

Facial emotion perception in schizophrenia: Does sex matter?

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Abstract

AIM: To review the literature on sex differences in facial

emotion perception (FEP) across the schizophrenia spectrum.

METHODS: We conducted a systematic review of empirical articles that were included in five separate meta-analyses of FEP across the schizophrenia spectrum, including meta-analyses that predominantly examined adults with chronic schizophrenia, people with early (onset prior to age 18) or recent-onset (experiencing their first or second psychotic episode or illness duration less than 2 years) schizophrenia, and unaffected first-degree relatives of people with schizophrenia. We also examined articles written in English (from November 2011 through June 2015) that were not included in the aforementioned meta-analyses through a literature search in the PubMed database. All relevant articles were accessed in full text. We examined all studies to determine the sample sizes, diagnostic characteristics, demographic information, methodologies, results, and whether each individual study reported on sex differences. The results from the meta-analyses themselves as well as the individual studies are reported in tables and text.

RESULTS: We retrieved 134 articles included in five separate meta-analyses and the PubMed database that examined FEP across the schizophrenia spectrum. Of these articles, 38 examined sex differences in FEP. Thirty of these studies did not find sex differences in FEP in either chronically ill adults with schizophrenia, early-onset or recently diagnosed people with schizophrenia, or first-degree relatives of people with schizophrenia. Of the eight studies that found sex differences in FEP, three found that chronically ill women outperformed men, one study found that girls with early-onset schizophrenia outperformed boys, and two studies found that women (including first-degree relatives, adults with schizophrenia, and the healthy control group) outperformed men on FEP tasks. In total, six of the eight studies that examined sex differences in FEP found that women outperformed men across the

schizophrenia spectrum.

CONCLUSION: Evidence to date suggests few sex differences in FEP in schizophrenia; both men and women across the schizophrenia spectrum have deficits in FEP.

Key words: Clinical high risk; Emotion; Facial emotion perception; Gender; Recent-onset schizophrenia; Schizophrenia; Sex differences

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Core tip: People with schizophrenia exhibit deficits in facial emotion perception (FEP) compared to healthy controls. These deficits are associated with poorer functioning and more severe symptoms. Although the literature to date suggests that there are few sex differences in FEP in schizophrenia, continued assessment of sex differences in FEP can help researchers and clinicians better understand other sex differences in the disorder and assist in treatment development aimed at improving functioning in people with schizophrenia. This review summarizes and critically evaluates the literature on FEP across the schizophrenia spectrum, focusing on the evidence related to sex differences in FEP.

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INTRODUCTION

"The movements of expression in the face and body, whatever their origin may have been, are in themselves of much importance for our welfare" (Charles Darwin, p. 229, *The Expression of the Emotions in Man and Animals*^[1]).

Facial emotion perception (FEP), or the ability to accurately identify the emotion on the face of another person, is an integral part of our everyday lives. FEP is a crucial component of our ability to function interpersonally in the world^[2]. Whether it is identifying happiness from a smiling infant or disappointment from an employer during a performance review, our perception of the emotions of others influences our thoughts ("She looks so peaceful in my arms", "I hope I don't get fired") and behaviors (smiling back, promising to improve performance) towards them. Without this ability, many of the interpersonal skills required to function in daily life - engaging in socially appropriate behaviors, empathy, prosocial behavior, conflict resolution - would suffer.

Due to its importance related to interpersonal skills, FEP has been studied extensively in schizophrenia, a

mental illness characterized by (among other features) poor social functioning, social cognition deficits, and emotion response deficits^[3,4]. People with schizophrenia are less accurate at FEP compared to people without schizophrenia^[5-9], and poorer accuracy on FEP tasks is positively correlated with poorer functioning, poorer social skills, and more severe symptoms, particularly negative symptoms, in schizophrenia^[3,8,10]. To illustrate, imagine a person with schizophrenia who consistently perceives the smiling face of his landlord as anger (inaccurate FEP). This may lead to confusion, where the person may not understand why his landlord is angry, which may further lead the person with schizophrenia to perceive his landlord's expressions as unjustified or cruel. These thoughts may enhance this person's feelings of mistrust regarding those around him and lead him to socially isolate himself more from others (increased symptom severity). This person may begin to feel so confused and frustrated by his landlord's unjustified anger that he shouts at his landlord, which may ultimately lead to eviction and temporary homelessness (impairment of functioning). While this is just a fictitious example, it is clear that poor FEP can impact a person with schizophrenia's capacity to function in the world day-to-day.

The relationship between FEP and functioning in schizophrenia has led to the development of cognitive remediation interventions that target emotion perception abilities, including FEP (e.g., teaching people with schizophrenia that a scowling face represents anger, a smiling face represents happiness, etc.). These interventions have been found to improve functioning (e.g., social skills, community functioning) in people with schizophrenia^[11]. Interestingly, a recent meta-analysis found that this relationship was moderated by sex: There was a stronger positive correlation between functional outcome and FEP in men compared to women with schizophrenia^[10]. In other words, men with schizophrenia appeared to benefit more (show improved functioning) from interventions targeting FEP compared to women.

Sex differences in schizophrenia have been studied extensively in many domains of the illness^[12-15]. For example, reviews and meta-analyses have shown that men have a 1.15-1.4:1 higher incidence of schizophrenia compared to women^[16-19]. Men also have an earlier age of onset compared to women across varying definitions of onset (e.g., first psychotic symptoms, first diagnosis, first hospitalization)^[20,21]. Women on average have a better treatment response to antipsychotic medications compared to men, including a more rapid treatment response and lower required dose to achieve a response^[12,22]. Further, women with schizophrenia tend to have a less severe course of the illness, including a lower frequency of hospitalization, less severe negative symptoms, better social skills, and better overall functioning^[23,24]. However, no review to date has examined sex differences in FEP.

One possibility is that women with schizophrenia are better at FEP compared to men. Women with schizophrenia (when compared to men) exhibit clinical features (less severe illness course, less severe negative symptoms, better overall functioning, better social skills) that are typically associated with better FEP performance. Further, healthy women are more accurate at FEP than healthy men^[25-27].

This review will examine the literature on FEP in schizophrenia and summarize relevant findings related to sex differences in chronically ill adults with schizophrenia, people with early or recent-onset schizophrenia, and people at clinical high risk for developing schizophrenia (specifically, unaffected first-degree relatives of people with schizophrenia). We will summarize relevant meta-analyses and studies included within the meta-analyses, focusing on results with regards to sex differences in FEP. We will also review the findings from the recent studies (2011-2015) that examined sex differences in FEP in schizophrenia but were not included in the summarized meta-analyses. Finally, we will offer a critical analysis of previous research on understanding sex differences in FEP and considerations for future research.

MATERIALS AND METHODS

Tasks that assess FEP can be divided broadly into two categories: Identification tasks and discrimination tasks. In identification tasks, participants view photographs or images of emotional faces that have been previously tested to categorically portray one emotion (e.g., Ekman stimuli)^[28] and are instructed to choose among a list of multiple emotion terms (forced-choice) the word that best describes the emotion portrayed on the face. Similarly, on identification tasks participants may be asked to rate on an anchored scale the valence (pleasant/unpleasant) the face is portraying or decide whether or not a face is portraying one emotion (e.g., happiness) vs another (e.g., sadness). Alternatively, on discrimination tasks participants are typically asked to view two emotional faces and state whether or not the stimuli match on emotion (label) or valence, or they may be asked to match a target face with the face among an array of facial stimuli that "matches" the target's emotion. Studies will be identified throughout the review as to whether they include an identification task or a discrimination task.

Within this review, we summarize recent meta-analyses of FEP in schizophrenia across the schizophrenia spectrum, including meta-analyses that predominantly examined adults with chronic schizophrenia (illness duration greater than 2 years)^[5,7,9], people with early (onset before age 18) or recent-onset (experiencing their first or second psychotic episode or illness duration less than 2 years) schizophrenia^[29], and unaffected first-degree relatives of people with schizophrenia^[30]. While meta-analytic results related to sex differences in FEP

will be discussed, an examination of all studies included in the meta-analyses will be conducted to determine the quantity, samples sizes, methodologies, and results of studies that examined sex differences in FEP to better compare studies that examined sex differences with those that did not.

In order to examine recent studies on sex differences in FEP that were not included in the meta-analyses, we conducted a literature review in the PubMed database. We searched for studies in English from November 2011 (the cut-off for studies included in Savla *et al.*^[9]) through June 2015. Keywords included in the search were "schizophrenia" or "psychosis" in the article title or abstract, and "gender difference" or "sex difference" and "emotion recognition" or "emotion percept*" in the body of studies. The original search resulted in 319 studies. Exclusion criteria included studies that: (1) did not examine people on the schizophrenia spectrum or a group of first-degree relatives of people with schizophrenia; (2) did not include at least one FEP task; (3) did not include a relevant nonclinical comparison group; (4) examined unconscious processing of facial stimuli; or (5) used dynamic stimuli (e.g., films). Following application of exclusion criteria, 22 relevant empirical articles were identified, including 20 studies with chronically ill adults with schizophrenia, one study with early-onset schizophrenia, and one study with people at clinical high risk for schizophrenia, including a group of unaffected first-degree family members (see Table 1 for summary of all studies that examined sex differences in FEP in schizophrenia).

RESULTS

Adults with chronic schizophrenia

Three recent meta-analyses have examined FEP in schizophrenia and have included sex as a potential moderating factor in their analyses^[5,7,9]. Predominantly, these meta-analyses included studies with chronically ill adults with schizophrenia, although they also included a smaller number of studies with early or recent-onset samples of people with schizophrenia as well as first-degree relatives of people with schizophrenia.

Kohler *et al.*^[7] analyzed 53 studies on FEP in people with schizophrenia published from 1970-2007. They found that irrespective of task type (identification or discrimination), people with schizophrenia showed impairments in FEP compared to healthy controls, with poorer performance correlated with both positive and negative symptoms, later age of onset, and inpatient status. There were no significant differences in the effect sizes of FEP performance between task types (identification vs discrimination). The authors investigated the effects of sex on FEP by examining whether the percentage of men with schizophrenia or men without schizophrenia moderated the effect sizes of the study results. They found that the percentage of male controls, but not the percentage of men with

Table 1 Description of studies across meta-analyses that examine sex differences in facial emotion perception in schizophrenia

Ref.	Cited from	SZ group(s)	SZ group description			CT group description		CHR group description		FEP task	Stimuli emotion description	Sex difference results
			<i>n</i>	% women	In/out	<i>n</i>	% women	<i>n</i>	% women			
Addington <i>et al</i> ^[44]	Chan, Kohler	Chronic	40	33	IN	40	43			ID and DISC	Anger, disgust, fear, happy, neutral, sad, surprise	None
Alfimova <i>et al</i> ^[84]	Lavoie	CHR, chronic	103	59	IN	99	67	55	49	ID	Anger, contempt, disgust, fear, happy, interest/excitement, neutral, sad, shame, surprise	Women > men
Amminger <i>et al</i> ^[73]	Barkl	CHR, first-episode	30	40	OUT	30	50	79	67	ID	Anger, disgust, fear, happy, neutral, sad, surprise	None
Bellack <i>et al</i> ^[45]	Chan	Chronic	35	49	IN	19	58			ID and DISC	Anger, disgust, fear, happy, sad, surprise	None
Bölte <i>et al</i> ^[76]	Kohler	CHR, early-onset	21	29	OUT	22	50			ID	Anger, disgust, fear, happy, neutral, sad, surprise	None
Borod <i>et al</i> ^[42]	Kohler, Savla	Chronic	20	5	OUT	21	48			DISC	Anger, disgust, fear, happy, neutral, sad, surprise	None
Castagna <i>et al</i> ^[69]	PubMed	Chronic	94	30	OUT	51	62			ID	Anger, disgust, fear, happy, neutral, sad, surprise	None
de Achával <i>et al</i> ^[31]	Savla	CHR, chronic	20	35	OUT	40	45	20	55	ID	Afraid, anger, disgust, distress, happy, sad, surprise	None
Donohoe <i>et al</i> ^[70]	PubMed	Chronic	487	28	OUT	163	60			ID	Not listed	None
Erol <i>et al</i> ^[80]	Lavoie	CHR, chronic	57	39	OUT	58	40	58	41	ID and DISC	Anger, fear, happy, sad, shame, surprise	None
Erol <i>et al</i> ^[72]	PubMed	Chronic	70	50	OUT	70	50			ID and DISC	Anger, fear, happy, sad, shame, surprise	Women with SZ = women and men CT
Gessler <i>et al</i> ^[50]	Chan	Chronic, recent-onset	60	38	Not described	20	50			ID	Happy, sad	Men > women
Habel <i>et al</i> ^[77]	Chan, Kohler	Early-onset, recent-onset	20	50	IN	20	50			ID	Happy, neutral, sad	Men > women
Kington <i>et al</i> ^[32]	Savla	Chronic	16	19	IN and OUT	16	19			ID	Afraid, anger, disgust, distress, happy, sad, surprise	None

Kohler <i>et al</i> ^[51]	Chan, Kohler, Savla	Chronic	35	43	OUT	45	44			ID	Happy, neutral, sad	Women > men
Kohler <i>et al</i> ^[33]	Kohler	Chronic	28	32	OUT	61	52			ID	Anger, disgust, fear, happy, neutral, sad	None
¹ Kohler <i>et al</i> ^[86]	PubMed	CHR, chronic	91	33	OUT	90	49	52	48	ID and DISC	Anger, fear, happy, neutral, sad	None
Kucharska-Pietura <i>et al</i> ^[58]	Chan	Chronic	50	48	IN	50	52			ID	Interest-excitement, enjoyment-joy, surprise-startle, distress-anguish, disgust, contempt, anger-rage, shame-humiliation, fear-terror	None
² Kucharska-Pietura <i>et al</i> ^[35]	Chan, Kohler, Savla	Chronic, recent-onset	100	49	IN	50	52			ID	Interest-excitement, enjoyment-joy, surprise-startle, distress-anguish, disgust, contempt, anger-rage, shame-humiliation, fear-terror	Women > men
Kucharska-Pietura <i>et al</i> ^[34]	PubMed	Chronic	84	48	IN	50	50			ID	Anger, disgust, fear, happy, neutral, sad, surprise	None
Leitman <i>et al</i> ^[46]	Kohler, Savla	Chronic	43	23	IN and OUT	34	59			ID and DISC	Anger, fear, happy, sad, shame, surprise	None
Leppänen <i>et al</i> ^[85]	Lavoie	CHR, chronic	36	28	OUT	22	50	23	65	ID	Anger, happy, neutral	Women > men
² Leung <i>et al</i> ^[74]	Barkl	Chronic, recent-onset	101	46	OUT	54	46			ID	Anger, disgust, fear, happy, sad, surprise	None
McCown <i>et al</i> ^[81]	Lavoie	CHR				50	50	50	50	ID	Disgust, fear, happy, neutral, sad, surprise	None
Mendoza <i>et al</i> ^[82]	Lavoie	CHR, chronic	93	33	OUT	109	63	110	41	ID	Anger, disgust, fear, happy, neutral, sad, surprise	None
Mueser <i>et al</i> ^[47]	Chan, Kohler, Savla	Chronic	28	53	IN	15	67			ID and DISC	Anger, disgust, happy, sad, shame, surprise	None
Muzekari <i>et al</i> ^[36]	Kohler	Chronic	32	50	IN	32	50			ID	Anger, fear, happy, sad	None
Novic <i>et al</i> ^[37]	Chan, Kohler, Savla	Chronic	17	24	IN	17	59			DISC	Not listed	None

Penn <i>et al</i> ^[43]	Chan, Kohler	Chronic	74	30	IN	40	53		DISC	Anger, disgust, happy, sad, shame, surprise	None	
Reske <i>et al</i> ^[75]	Barkl, Savla	Recent-onset	18	44	OUT	18	44		ID	Happy, neutral, sad	None	
Rubin <i>et al</i> ^[38]	Savla	Chronic	48	46	IN and OUT	57	54		ID	Happy, neutral, sad	None	
Sachs <i>et al</i> ^[48]	Kohler, Savla	Chronic	40	38	IN	43	44		ID and DISC	Happy, sad	None	
Schneider <i>et al</i> ^[39]	Chan, Kohler	Chronic	40	48	IN and OUT	40	48		ID	Happy, sad	None	
Schneider <i>et al</i> ^[40]	Chan, Kohler, Savla	Chronic	20	50	IN	20	50		ID	Anger, fear, happy, neutral, sad	None	
Scholten <i>et al</i> ^[52]	Chan, Kohler, Savla	Chronic	53	47	IN and OUT	42	50		ID	Anger, disgust, fear, happy, sad, surprise	Women > men	
Walker <i>et al</i> ^[41]	Kohler	Chronic, recent-onset	48	48	IN	48	48		ID	Afraid, ashamed, curious, disgust, joy, mad, sad, surprise	None	
Weniger <i>et al</i> ^[49]	Chan, Kohler, Savla	Chronic	45	38	IN and OUT	30	50		ID and DISC	Anger, disgust, fear, joy, neutral, surprise	None	
Wolf <i>et al</i> ^[83]	Lavoie	CHR				25	52	20	55	ID	Anger, fear, happy, neutral, sad	None

¹Only first-degree relatives of people with schizophrenia included in "CHR group description"; ²Chronic and recent-onset groups combined in "SZ group description". SZ: Schizophrenia; CT: Control; CHR: Clinical high risk; IN: Inpatient; OUT: Outpatient; ID: Identification task; DISC: Discrimination task.

schizophrenia, significantly moderated the effect sizes of FEP results. Specifically, the higher the percentage of male controls included in studies, the smaller the magnitude of group differences in FEP between controls and people with schizophrenia. The authors suggested that because healthy men perform worse on FEP than healthy women^[27], having more women in the control group may have boosted the overall control group mean, thus amplifying group differences between people with and without schizophrenia. Furthermore, because the percentage of men with schizophrenia did not significantly moderate the effect sizes in FEP, the authors concluded that men and women with schizophrenia performed similarly on FEP tasks.

Chan *et al*^[5] analyzed 28 FEP studies in schizophrenia published from 1980-2008. This meta-analysis differed from Kohler *et al*^[7] in that their study inclusion criteria required that the study not only include an identification and/or discrimination FEP task, but also a "control" facial processing task (e.g., identifying the age or sex of the facial stimuli) in addition to an FEP task. In examining this smaller pool of studies, they found that people with schizophrenia showed impairments in both identification and discrimination FEP tasks compared to healthy controls. However, unlike Kohler *et al*^[7], their results showed that poorer FEP performance was

only correlated with negative, not positive, symptoms. Furthermore, through meta-regression analyses, the authors found that sex did not have a significant effect on FEP performance in schizophrenia. That is, men and women with schizophrenia performed similarly on FEP tasks in the studies included in their meta-analysis.

Savla *et al*^[9] conducted a meta-analysis on 112 studies published from 1980-2011 to examine seven aspects of social cognition in schizophrenia. They included 62 studies that examined "emotion perception" broadly in schizophrenia, including studies that asked participants to identify the emotion portrayed on facial stimuli, through the vocal prosody of audio stimuli, and/or as portrayed by actors in film stimuli. Of these 62 studies, 54 included an FEP task. They found that people with schizophrenia were significantly worse at identifying emotions across different emotion perception tasks compared to healthy controls. They found that inpatient status (compared to outpatient status) significantly contributed to the heterogeneity of effect sizes across studies, suggesting that inpatients showed greater deficits in emotion perception. The percentage of male participants did not significantly account for variability in study effect sizes.

In sum, across 81 non-overlapping studies of FEP in three meta-analyses, sex was not a significant

moderator of effect sizes for the schizophrenia group. In other words, it does not appear as if men and women with schizophrenia differ in FEP, and that both men and women with schizophrenia perform worse than healthy controls. However, the meta-analyses may have been underpowered to detect sex differences as not every study within the meta-analyses included a substantial number of women with schizophrenia. Indeed, only 22 of the 81 studies included a sample of at least 39%-40% women. Further, these meta-analyses examined studies that included samples other than only chronically ill adults with schizophrenia. To more systematically examine sex differences in FEP in adults with chronic schizophrenia, we reviewed the specific studies from the meta-analyses.

Of the 81 non-overlapping studies from Kohler *et al.*^[7], Chan *et al.*^[5] and Savla *et al.*^[9], 59 studies either failed to report on sex differences in FEP or statistically controlled for sex in their analyses. Twenty-two studies examined sex differences in FEP in adult samples of chronically ill people with schizophrenia. The majority of these studies ($n = 19$) did not find sex differences in FEP, either on identification tasks^[31-41], discrimination tasks^[42,43], or in studies that included both task types^[44-49].

Three studies included in Kohler *et al.*^[7], Chan *et al.*^[5], and Savla *et al.*^[9] found sex differences in FEP performance on identification tasks in adults with chronic schizophrenia. One study found that men outperformed women overall (*i.e.*, in both the control and schizophrenia groups)^[50]. Two studies found that women, regardless of diagnostic status, performed better than men^[51,52]. Specifically, Kohler *et al.*^[51] found that sex was a moderator in participant performance on a task where participants were asked to rate on a seven-point scale (varying from very sad, to neutral, to very happy) the emotion of putatively happy, sad, and neutral faces: Women with and without schizophrenia made significantly fewer errors in identifying emotion compared to men. Scholten *et al.*^[52] found that overall, women performed better than men on an FEP identification task only for negative faces (including facial stimuli portraying fear, sadness, and disgust). To summarize, when comparing chronically ill people with schizophrenia to healthy controls, only two of the 22 studies that examined sex differences provided evidence that women with schizophrenia outperform men on FEP tasks.

From our PubMed search of more recent studies not included in the meta-analyses, a total of 16 of the 20 studies that examined adults with chronic schizophrenia either did not report on sex differences or controlled for sex in their FEP analyses^[53-67], with one study including an all-male sample^[68]. Of the remaining four studies, three studies did not find sex differences on an FEP identification task^[69-71]. By contrast, Erol *et al.*^[72] found sex differences in FEP: Chronically ill women with schizophrenia performed equivalently to men and

women without schizophrenia on both identification and discrimination FEP tasks, while men with schizophrenia performed worse on both tasks. In sum, out of four recent studies, only one found that women outperformed men with schizophrenia in FEP^[72].

In total, out of 101 studies that examined FEP in chronically ill adults with schizophrenia, 26 examined sex differences. Twenty-two out of 26 studies did not find sex differences in FEP performance. One study found that men outperformed women regardless of diagnostic status on an identification task^[50] and three studies found that women outperformed men on an identification task^[51,52,72] and discrimination task^[72]. Taken together, the evidence suggests that men and women with chronic schizophrenia perform comparably on FEP.

Early and recent-onset schizophrenia

To ascertain whether there are sex differences in FEP early in the course of the illness, we examined studies in people with early or recent-onset schizophrenia. Barkl *et al.*^[30] conducted a meta-analysis of 12 FEP studies in people with early-onset schizophrenia (2 studies) or in people who recently had their first psychotic episode (10 studies) published from 1806-2013. Similar to studies with chronically ill adults with schizophrenia, they found that people during the early stages of the illness showed impairments in FEP compared to healthy controls. Of the 12 studies included in Barkl *et al.*^[30], only three examined sex differences in FEP. None of the three studies found sex differences in FEP on identification tasks in recent-onset samples^[73-75].

Of the 81 non-overlapping studies that examined sex differences in FEP in schizophrenia included in Kohler *et al.*^[7], Chan *et al.*^[5], and Savla *et al.*^[9], four studies examined sex differences in FEP in samples of either recent-onset schizophrenia or children and adolescents diagnosed with schizophrenia-spectrum disorders (these studies were not included in Barkl *et al.*^[30]). Two studies did not find sex differences in FEP in children or adolescents diagnosed with schizophrenia^[41,76]. One study found that men outperformed women regardless of diagnostic group in a sample of people ages 11-20 with and without schizophrenia-spectrum disorders^[77]. Kucharska-Pietura *et al.*^[35] compared inpatients who were either: (1) experiencing their first or second psychotic episode; or (2) chronically ill with schizophrenia with a healthy control group and found that women, regardless of diagnostic status, were more accurate at identifying emotions in a variety of affective facial stimuli compared to men. When the authors examined whether sex differences existed within each diagnostic group separately (examining sex differences in the recent-onset group vs the chronically ill group), they found that sex differences only existed within the recent-onset group: Women who were experiencing their first or second psychotic episode outperformed men on FEP tasks^[35]. We found one study that

examined FEP in an early onset group in our PubMed search, but the authors did not report sex differences^[78].

In summary, out of seven studies of FEP in early or recent-onset schizophrenia that examined sex differences, five did not find sex differences^[41,73-76]. One study found that boys outperformed girls^[77] and one study found that recently diagnosed women outperformed men^[35].

Unaffected first-degree relatives

In order to examine sex differences in a clinical high risk group, we examined studies in unaffected first-degree relatives of people with schizophrenia. Lavoie *et al.*^[29] conducted a meta-analysis examining 29 studies published from 1985-2011 on five aspects of social cognition in unaffected first-degree relatives. Within this meta-analysis, they examined 20 studies examining "emotion processing", including one study that used affective facial stimuli but was not an FEP task (thus, is not included in this review)^[79] and 19 studies that included an FEP task. They found that unaffected, first-degree relatives of people with schizophrenia performed significantly worse on these tasks compared to control groups, although the effect sizes were smaller than effect sizes found in studies that compare people with schizophrenia to healthy controls. They also found a significant difference in task type: First-degree family members performed significantly worse on identification tasks vs "differentiation" tasks (tasks where participants state whether a face is emotional vs neutral or positive vs negative).

Of the 29 studies included in Lavoie *et al.*^[29], eight examined sex differences on an FEP task. Six studies did not find differences between men and women on an identification task^[31,76,80-83] or on a discrimination task^[80]. Two studies found that women, across diagnostic groups of first-degree relatives, outperformed men on FEP identification tasks^[84,85].

Across the meta-analyses of Kohler *et al.*^[7], Chan *et al.*^[5], Savla *et al.*^[9], and Barkl *et al.*^[30], one study did not find sex differences on an identification FEP task in a clinical high risk group, a first-episode group, and a healthy control group^[73]. We found one study through our PubMed literature search that examined FEP in two clinical high risk groups (one group with prodromal symptoms and another group of unaffected first-degree relatives); results indicated no sex differences in performance on either an identification or discrimination FEP task^[86].

In sum, of 10 studies that examined sex differences in samples that included a group of unaffected first-degree relatives of people with schizophrenia, eight did not find sex differences on either identification or discrimination tasks^[31,73,76,80-83,86]. Two studies found that women, including first-degree relatives, people with schizophrenia, and healthy controls, outperformed men on an identification FEP task^[84,85].

DISCUSSION

Across five separate meta-analyses including people with chronic schizophrenia, early or recent-onset schizophrenia, and a clinical high risk group of unaffected first-degree relatives of people with schizophrenia, the evidence suggests that men and women across the schizophrenia spectrum show equivalent performance in FEP, and they both show poorer performance compared to healthy controls. Women with schizophrenia do not appear to retain the superiority in FEP that is found in their healthy counterparts. Thus, it does not appear likely that FEP ability contributes to women with schizophrenia having less severe negative symptoms, better social skills, and better functioning compared to men with schizophrenia. Women may exhibit strengths in other skills besides FEP that they rely on to navigate the social world. It would be important to understand why women with schizophrenia have better social functioning despite showing equivalent FEP ability compared to men, and whether there are other treatment targets outside of FEP that may better benefit both men and women with schizophrenia in improving functioning.

It also remains unclear why men with schizophrenia would benefit more from cognitive remediation treatments that target FEP compared to women^[10] when they both show equivalent deficits in FEP. Again, women may have other social or emotional skills that may help them function in the world despite their deficits in FEP, thus improving this one skill may not benefit them as much as it benefits men. Future studies should continue to examine whether FEP is an effective treatment target in improving functioning in women as well as men with schizophrenia.

Despite the seemingly overwhelming evidence that there are no sex differences in FEP in schizophrenia, there are limitations to the existing body of literature worth noting. First, the studies that do examine sex differences vary widely in the percentage of female participants, ranging from 5% to over 50% of women in the schizophrenia group. Indeed, only 22 studies included 39%-40% or more women in both their schizophrenia and control samples. These percentages of female participants are unrepresentative of the incidence rate of schizophrenia among women in the general population, which is closer to 40%-50% of people with schizophrenia^[17]. A recent review found that across studies of schizophrenia, men outnumber women almost 2:1, suggesting that the majority of knowledge we have about schizophrenia, including FEP, comes from studies that include more (or sometimes, only) men^[87]. Further, the majority of treatment intervention studies that target FEP have included predominantly male samples^[11]. While some researchers examine sex differences within or across their study groups, others either control for sex during their analyses prior to examining main effects or interactions of sex on their outcome variable or fail to examine sex differences at

all. In short, while there are not many studies that have adequately examined sex differences in FEP, those that have done so with reasonably balanced and sufficiently large sample sizes do not find sex differences in FEP.

A second limitation is that among the studies that examine sex differences, the majority do not examine differences in clinical features - such as symptom severity - that differ between men and women and that are also related to performance on FEP tasks. Men with schizophrenia tend to have more severe negative symptoms, are more likely to be inpatients, and have a younger age of onset compared to women. Negative symptoms and inpatient status are associated with poorer performance on FEP tasks. On the other hand, Kohler *et al.*^[7] found that older age of onset was associated with more impairment in FEP, a clinical feature associated more with women than men with schizophrenia^[21]. It may be the case that the relationships between FEP and symptoms may differ between men and women; for example, negative symptoms might only be associated with poorer FEP ability in men. Examining sex differences in these clinical features in addition to FEP performance would illuminate whether FEP performance is partially related to clinical features alone, sex, or both.

Of the 38 studies included in this review that examined sex differences in FEP, only four reported on the relationship between sex and symptoms. Taken together, the evidence from these studies is mixed: When symptoms and/or other clinical features (e.g., duration of illness, number of hospitalizations) do not differ between men and women with schizophrenia, two studies do not find sex differences in FEP performance^[38,48] and two studies find that women outperform men^[52,72]. The studies that found that women outperformed men examined positive and negative symptoms separately, while the studies that did not find sex differences either did not examine symptoms at all^[48] or only examined total symptom scores as measured by the PANSS^[38]. In other words, women outperformed men in FEP performance in two studies where they did not differ in either negative or positive symptoms. It remains unclear how or whether symptoms and other clinical features affect sex difference findings (or the lack thereof) in FEP studies in schizophrenia as the majority of studies do not examine sex differences in symptoms. Future studies should examine both facets - sex and clinical features - to better understand how these factors may or may not be interacting and influencing performance on FEP tasks.

While the majority of studies on FEP do not find sex differences in schizophrenia, there are similarities across studies that do find sex differences. First, the majority of these studies find that, regardless of diagnostic status, women outperform men^[35,51,52,72,84,85]. Second, the majority of studies that find sex differences do so using FEP identification tasks^[35,51,52,84,85]. Third, all but one study^[85] have included at least 40% women with

schizophrenia in their samples. Fourth, the natures of samples are such that sex differences have been found in inpatients^[35,84], outpatients^[51,72,85], or both^[52]. Fifth, of the few studies that report better FEP performance for women than men, this appears to be found across the schizophrenia spectrum, including in chronically ill adults^[51,52,72], recent-onset samples^[35], and in unaffected first-degree relatives^[84,85].

While it may seem non-critical to focus on sex differences in FEP in schizophrenia when the majority of existing evidence suggests that none exist, the above noted limitations to the pre-existing literature suggest that it is worth additional study. Future studies should include more women with schizophrenia in their samples, examine the relationship between symptoms and clinical features and sex, and continue to study early or recent-onset populations in addition to clinical high risk populations. Further clarification on sex differences in FEP would also help us understand why men with schizophrenia appear to benefit more from interventions that target FEP when compared to women and whether women with schizophrenia show strengths in other social skills to compensate for their deficits in FEP. Controlling for sex differences or ignoring potential sex differences in FEP tasks, as well as other tasks that may be related to functioning and symptoms in schizophrenia, is limiting our ability to uncover potentially important differences between men and women with schizophrenia, such as why women with schizophrenia overall show better functioning and less severe negative symptoms when compared to men. Finally, while the magnitude of sex differences in FEP may be small, a recent meta-synthesis of 106 meta-analyses of sex differences in nonclinical populations found that the effect sizes for all sorts of sex differences are typically relatively small, suggesting that men and women are more similar than dissimilar on a variety of psychological outcomes^[88]. However, the authors cautioned that although such differences "are typically small, they should not be regarded as trivial, as even small effects can have important everyday consequences" (p. 17)^[88]. Thus, it may well prove fruitful to continue to study the relationship between FEP and sex across the schizophrenia spectrum.

In conclusion, men and women across the schizophrenia spectrum - including chronically ill adults, people with early and recent-onset schizophrenia, and unaffected first degree relatives of people with schizophrenia - do not exhibit large differences in FEP. Both men and women across the schizophrenia spectrum perform more poorly on FEP tasks compared to people not on the spectrum. However, there are noteworthy limitations in the existing literature that can be addressed, including the inclusion of more women in studies and understanding the role of symptoms and sex differences in FEP in schizophrenia. The continued assessment of sex differences in FEP remains important to help researchers and clinicians further understand

other sex differences in the disorder as well as develop future treatment targets to improve functioning in both men and women with schizophrenia.

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COMMENTS

Background

Facial emotion perception (FEP) refers to the ability to identify the emotion on the face of another person and is typically assessed with laboratory tasks.

Research frontiers

To the best of our knowledge, no systematic review of sex differences in FEP across the schizophrenia spectrum has previously been published. The objective of this study was to systematically review all studies on sex differences in FEP across the schizophrenia spectrum and critically evaluate the available literature.

Innovations and breakthroughs

The majority of studies examined in this review suggest that men and women across the schizophrenia spectrum do not differ in FEP ability. However, the limitations of the available literature warrant further investigation.

Applications

Future studies on FEP in schizophrenia should include more women in their studies, continue to examine the relationship between symptoms and clinical features and sex, and continue to study early and recent-onset populations in addition to clinical high risk populations. Future studies should also attempt to understand whether men might benefit more from interventions that target FEP than women with schizophrenia.

Terminology

Schizophrenia is characterized by positive symptoms (hallucinations and delusions), negative symptoms (blunted affect, avolition, and anhedonia), and disorganization symptoms. Approximately 1% of the general population has schizophrenia and the prevalence of the disorder is approximately the same between men and women.

Peer-review

This is a nice and complete study. It is nicely written, readable and documented.

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