Chapter 3.0

REVIEW OF SCIENTIFIC LITERATURE

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3.1 SCHIZOPHRENIA

Schizophrenia is a chronic psychotic disorder with cognitive, behavioural and emotional dysfunction. It's diagnosed as per DSM 5 (American Psychiatric Association, 2013a) with the following criteria,

1. Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated). At least one of these must be (1), (2), or (3):
    1. Delusions.
    2. Hallucinations.
    3. Disorganized speech (e.g., frequent derailment or incoherence).
    4. Grossly disorganized or catatonic behavior.
    5. Negative symptoms (i.e., diminished emotional expression or avolition).
2. For a significant portion of the time since the onset of the disturbance, level of functioning in one or more major areas, such as work, interpersonal relations, or self-care, is markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, there is failure to achieve expected level of interpersonal, academic, or occupational functioning).
3. Continuous signs of the disturbance persist for at least 6 months. This 6-month period must include at least 1 month of symptoms (or less if successfully treated) that meet Criterion A (i.e., active-phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or by two or more symptoms listed in Criterion A present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences).

4. Schizoaffective disorder and depressive or bipolar disorder with psychotic features have been ruled out because either 1) no major depressive or manic episodes have occurred concurrently with the active-phase symptoms, or 2) if mood episodes have occurred during active-phase symptoms, they have been present for a minority of the total duration of the active and residual periods of the illness.

5. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.

6. If there is a history of autism spectrum disorder or a communication disorder of childhood onset, the additional diagnosis of schizophrenia is made only if prominent delusions or hallucinations, in addition to the other required symptoms of schizophrenia, are also present for at least 1 month (or less if successfully treated).

3.2 COGNITION

The term ‘cognition’ refers to many different processes by which individuals understand and make sense of the world. Social cognition concerns the various psychological processes that enable individuals to take advantage of being part of a social group(Frith & Frith, 2008). Brothers defined social cognition as the ‘‘mental operations underlying social interactions, which include the human ability and capacity to perceive the intentions and dispositions of others’’ (Brothers, 1990).

Broadly cognition can be classified as neurocognition (which includes attention, executive function, learning & memory, language & perceptual motor function) and social cognition.

3.3 SOCIAL COGNITION & ITS DOMAINS

Social cognition has not been studied widely among patient population until recently when a NIMH workshop consensus statement came up with various domains of social cognition and its application in research.

The NIMH workshop defined social cognition as "the mental operations that underlie social interactions, including perceiving, interpreting, and generating responses to the intentions, dispositions, and behaviours of others. As per the NIMH workshop consensus statement (Green et al., 2008), significant domains under which different items are grouped for clinical and research utility for social cognition that are applied frequently are a) Theory of mind, b) emotion processing, c) attributional styles and d) social perception & social knowledge.

These social cognition domains, their method of assessment and the neural correlates are described briefly in the following section including Mirror Neuron Activity (MNA), a phenomenon closely related to social cognition.

Theory of Mind (ToM)

Theory of Mind is the ability to infer the intentions and beliefs of others (Premack & Woodruff, 1978). ToM is also referred by various names as mentalizing, mental state attribution and social intelligence. This ToM capacity usually develops around the age of 4-5 years normally. ToM is assessed very commonly with simple short written stories of people interacting with each other with the subject asked to infer the intention or mental state of the people involved in the conversation. It can also be tested with short videos of geometrical shapes interacting with each other.

Different levels of ToM

ToM can be of varying complexity as follows,

1st order: The capacity to infer "*A* believes that *x*"

2nd order: The capacity to infer "*A* believes that *B* believes that *x*"

Stories with social blunders (Faux Pas and irony) are also considered as higher order ToM.

ToM assessment

Most of the literature available on ToM are in children comparing the normal and abnormal development of ToM. These ToM measures used in children with autism has been extended to patients with schizophrenia as well, due to similarity of social dysfunction in autism and schizophrenia. Though most of

the studies assessing ToM in adult patients has used false belief task developed for children, there are some measures developed for use in adults specifically, like The Awareness of Social Inference Test (TASIT)(McDonald, Flanagan, Rollins, & Kinch, 2003), reading the mind in the eyes test (Eyes test)(Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001), etc.

Brain regions involved in ToM

Several brain regions involving medial prefrontal cortex (mPFC)(Amodio & Frith, 2006), bilateral temporoparietal junction (TPJ)(Mitchell, Heatherton, & Macrae, 2002) and precuneus were found to be activated during ToM task in healthy adults. Superior Temporal Sulcus (STS) and inferior frontal gyrus (IFG) are also activated in ToM task involving geometrical shape and inferring emotions from eyes respectively(Heider & Simmel, 1944).

Emotional Processing (EP)

Emotional processing is about perceiving and using emotions adaptively(Green & Horan, 2010). Emotions could be perceived through face, voice and bodily gestures. According to an influential model proposed by Salovey and colleagues emotional processing has four components which includes identifying emotions, facilitating emotions, understanding emotions and managing emotions(Mayer & Salovey, 1995). Face perception (affective and non-affective) and voice perception are also used to study emotion processing.

Emotional Processing assessment

Face perception is very commonly used tool for emotional perception. It's also an important aspect of social cue perception. Non-affective face perception involves processing of non-emotional information from the face like the age, sex or identity of a person. Affective face perception involves processing the emotions expressed in face of others.

Another tool which is a part of MATRICS cognitive battery is Mayer Salovey Caruso Emotional Intelligence Test or MSCEIT(Mayer, Salovey, Caruso, & Sitarenios, 2003). With this tool emotional processing is assessed in the following 4 abilities or branches: perceiving emotions, using emotions to facilitate thinking, understanding emotions, and managing emotions.

Brain regions involved in emotional processing

Affective face perception is associated with increased activation in limbic regions (amygdala, Parahippocampal gyrus and posterior cingulate cortex), inferior frontal gyrus (IFG), medial prefrontal gyrus and putamen (Fusar-Poli et al., 2009)(Vuilleumier & Pourtois, 2007)

Non- affective face perception is associated with increased activation in the bilateral fusiform face area (FFA; also known as lateral fusiform gyrus), visual extrastriate cortex, lateral occipital gyri, anterior temporal pole and posterior superior temporal gyrus (pSTG)(Fairhall & Ishai, 2007)(Gauthier et al., 2000)

Voice perception could be related to identity of the speaker, content/comprehension of the speech and affect of the content(Belin, Bestelmeyer, Latinus, & Watson, 2011). Anterior temporal-lobe regions of the right hemisphere, particularly right anterior STS regions, are associated in processing information related to speaker identity. Affective nonverbal vocalizations such as laughs, cries, groans are associated with activation of amygdala and anterior insula. Right temporal lobe and right inferior prefrontal cortex activation is associated with perceiving emotions from the prosody of speech. Comprehension of the speech is found to activate anterior regions of the left STS/superior temporal plane(Belin, Fecteau, & Bédard, 2004)

Attribution Style (AS)

Attribution bias or style refers to the manner in which individuals interpret, explain, or make sense of the positive and negative social events encountered in life and is thought to have a significant impact on behaviours(Green et al., 2008). Attributional bias may be external personal attributions (i.e. causes attributed to other people), external situational attributions (i.e. causes attributed to situational factors), and internal attributions (i.e. causes due to oneself). There are numerous factors which influences the attribution style including the actor's intention, perceiver's motivation and cultural differences.

Based on whether the attribution style favours the perceiver's motive or intention, attribution could be a categorized as self-serving bias/personalizing bias and externalizing bias(Bentall, Corcoran, Howard, Blackwood, &

Kinderman, 2001)(Combs, Penn, Wicher, & Waldheter, 2007). Attributing positive events to the self or negative events to others is self-serving bias and the vice versa is externalizing bias

Various models have been proposed for explaining the process of attribution. The most influential being the three-stage model proposed by Gilbert & colleagues(Gilbert, Krull, & Pelham, 1988). This three-stage model includes,

a) categorization/identification stage

b) characterization stage

c) correction stage

Categorization stage is identifying the cues of target, situation and cues experienced from the target person in past. Characterization involves a correspondent dispositional inference which is automatic/reflexive and correction stage involves a reflective stage where the dispositional inference is adjusted for the situational forces.

Attribution style assessment

Assessment of attribution style dates back to the beginning of social cognition in the in 1940s with the classical film created by Heider and Simmel (1944)(Heider & Simmel, 1944) of geometrical shapes moving against a white background.

The most commonly used tool is Internal Personal Situational Attribution Style Questionnaire-IPSAQ (an extension of Attribution Style Questionnaire-ASQ)(Kinderman & Bentall, 1996). IPSAQ gives a set of imaginary situations for which the subject has to attribute the causes-external (personal/ situational) or internal

Brain regions involved in attribution

As attribution involves both automatic and reflexive processing, it is speculated that corresponding brain regions might be activated(Gilbert, 1989). For example, when dispositional inference is adjusted for the situational factors, prefrontal cortex is found to be associated with this correction stage of attribution process. This is further supported by studies which has demonstrated

the disruption in correction dispositional inference stage by the cognitive demand of daily lives like making a positive impression(Gilbert & Malone, 1995). During automatic processing stage of attribution lateral temporal cortex and superior temporal sulcus are involved.

Social perception(SP) and social knowledge

Social perception is the ability to judge social roles and rules in a social context(Corrigan & Green, 1993a). Social perception overlaps with two other areas - emotion perception and social knowledge.

Though similar to emotion perception, it differs in the type of judgement. In social perception, social cues are inferred to situational events that generated the cue unlike emotion perception where emotional qualities are inferred from facial expression or voice tone.

Social knowledge is about the roles and rules that characterize a specific social situation(Corrigan, Wallace, & Green, 1992). Example- role of a doctor in clinic, role of a waiter in a restaurant. Social knowledge overlaps with social perception as some amount of social knowledge is required for appropriate social perception.

Social perception & social knowledge assessment

Social perception is assessed with short video clips of 2-3 people interacting with each other. Subjects is supposed to answer set of questions from the video clips inferring about the rules, affect and the roles guiding the person's behaviour. Social Cue Recognition test (SCRT)(Corrigan & Green, 1993a) is the tool commonly used for social perception assessment.

Social knowledge is a paper and pencil measure in which the participants are asked to identify some features from a list of descriptors that define a familiar situation. It's assessed using the Situational Features Recognition Test (SFRT)(Corrigan & Green, 1993b)

Brain regions associated with social perception and social knowledge

Ventromedial prefrontal cortex has been implicated in social knowledge and behaviour especially in brain injury studies in primates and human beings. In

humans lesions of ventromedial prefrontal cortex are associated with difficulty in incorporating emotional information in to the social context and make social reasoning and judgement. Adolph has reported that patients with prefrontal lesions were more accurate in reasoning from a non-social scenario than a social scenario compared to the comparison subjects(Adolphs, 1999).

Mirror Neuron Activity (MNA)

Mirror neuron system is a specialized network of neurons which are activated when one performs an action as well as when he / she observes such action and it is an underlying process of all social interactions(Di Pellegrino, Fadiga, Fogassi, Gallese, & Rizzolatti, 1992).

Recently it has been speculated as a mediator for automatic cognitive processing in the Dual Processing(DP) theory of social cognition.

MNA Assessment

Mirror neuron activity has been demonstrated by direct method, single-cell electrode recordings (Mukamel, Ekstrom, Kaplan, Iacoboni, & Fried, 2010) and indirect methods such as, functional magnetic resonance imaging or functional MRI (fMRI) (Rizzolatti & Craighero, 2004), electroencephalogram (EEG) (Pineda & Hecht, 2009) (Oberman, Ramachandran, & Pineda, 2008) magnetoencephalography(MEG) (Kato et al., 2011) and transcranial magnetic stimulation (TMS) (Mehta, Basavaraju, Thirthalli, & Gangadhar, 2012). Functional Near Infra Red Spectroscopy fNIRS) is an emerging technique of brain imaging to study cortical responses measured by hemodynamic variations. fNIRS has also been used in assessing MNA in a recent study with Pervasive Developmental Disorders(PDD)(Kajiume, Aoyama-Setoyama, Saito-Hori, Ishikawa, & Kobayashi, 2013). Different indirect methods of MNA assessment are as follows,

Table-3.1 MNA assessment-indirect methods

S.No	Method	Putative measure of MNA
1	fMRI	Blood oxygenation level–dependent changes

2	TMS	Motor evoked potential (MEP) Enhancement
3	EEG	mu Rhythm suppression
4	PET	Blood flow changes & Glucose metabolism
5	MEG	Alpha band suppression and gamma band amplifications
6	fNIRS	Blood oxygenation level–dependent changes

Brain regions associated with MNA

Specific sets of temporal, parietal and frontal areas contribute to different aspects of MNA in human beings.

The overall mirror neuron circuitry of humans is composed of core circuit of premotor cortex and parietal (posterior parietal lobule) cortex containing the mirror neurons (Rizzolatti & Craighero, 2004), and visual cortex of the temporal lobe (posterior temporal sulcus) intimately linked to these two areas. The visual cortex of the temporal lobe provides visual input to the core mirror areas and also receives information about motor intentions (Iacoboni et al., 2005).

3.4 COGNITIVE DEFICIT IN SCHIZOPHRENIA

People with schizophrenia generally perform 1.5 to 2 standard deviations below the healthy normal people in cognitive (neurocognition) function tests (Saykin & Gur, 1991). Patients with schizophrenia show impairment in most of the domains of neuro-cognition and social cognition. Social cognition deficits are present in schizophrenia patients even when in remission (Mehta, Bhagyavathi, Thirthalli, Kumar, & Gangadhar, 2014).

3.5 COGNITIVE DEFICIT AND FUNCTIONAL OUTCOME IN SCHIZOPHRENIA

Cognitive deficits both neurocognition and social cognition has been very well documented in schizophrenia (Fett, Viechtbauer, Dominguez, et al., 2011). Indeed, social cognitive deficits play a key role in determining the functional

outcome including social and vocational capacities in schizophrenia (Fig-3.1). Social cognitive abilities make one interact effectively in social environment and lack of social cognition might lead to poor or maladaptive understanding and experience of the social situations leading to social withdrawal(D. L. Penn, Sanna, & Roberts, 2008). Studying social cognitive deficit would also enable us to understand the clinical symptoms like paranoia and negative symptoms much better.

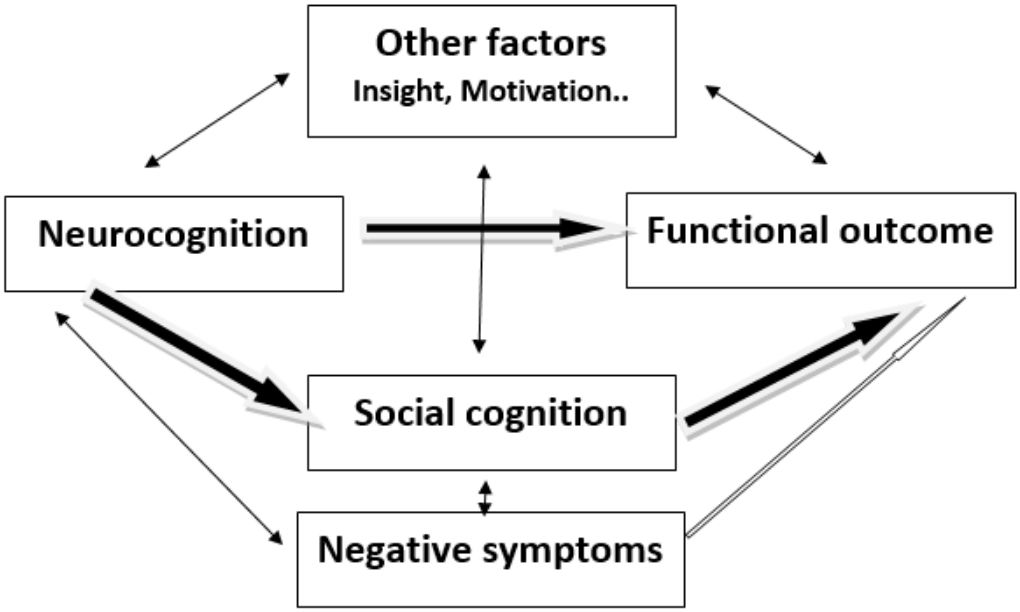

Figure-3.1 Social cognition & functional outcome

3.6 SOCIAL COGNITIVE DEFICIT IN SCHIZOPHRENIA

Social cognition is an emerging topic in the field of mental health. Though research on attribution (mostly on healthy population) formed the core for social cognition development in the beginning, its recent application in diseased population has brought out different domains which are evolving progressively over time with emerging empirical evidences. For example, the same four domains of social cognition-ToM, EP, AS and SP were organized conceptually in a little different way by Green et al (Green, Horan, & Lee, 2015) in a recent review, with some more additions like, MNA, empathy, etc under the same umbrella theme of social cognition.

The following section gives details of social cognition deficit based on the conceptual framework of Green et al (2015).

But, before going to details of social cognition deficit in schizophrenia, it would be useful to understand the theoretical model of social cognition.

Model for understanding social cognition

One of the most influential model in social cognition is the Dual Processing (DP) theory (Evans, 2008). The dual processing framework views social cognitive judgements as results of interaction between the automatic and controlled cognitive processing (Chaiken & Trope, 1999).

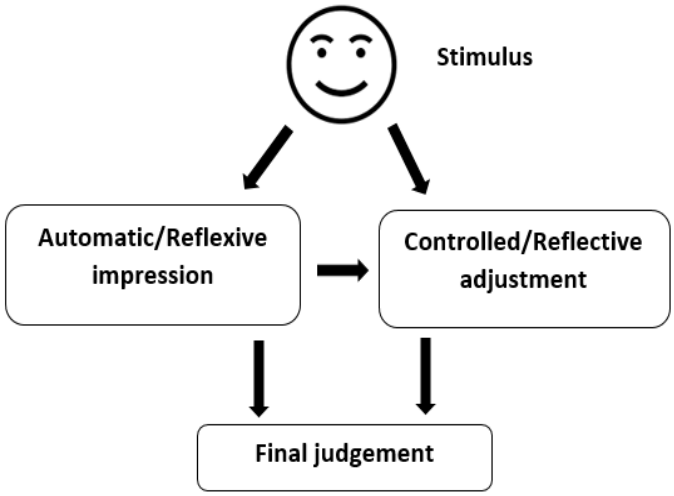

Fig- 3.2 Dual Processing (DP) theory of social cognition

Automatic processing is the primary mechanism for generating initial social cognitive representation, which may later be manipulated as per the need of the self & situation. It is fast and efficient and largely happens outside of one's conscious awareness. Automatic generation of social cognitive representations draws on early perception-based representations of others' facial features and bodily motion, mediated in part by fusiform gyrus and superior temporal sulcus, respectively. It also draws on well-rehearsed interpersonal scripts or stereotypes, and emotional experiences and representations of the subject's own bodily and physiological states, as mediated by subcortical structures such as the amygdala and insula (Lieberman, 2007). Actual neural mechanisms by which automatic process sub serves the heuristic manipulations and hence the automatic social cognitive representations are not understood. One speculation

that gained empirical support in recent years is mirror neuron system (Carr, Iacoboni, Dubeau, Mazziotta, & Lenzi, 2003).

Controlled processing is the capacity to consciously manipulate the cognitive representations, allowing the subject to strategically evaluate, modify or suppress the automatic impressions which are maladaptive or inconsistent with the subject's goals.

The basic DP model of social cognition is illustrated in figure 3.2. Automatic processing responds immediately to a social stimulus, quickly and unconsciously generating an actionable impression on the basis of whatever combination of perceptions, emotion, cognitive schemas, and physiological inputs happen to be most salient at the time. After roughly 500 ms post stimulus onset, controlled processing may or may not be engaged to modify or suppress this initial impression, depending on multiple factors. Controlled processing is less likely to be engaged if the automatic impression is highly salient; if the subject is experiencing cognitive load, emotional arousal, or distraction; is cognitively impaired; is unaware that the initial impression may be maladaptive; or is not motivated to question the initial impression. Failure to actively engage controlled cognition results in passive endorsement of the automatic impression, and subsequent controlled processing will be biased toward its continued endorsement.

Applying the Dual-Process Framework to Social Cognition in Schizophrenia

The social cognitive deficits in schizophrenia can be conceptualized in the light of dual processing framework as follows,

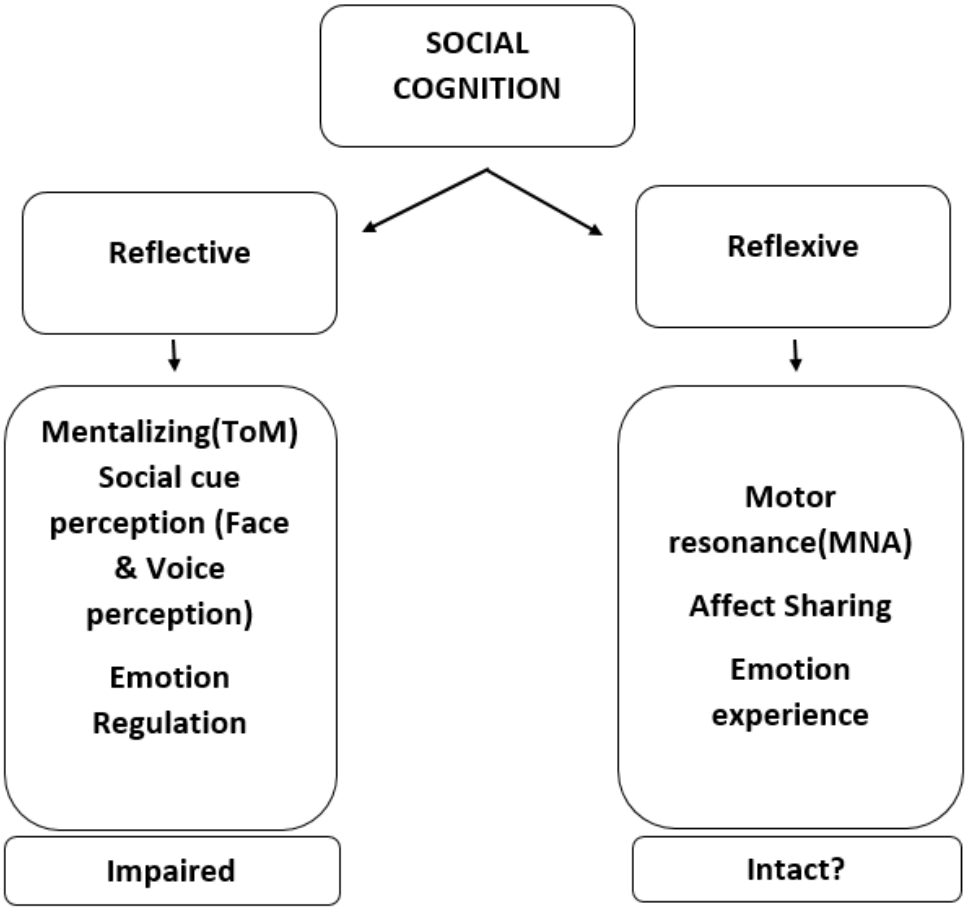

Fig-3.3 Social cognitive deficits in schizophrenia in the light of DP framework

Social cognitive abnormality in schizophrenia results from two factors:

(1) diminished controlled processing capacity and

(2) excessively salient and aberrant automatic social cognitive impressions.

There is broad support in the literature for the first factor, as schizophrenia is linked to diminished prefrontal functioning (Ragland, Yoon, Minzenberg, & Carter, 2007). There is also support for the second factor in the literature on dopamine-mediated aberrant salience experience (Kapur, Mizrahi, & Li, 2005), including evidence that dysregulated neural signalling causes feelings of social threat, alien control, and other forms of aberrant intentionality. This two-factor model predicts the generation of highly salient but maladaptively biased automatic social cognitive impressions (e.g., the impression of being the object of hostility) in combination with a handicapped ability to evaluate, suppress, or modify these dysfunctional impressions.

Mentalizing (ToM) Deficit

Neuroimaging studies showed that patients with SCZ had decreased activity in some core regions of the mentalizing system. During a task that required subjects to use the perspectives of others to correctly identify objects, patients showed reduced activation of the ventromedial PFC (vmPFC) and orbitofrontal cortex (Eack, Wojtalik, Newhill, Keshavan, & Phillips, 2013).Patients also showed decreased activation of the mPFC and TPJ while making inferences about the beliefs of others (Lee, Quintana, Nori, & Green, 2011) (Dodell-Feder, Tully, Lincoln, & Hooker, 2014). Controls showed less activation in the mentalizing system when inferring the intentions of a person in isolation compared with inferring the intentions of a person who is participating in a social interaction, and patients failed to show this modulation (Walter et al., 2009). Another study found that, compared with controls, people with schizophrenia exhibited increased activity in the superior temporal gyrus (STG), dorsomedial PFC (dmPFC) and precuneus when inferring the intentions of others (Brüne et al., 2008). In both of these studies, the individuals with schizophrenia showed intact performance, suggesting that they required greater levels of neural activity to achieve the same levels of performance on mentalizing tasks as controls.

To summarize, the patterns of aberrant activation on mentalizing tasks are not consistent across studies. Most studies report hypoactivation of the core mentalizing system and impaired mentalizing ability in behavioural tasks. A few studies found hyperactivation of brain regions associated with mentalizing. Individuals with schizophrenia may need greater activation in these regions to achieve the same level of mentalizing proficiency, suggesting neural inefficiency – potential to result in delayed activation of this network.

Non-affective face perception

Patients with schizophrenia have less difficulty with coarse judgments of facial features but have more difficulty with finer-grained judgments (Darke, Peterman, Park, Sundram, & Carter, 2013) (Bortolon, Capdevielle, & Raffard, 2015). Individuals with and without schizophrenia have similar levels of neural activation in the FFA during non-affective face perception (Walther et al.,

2009). Patterns of neural activation across FFA voxels during a non-affective face-perception task were less cohesive in patients with schizophrenia (Yoon, D'Esposito, & Carter, 2006).

Affective face perception

Individuals with schizophrenia show less activation in the right inferior occipital gyrus, right fusiform gyrus, left amygdala and hippocampal regions, anterior cingulate cortex (ACC), medial prefrontal cortex (mPFC) and thalamus. However, they show greater activation in the insula, cuneus, parietal lobule and STG during affective face perception (Li, Chan, McAlonan, & Gong, 2009) (Taylor et al., 2012) (Delvecchio, Sugranyes, & Frangou, 2013). Blunted response in the amygdala seen in individuals with schizophrenia during contrasts of emotional versus neutral conditions might be due to increased activation in response to neutral stimuli (Anticevic et al., 2010). Studies using ERP to assess neural activation during face perception have focused on two components:

1) N170 at occipitotemporal sites, which is associated with structural information of
faces (Bentin, Allison, Puce, Perez, & McCarthy, 1996)
2) N250 at frontocentral sites, which is associated with facial emotional information (Marinkovic & Halgren, 1998).

A meta-analysis of various schizophrenia studies revealed robust deficits in N170 and N250 components during affective face perception (McCleery et al., 2015).

To summarize, studies of non-affective face processing in schizophrenia have yielded conflicting results, whereas studies of affective face processing in schizophrenia are more consistent. Patients with schizophrenia demonstrate hypoactivation in brain regions associated with affective face perception and hyperactivation in regions not typically associated with face perception. Patients may recruit other areas to compensate for dysfunction in the key face-processing regions.

Voice perception

These are acoustic properties of speech that provide critical information beyond the meaning of words or grammatical structure, such as emotional state, emphasis, contrasts and focuses. Findings of non-affective prosody in schizophrenia are mixed, in that patients correctly perceive certain features of non-affective prosody and have difficulties with perceiving pitch and rhythm. Studies on affective prosody perception have shown consistent behavioural impairment, and the few neuroimaging studies carried out to date suggest hypoactivation in key regions, for example, the STG and IFG.

Emotion regulation

The emotion regulation system influences expression of emotions within appropriate social contexts and includes brain regions that overlap with the amygdala and the ventral and dorsal lateral prefrontal cortices. Dysfunctional neural activity in these brain regions has regularly been demonstrated in schizophrenia.

In two fMRI studies schizophrenia patients showed ventro-lateral prefrontal cortex hypoactivation while emotional responses were decreased and vlPFC hyperactivation while emotional responses were increased. Neural activity in the amygdala was inversely coupled with prefrontal activation activation in controls, but not in those with schizophrenia (Morris, Sparks, Mitchell, Weickert, & Green, 2012) (van der Meer et al., 2014)

To summarize, converging evidence suggests that the use of cognitive reappraisal strategies is disrupted in schizophrenia, a conclusion that is consistent with the neural impairments in cognitive control processes in this disorder (Nuechterlein, Luck, Lustig, & Sarter, 2009) (Carter, Bowling, Reeck, & Huettel, 2012) . The interface between cognitive control and emotional processes is an active area of translational research in schizophrenia.

Motor resonance/MNA

Evidence available for MNA in schizophrenia is mixed, which is listed as follows,

fMRI studies:

Two fMRI studies of motor resonance in schizophrenia have provided conflicting results. Patients with schizophrenia showed decreased activation in the right inferior parietal lobule (IPL) and posterior superior temporal sulcus (STS) during action observation, but increased activation in these regions during imitation of finger movements (Thakkar, Peterman, & Park, 2014). Patients and controls showed similar activation in the expected brain regions across conditions, including inferior frontal, premotor and inferior parietal cortices, suggesting intact motor resonance in schizophrenia (Horan, Pineda, Wynn, Iacoboni, & Green, 2014).

TMS studies:

Two TMS studies yielded mixed findings, showing evidence of either diminished or intact mirror neuron system activation (Enticott et al., 2008) (Mehta, Thirthalli, Basavaraju, Gangadhar, & Pascual-Leone, 2013).

EEG studies:

'Mu' wave suppression: - Suppression of mu during observation and execution of actions has been found and is thought to be a physiological index of mirror neuron system activity. Three studies found no differences in mu suppression between individuals with schizophrenia and healthy subjects (McCormick et al., 2012) (Singh, Pineda, & Cadenhead, 2011) (Horan et al., 2014). But one study found diminished mu suppression in patients compared with healthy controls (Mitra, Nizamie, Goyal, & Tikka, 2014).

MEG studies:

Two small MEG studies reported diminished mirror neuron system activity in individuals with schizophrenia compared with healthy controls and with healthy co-twins (SchÜrmann et al., 2007) (Kato et al., 2011).

To summarize, the findings from motor resonance studies of schizophrenia are mixed. This area of research is still relatively new and the scientific approaches used are highly diverse, which may account for some of the discrepancies in the findings.

Affect sharing

Neural activation in certain limbic regions, particularly the amygdala, insula and cingulate gyrus occurs when an individual executes facial expressions of emotion and when an individual observes another person making such expressions. Studies of affect sharing have also focused on the perception of others when they display physical pain. Studies in healthy people demonstrate that the anterior insula and dorsal ACC, which are involved in the affective and motivational processing of schizophrenia, are also activated by the observation of others' pain (Lamm, Decety, & Singer, 2011).In self-report studies, patients score similarly to healthy controls for personal traits associated with affect sharing, and some showed tendency to be overly sensitive and reactive to the feelings of others compared with healthy controls (Michaels et al., 2014). Patients and controls showed a similar pattern of mu suppression in response to stimuli depicting various social interactions (Horan et al., 2014).In another study, individuals with recent-onset schizophrenia showed normal mu suppression for stimuli depicting social interaction stimuli, although they displayed diminished mu suppression while viewing stimuli depicting human biological motion. (Singh et al., 2011). Early event related potential (ERP)-processing components (N110, P180 and N240) during an affect-sharing task both patients and healthy controls showed similar levels of sensitivity to pain relevant stimuli (Corbera, Ikezawa, Bell, & Wexler, 2014). In a fMRI study, although imitation and execution of emotional expressions were impaired in patients, both groups showed similar levels of activation in regions associated with affect sharing, including inferior prefrontal, premotor, and inferior and superior parietal cortices (Horan et al., 2014)

To summarize, several studies using various methods report normal, or even enhanced, affect sharing in schizophrenia. Thus, affect sharing may reflect a relatively preserved aspect of social cognition in schizophrenia.

Emotion experience

Emotion experience activates the amygdala, anterior hippocampus, ACC and anterior insula. Emotion experience in schizophrenia is largely intact during exposure to both pleasant and unpleasant stimuli (Horan, Foti, Hajcak, Wynn,

& Green, 2012) (Pinheiro et al., 2013).The capacity to effectively regulate negative emotions would therefore be critical for normal adaptive functioning in schizophrenia.

Attribution style in schizophrenia

Individuals with persecutory delusions often attribute negative outcomes to others, rather than situations. This is known as a personalizing bias (Bentall et al., 2001). Similarly, schizophrenia patients also found to have hostile attributional biases or the tendency to attribute hostile intentions to others' actions (Combs, Penn, et al., 2007).

3.7 SUMMARY OF SOCIAL COGNITIVE DEFICIT IN SCHIZOPHRENIA

From the behavioural and neuroscientific studies discussed above, we can conclude that there is strong evidence to suggest that people with schizophrenia have impairments in some, but not all, social processes. There is consistent evidence to suggest schizophrenia is associated with impairments in face and prosody perception, mentalizing and emotion regulation. By contrast, the findings regarding emotion experience in schizophrenia suggest that this process is largely intact. In addition, some evidence suggests that motor resonance and affect sharing are intact in schizophrenia. However, it is important to note that there are relatively few studies on experience sharing to date and that some of the findings of these studies are inconsistent; hence, it is difficult to make firm conclusions. Nonetheless, the available data suggest that any impairment in experience sharing may be subtle.

Another interesting observation is, all the social cognitive process which are reflective are impaired but not the reflexive social cognitive process.

3.8 BRAIN REGIONS ASSOCIATED WITH SOCIAL COGNITION DEFICIT IN SCHIZOPHRENIA

Social cognition can be divided into several distinct processes, which involve many different brain regions, some of which show overlap between processes. Perceiving social cues incorporates face perception, which is associated with

activation of the amygdala and fusiform face area (FFA), and voice perception, which activates the superior temporal gyrus (STG) and inferior frontal gyrus (IFG). Experience sharing includes the processes of motor resonance, which activates the inferior

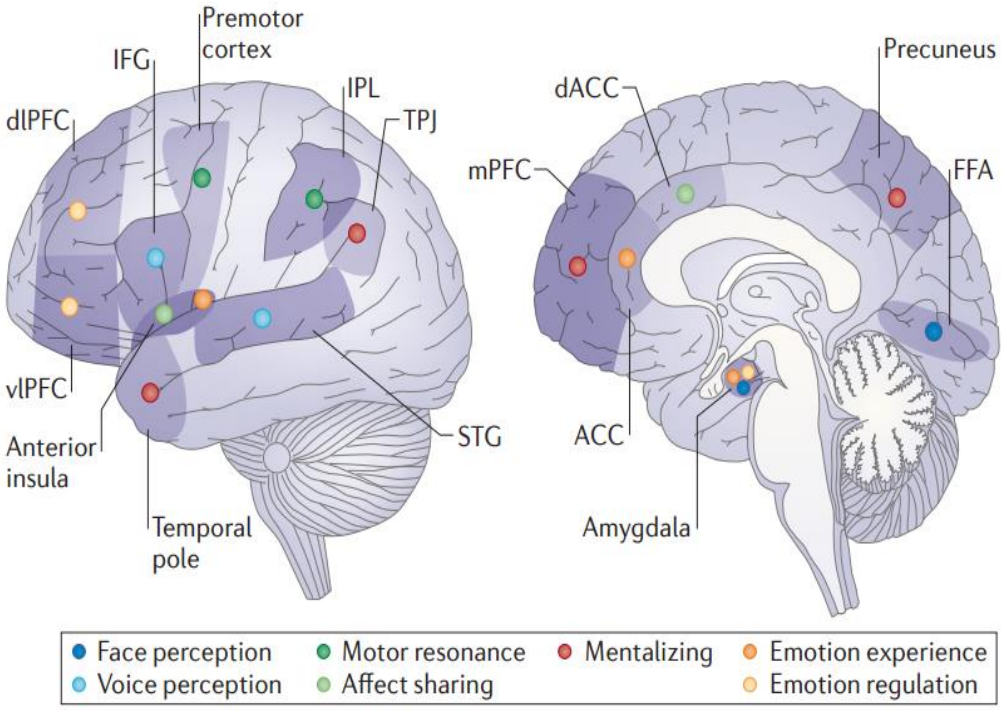

Fig-3.4 Brain regions in social process (from Green et al, 2015)

parietal lobule (IPL) and premotor cortex, and affect sharing, which activates the dorsal anterior cingulate cortex (dACC) and anterior insula. Mentalizing activates various regions, including the temporoparietal junction (TPJ), temporal pole, precuneus and medial prefrontal cortex (mPFC). Emotion experience activates the amygdala, anterior hippocampus (not shown), ACC and anterior insula, and emotion regulation activates brain regions including the dorsolateral PFC (dlPFC), ventrolateral PFC (vlPFC) and amygdala. These brain regions and associated social processes are not entirely separate; for example, the anterior insula is involved in both affect sharing and emotion experience, and the amygdala is involved in face perception, emotion experience and emotion regulation. Note that these regions are a representative, but not comprehensive, listing of relevant brain regions for each social cognitive process.

3.9 MNA AND SOCIAL COGNITIVE DEFICIT-THE RELATIONSHIP

In recent years, theories have come up trying to place MNA as one of the key contributor for social cognition. For example, ToM is explained based on one of the theories called simulation theory. Simulation theory is based on the fact that we are able to understand others intuitively, as we all have similar kind of representations within ourselves. With this theory, MNA goes hand in hand with ToM. There is recent speculation that MNA might underlie the automatic processing of social cognitive representation, as per the DP theory of social cognition (Carr et al., 2003).

Similarly, the neural correlates of empathy include inferior frontal gyrus (IFG), right superior temporal sulcus (STS), right inferior parietal lobe (IPL), anterior cingulate cortex (ACC), ventromedial prefrontal cortex (VMPFC), somatosensory cortex, amygdala, precuneus, insula and the posterior cingulate. Thus, empathy involves a significant interaction of the core MNS and its limbic extension (Iacoboni, 2005).

In summary, considering social cognition in the context of social learning through imitation, there is emerging evidence to speculate MNA as a key contributor of social cognition.

3.10 TREATMENT FOR COGNITIVE DYSFUNCTION

Most of the biological treatments work better for the positive symptoms of schizophrenia, but not for the negative symptoms or the cognitive dysfunction (Szöke, Trandafir, Dupont, Méary, Schürhoff, Schu, et al., 2008) (Moncrieff, 2011).Social cognition deficits persist despite antipsychotic treatment.

Interventions for social cognitive deficit

Social cognition training is not a new comer in the area of psychosocial rehabilitation. Its origin can be traced back to social skills training and neurocognitive remediation.

Although social skills training and neurocognitive remediation has the same goal of improving social and community functioning, the targets are different

in these programs. Social skills training program were developed based on social learning theory and operant conditioning techniques and focuses mainly on motor behaviours like eye contact, speech content, duration and loudness, whereas neurocognitive remediation focuses on attention, memory and problem solving. (as literature shows significant link between neurocognition and various functioning)

Concept of social cognition training is a combination of both social skills and basic cognition training. Nonetheless, there are various manual based training programs for improving the community and social functioning targeting only social domains (few domains or comprehensive) with or without neurocognitive training.

Accordingly, social cognitive training programs can be broadly classified as

1) Targeted treatments

2) Comprehensive treatments

3) Broad based treatment approaches

Table-3.2 Social cognitive training programs

S. No	**Treatments**	**Approach**	**Focus**
1	Training in Affect Recognition (TAR)	Targeted	Affect perception
2	Social Cognition Enhancement Training (SCET)	Targeted	Social perception
3	Emotion & ToM Imitation Training(ETIT)	Targeted	ToM & Emotion processing
4	Social Cognition Interaction Training(SCIT)	Comprehensive	Full range of Social cognition

5	Social Cognition Skills Training(SCST)	Comprehensive	Similar to SCIT with add-on TAR
6	Meta Cognitive Therapy (MCT)	Comprehensive	ToM, Attribution, Memory & Cognitive biases
7	Integrated Psychological Therapy (IPT)	Broad based	Basic cognitive (CBT based) & social cognitive remediation with psychosocial rehabilitation
8	Cognitive Enhancement Therapy(CET)	Broad based	Social cognition with neurocognition
9	Integrated Neurological Therapy (INT)	Broad based	Social cognition & Neurocognition with MATRICS defined domains

Brief descriptions of available treatments for social cognitive deficit:

Training in Affect Recognition (TAR)

TAR is a 6-week, 12-session, manualized treatment consisting of three segments: identification of prototypical components of basic emotions, integration of facial elements to form quick decisions about affect, and application of learned information to the processing of non-prototypical, ambiguous facial expressions. The training relies on both compensatory and restorative techniques, includes both computerized stimuli and "desk work," and relies heavily on strategies like verbalization and self-instruction.

In an efficacy trial of TAR, Wolwer and colleagues (Wölwer et al., 2005) randomly assigned 77 post-acute schizophrenia inpatients and outpatients to TAR, cognitive remediation therapy (CRT), or treatment as usual (TAU). CRT

consisted of 12 sessions of computerized training in attention, memory, and executive function, as well as dyad training in cognitive strategies. An intent-to-treat analyses, the authors reported significant group differences in affect recognition and basic neurocognitive performance. Individuals in the TAR group improved significantly more than the other two groups on pre–post measures of affect recognition, whereas individuals in CRT improved significantly more than TAU on measures of memory and learning.

Social Cognition Enhancement Training (SCET)

Social Cognition Enhancement Training (SCET) (Choi & Kwon, 2006), which focuses on improving social context appraisal and perspective-taking abilities through practice with arranging cartoons of social situations, has been shown to improve social perception, although the training did not generalize to affect recognition.

Van der Gaag and colleagues (van der Gaag, Kern, van den Bosch, & Liberman, 2002) have also evaluated the efficacy of a social perception combined with emotion recognition training. Evaluated in a sample of 42 inpatients with schizophrenia randomized to either the treatment or time-matched leisure activities, the training led to improvements in social perception, with a 23% reduction in errors on emotion matching and a 49% reduction in errors on emotion labelling. There was also some evidence of improvements in executive function; however, these were only observed in within- group paired t-tests.

Emotion & ToM Imitation Training (ETIT)

Roncone and colleagues (Roncone et al., 2004) randomly assigned 20 inpatients with residual schizophrenia to Instrumental Enrichment Program (IEP) or a usual treatment control condition. IEP, which the authors compare to Hogarty and colleagues' Cognitive Enhancement Therapy, focuses on exposing participants to new situations and decreasing ToM impairments by "teaching and learning how to change cognitive structure by transforming a passive dependent cognitive style to an autonomous one".

IEP was conducted in a single 6-month weekly group, which included ten patients and five therapists. Compared to the control condition, IEP was

associated with decreases in negative symptoms, improvements in ToM (both first- and second-order false beliefs), executive functions, strategic thinking, and affect recognition for two types of emotions—sadness and fear.

In another study of the malleability of ToM impairments, Mazza and colleagues (Mazza et al., 2010) compared changes in ToM performance following 12 sessions of Emotion and ToM Imitation Training (ETIT) or Problem-Solving Skill Training (PST) administered to 33 outpatients with schizophrenia. ETIT is a group-based treatment consisting of four training phases: observing others' eye direction, imitating facial emotions, inferring others' mental states, and making attributions of intentions based on observations of others' actions. Compared to the active control condition, individuals randomized to ETIT evidenced improvements in several ToM measures, affect recognition, empathy, clinician-rated social functioning, and positive symptoms. Improvements in memory were observed only in the group receiving PST.

Social Cognition Interaction Training (SCIT)

Social Cognition and Interaction Training (SCIT) is a comprehensive, standalone manual-based group intervention that targets the three-core social cognitive deficits in schizophrenia: emotion perception, theory of mind (ToM), and attributional style (Roberts, Penn, Labate, Margolis, & Sterne, 2010).

SCIT is comprised of three distinct phases, lasts 20–24 weeks, and is built around a weekly 1-hour group therapy session. SCIT involves the use of didactic instruction, videotape and computerized learning tools, and role-play methods to improve social cognition. SCIT involves weekly homework assignments and uses optional phone-in contacts and practice partners to consolidate gains made in the sessions.

SCIT has shown improvements in both inpatients and outpatients with schizophrenia (Combs, Adams, et al., 2007) (D. Penn et al., 2005) (Roberts & Penn, 2009) and these gains persist at 6-month follow-up (Combs et al., 2009). SCIT has the potential to become an evidence based treatment for schizophrenia (D. L. Penn, Roberts, Combs, & Sterne, 2007).

Social Cognition Skills Training (SCST)

Social Cognitive Skill Training (SCST) was developed by Green, Horan, and colleagues at the University of California at Los Angeles (UCLA) and combines and expands on elements from other social cognitive treatments including SCIT and TAR.

In the first evaluation of the feasibility and tolerability of SCST (Horan et al., 2009), 34 schizophrenia spectrum outpatients, social cognitive training was associated with significant improvements in affect recognition, with large between-group and medium to large within-group effect sizes; these improvements were independent of any change in neurocognitive function or clinical symptoms. There were also trend-level improvements on measures of attributional bias and ToM.

In a subsequent evaluation of the now-expanded SCST treatment (Horan et al., 2011), 85 individuals with psychotic disorders were randomized to receive one of four time-matched treatments: SCST, computerized neurocognitive remediation, a hybrid intervention that included both SCST and neurocognitive remediation components, and a standard illness management skills training group. There were no significant between-group differences on measures of social perception, attributional bias, or ToM, nor on neurocognition or psychiatric symptoms. There was a trend-level improvement for social skill ability in both the SCST and the neurocognitive remediation group. But differential effects favouring SCST were found for affect recognition, which generalized to emotion management. Because effects on emotion processing were specific to the SCST group, the authors conclude that this intervention has a specific effect on social cognition not observed for the other three treatment conditions, and they suggest that efforts at improving social cognition may be successful in stand-alone social cognitive treatments that do not require concomitant neurocognitive remediation.

Meta Cognitive Therapy (MCT)

Metacognitive training (MCT; from metacognition, "thinking about one's thinking") is a novel approach founded in the tradition of psychoeducation, cognitive remediation, social cognition training and CBT. MCT targets cognitive biases putatively involved in delusion formation, for which patients

often lack adequate awareness. Another explicit aim of MCT is to foster improved social cognition and theory of mind.

Various studies have asserted the feasibility of the MCT (S Moritz, Veckenstedt, Randjbar, Vitzthum, & Woodward, 2011) (Steffen Moritz & Woodward, 2007) in German and other languages. Researchers, have also shown a positive impact on symptoms (Aghotor, Pfueller, Moritz, Weisbrod, & Roesch-Ely, 2010) (Kumar et al., 2010) (Ross, Freeman, Dunn, & Garety, 2009). Although there is increasing support for the efficacy of the MCT as a stand-alone program, it is probably best to use it with along with other therapies like CBT.

Integrated Psychological Therapy (IPT)

IPT was one of the very first comprehensive and manual-driven group therapy approaches for schizophrenia patients. IPT is a "bottom-up" and "top-down" approach, addressing both basic cognitive building blocks and higher order integrative processing. It consists of five subprograms, each with incremental steps. IPT starts with a subprogram addressing the neurocognitive domain, followed by a second subprogram to enhance social cognition. In a third stage, IPT focuses on interpersonal and social context using verbal communication tools, thereby bridging the gap between cognitive and social functioning. Finally, social competence is targeted with exercises to improve social skills (fourth subprogram) and to increase patients' mastery in coping with interpersonal and social problems (fifth subprogram) for more independent living.

A meta-analysis of the efficacy of IPT (Roder, Mueller, Mueser, & Brenner, 2006), however, indicates efficacy in all examined domains, including neurocognition, psychiatric symptoms, and psychosocial functioning, with within-group effect sizes in the medium range. This pattern of findings persists when only methodologically rigorous IPT studies with large samples are included, and it generalizes to a broad range of assessment types, settings, and treatment phases. There is also evidence that the effects of IPT are maintained or even enhanced during an average follow-up period of over 8 months.

Cognitive Enhancement Therapy(CET)

CET is a broad-based psychosocial treatment combining neurocognitive remediation and social cognitive group training. Although from the beginning CET has been conceptualized as a social cognitive treatment, it nevertheless includes a significant neurocognitive training component, with neurocognition seen as a necessary building block for successful social behaviour.

In the first published evaluation of CET (Hogarty et al., 2004) with 121 chronically ill patients with schizophrenia randomized to 2 years of CET or an illness self-management focused intervention called Enriched Supportive Therapy (EST), group differences favouring CET were observed on processing speed, neurocognition, and social adjustment, with trend-level improvements for social cognition and cognitive style were observed at the end of one year.

At the end of the 2-year treatment, observed group differences remained or were enhanced, with large effect size improvements for CET on all assessed composite scores, with the exception of psychiatric symptoms. Most importantly perhaps, at the end of treatment, the groups differed significantly on measures of social functioning and social adjustment, including vocational and interpersonal effectiveness, instrumental task performance, and adjustment to disability. In an effort to disentangle relevant patient variables associated with treatment efficacy, the authors report that when the sample was divided into more versus less chronic patients (those ill for more or less than 15 years), among more chronic patients, CET participants improved more than EST participants only on measures of reaction time, whereas for the less chronic patients, group differences were observed on several of the assessed domains, including social functioning, suggesting that CET may be particularly helpful to individuals earlier in the course of illness.

In a subsequent report of the durability of CET effects 1-year after the conclusion of treatment (Hogarty, Greenwald, & Eack, 2006), follow-up data were available for close to 90% of the originally randomized sample. Posttreatment CET improvements were maintained on processing speed, cognitive style, social cognition, and social adjustment, and there was evidence that early (first year) improvements in processing speed mediated

improvements in social cognition and social adjustment in the CET group. Perhaps of most interest is that at the follow-up assessment, group differences were noted on several real-world outcomes, including participation in social, recreational, or therapeutic group activities, with 30% of the CET group (vs. only 9% of EST group) engaged in these types of activities.

A similar kind of study (Eack, Greenwald, Hogarty, & Keshavan, 2010) with early course illness from the same researchers have shown results favouring the CET with maintenance of effect at one year follow up.

CET has also been reported to be associated with changes in brain morphology (Eack, Hogarty, et al., 2010). In a subsample of 53 of the 58 early-course schizophrenia patients described above, magnetic resonance imaging (MRI) assessments were conducted at baseline, 1 year, and 2 years. Comparing regional volume changes between the two groups at the end of treatment, CET seemed to provide a neuroprotective effect against gray matter loss in temporal lobe structures.

Integrated Neurocognitive Therapy (INT)

INT includes both computerized exercises, as well as cognitive-behavioural group sessions and homework assignments meant to promote generalization of training to real-world functioning. Neurocognitive training focuses on processing speed, learning and memory, executive functions, and working memory, whereas social cognitive training focuses on emotion perception, social perception, social schema, and attributional style.

Though INT is a new comer in this area of social cognition intervention, preliminary analyses (Mueller, Schmidt, & Roder, 2011) indicate good treatment tolerability and acceptance of the treatment. Compared to TAU, INT led to improvements in neurocognition, symptoms, functioning, and social cognition, with some indication that treatment gains were maintained or even enhanced at the follow-up assessment. There is also evidence that social cognition and negative symptoms may mediate the relationship between neurocognition and functional outcomes in INT participants (Roder, 2010).

Summary of available social cognition interventions in schizophrenia:

As for as pharmacotherapy is concerned, drugs are yet to be discovered for the treatment of cognitive symptoms including social cognitive deficits. At present psychosocial interventions are the effective available interventions. All the psychosocial interventions have been discussed briefly above and the efficacy/preliminary evidences of various interventions are tabulated below table-3.3.

Apart from psychological interventions, physical exercise including aerobic training had been found to improve social cognition, though the number of studies were just two and the social cognition assessments were not comprehensive(Kimhy et al., 2015) (Firth et al., 2016)

3.11 YOGA FOR SOCIAL COGNITION IN SCHIZOPHRENIA

Schizophrenia has also been described in past as split mind/personality. On the other hand, yoga has been defined as *'Citta vṛtti nirodaha'* (controlling the modifications of the mind). In some yoga texts like, Yoga Sutras of Patanjali there are descriptions of experiences like clairaudience and clairvoyance (Iyengar BKS, 2007) which accomplished yoga practitioners cultivate consciously and use for spiritual progress, whereas similar experiences which forms the symptoms of schizophrenia makes the patients socially dysfunctional. Hence, it's likely that the key difference in social functioning and its precursor/predictor – the social cognition could be managed with add-on yoga therapy. In this light, yoga has the potential to be used as an add-on complementary therapy in schizophrenia. Previous studies have demonstrated the efficacy of yoga in schizophrenia for clinical symptoms including some aspects of social cognition like FERD (Jayaram et al., 2013) (R V Behere et al., 2011). To comment on the definite role of yoga for improving symptoms, larger multicentric trials are warranted, as there are only few studies available currently and majority are from India. Hence apparently the evidence available is weak(Broderick, Knowles, Chadwick, & Vancampfort, 2015) and in general there is a trend for yoga studies conducted in India to be positive than in other countries(Cramer, Lauche, Langhorst, & Dobos, 2015)

Table 3.3 Interventions for Social Cognition training

S.No	Author	Study Design	Gender	Patient characteristics	Intervention	Control	Duration of illness	Results
1	Bechi et al. (2012)	RCT(3 groups; random allocation only for the experimental conditions not for controls)	SRT 63%; SCT 68%; NT 67%	Schizophrenia (n=51); Outpatients. SRT 24, 0 dropout; SCT 28, 1 dropout; NT 24, 2 dropouts	Video based training in AR and ToM; 12 weeks of 1 h session	Social rehabilitation training,CRT 2 one hour sessions per week, for 12 weeks	SRT 15; SCT 14; NT 17	statistically significant improvement in ToM abilities, but no changes with respect to EP
2	Bechi et al. (2013)	RCT	ToMI 42%; ACG 54%	Schizophrenia(n=30); 30 outpatients (19 treatment no dropouts; 11 no dropouts)	Theory of Mind Intervention (ToMI); 18 weeks, 1 h sessions twice a week	18 1 h session twice a week Active control (newspaper discussion group)	ToMI 10.8; ACG 15.4	significant improvement of ToM abilities among subjects allocated to ToMI compared to ACG
3	Bechi et al. (2015)	RCT (3 groups)	ToMI 53%; SCT 67%; ACG 53%	Schizophrenia(n=75); 75 outpatients; ToMI 32; SCT 24; ACG 19. Dropouts not Mentioned.	ToMI 18 1 h sessions twice a week; SCT 1 h 12 weeks; plus CRT two 1 h sessions a week	16 1 h session once a week Active control (newspaper discussion group)	ToMI 16.3; SCT 13.9; ACG 14.94	SCT and ToMI groups improved significantly in ToM measures, whereas the ACG did not. paranoid and non-paranoid subjects improved significantly after ToMI and SCT, without differences between groups, despite the better performance in basal ToM found among paranoid patients.
4	Choi and Kwon (2006)	RCT	SCET 52%; Control 58%	Schizophrenia (n=33); Schizoaffective (n=1) Outpatients 17 SCET (7 dropouts); 17 control; 10 Dropouts)	Social Cognition Enhancement Training (SCET) 36 sessions, 1.5 h	Standard psychiatric rehabilitation training (coping skills, medication adherence)	SCET 9.3; Control 13.1	SCET group significantly improved their performance relative to those in the standard group on one measure of social cognitive ability (PA of WISC-R)
5	Combs et al. (2007)	Non randomized controlled trial	SCIT 67%; control 90%	Schizophrenia (n=18); 28 forensic inpatients (18 SCIT; 10 control) no information on dropouts	SCIT; 18 h ; 1 session per week	18 h coping skills group	SCIT 18.4; control 19.7	compared to the control group, SCIT participants improved on all of the social cognitive measures and showed better selfreported social relationships and fewer aggressive incidents.Change was independent of changes in clinical symptoms
6	Combs et al. (2008)	RCT (3 groups)	65.00%	Schizophrenia (n=60); inpatients (20 in each group, no mention of dropouts)	Emotion Perception Intervention (based on attention or monetary incentive) for AR	FEIT only with no training	Not reported	attentional-shaping condition had significantly higher scores on the FEIT at intervention, post-test, and follow-up compared to monetary reinforcement and repeated practice
7	Corrigan et al. (1995)	RCT	Intervention 45%; control 45%	Schizophrenia (n=46); Inpatient and outpatient; 20 in each group	1 h session Vigilance plus memory training for social perception (self-instruction, salient cues, repeated practice)	1 h session Vigilance alone	59.9 day hospitalised exp.; 61.6 days hospitalised control	subjects in the vigilance-plus-memory condition were able to identify social cues in the videotaped training materials significantly better than subjects in the vigilance-alone condition. Difference was evident in an independent measure of social cue recognition and was present at a 48 h follow-up

8	Eack et al. (2009)	RCT	ET 65%; EST 74%	Schizophrenia (n=58); inpatient and outpatient, CET 31, EST 27 (9 dropouts at 1 year, 12 at 2 years)	Cognitive Enhancement Therapy. Two years including 45 1.5 h social cognitive therapy	Enriched Supportive Therapy (EST; incl individual sessions on psychoeducation, relapse prevention)	CET 3.1; EST 3.3	significant differential effects favoring CET on social cognition, cognitive style, social adjustment, and symptomatology composites during the first year of treatment. After two years, moderate effects (d=.46) were observed favoring CET for enhancing neurocognitive function. Strong differential effects (d>1.00) on social cognition, cognitive style, and social adjustment composites remained at year 2
9	Eack et al. (2015)	RCT	CET 68%; TAU 78%	Schizophrenia (n=31); Outpatients with substance misuse. CET 22 (posttreatment 12); TAU 9 (posttreatment 8)	Cognitive Enhancement Therapy. 45 sessions 1.5 h	Treatment as usual	CET 15.2; TAU 11.8	CET is a feasible and potentially effective treatment for cognitive impairments in patients with schizophrenia who misuse alcohol and/or cannabis.
10	Garcia et al. (2003)	Non randomized controlled trial	IPTS 82% control 55%	Schizophrenia (n=30); 23 community (IPTS 5: 2 dropouts pre intervention, 6 lost to FU); 7 control (1 before test, 2 lost to FU)	Integrated Psychological Therapy for Schizophrenia Patients (IPTS)	No training condition	IPTS 21; control 15	instrument has been sensitive to changes in the pre-treatment and post-treatment measures, showing that schizophrenics patients have improved their ability to perceive and to interpret reality in a more adequate way.
11	Gil Sanz et al. (2009)	RCT	PECS 57%; control 43%	Schizophrenia (n=14); 14 community patients (PECS 7; control 7) no information on dropouts	Social Cognition Training Program (PECS)	nclear but difference is that control group only received ER training, not SP	PECS 13.4; control 20.6	improvement in social perception and interpretation in the experimental group, in comparison with the control group, but not in emotion recognition. No significant correlations were obtained between social cognition training and other variables tested.
12	Gil-Sanz et al. (2014)	RCT	PECS 40%; control 66%	Schizophrenia (n=83); 83 community patients (PECS 44; control 39) no information on dropouts	Social Cognition Training Program (PECS)	Attention and memory	PECS 12; control 16	experimental group showed a higher performance compared to patients in the control task group in the Hinting Task Test and in the emotion recognition of sadness, anger, fear, and disgust
13	Gohar, Hamdi, El Ray, Horan and Green (2013)	RCT	SCST 72%; control 90%	Schizophrenia (n=42); outpatients (SCST 22; Control 20. No dropouts)	Social Cognitive Skills Training.2 sessions per week for 8 weeks	Skills Training Control Group. 16 sessions	SCST 21.6; control 22.5	SCST group demonstrated significant treatment effects on total emotional intelligence scores, as well as the sub-areas of Identifying Emotions and Managing Emotions , compared with those in the control condition. There were no treatment benefits for neurocognition for either condition, and both interventions were well-tolerated by patients

14	Hasson-Ohayon et al. (2014)	RCT	69.00%	Schizophrenia (n=55) community patients (SCIT-34, control-21); no drop outs	SCIT, plus social mentoring 8 weeks, one hour sessions	Social mentoring, Three times per week, 1 h	Not reported	preliminary evidence that SCIT plus social mentoring improves social cognition and functioning among persons with severe mental illness who are living in the community
15	Habel et al. (2010)	RCT	100%	Schizophrenia(n=30) 30 inpatient and outpatient (10 treatment group 4 dropouts; 10 TAU 2 dropouts;	12 sessions of 45 mins Training in Affect Recognition (TAR)	Treatment as usual (no additional information); Healthy controls	Not reported	patients differentially impaired in the identification of the emotional aspects of facial expressions (but not age discrimination) compared to healthy participants. increased number of correct identifications was observed in trained patients only. an increase in activation was noted in the left middle and superior occipital lobe, the right inferior and superior parietal cortex, and the inferior frontal cortex bilaterally in TAR patients compared to the TAU group. These activation changes in TAR patients correlated with their behavioral improvement,
16	Horan et al. (2009)	RCT	SCT 87%; Control 100%	Schizophrenia (n=34) (SCIT 15 2 dropouts; Control 16 1 dropout)	Social Cognitive Training; 12 1 h once a week	Active control group 12 1 h once a week; illness management and relapse prevention skills training	SCT 20.2; control 18.0	individuals who received the social cognitive intervention demonstrated significant improvements in facial affect perception, one of the four targeted social cognitive domains. These improvements were not attributable to changes in neurocognitive functioning or clinical symptoms.
17	Horan et al. (2011)	RCT	SCST 93.8%; NR 89.5%, ST 78.9%; Hybrid 92.9%	68 patients ((48 schizophrenia,13 schizoaffective,7 psychosis NOS) (SCST 16, 3 dropouts; NR 19, 5 dropouts; Hybrid 14 (7 dropouts)	Social Cognitive Skills Training;24 sessions, Neurocognitive remediation; Hybrid combination.	ST – standard illness management training. Matched for contact time.	SCST 19.7 yrs.; NR 22.7 yrs.; ST 24.1 yrs.; Hybrid 23.4 yrs	The SCST group demonstrated greater improvements over time than comparison groups in the social cognitive domain of emotional processing, including improvement on measures of facial affect perception and emotion management. There were no differential benefits among treatment conditions on neurocognitive or clinical symptom changes over time.
18	Kayser et al. (2006)	RCT	Intervention 60%; control 84%	Schizophrenia (n=14) (13 outpatients, 1 being discharged) (8 exp.; 6 control) dropouts not reported	2 one hour training sessions, Video clips showing social interactions, with training in theory of mind	Treatment as usual	Intervention 12.3; control 11.5	patients showed less disorganisation signs on the second evaluation when compared to the first (there seems to be a possible improvement of the participants' communication disorders and their ability to attribute intentions to others)

19	Mazza et al. (2010)	RCT	59%	Schizophrenia (n=33) ETIT group 17; control group 16. 0 dropouts	Two days a week, 12 weeks 50 mins. Emotion and ToM Imitation Training (ETIT)	Problem solving group	Intervention 6.3; control 6.5	ETIT participants improved on every social cognitive measure and showed better social functioning at posttest than controls . Improvement in social cognition, in particular in emotion recognition, is also supported by ERP responses: we recorded an increase in electroactivity of medio-frontal areas only after ETIT treatment.
20	Penn and Combs (2000)	RCT (4 groups)	58%	Schizophrenia (n=40) (10; 12; 9; 9 group split) dropout info not reported	Reinforcement, facial feedback and combination targeting FAR.	Repeated practice condition with no feedback	17.1	all groups of subjects, with the exception of those in the repeated practice group, improved in their ability to identify facial affect, with these effects showing some stability over time. There was limited evidence of these effects generalizing to the test of facial affect discrimination.
21	Popova et al. (2014)	RCT(3 groups)	66%	Schizophrenia (n=57) FAT 29, 10 dropouts; TAU 24, 5 dropouts); CE 27, 8 dropouts	FAT consisted of training in affect recognition and working memory. 20 daily 1 h sessions over 4 weeks	CE standardised program of cognitive training, and treatment as usual	Not reported	alpha power increase during the dynamic facial affect recognition task was larger after affect training than after treatment-as-usual, though similar to that after targeted perceptual–cognitive training. Alpha power modulation was unrelated to general neuropsychological test performance, and it improved in all group
22	Roberts et al. (2014)	RCT	SCIT 67% TAU; 67%	Schizophrenian (n=66) (SCIT 33, 2 drop outs; TAU 33, 1 dropout)	20–24 Weekly hour long sessions of SCIT	TAU	SCIT 23; TAU 23	SCIT may improve social functioning, negative symptoms, and possibly hostile attributional bias. Post-hoc analyses suggest a dose– response effect.
23	Roncone et al. (2004)	RCT	Intervention 60%; control 70%	Schizophrenia (n=20) (10 exp.; 10 control) dropouts not mentioned	Metacognitive Intervention Programme; 22 h of training to change social cognitive structure	Medication and supportive psychotherapy “where needed”	Intervention 16.9; control 11.1	Social cognition, neurocognition, clinical variables, and community functioning improved significantly following metacognitive training based rehabilitation
24	Russell et al. (2008)	RCT	Intervention 65%; 71% control	Schizophrenia (n=40) (26 in exp. groups, 13 in control 1 dropout in ctrl)	METT	Repeated exposure	Intervention 21.6; control 23.6	first evidence that improvements in emotion recognition following METT training are associated with changes in visual attention to the feature areas of emotional faces

25	Sachs et al. (2012)	RCT	TAR 60%; TAU 40%	Schizophrenia (n=40) inpatients and outpatients (TAR 20, 0 dropouts; control 18, 2 dropouts)	12 sessions over 6 weeks; Training in Affect Recognition	12 sessions over 6 weeks Treatment as usual	TAR 24.3; TAU 24.3	TAR group achieved significant improvements in facial affect recognition, in particular in recognizing sad faces and, in addition, in the quality of life domain social relationship. TAR training contributes to enhancing some aspects of cognitive functioning and negative symptoms. improvements in facial affect recognition and quality of life were independent of changes in clinical symptoms and general cognitive functions.
26	Tas et al. (2012)	RCT	F-SCIT 57.9%; SS 46.2%	Schizophrenia (n=49) outpatients (F-SCIT 19, 3 dropouts; SS 26, 1 dropout)	14 weeks; based on SCIT program	14 weeks; Social Stimulation (SS)	F-SCIT 12.6; SS 11.9	Patients who received FSCIT significantly improved in quality of life, social functioning and social cognition, whereas the SS group worsened in nearly all outcome variables. Family-assisted SCIT is effective in improving quality of life, social functioning and social cognition
27	Taylor et al. (2015)	RCT	100% (single sex ward)	Schizophrenia (n=45) forensic inpatients (SCIT 21, 5 dropouts; TAU 15, 4 dropouts)	16 sessions, twice a week for 45 min. Based on SCIT	TAU	SCIT 25,2; TAU 22.3	SCIT group showed a significant improvement in facial affect recognition compared to TAU
28	van der Gaag et al. (2002)	RCT	Intervention 62%; control 66%	Schizophrenia (n=42) inpatients (21 per group, 3 dropouts	22 sessions, training on perception; reasoning, emotion perception and social situations	Treatment same as experimental group, but leisure activities substituted for intervention	Not reported	cognitive training program improved emotion perception, with some evidence of generalization to measures of executive functioning; other areas of neurocognitive functioning were largely unaffected
29	Veltro et al. (2011)	RCT	Not reported	Schizophrenia (n=24) outpatients	24 sessions, 90 min Cognitive Emotional Rehabilitation (REC)	24 sessions, 90 min Problem solving training (PST)	REC 14.2; PST 11.9	both training methods(REC & PST) were found to be effective in psychopathological measures and in social functioning. On cognitive function improvements were specific to the rehabilitative approach. PST are mainly improved capacities for planning and memory, while the REC improved measures such as social cognition Theory of mind and emotion recognition
30	Wang et al. (2013)	RCT	SCIT 54.5%, TAU 47.1%	Schizophrenia (n=43) outpatients (SCIT 22, 0 dropouts; Control 21, 4 dropouts)	20 weeks based on SCIT	Treatment as usual	Not reported	Patients in SCIT group showed a significant improvement in the domains of emotion perception, theory of mind, attributional style, and social functioning compared to those in waiting-list group.

31	Wolwer et al. (2005)	RCT (3 groups)	TAR 90%; CRT 58%; control 84%	Schizophrenia (n=77) inpatients & outpatients TAR 28; CRT 24; 25 TAU (24 dropouts)	12 sessions TAR facial affect recognition; 12 sessions CRT neurocognition	TAU	Number of previous hospitalisations (TAR 4.8; CR T 6.2; TAU 3.3)	Patients under TAR significantly improved in facial affect recognition, with recognition performance after training; Patients under CRT and those without special training (TAU) did not improve in affect recognition, though patients under CRT improved in verbal memory functions
32	Wolwer and Frommann (2011)	RCT	68%	Schizophrenia (n=38) inpatients (TAR 20, 5 dropouts; CRT 18, 3 drops outs)	TAR facial affect recognition; 12 sessions 45–60 min	CRT neurocognition;12 sessions 45–60 min	7 first episode, 13 2–4 episodes, 13 had 5 or more	Intentionto-treat analyses found significantly larger pre–post improvements with TAR than with CRT in prosodic affect recognition, ToM, and social competence and a trend effect in global social functioning.