoking. Siqueira et al. (2000) explored this relationship in a general population sample of adolescents with a mean age of 17 ( $N = 954$ ), in which negative life events were related to smoking status. Furthermore, a study in people at clinical high-risk of psychosis ( $N = 764$ ) showed that stressful life events increased the risk of smoking (Ward et al., 2019). In psychosis studies, coping styles have been found to play a mediating role between life events and several symptom domains (e.g. obsessive-compulsive (Renkema et al., 2020), psychotic experiences, (Ered et al., 2017) and subjective well-being (van Dijk et al., 2019)). This suggests an interplay between experiences of life events/stress, coping strategies, and functional or clinical outcomes in psychosis (van Dijk et al., 2019). The potential involvement of mediating coping pathways on the outcome of substance use was explored by Dariotis and Chen (2020). In this longitudinal study in a non-psychiatric population, *avoidance coping* acted as a mediator between life events and substance use (including tobacco, alcohol, marijuana, and other illicit drugs). In the current study, we did not explore mediating effects of *avoidant coping* since an association between this coping style and tobacco smoking was lacking. However, given the fact that the subscales *avoidance coping* and *passive coping* are highly correlated (Schreurs et al., 1993) and both can be viewed as

maladaptive, these results point in the same direction.

In the current study, we found no significant association between coping strategies and the risk of cannabis use. Based on previous literature in the general population, we expected that maladaptive coping strategies would be related to the use of cannabis. For example, one study (Sadaf et al., 2021) found that avoidance coping (measured with the brief COPE (Carver, 1997)) was an important predictor for cannabis use. Hence, it was somewhat surprising that a relationship was lacking between maladaptive coping and the use of cannabis. There are several (non-mutually exclusive) hypotheses that could explain the relationship between cannabis and psychosis. A frequently mentioned mechanism is the self-medication hypothesis, which proposes that patient are using cannabis as a form of self-medication for psychotic symptoms. However, a recent systematic review evaluating longitudinal associations between cannabis use and psychopathology in psychosis (Athanasidou et al., 2021) found evidence for poorer psychotic outcomes (i.e. relapses or changes in positive symptoms) in patients using cannabis compared to non-users. This suggests that hypotheses other than self-medication and maladaptive coping could play a role in the high cannabis prevalence, including a shared genetic and environmental vulnerability (Shakoor et al., 2015; Sherva et al., 2016) and a strong association between psychosis and cannabis (Livne et al., 2021; Pasman et al., 2018), although the evidence for and direction of a causal relationship remains unclear (Johnson et al., 2021).

Furthermore, it must be emphasized that a potential type-II error was introduced by applying Bonferroni correction, as our second model did show an association between the avoidance/await coping and the risk of cannabis use (OR 1.72, [1.03–2.87],  $p = 0.037$ ), but not survived Bonferroni correction ( $p = 0.017$ ). Lastly, it is worth mentioning that different instruments were used to assess copings strategies, thereby introducing complexity to the comparison of study results. There are several options for grouping coping strategies (such as active versus passive coping (Nielsen and Knardahl, 2014), adaptive versus maladaptive coping (Moritz et al., 2016a), and problem-focused versus emotion-focused coping (Lazarus and Folkman, 1984)) and there is no consensus regarding the best method (Carver and Connor-Smith, 2010).

The present study found no evidence that the use of specific coping strategies was associated with alcohol consumption. In contrast, one previous study (Yigitoglu and Keskin, 2020) in psychosis concluded that dysfunctional coping was associated with the use of alcohol. However, the authors did not account for important confounding variables (e.g., antipsychotic medication), the study size was relatively small (6 alcohol users vs. 47 non-users), and detailed information about the heaviness of use of alcohol was missing. Physiological mechanisms regarding the use of alcohol in psychosis may differ between patients using nicotine and/or cannabis. Illness-related symptoms are thought to influence coping strategies in psychosis (Scholte-Stalenhoef et al., 2016). It might be that the link between illness-related symptoms and alcohol is less clear when compared with smoking and cannabis use. One study found that patients who use tobacco smokers and cannabis users had higher scores on positive symptoms, whereas alcohol use was not significantly related to positive symptoms (Oluwoye et al., 2019). In addition, it appeared that negative symptoms were associated with less alcohol use and less alcohol craving (Batki et al., 2008). What is more, the use of alcohol was more prevalent in siblings (31%) and controls (33%), compared to patients (22%), thereby contrasting the differences in prevalence rates of smoking and cannabis. This might indicate that potential social

motivated reasons (i.e. to enhance social inclusion) are related to alcohol use in psychosis. Future studies could explore possible links between coping and problematic alcohol use.

In siblings and controls, we found that coping styles were not related to participants' substance use. This is at odds with previous literature (Cerea et al., 2017; McConnell et al., 2014; Siqueira et al., 2000). In two large adolescent populations ( $N = 1352$  and  $N = 954$ ), coping was associated with the use of nicotine (McConnell et al., 2014; Siqueira et al., 2000) and cannabis (McConnell et al., 2014). However, the presence of psychosis was not an exclusion criterion in the selection of participants in these studies, thus limiting comparisons with our siblings and control group. Compared to patients, protective or buffer mechanisms (i.e. more social support and less (self-) stigma) could be more profound in these individuals, preventing them from using substances. Furthermore, methodological differences regarding the evaluation of coping may also have played a role (Wills and Hirky, 1996). Regarding the use of alcohol, one study (Cerea et al., 2017) found indeed a significant relationship between coping and alcohol use disorder according to DSM-5. However, we did not evaluate substance disorders but focused on frequency of use as assessed with the CIDI. This might be an explanation for our failure to find a relationship between coping styles and alcohol use.

#### 4.3. Proposed mechanisms

Patients with psychosis are known to have an increased vulnerability to minor stressors (Myin-Germeys et al., 2003) and to show more maladaptive coping strategies compared to the general population (Moritz et al., 2016b; van Dijk et al., 2019). The current study examined whether these mechanisms would be associated with the risk of substances use in this patient group, siblings, and controls. Findings implicate that maladaptive coping might contribute to the high tobacco smoking prevalence in patients with psychosis. Environmental factors such as negative life events occur more frequently in patients with psychosis (Beards et al., 2013). Both are likely to come with difficulties in applying appropriate coping strategies which may also increase the risk of tobacco use. Furthermore, these patients may also smoke to cope with life events and stress, trying to reduce negative affect, which is in line with the stress-coping model of addiction (Wills et al., 2001). However, at least for smoking, it is known that tobacco smoking actually causes stress and negative affect (Aronson et al., 2008). This highlights the complexity and bidirectional pathways between life events/stress, coping strategies, and smoking behaviour. Future prospective studies are needed to evaluate causal associations.

#### 4.4. Strengths and limitations

Strengths of the current study are the relatively large sample size, the inclusion of patients, siblings, and controls, and the evaluation of the association between different coping styles and specific substances. However, the current study has several limitations. First, the cross-sectional design of the current study lacks the capability of evaluating short- and long-term effects of coping in relation to substance use. Second, reverse causality and residual confounding cannot be ruled out due to the cross-sectional analyses and observational design. Third, the GROUP-cohort includes a sample of relatively high-functioning patients (Korver et al., 2012b). Hence, underestimation of maladaptive coping and substance use cannot be ruled out. In addition, the current sample only included a subsample of GROUP participants due to the inclusion of participants at the 3-year and 6-year follow up. Therefore, a selection bias (i.e., selecting less avoidant coping participants) might have occurred, and the generalizability of findings to other samples of patients with psychotic disorders should be made with caution. Fourth, information concerning the duration of use of antipsychotics was missing. Lastly, the current study determined the use of alcohol by the number of units (more than 12 yes/no) within two weeks, which

captured both frequent and moderate drinkers (e.g. one unit/day for two weeks) as well as infrequent but severe drinkers (e.g. 12 units in one day). Hence, both hazardous and non-hazardous alcohol users might be included which should be taken into account when interpreting the outcomes.

In conclusion, the data in the current study suggest that a passive way of coping with stress and negative life events by patients is related to tobacco smoking but not to cannabis or alcohol use. Previous literature in the general population found a role for specific coping strategies in smoking cessation and relapse prevention (Siqueira et al., 2001). Furthermore, an increase (or respectively decrease) in smoking behaviour in patients with psychosis has also been found to increase (or respectively decrease) the use of cannabis (Nguyen et al., 2021). Future studies are necessary to examine whether enhancing healthy coping strategies decreases tobacco use in patients with psychosis and whether they might play a role in substance initiation or cessation.

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#### CRedit authorship contribution statement

All authors are responsible for reported research and all authors have participated in the concept and design; analysis and interpretation of data; drafting or revising of the manuscript, and they have all approved the manuscript as submitted.

#### Declaration of competing interest

None.

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#### Appendix A. Supplementary data

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