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Patterns of executive functions and theory of mind in adults with a family history of alcohol use disorder: Combined group and single-case analyses

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Abstract

Background: Impairments in executive function and social cognition are highly prevalent in individuals with an alcohol use disorder (AUD). Some studies show that similar difficulties are displayed by individuals with a positive family history of AUD (FH+) compared with individuals with a negative family history (FH-). Yet, no studies have jointly investigated cognitive and affective theory of mind at the behavioral level. Moreover, some studies show preserved executive and socioemotional functioning in FH+ participants. One possible explanation for these divergent results is that FH+ individuals are cognitively heterogeneous. In this study, we examined the frequency and co-occurrence of difficulties in executive function and social cognition among FH+ individuals at the individual level.

Methods: Sixty FH+ and 60 FH- participants matched on age, sex, and education level were included. They completed tasks assessing executive functions (Stroop, Trail Making Test) and affective and cognitive theory of mind (Movie for the Assessment of Social Cognition). They also completed self-report questionnaires measuring impulsivity, alexithymia, and empathy. Single-case analyses assessed the proportion of FH+ participants with difficulties in executive function and/or theory of mind.

Results: FH+ individuals exhibited difficulties in response inhibition and made more errors during theory of mind processing, indicating an absence of mental state representation, compared with FH- individuals. In the FH+ sample, 53.33% had executive function and/or theory of mind difficulties. Those with lower theory of mind scores reported higher alexithymia and lower empathy on self-report measures.

Conclusions: FH+ individuals display heterogeneous executive function and theory of mind abilities. Given that they mostly occur independently of one another, executive function and theory of mind difficulties may be distinct vulnerability markers in AUD.

KEYWORDS

alcohol use disorder, executive functions, family history, social cognition, theory of mind

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INTRODUCTION

Alcohol use disorder (AUD) constitutes one of the mental health issues with the highest prevalence rates worldwide (Rehm & Shield, 2019). A Positive Family History (FH+) of AUD increases the risk of developing the disorder through a combination of shared genetic and environmental factors (Kosty et al., 2020). Although studies have shown that FH+ individuals often initiate alcohol use earlier in adolescence (Dawson, 2000) and have higher AUD lifetime prevalence rates (Jenkins et al., 2011) than individuals with a negative family history (FH-) of AUD, most never develop AUD. FH+ individuals share 50% of their genes with their first-degree relative(s) affected by AUD. Shared environmental factors (i.e., childhood trauma, attachment style, precarious economic living conditions) may further add to this genetic overlap. It has therefore been suggested that FH+ individuals possess some of the vulnerability factors associated with AUD. In fine, the interplay between vulnerability and resiliency factors in FH+ individuals may contribute to the development of AUD or any other mental health condition in the long run.

Differences in cognitive functioning have been evoked as factors that may contribute to this increased risk for AUD in FH+ individuals (Cservenka, 2016). More specifically, authors have suggested that executive function (EF) and social cognition (SC) processes may be predisposing vulnerability factors for AUD. EF and SC weaknesses may already be present prior to AUD development and may subsequently be amplified by chronic alcohol intake (Kumar et al., 2022, 2023).

EF are defined as a set of higher order processes that allow individuals to flexibly adjust their behavior in nonroutine situations (Snyder et al., 2015). These processes typically include the inhibition of preponderant responses, mental flexibility, and updating in working memory (Miyake et al., 2000). SC processes allow individuals to perceive, interpret, and respond to social cues, in order to engage in adaptive social interactions. They include emotion recognition, theory of mind (ToM; i.e., ability to understand other people's mental states), and empathy (Cassel et al., 2019). It is common to distinguish affective and cognitive SC components (Etchepare & Prouteau, 2018). While affective SC components refer to the processing of emotional information, cognitive SC components refer to the interpretation and understanding of intentions and other non-emotional mental states. This distinction of affective and cognitive components has been widely applied in ToM research which has reported dissociations between affective and cognitive ToM (Abu-Akel & Shamay-Tsoory, 2011). In addition, SC comprises low- and high-level processes which differ in the complexity of social stimuli processing. Low-level processes englobe emotion recognition and the simple perceptual decoding of mental states while high-level processes refer to mental state reasoning and the contextual integration of social cues (Etchepare & Prouteau, 2018).

AUD patients fairly consistently exhibit EF and SC impairments and both have been associated with moderate to large effect sizes (Bora & Zorlu, 2017; Stephan et al., 2017). Regarding EF, AUD

patients have difficulties inhibiting automated responses and flexibly alternating between response sets (Wilcox et al., 2014). Some studies have also reported difficulties for updating working memory content in AUD patients (Pitel et al., 2007, 2009); however, working memory impairments seem to be less consistent in AUD than inhibition and mental flexibility deficits (Wilcox et al., 2014). Regarding SC, AUD patients frequently mislabel other people's emotional facial expressions (Maurage et al., 2021), have difficulties understanding other's mental states (Cox et al., 2018), and exhibit reduced empathic abilities (Grynberg et al., 2017). In AUD, SC deficits have been reported for both, affective and cognitive SC components, and low- and high-level SC processes (Cox et al., 2018; Pabst et al., 2022). Yet, mental state reasoning seems to be more severely impaired in AUD than mental state decoding according to a meta-analysis on SC (Bora & Zorlu, 2017).

Even though EF and SC are generally considered distinct cognitive domains, there is ample evidence indicating a reciprocal relationship between EF and SC in the general population (Apperly et al., 2005). On the neural level, overlapping neural networks may partly explain this reciprocal relationship. Studies indicate for instance that both, EF and SC processes, are associated with increased frontoparietal and reduced default mode network activity (Xin & Lei, 2015). Associations between EF and SC processes have also been reported in AUD, especially between inhibition, mental flexibility, and ToM processes (Cox et al., 2018; Quaglino et al., 2015). Studies have argued that the inhibition of distracting information, especially of one's own perspective, and the ability to flexibly alternate between different mental states may be crucial for the completion of ToM tasks in AUD patients (Maurage et al., 2015). Still, research suggests that EF and SC may best be considered separate albeit interrelated cognitive domains in AUD and recommends a joint investigation of EF and SC in neuropsychological assessments (Schmid et al., 2022).

Interestingly, some studies conducted among healthy FH+ participants have revealed cognitive weaknesses similar to those described in AUD patients (Cservenka, 2016). Regarding EF, FH+ individuals exhibit less efficient inhibition abilities, as reflected by lower resistance to interference in the Stroop test (Lovallo et al., 2006) and produce fewer correct responses in Stop Signal and Go/No-go tasks compared with FH- individuals (Filippi et al., 2019; Lees et al., 2020). Moreover, FH+ individuals have longer completion times in the Trail Making Test Part B and commit more perseverative errors in the Wisconsin Card Sorting Test than FH- individuals, suggesting less efficient mental flexibility (Gierski et al., 2013; Henderson et al., 2018). Imaging studies, comparing FH+ and FH- adolescents and adults on EF tasks, revealed differential activations in several brain regions, notably the dorsolateral and orbitofrontal cortices (Silveri et al., 2011), inferior frontal cortex (DeVito et al., 2013) and cingulate gyrus (Acheson et al., 2014), and found connectivity differences in visual, default mode, and attentional networks (Amico et al., 2020).

While several studies have investigated EF in FH+ individuals, studies on SC processes are scarce. Most FH+ studies have investigated the implicit processing of socio-emotional stimuli (i.e., emotional

facial expressions, emotionally valenced words), without requiring any interpretation or generation of responses to these cues (see Cservenka, 2016, for review). Few FH+ studies have used common behavioral SC tasks requiring explicit processing of social cues in FH+ samples. Still, existing SC studies further corroborated the presence of neural and/or behavioral differences in FH+ individuals.

Regarding emotion recognition, Khemiri et al. (2022) reported longer response latencies in a facial emotion recognition task in FH+ versus FH- individuals. Kirk-Provencher et al. (2023) found higher brain activations in the right middle and superior frontal cortices during the reappraisal of negative emotional scenes in an emotion regulation task in FH+ individuals. Finally, Hill et al. (2007) found differential brain activations in the middle temporal cortex and superior and inferior frontal cortices in FH+ individuals, compared with FH- individuals during the Reading the Mind in the Eyes test, a measure of affective ToM. Conversely, all these studies have taken an interest in affective and low-level SC processes while affective and higher order SC processes have remained largely unexplored. To fill this gap of the literature, our team recently conducted an fMRI study investigating both, affective and cognitive SC processes, in FH+ adults through a ToM task requiring high-level mental state reasoning (Schmid et al., 2023). The results highlighted differences in terms of neural activations between the FH+ and FH- groups during affective ToM processing in the left insula and inferior frontal cortex. However, if these neural differences also exist at the behavioral level when using common neuropsychological SC tasks remains an open question to date.

Moreover, although studies have highlighted EF and socioemotional weaknesses in FH+ groups, several studies have reported comparable performances across FH+ and FH- individuals (Hardee et al., 2014; Schmidt et al., 2017). One possible explanation for these discordant results may lie in the cognitive heterogeneity of the FH+ groups which could have presented various executive and socioemotional abilities at the behavioral level. Whereas some FH+ individuals may have EF and SC difficulties, others may have no such cognitive specificities (Long et al., 2017). The fact that, in a parallel way, several studies have highlighted heterogeneous EF (Schmid et al., 2021) and SC (Maurage et al., 2021) abilities among detoxified patients with AUD lends further weight to this hypothesis. Up to now, studies among FH+ individuals have relied on group comparisons to assess the presence of EF and SC specificities. Yet, it seems important to describe patterns of EF and SC abilities of FH+ individuals if we are to hone our understanding of EF and SC processes as vulnerability markers for AUD and potentially identify FH+ individuals at greater risk for developing this disorder.

The aim of this study was twofold: our first objective was to offer a more concise characterization of SC difficulties in FH+ individuals at the behavioral level and to study the extent of these difficulties compared with commonly reported EF difficulties. Although, EF and SC processes have been shown to be interrelated in AUD, only one study has investigated EF and SC processes in the same FH+ sample (Khemiri et al., 2022). We therefore set out to investigate EF and SC in unaffected first-degree relatives of individuals with AUD and used

a task assessing affective and cognitive SC components (i.e., ToM task requiring mental state reasoning). Even though AUD is characterized by affective and cognitive SC impairments and especially affects high-level SC processes, no prior FH+ study has used common behavioral tasks targeting these cognitive processes.

The second objective of this study was to assess the cognitive heterogeneity of FH+ individuals in terms of EF and SC functioning. For this purpose, we used single-case analyses (Crawford & Howell, 1998) to explore the proportions of EF and/or ToM difficulties in FH+ healthy adults. Single-case analyses are powerful tools for gaining an in-depth understanding of cognitive functioning and complement group analyses (Nickels et al., 2022).

Given that AUD yields important EF and SC impairments, we expected FH+ individuals to present both, EF and SC difficulties, at the group level and hypothesized that FH+ individuals will present difficulties in a high-level SC task requiring mental state reasoning, in addition to the mental state decoding difficulties described in the literature. Moreover, given the presumed heterogeneity of FH+ individuals in terms of EF and ToM abilities, we expected some FH+ participants to display less efficient EF and/or ToM, and others to display EF and ToM equivalent to those of FH- individuals in single-case analyses. EF and ToM are generally regarded as two distinct albeit interrelated cognitive domains, and are thought to increase AUD vulnerability through different cognitive mechanisms (Cassel et al., 2019). For these reasons, we expected some FH+ participants to mainly exhibit EF difficulties and others to mainly exhibit ToM difficulties compared with FH- participants.

MATERIALS AND METHODS

Participants

Participants were 120 adults (60 FH+, 60 FH-). FH+ participants were unaffected (i.e., without AUD) adults who had at least one first-degree relative (father or sibling) with current or past AUD according to DSM-5 criteria (American Psychiatric Association, 2013). Participants who had a mother with a current or past AUD were excluded to avoid the potential impact of alcohol consumption during pregnancy on cognitive performances. FH- participants had no first-degree relative with a current or past AUD.

The FH+ and FH- groups were matched on age, sex, and education level (Table 1). Participants were eligible if they were aged 18–60 years, were native French speakers, and had no current or past diagnosis of alcohol abuse or alcohol dependence. Exclusion criteria for both groups were the presence of any substance use disorder (except nicotine dependence), or major neurological or psychiatric disorder. The absence of alcohol consumption prior to testing was ascertained with a breathalyzer.

This study was approved by an institutional review board (ID-RCB: 2020-A00784-35) and preregistered on [ClinicalTrials.gov](https://clinicaltrials.gov) (NCT04647422). Participants provided written informed consent and were compensated with €40 on study completion.

TABLE 1 Demographic and clinical characteristics of FH+ and FH- participants.

	FH+ group (n = 60)	FH- group (n = 60)	p Value
Demographics			
Age (years)	38.07 (11.15)	39.70 (10.95)	0.420
Sex ratio (F/M)	40/20	31/29	0.095
Education level (years)	13.90 (2.11)	13.75 (1.85)	0.679
NART total IQ	107.63 (6.63)	106.90 (7.46)	0.573
Alcohol and tobacco use			
AUDIT total score	3.88 (2.59)	3.10 (2.09)	0.070
Alcohol units per week	2.94 (3.09)	2.35 (2.60)	0.259
Age first drunkenness ^a	18.75 (5.74)	17.75 (2.64)	0.259
Current smokers (%)	20.00	16.67	0.734
Pack years ^b	9.75 (5.81)	5.77 (5.58)	0.138
FTND score ^b	3.58 (1.98)	1.90 (2.38)	0.085
Family drinking history			
Number of AUD first degree relatives	1.55 (0.91)	-	
Fathers with AUD (%)	88.30	-	
Siblings with AUD (%)	43.30	-	
FHD score	0.40 (0.15)	-	
Other self-report measures			
BDI-13	4.72 (3.60)	1.88 (2.53)	<0.001
STAI-A	29.43 (8.16)	25.88 (8.70)	0.023
STAI-B	40.55 (9.40)	33.80 (9.17)	<0.001
Lifetime MDE (%)	18.33	11.67	0.306
Lifetime suicide attempts (%)	16.67	1.67	0.004
Anxiety disorders (%)	28.33	11.67	0.022
CTQ total score	45.18 (17.22)	32.67 (7.33)	<0.001
UPPS-P Negative Urgency	9.08 (3.13)	7.07 (2.14)	0.083
UPPS-P Positive Urgency	9.97 (2.80)	8.60 (2.44)	0.197
UPPS-P Premeditation	6.98 (2.20)	6.23 (1.77)	0.101
UPPS-P Perseverance	6.42 (2.30)	5.92 (2.04)	0.992
UPPS-P Sensation Seeking	8.73 (2.98)	8.63 (2.56)	0.947
BVAQ-B Fantasize	10.18 (3.63)	10.48 (3.33)	0.671
BVAQ-B Identify	8.32 (2.72)	7.03 (2.80)	0.741
BVAQ-B Analyze	7.83 (2.48)	7.17 (2.51)	0.342
BVAQ-B Verbalize	11.45 (4.25)	10.92 (4.10)	0.527
BVAQ-B Emotionalize	9.40 (3.04)	9.32 (2.49)	0.170
BVAQ-B Affective	19.58 (5.06)	19.80 (4.34)	0.625
BVAQ-B Cognitive	27.60 (7.82)	25.12 (7.15)	0.928
IRI Concern	27.25 (6.19)	28.32 (4.41)	0.409
IRI Distress	18.40 (4.73)	18.07 (5.53)	0.061
IRI Fantasy	25.37 (5.64)	23.17 (6.22)	0.289
IRI Perspective-taking	23.88 (4.92)	25.23 (4.80)	0.594
IRI Affective	45.65 (7.86)	46.38 (7.82)	0.077
IRI Cognitive	49.25 (7.96)	48.40 (8.58)	0.667

Note: Data are means (standard deviation), unless otherwise specified. Significant *p* values are highlighted in bold for *p* < 0.05. Group comparisons of impulsivity, alexithymia, and empathy controlled for age, anxiety, and depressive symptoms.

Abbreviations: AUDIT, Alcohol Use Disorder Identification Test; BDI-13, 13-item Beck Depression Inventory; BVAQ-B, Bermond-Vorst Alexithymia Questionnaire - Version B; CTQ, Childhood Trauma Questionnaire; FH-, Negative Family History; FH+, Positive Family History; FHD, Family History Density; FTND, Fagerström Test for Nicotine Dependence; IRI, Interpersonal Reactivity Index; MDE, Major Depressive Episode; NART, National Adult Reading Test; STAI, State Trait Anxiety Inventory; UPPS-P, UPPS Impulsive Behavior Scale.

^aMeans were calculated for participants who experienced drunkenness only ($n_{FH+} = 53$, $n_{FH-} = 44$).

^bMeans were calculated for smokers only ($n_{FH+} = 12$, $n_{FH-} = 12$). Data of two participants were missing for pack years ($n_{FH+} = 11$, $n_{FH-} = 11$).

Sociodemographic and clinical measures

Sociodemographic characteristics were collected through an extensive face to face interview with a trained investigator. The National Adult Reading Test (NART; Mackinnon & Mulligan, 2005) assessed general intellectual functioning. The Mini-International Neuropsychiatric Interview (MINI) for DSM-IV (Sheehan et al., 1998) was used to assess possible psychiatric disorders, including alcohol abuse and dependence, past major depressive episodes, suicide attempts, and anxiety disorders. The Alcohol Use Disorder Identification Test (AUDIT; Gache et al., 2005) screened for problematic alcohol consumption. The Fagerström test (Heatherton, 1991) assessed nicotine dependence. Depressive symptoms and anxiety were assessed with the 13-item Beck Depression Inventory (BDI-13; Collet & Cottraux, 1986), and the State Trait Anxiety Inventory (STAI; Spielberger et al., 1983). The presence of childhood trauma was evaluated with the Childhood Trauma Questionnaire (CTQ; Paquette et al., 2004).

Family history of alcohol and substance use disorders

The semi-structured Family Informant Schedule, and Criteria (Mannuzza et al., 1985) interview was used to assess the presence of any family history of AUD and other substance use disorders in biological relatives (parents, siblings, half-siblings, and children). Based on this information, we computed ratio scores of family history density (FHD) to go beyond the dichotomous FH+/FH- distinction. FHD scores allow to account for the number of family members with AUD relative to the total number of affected and unaffected family members (see Pandey et al., 2020, for the full equation). Only nondescendant first-degree relatives (parents, full siblings) were included in the equation.

Neuropsychological tasks

EF were evaluated with the Stroop Color-Word test (Golden, 1978), a measure of prepotent response inhibition, and the Trail Making Test Parts A and B (TMT; Reitan, 1958), a measure of mental flexibility. Both tasks include control conditions (Word and Color conditions in the Stroop test, Part A in the TMT), allowing to partially account for the multifaceted nature of EF tasks (Snyder et al., 2015) and both have been shown to be severely impaired in AUD (Stephan et al., 2017). For the Stroop test, the main outcomes were the number of items completed in 45s and the total number of errors for each condition. Based on these outcomes, we computed interference scores for completion times (see Golden, 1978) and difference scores for error rates as purer measures of inhibition abilities. For the TMT, the main outcomes were completion times (in s) and number of errors for Parts A and B. We calculated difference scores for completion times and errors (TMTB-A) as more explicit cognitive flexibility indices.

ToM abilities were evaluated with the Movie for the Assessment of Social Cognition (MASC; Dziobek et al., 2006). Participants were shown a 15-min movie featuring four protagonists having a dinner party on a Saturday night. From time to time, the movie was paused, and participants had to answer questions about the protagonists' mental states (i.e., emotions, thoughts, intentions). The MASC yields affective (i.e., comprehension of emotions) and cognitive (i.e., comprehension of thoughts and intentions) ToM scores. We also assessed the percentages of three error types, namely *excessive ToM* (overinterpretation of mental states), *reduced ToM* (understatement of mental states), and *absence of ToM* (responses not referring to mental states).

Other self-report measures

Participants completed the UPPS Impulsive Behavior Scale (UPPS-P; Billieux et al., 2012) assessing five impulsivity facets: negative urgency, positive urgency, lack of premeditation, lack of perseverance, and sensation seeking. The UPPS-P has been reported to have good internal consistency in the French population with Cronbach's alphas ranging from 0.70 to 0.84 for the various subscales (0.79–0.87 in our sample). The Bermond-Vorst Alexithymia Questionnaire (BVAQ-B; Zech et al., 1999) assessed alexithymic traits via five subscales: ability to fantasize, to identify emotions, to analyze emotions, to verbalize emotions, and to be emotionally aroused (emotionalizing). Two of these subscales (fantasizing, emotionalizing) reflect affective alexithymia and three reflect cognitive alexithymia (identifying, analyzing, and verbalizing). Cronbach's alphas for the BVAQ-B subscales indicate high internal consistency and ranged from 0.68 to 0.86 in the French population (0.36–0.79 in our sample). The Interpersonal Reactivity Index (IRI; Gilet et al., 2013) measured empathy via four subscales: empathic concern, personal distress, fantasy, and perspective-taking. Two of these subscales assess affective empathy (empathic concern, personal distress) and two assess cognitive empathy (fantasy, perspective-taking). The IRI has good internal consistency in the French population with Cronbach's alphas ranging from 0.70 to 0.81 for the various subscales (0.74–0.84 in our sample).

Data analysis

First, we explored differences between the FH+ and FH- participants at the group level. Chi-square tests were used for categorical variables and independent t tests for numerical variables for comparisons on sociodemographic and clinical variables. Then, Pearson correlation coefficients were computed to assess the relationship of age, anxiety, and depressive symptoms with EF, ToM, and self-report measures. Age, anxiety, and depressive symptoms have been shown to impact EF and ToM functioning in healthy adults (Grainger et al., 2023; Roye et al., 2022). For this reason, all subsequent group comparisons in this study were run with and without these variables

as covariates. For the analyses without covariates, we used independent sample *t* tests and for the analyses with covariates, we used univariate analyses of covariance (ANCOVAs) with group (FH+ vs. FH-) as the independent variable, the various EF, ToM, and self-report measures as dependent variables and age, BDI total scores and STAI-B total scores as covariates. Follow-up correlational analyses were used to investigate the link between EF, ToM, self-report measures, and family history density of AUD (FHD scores) in the FH+ sample ($n=60$).

Second, to test for EF and ToM difficulties at the individual level, we computed single-case analyses (modified *t* tests; Crawford & Howell, 1998). In the modified *t* tests, the test performance of each FH+ participant was compared with the mean performance of the matched control group (i.e., the FH- group): $t = (\text{FH+ participant score} - \text{mean FH- score}) / \text{SD FH-} \sqrt{(n_{\text{FH-}} + 1) / n_{\text{FH-}}}$. By treating the characteristics of the control group as statistics instead of parameters, this technique has been shown to substantially reduce the frequency of Type I errors (Crawford & Garthwaite, 2005). Modified *t* tests were computed for each EF and ToM main outcome and any score below -1.65 was deemed to reflect EF or ToM difficulties (one-sided $p < 0.05$).

We then assessed the proportions of FH+ participants exhibiting either EF difficulties (i.e., at least one EF measure below the standard cutoff), ToM difficulties (i.e., at least one ToM measure below the standard cutoff), or both (i.e., at least one EF and one ToM measure below the standard cutoff). This procedure allowed us to identify different EF and ToM patterns in FH+ participants. We then performed ANCOVAs, controlling for age, anxiety, and depressive symptoms, to assess differences between these cognitive FH+ patterns in EF and ToM tasks. FH+ subgroups were also compared on self-report measures and on sociodemographic and clinical variables. Post hoc pairwise comparisons were performed for significant differences between subgroups and were Bonferroni-corrected.

Group comparisons were considered significant at $p < 0.05$. Statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS 24 IBM Corp., Armonk, NY, USA).

RESULTS

Sociodemographic and clinical characteristics

The FH+ and FH- groups were comparable in terms of age, sex, education level, intellectual functioning, and alcohol and nicotine consumption (all $ps > 0.070$) (Table 1). Current depressive symptoms (BDI, $p < 0.001$) and trait anxiety (STAI-B, $p < 0.001$) were higher in the FH+ group than in the FH- group, but remained within the low range for all participants, according to clinical norms. Nevertheless, the FH+ group was characterized by a higher number of past suicide attempts ($p = 0.004$) and anxiety disorders ($p = 0.022$), according to the MINI. Childhood trauma was higher in the FH+ group than in the FH- group (CTQ, $p < 0.001$). According to the CTQ interpretation

guidelines, scores fell in the low to moderate range for the FH+ group (19 participants above the standard cutoff) and in the low range for the FH- group (six participants above the standard cutoff).

Correlations of age, anxiety, and depressive symptoms with neuropsychological and self-report measures

In the total sample ($n=120$), age showed a significant negative correlation with several impulsivity and alexithymia facets: UPPS-P Negative Urgency ($r = -0.20$, $p = 0.030$), UPPS-P Positive Urgency ($r = -0.25$, $p = 0.005$), UPPS-P Sensation Seeking ($r = -0.29$, $p = 0.001$), BVAQ-B Identify ($r = -0.19$, $p = 0.040$), and BVAQ-B Emotionalize ($r = -0.20$, $p = 0.028$). Age was also negatively correlated with Stroop interference scores ($r = -0.42$, $p < 0.001$) and cognitive ToM scores ($r = -0.21$, $p = 0.020$). Depressive symptoms were positively correlated with several impulsivity and alexithymia facets: UPPS-P Negative Urgency ($r = 0.53$, $p < 0.001$), UPPS-P Positive Urgency ($r = 0.32$, $p < 0.001$), UPPS-P Perseverance ($r = 0.26$, $p = 0.004$), BVAQ-B Identify ($r = 0.45$, $p < 0.001$), and BVAQ-B Verbalize ($r = 0.26$, $p = 0.005$). They were also significantly correlated with empathy subscales, except for the empathic concern subscale (IRI Concern, $r = -0.09$, $p = 0.349$). Finally, anxiety showed significant positive correlations with all impulsivity, alexithymia, and empathy facets, except for UPPS-P Sensation Seeking ($r = 0.91$, $p = 0.322$), BVAQ-B Fantasizing ($r = -0.14$, $p = 0.134$), BVAQ-B Analyzing ($r = 0.08$, $p = 0.388$), and IRI Concern ($r = 0.06$, $p = 0.552$) subscales. The subsequent group comparisons have been run with and without age, anxiety, and depressive symptoms as covariates.

Group comparisons on self-report measures

The FH+ group reported greater impulsivity than the FH- group in terms of negative urgency (UPPS-P Negative Urgency, $p < 0.001$), positive urgency (UPPS-P Positive Urgency, $p = 0.005$), and lack of premeditation (UPPS-P Premeditation, $p = 0.042$) and had more alexithymic traits, especially difficulties identifying emotions (BVAQ-B Identify, $p = 0.012$). As for empathy, the FH+ group had a greater tendency to transpose themselves into fictional situations than the FH- group (IRI Fantasize, $p = 0.045$). All these intergroup differences became nonsignificant when controlling for age, anxiety, and depressive symptoms (Table 1). FHD scores were not significantly correlated with any of the self-report measures within the FH+ group (all $ps > 0.160$).

Group comparisons on executive function and theory of mind measures

The FH+ and FH- groups differed significantly on the error difference score of the Stroop test ($p = 0.002$), highlighting lower resistance

TABLE 2 Comparison of FH+ and FH- groups on executive function and theory of mind measures.

	FH+ group (n=60)	FH- group (n=60)	Partial η^2	p Value
Executive functions				
Stroop interference score	3.66 (6.58)	3.83 (7.42)	0.003	0.543
Stroop error difference score	0.79 (1.19)	0.18 (0.83)	0.069	0.004
TMTB-A (time in s)	29.80 (16.28)	27.88 (12.94)	0.002	0.598
TMTB-A (errors)	0.07 (0.94)	0.10 (0.57)	0.002	0.640
Social cognition				
MASC Affective (% correct)	68.15 (11.70)	68.52 (11.05)	0.001	0.682
MASC Cognitive (% correct)	71.92 (9.35)	70.32 (10.51)	0.006	0.396
MASC Excessive ToM errors (%)	12.88 (5.03)	12.95 (4.83)	0.002	0.608
MASC Reduced ToM errors (%)	12.01 (5.55)	14.28 (6.07)	0.018	0.149
MASC Absent ToM errors (%)	4.74 (3.95)	3.18 (3.14)	0.041	0.029

Note: Data are means (standard-deviation). Group differences were examined with univariate analyses of variance controlling for age, anxiety, and depressive symptoms. Significant *p* values are highlighted in bold for $p < 0.05$.

Abbreviations: FH-, Negative Family History; FH+, Positive Family History; MASC, Movie for the Assessment of Social Cognition; TMT, Trail Making Test; ToM, theory of mind.

to interference in FH+ participants. Furthermore, FH+ participants differed on the types of errors made on the MASC: They less frequently chose response options reflecting *reduced ToM* ($p=0.034$), and more frequently chose response options reflecting an *absence of ToM* ($p=0.019$). All other EF and ToM measures were comparable across the FH+ and FH- groups (all $ps > 0.281$). When controlling for age, anxiety, and depressive symptoms, the error difference score of the Stroop test and the percentage of errors reflecting an *absence of ToM* still significantly differed between groups (Table 2). FHD scores were not significantly correlated with any EF or ToM measure within the FH+ group, even though the correlation between FHD scores and cognitive ToM scores was close to significance ($r = -0.21$, $p = 0.053$).

Correlations between executive function, theory of mind, and self-report measures

In the FH+ group, the Stroop interference score showed a positive correlation with the UPPS lack of perseverance subscale (UPPS-P Perseverance) which remained significant after controlling for multiple comparisons ($r = 0.42$, $p = 0.020$). No other self-report measure was significantly correlated with EF or ToM measures after applying corrections (all $ps > 0.289$).

Single-case analyses

In the FH+ group, 25% ($n=15$) of the participants had difficulties on at least one EF outcome, 16.67% on at least one ToM outcome ($n=10$), and 11.67% on at least one EF and one ToM outcome ($n=7$) compared with FH- participants. Hence, a total of 53.33% ($n=32$) of FH+ participants exhibited some cognitive weaknesses (EF, ToM, or both) while 46.67% ($n=28$) of FH+ participants had EF and ToM performances within the normal range (Figure 1).

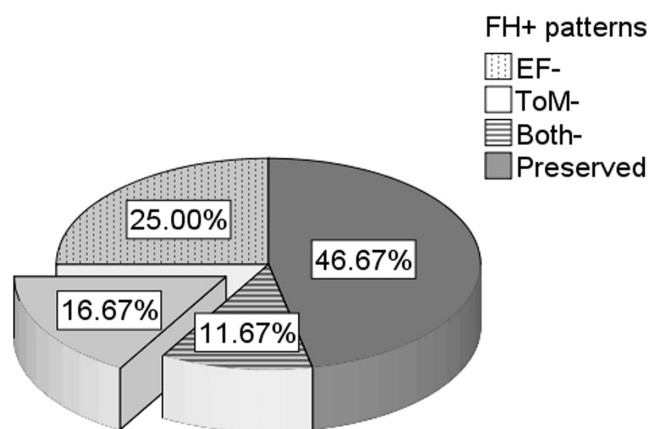


FIGURE 1 Proportions of FH+ participants ($n=60$) displaying executive function (EF) difficulties (EF-), theory of mind (ToM) difficulties (ToM-), EF and ToM difficulties (Both-), or preserved EF and ToM abilities (Preserved).

Among the FH+ participants with EF and/or ToM weaknesses, 59.38% had difficulties on one outcome ($n=19$), 21.88% on two outcomes ($n=7$), 12.50% on three outcomes ($n=4$), and 6.25% on four outcomes ($n=2$).

Comparisons of FH+ subgroups

FH+ participants who exhibited only EF difficulties were compared with FH+ who exhibited only ToM difficulties and with FH+ participants who were characterized by preserved EF and preserved ToM, controlling for age, anxiety, and depressive symptoms (Table 3). As only a small number of FH+ cases exhibited both, EF and ToM, difficulties ($n=7$), they were dropped from subgroup comparisons.

TABLE 3 Comparisons of FH+ subgroups on executive function and theory of mind measures.

	FH+ patterns		Preserved (n = 28)	FH- group (n = 60)	Group comparison	Post hoc comparisons ^a
	EF- (n = 15)	ToM- (n = 10)				
Executive functions						
Stroop interference score	1.71 (5.07)	6.90 (7.67)	4.72 (6.08)	3.83 (7.42)	$F(2,47)=3.31, p=0.045$	EF- < ToM-
Stroop error difference score	2.00 (0.93)	0.25 (0.72)	0.07 (0.62)	0.18 (0.83)	$F(2,47)=36.32, p<0.001$	EF- > (ToM-, Preserved)
TMTB-A (time in s)	31.33 (19.43)	26.40 (9.42)	25.25 (9.13)	27.88 (12.94)	$F(2,47)=0.92, p=0.406$	-
TMTB-A (errors)	0.53 (1.19)	-0.10 (0.74)	-0.21 (0.50)	0.10 (0.57)	$F(2,47)=4.22, p=0.021$	EF- > Preserved
Social cognition						
MASC Affective (% correct)	71.85 (7.41)	57.78 (12.34)	72.22 (9.18)	68.52 (11.05)	$F(2,47)=8.58, p=0.001$	ToM- < (EF-, Preserved)
MASC Cognitive (% correct)	75.38 (10.26)	65.39 (6.28)	74.59 (7.80)	70.32 (10.51)	$F(2,47)=4.72, p=0.014$	ToM- < (EF-, Preserved)
MASC Excessive ToM errors (%)	10.61 (4.52)	15.23 (4.68)	12.83 (2.92)	12.95 (4.83)	$F(2,47)=5.02, p=0.011$	ToM- > EF-
MASC Reduced ToM errors (%)	12.12 (4.83)	13.41 (8.12)	10.39 (3.30)	14.28 (6.07)	$F(2,47)=0.95, p=0.394$	-
MASC Absent ToM errors (%)	3.33 (2.25)	9.09 (4.29)	3.17 (2.58)	3.18 (3.14)	$F(2,47)=16.54, p<0.001$	ToM- > (EF-, Preserved)

Note: Data are means (standard-deviation). Group differences were examined with univariate analyses of variance controlling for age, anxiety, and depressive symptoms. Means for the EF- and ToM- groups that significantly differed from those of the FH- group are highlighted in bold.

Abbreviations: EF-, Executive function difficulties, FH-, Negative Family History, FH+, Positive Family History, MASC, Movie for the Assessment of Social Cognition, Preserved, No executive function or theory of mind difficulties, TMT, Trail Making Test, ToM-, theory of mind difficulties, ToM, theory of mind.

^aBonferroni corrections were applied to *p* values. Only pairwise comparisons reaching significance are listed in the table.

FH+ participants with EF difficulties had lower performances on the Stroop test than the other two FH+ subgroups as reflected by both, interference scores ($p=0.045$) and error difference scores ($p=0.021$). Moreover, they had higher error difference scores on the TMT compared with the other FH+ subgroups ($p<0.001$). Compared with the FH- participants, the error difference scores in the Stroop test were significantly higher in this FH+ subgroup ($p<0.001$).

FH+ participants with ToM difficulties performed more poorly on all the MASC outcome measures (affective and cognitive ToM scores, errors reflecting *excessive ToM* and an *absence of ToM*), except for the proportion of *reduced ToM* errors which was comparable across FH+ subgroups ($p=0.362$). Compared with the FH- group, this subgroup had significantly lower affective ToM performances ($p=0.004$) and a higher proportion of errors reflecting an *absence of ToM* ($p<0.001$).

As shown in Table 4, FH+ participants with ToM difficulties were characterized by higher affective alexithymia compared with the other FH+ subgroups (BVAQ-B Affective, $p=0.035$) and compared with the FH- group (BVAQ-B Affective, $p=0.026$), and notably reported reduced abilities to be emotionally aroused (BVAQ-B Emotionalize, $p=0.005$). Moreover, FH+ participants with ToM difficulties had less cognitive empathy (IRI Cognitive, $p=0.002$) than the other FH+ subgroups, as indicated by lower scores on the fantasizing (IRI Fantasizing, $p=0.032$) and perspective-taking (IRI Perspective-taking, $p=0.005$) subscales. Also, the FH+ participants with ToM

difficulties had lower scores on the empathic concern subscale than the FH+ participants with EF difficulties (IRI Concern, $p=0.010$). Compared with the FH- group, FH+ participants with ToM difficulties had significantly less affective empathy (IRI Affective, $p=0.017$), especially on the empathic concern subscale (IRI Concern, $p=0.010$). Impulsivity scores did not differ across FH+ subgroups (UPPS-P, all $ps>0.086$).

The FH+ subgroups were similar on sociodemographic and clinical measures (all $ps>0.274$). The results of these comparisons are included as supplemental material (Table S1).

DISCUSSION

Using a combination of group and single case analyses, this study highlighted differences between FH+ (i.e., healthy unaffected adults having at least one first-degree relative with a current or past AUD) and FH- participants for EF and ToM processes. Overall, group comparisons revealed that the FH+ group presented reduced abilities during tasks evaluating the inhibition of prepotent responses (i.e., Stroop test) and ToM (i.e., MASC) compared with those of the FH- group. These results echo previous findings that suggested specificities in EF (Gierski et al., 2013; Lees et al., 2020) and SC (Hill et al., 2007; Khemiri et al., 2022) processes in FH+ individuals but provide additional insights.

TABLE 4 Comparisons of FH+ subgroups on self-report measures of impulsivity, alexithymia, and empathy.

	FH+ patterns			FH- (n = 60)	Group comparison	Post hoc pairwise comparisons ^a
	EF- (n = 15)	ToM- (n = 10)	Preserved (n = 28)			
UPPS-P Negative Urgency	8.93 (3.33)	8.00 (2.83)	9.32 (3.43)	7.07 (2.14)	$F(2,47)=0.72, p=0.931$	-
UPPS-P Positive Urgency	9.67 (3.62)	9.80 (2.15)	10.04 (2.70)	8.60 (2.44)	$F(2,47)=0.23, p=0.798$	-
UPPS-P Premeditation	6.13 (1.77)	7.00 (2.16)	7.04 (2.38)	6.23 (1.77)	$F(2,47)=0.88, p=0.421$	-
UPPS-P Perseverance	5.60 (1.81)	7.30 (3.47)	6.25 (1.80)	5.92 (2.04)	$F(2,47)=2.58, p=0.086$	-
UPPS-P Sensation Seeking	8.73 (3.13)	9.10 (3.21)	8.36 (2.73)	8.63 (2.56)	$F(2,47)=0.46, p=0.635$	-
BVAQ-B Fantasize	10.47 (4.09)	11.30 (2.31)	9.79 (3.79)	10.48 (3.33)	$F(2,47)=0.64, p=0.532$	-
BVAQ-B Identify	7.40 (2.47)	8.50 (2.76)	9.18 (2.75)	7.03 (2.80)	$F(2,47)=2.29, p=0.113$	-
BVAQ-B Analyze	6.87 (2.00)	8.80 (3.68)	8.07 (2.28)	7.17 (2.51)	$F(2,47)=2.07, p=0.137$	-
BVAQ-B Verbalize	9.53 (3.54)	12.90 (4.18)	12.64 (4.35)	10.92 (4.10)	$F(2,47)=3.73, p=0.031$	-
BVAQ-B Emotionalize	8.40 (2.17)	12.30 (4.19)	8.93 (2.42)	9.32 (2.49)	$F(2,47)=5.96, p=0.005$	ToM- > (EF-, Preserved)
BVAQ-B Affective	18.87 (5.08)	23.60 (4.84)	18.71 (4.56)	19.80 (4.34)	$F(2,47)=3.60, p=0.035$	ToM- > Preserved
BVAQ-B Cognitive	23.80 (6.26)	30.20 (8.73)	29.89 (7.88)	25.12 (7.15)	$F(2,47)=4.30, p=0.019$	(ToM-, Preserved) > EF-
IRI Concern	29.80 (3.41)	22.10 (9.02)	27.46 (5.72)	28.32 (4.41)	$F(2,47)=4.78, p=0.013$	ToM- < EF-
IRI Distress	18.20 (6.75)	17.70 (3.27)	18.14 (4.16)	18.07 (5.53)	$F(2,47)=0.16, p=0.849$	-
IRI Fantasy	26.47 (5.90)	20.40 (6.02)	26.00 (5.09)	23.17 (6.22)	$F(2,47)=3.69, p=0.032$	ToM- < (EF-, Preserved)
IRI Perspective-taking	27.13 (4.00)	21.60 (6.02)	23.14 (4.58)	25.23 (4.80)	$F(2,47)=5.84, p=0.005$	(ToM-, Preserved) < EF-
IRI Affective	48.00 (7.31)	39.80 (10.28)	45.61 (7.08)	46.38 (7.82)	$F(2,47)=2.92, p=0.064$	-
IRI Cognitive	53.60 (6.59)	42.00 (9.32)	49.14 (7.18)	48.40 (8.58)	$F(2,47)=7.13, p=0.002$	ToM- < (EF-, Preserved)

Note: Data are means (standard-deviation). Group differences were examined with univariate analyses of variance controlling for age, anxiety, and depressive symptoms. Means for the EF- and ToM- groups that significantly differed from those of the FH- group are highlighted in bold.

Abbreviations: BVAQ-B, Bermond-Vorst Alexithymia Questionnaire - Version B; EF-, Executive function difficulties; FH-, Negative Family History; FH+, Positive Family History; IRI, Interpersonal Reactivity Index; Preserved, no executive function or theory of mind difficulties; ToM-, theory of mind difficulties; UPPS-P, UPPS Impulsive Behavior Scale.

^aBonferroni corrections were applied to *p* values. Only pairwise comparisons reaching significance are listed in the table.

Previous studies have mainly investigated socioemotional processes during the implicit processing of emotional facial expressions in FH+ participants (Cservenka, 2016). Few studies have explored common SC components (i.e., emotion recognition, empathy, and ToM), and if so, they have only targeted affective SC components such as emotion recognition, emotion regulation or affective ToM (i.e., mental state decoding). ToM, a key component of SC, has been shown to be severely impaired in individuals with AUD (Bora & Zorlu, 2017), but only one prior fMRI study has investigated affective and cognitive ToM performances in FH+ individuals (Schmid et al., 2023). This study reported higher brain activation in the left insula and inferior frontal cortex in FH+ compared with FH- individuals. Our results extend these findings and indicate that differences in terms of ToM processing not only exist at the neural level in FH+ participants but can also be found at the behavioral level, in a higher order SC task assessing mental state reasoning.

Furthermore, our study was the first to investigate EF and ToM heterogeneity in FH+ individuals through single-case analyses (Crawford & Howell, 1998). Results indicated that EF and ToM specificities were present in approximately half of FH+ participants (53.33%), whereas the other FH+ participants had EF and

ToM performances within the normal range (47.67%). This result echoes previous findings in AUD which have reported EF and ToM alterations in one out of two patients, suggesting heterogeneous cognitive patterns in this pathology (Maurage et al., 2015; Schmid et al., 2021). Prior studies of EF and SC abilities in FH+ individuals have yielded divergent results, with some suggesting EF and SC alterations (Dougherty et al., 2015; Henderson et al., 2018) and others equivalent behavioral performances across FH+ and FH- individuals (DeVito et al., 2013; Schmidt et al., 2017). The fact that FH+ individuals are not a homogeneous group at the cognitive level may explain these apparently contradictory results. Many FH+ individuals have no cognitive difficulties, consistent with FH+ studies reporting only small to medium effect sizes with EF and SC tasks (Kirk-Provencher et al., 2023).

Moreover, some FH+ individuals mainly display EF difficulties, suggesting reduced cognitive control, while others mainly display SC difficulties. Prior literature has indeed suggested that EF and ToM processes may best be represented as two interrelated but independent cognitive domains (Apperly et al., 2005). The double dissociations observed within the FH+ group of this study corroborate this idea and suggest that EF and ToM specificities may constitute two different mechanisms which may be driving

AUD vulnerability. It is noteworthy that the SC difficulties of FH+ participants manifested themselves not only in the ToM task used in this study, but also in the self-report measures of alexithymia and empathy. The FH+ participants with reduced ToM abilities reported diminished emotional arousal (higher alexithymic traits) as well as difficulties in fantasizing and perspective-taking (lower empathy), relative to the other FH+ subgroups, indicating the presence of wide-ranging socioemotional weaknesses in this FH+ subgroup.

Considering the fact that differences on self-report measures were observed between FH+ subgroups, it may seem surprising that self-report measures did not differ between the FH+ group and the FH- group and that EF, ToM, and self-report measures were only weakly correlated in the FH+ sample. An explanation for these findings may lie in the poor reliability of most behavioral measures and the fact that behavioral and self-report measures involve different response processes as pointed out by Dang et al. (2020). For these reasons, behavioral and self-report measures may show weak associations even when evaluating similar or related psychological constructs.

The cognitive difficulties in EF and SC tasks observed in FH+ participants seem to indicate the presence of cognitive vulnerability factors in this population. This is all the more likely when considering that AUD patients commonly present EF and SC impairments on these same tasks and that FH+ participants share genetic and environmental factors with their family members affected by AUD. In the FH+ group of this study, FHD scores were mostly unrelated to EF, SC, and self-report measures and the FH+ patterns did not differ on FHD scores in subgroup comparisons. It is possible that EF and SC difficulties of FH+ participants are associated with the presence versus the absence of any first-degree family member with AUD *per se* rather than with the number of family members and the familial loading of AUD. However, this finding needs to be treated with caution and should be further investigated with FH+ samples including individuals from multiplex alcohol use disorder families who present higher FHD scores.

In our study, vulnerability factors in FH+ participants were not only present in terms of cognitive performances but also at the clinical level in terms of mental health symptoms. FH+ participants were indeed characterized by more anxiety and depressive symptoms, more frequent childhood trauma, and a higher number of suicide attempts compared with FH- participants. Even though these symptoms were not in the clinical range and even though FH+ participants were exempt of AUD, substance use disorders, and major psychiatric disorders, the presence of such mental health symptoms may increase the risk for heavy drinking. As pointed out by several studies, psychopathological symptoms and negative affect represent one out of various pathways which may lead to alcohol misuse and possibly AUD (Guinle, 2020; Ham et al., 2009).

Still, this study included healthy FH+ participants and most of them were characterized by low alcohol consumption. Hence, while these FH+ participants may have had risk factors for AUD development compared with FH- participants, they were also likely to

have resiliency factors protecting against mental health issues (Long et al., 2017). A dimensional approach to AUD vulnerability may be the most opposite one, with FH+ individuals being placed on a vulnerability-resiliency continuum. The balance between vulnerability and resiliency factors may be decisive in this population and determine whether an individual goes on to develop any problematic alcohol consumption or AUD.

Future research is necessary to identify FH+ individuals with a higher degree of clinical and cognitive vulnerability for preventive purposes. Moreover, studies should examine if the EF and SC differences between the FH+ patterns of this study are associated with differences in terms of AUD vulnerability. In this context, longitudinal studies are needed to assess clinical variables, cognitive performances, and their mutual relationships over time. Also, studies on EF and SC abilities in FH+ participants should more systematically explore the relationships between clinical variables and cognitive performances in their FH+ sample. Studies may especially explore differences between the identified FH+ patterns on clinical variables which have not been evaluated in this study (e.g., attachment style, sleep quality, personality traits, and self-esteem). In the long run, such an approach may hone our understanding of the relationship between cognitive performances and clinical vulnerability and inform about possible mediating/moderating factors in FH+ individuals.

This study had several strengths, notably the combined use of group and single-case analyses to advance our current understanding of EF and ToM processes in FH+ individuals. We nevertheless need to acknowledge several limitations. First, the cross-sectional nature of this study meant that we could not establish whether EF and ToM specificities in FH+ individuals constitute actual triggers for AUD or for other mental health conditions. In this context, it should be noted that the presence of a family history of disorders other than AUD and substance use disorders was not collected in this study. Participants may thus have had first-degree family members affected by other mental health disorders. Second, the comparisons of FH+ subgroups did not include FH+ individuals with concomitant EF and ToM difficulties owing to the very low number of FH+ cases with this cognitive pattern. Further research is warranted to investigate the combined effects of EF and ToM difficulties in FH+ individuals. Third, our sample included more women than men. Given that some studies have highlighted the effects of sex on EF and ToM processes in FH+ individuals (Elton et al., 2023), FH+ patterns may vary according to sample characteristics.

To conclude, FH+ participants showed difficulties in terms of EF and ToM processing compared with FH- participants. This study is the first to highlight ToM difficulties in FH+ participants in a task assessing cognitive and affective ToM (i.e., mental state reasoning), thereby showing that differences during ToM processing are not only found at the neural but also at the behavioral level in this population. However, FH+ individuals form a heterogeneous group and differ considerably on EF and ToM abilities. It may be that EF and ToM difficulties represent distinct vulnerability factors for AUD

even though further research is warranted to examine the respective contribution of these two cognitive domains to AUD development.

AUTHOR CONTRIBUTIONS

Each author contributed significantly to this study and approved the final version of the article. FS was responsible for study conception and design, data collection, data analysis, drafting and revising the article. AH was responsible for study conception and design, supervision of analyses, drafting and revising the article. FB was responsible for data collection and revising the article. SB was responsible for participants' recruitment, data collection, and revising the article. JG was responsible for data collection and revising the article. AK was responsible for funding, supervision of analyses, and revising the article. FG was the principal investigator of this study and was responsible for study conception and design, supervision of analyses, drafting and revising the article.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to disclose.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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