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Research Article

The Relationship between Motor Symptoms, Signs, and Parkinsonism with Facial Emotion Recognition Deficits in Individuals with 22q11.2 Deletion Syndrome at High Genetic Risk for Psychosis

Tommaso Accinni,[1] **Martina Fanella**,[1] **Marianna Frascarelli**,[1] **Antonino Buzzanca**,[1] **Georgios D. Kotzalidis**,[2] **Carolina Putotto**,[3] **Bruno Marino**,[3] **Alessia Panzera**,[1] **Antonella Moschillo**,[2] **Massimo Pasquini**,[1] **Massimo Biondi**,[1] **Carlo Di Bonaventura**,[1] **and Fabio Di Fabio**[1]

[1]*Department of Human Neurosciences, Sapienza University of Rome, Faculty of Medicine and Dentistry, Piazzale Aldo Moro 5, 00185 Rome, Italy*
[2]*Department of Neurosciences, Mental Health and Sensory Organs, Sapienza University, Faculty of Medicine and Psychology, Via di Grottarossa 1035-1039, 00189 Rome, Italy*
[3]*Department of Pediatrics, Obstetrics and Gynecology, Sapienza University of Rome, Viale Regina Elena, 324, 00161 Rome, Italy*

Correspondence should be addressed to Tommaso Accinni; tommaso.accinni@uniroma1.it

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Background. The 22q11.2 Deletion Syndrome (22q11.2DS) is a genetic condition at high risk of developing both psychosis and motor disorders. Social Cognition (SC) deficits have been associated not only with schizophrenia but also with Parkinson's disease (PD). The present study assessed SC deficits in 22q11.2DS and investigated the interaction between motor symptoms and deficits in Facial Emotion Expressions (FEE) recognition and in Theory of Mind (ToM) tasks in people with 22q11.2DS. *Methods*. We recruited 38 individuals with 22q11.2DS without psychosis ($N = 38$, DEL) and 18 with 22q11.2DS and psychosis ($N = 18$, DEL_SCZ). The *Positive And Negative Syndrome Scale* (PANSS), *Ekman's 60 Faces Test* (EK-60F), the *Awareness of Social Inference Test* (TASIT EmRec), and the *Movement Disorder Society-Unified Parkinson's Disease Rating Scale part III* (UPDRS III) were administered. Correlations were sought between UPDRS III and both TASIT EmRec and EK-60F scores. Analyses were conducted separately for each psychopathological subgroup. *Results*. Higher UPDRS III ($p = 0.04$) and lower EK-60F ($p = 0.025$) scores were observed in the DEL_SCZ group. We found inverse correlations between UPDRS III and both TASIT EmRec ($r = -0.289$, $p = 0.031$) and EK-60F ($r = -0.387$, $p = 0.006$) scores in the whole sample. Correlations were no longer significant in the DEL_SCZ group (UPDRS III-TASIT EmRec $p = 0.629$; UPDRS III-EK60F $p = 0.933$) whilst being stronger in the DEL group (TASIT EmRec, $r = -0.560$, $p < 0.001$; EK60F, $r = -0.542$, $p < 0.001$). Analyses were adjusted for CPZ Eq and IQ. *Conclusions*. A modulation between FEE recognition deficits and motor symptoms and signs was observed in the 22q11.2DS group, likely affecting patients' quality of life.

1. Introduction

Social Cognition (SC) involves several neurocognitive processes aimed at representing other's mental state by enabling individuals to infer their beliefs, feelings, and emotions up to predict their intentions and purposes [1]. It consists of a set of functions of both affective and cognitive nature that are relevant for social interactions [2]. Different cognitive domains participate in SC, like Theory of Mind (ToM) [3, 4], which is specifically aimed at other's mental state representation to

build effective interactions and provide reasonable reactions to other's intentions. Other SC components serve to infer social rules and roles, to correctly interact and to recognize other's emotional content. In the last years, SC processes have been progressively studied to shed line on their dysfunctions and clinical correlates, but several aspects still require to be clarified, like specific SC cognition components and their mutual relationships [1]. SC deficits have been tightly associated with neurodegenerative disorders and neurodevelopmental, in particular with schizophrenia [5, 6]. These are described as related to the psychopathological core of this illness more than positive, negative and disorganisation symptoms [7, 8]. SC deficits concern both dysfunctions in decoding and elaborating social inputs and significant functioning impairments; they may be intended as an endophenotype of vulnerability to psychosis [6, 9, 10]; this results in appearing similar in both chronic and first-episode psychosis patients [11]. Of note, theory of mind deficits have been associated with poor quality of life (QoL) in patients with schizophrenia as well, likely due to their impact on patients' valuations and life satisfaction, and on their degree of autonomy [12].

Deficits in SC have been described in the 22q11.2 Deletion Syndrome (22q11.2DS) [13–15], which is caused by an autosomal dominant microdeletion at the 11.2 strand on the long arm (q) of chromosome 22 [16]. This syndrome to date is the most common multi-systemic syndrome arising from a Copy Number Variation (CNV) with an incidence ranging from 1 : 3000 to 1 : 6000 according to literature and involving a hemizygotic deletion of 1.5 to 3 megabases of DNA [16, 17]. The 22q11.2 microdeletion represents one of the most important genetic risk factors for schizophrenia (SCZ); 22q11.2DS represents a simplified biological model for studying neuropsychiatric disorders [17]. Indeed, a large set of clinical features is present due to a common neurodevelopmental defect affecting neural crest cells. Besides specific disorders concerning several organs and biological systems, individuals with 22q11.2DS display a higher risk to develop SCZ compared to the general population [18, 19], with an increased incidence ranging across different studies from 23% to 43% during the lifespan. Similarly, a higher incidence of Parkinson's Disease (PD) in 22q11.2DS compared to the general population has also been described [20, 21]. It is estimated that 22q11.2 microdeletion accounts for 0.5% of Early Onset Parkinson Disease (EOPD) and in turn, an estimated 20- to 70-fold increased risk of PD in 22q11.2DS compared to the general population has been reported [22].

People with 22q11.2DS and PD differ little from patients with idiopathic PD, save for their age of onset, which is younger in the former, and some of their symptoms, like early dystonia and psychotic symptoms, usually precede the onset of PD [22, 23]. Specific nonmotor features characterise both 22q11.2DS and prodromal or full-blown idiopathic PD, like sleep disorders, olfactory deficits [24, 25] and constipation [26]. There is no agreement whether these clinical features are predictive of future PD development in 22q11.2DS.

In addition to motor features arising from specific dysfunctions of the nigrostriatal dopaminergic circuits aimed at motor control [27], PD displays psychiatric symptoms. These include depression, anxiety, apathy, gambling addiction, and psychosis [28], impulsive-compulsive symptoms [29], and cognitive impairments. These may lead to dysfunctions in social inference abilities involving mind-reading, decision making processes, and Facial Emotion Expression (FEE) recognition [30, 31]. FEE represents a fundamental part of SC skills [32, 33], pointing to basically universal abilities to display and recognize human emotions based on movements of the facial musculature, independently from contextual and cultural influences [34, 35]. Emotion processing deficits in PD have been particularly described in regard of affective prosody decoding [36, 37], besides being associated with social functioning impairments [33].

Evidence is accumulating that deficits in SC are steadily present at the early stages of PD [38, 39], even long before motor manifestations and without other significant cognitive impairments. SC deficits have been associated with EOPD [40]. In fact, nondemented individuals with EOPD have been observed to perform worse in different SC domains involving facial emotion recognition, social reasoning, ToM and decision making compared to matched healthy controls (HCs). Interestingly, none of the abovementioned SC domains appeared to be influenced by the cognitive level except for decision making abilities [39] and several studies have confirmed that emotion processing deficits in PD are independent from cognitive status [40–42]. Common neurophysiopathological underpinnings have been advanced to explain both motor and neurocognitive symptoms of PD and abnormalities in the dopaminergic circuits of the mesocorticolimbic system have been pointed out [43, 44]; considering that mechanisms of the interactions between SC deficits and motor symptoms are still unclear, it could be useful to shed light on such modulations by investigating a genetic model associated with neurocognitive, neuropsychological, and motor features.

2. Objectives

The main aim of the present study was to investigate potential SC deficits in a population of individuals affected by 22q11.2DS, at high genetic risk of developing schizophrenia and motor symptoms as well, analysing patients' performance both on ToM and on FEE recognition tasks. The second aim was to identify possible correlations between performances in FEE recognition and in ToM tasks and early motor signs and symptoms of parkinsonism in patients with 22q11.2DS.

3. Methods

The sample consisted of 38 individuals affected by 22q11.2DS without psychosis ($N = 38$, DEL) and 18 individuals with 22q11.2DS and psychosis ($N = 18$, DEL_SCZ). Recruited individuals were between 18 and 47 years of age; they were consecutively enrolled at the Outpatient Clinic for psychosis and 22q11.2DS of the Department of Human Neurosciences of the Policlinico Umberto I Hospital, Sapienza University of Rome, from January 2017 to January 2018. Each participant signed free, informed consent before

being enrolled in the study. The study adopted the Helsinki Principles of Human Rights of 1964 and received the approval of the Ethics Committee of the Umberto I University Hospital, Rome, Italy. All data were anonymised. Patient eligibility and diagnosis of psychotic disorder were based on the Structured Clinical Interview for DSM-5 Disorders-Clinician Version (SCID-5-CV) [45, 46], with the aim to investigate the presence of other previous or current psychiatric symptomatology that would meet criteria for a DSM-5 diagnosis. Each participant was assessed by a neurologist, who investigated and reported symptoms and signs of parkinsonism or PD with the aid of specific rating scales. Genetic diagnosis of recruited patients was ascertained through Fluorescent *In Situ* Hybridization (FISH) at their original assistance centres, before they were referred to our outpatient clinic for specialistic care of mental disorders.

3.1. Social Cognition Assessment. Data about sociodemographic variables with age, years of education, working status, social status, and marital status were collected during clinical interview. Patients' symptoms were assessed by a psychiatrist using *The Positive And Negative Syndrome Scale* (PANSS) to assess symptom severity [47]. The PANSS has shown validity and reliability with an interrater reliability of about 0.8 [48].

After PANSS completion, the clinician administered the *Eckman 60 Faces Test* (EK-60F) [49]. This is a tool to assess ability to promptly recognize facial emotional expressions. Each participant was asked to observe on a screen a set of pictures representing different individuals (6 women and 4 men) statically reciting the following basic facial emotional expressions: *rage (R), fear (F), sadness (SA), happiness (H), surprise (SU), and disgust (D),* as well as a *neutral (N)* expression, and then asked to classify each picture according to this range. EK-60F consists of two sections comprising 55 images each (maximum total score is 55; the percentage of correct answers concerning specific emotion recognition is recorded, based on participant's performance). Each image remains on the screen for 5 seconds. Answers are provided through touching appropriate keys on the keyboard, with latency times being recorded.

The *Awareness of Social Inference Test* (TASIT) [50] has been employed to assess SC of the sample by means of a computerized task concerning social perception. The test proved to be valid in both patient [51] and healthy populations [52]. Participants were asked to identify thoughts, feelings and intentions of actors playing in brief video vignettes. They were required to recognize lies and sarcasm in the frame of social interactions as represented in 16 vignettes of about 15-60 seconds each. Participants, once viewing each video, were asked to answer specific questions, i.e., what he/she is doing to another one? What he/she is trying to say to another one? What he/she is truly thinking about? What he/she is truly feeling? TASIT consists of seven scales organised in the following three sections: emotion recognition (positive emotions, PE; negative emotions, NE; sincere, SI); social inference-minimal (simple sarcasm, SS; paradoxical sarcasm, PS); and social inference-enriched (lie, LI; enriched sarcasm, ES). In this study, we employed the first section of TASIT (TASIT EmRec) since it describes the subject's ability in emotional recognition by means of a dynamic measurement. This social perception task has been previously employed with significant reliability, both with people at Clinical High Risk (CHR) for psychosis and chronic patients [13]. IQ for each participant was assessed by employing the Raven's Progressive Matrices [53].

3.2. Neurological Assessment. All participants underwent a thorough neurological evaluation by an expert neurologist. A comprehensive neurological examination including an assessment of cognition, cranial nerves, motor, sensory, cerebellar, gait, reflexes, and long tract signs was performed in all patients. The Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) [54] was administered to all patients to improve the evaluation of motor aspects. UPDRS consists of 4 parts: part I, nonmotor aspects of daily life experiences (13 items); part II, motor aspects of daily life experiences (13 items); part III, motor examination (18 items providing 33 scores for localisation and lateralisation); and part IV, motor complications (6 items). Parts III of the scale were rated in all patients. We evaluated the motor aspects of disability including facial expression, tremor, rigidity, gait, body bradykinesia, and posture.

3.3. Statistical Analysis. Descriptive statistics (i.e., mean and standard deviation for continuous variables and frequencies for categorical variables) were obtained for clinical (psychiatric diagnosis, IQ), demographic (age, gender) and behavioral (UPDRS III, TASIT Emotion Recognition and EK-60F scores) data. Differences between groups (i.e., DEL_SCZ and DEL) in behavioral data were investigated through the t-test for independent samples.

To identify correlations between UPDRS III scores and both TASIT Emotion Recognition and EK-60F scores, we conducted Pearson's r correlations in the entire sample. Pearson's correlation was also conducted between IQ and both TASIT Emotion Recognition and EK-60F. Partial correlations between the same variables were conducted introducing as control variables IQ and Chlorpromazine Equivalents as well. The same correlation analyses were conducted in the two diagnostic groups (i.e., DEL_SCZ and DEL) separately. All analyses were implemented using the Statistical Package for the Social Sciences (SPSS), version 28.0 (IBM SPSS Statistics, Armonk, New York, May 2021).

4. Results

Clinical and demographical characteristics of the sample are reported in Table 1. Differences in test performances were significant for UPDRS III and EK-60F between the DEL_SCZ and DEL groups (Table 2).

A significant positive correlation was found between IQ and both TASIT EmRec ($r = 0.404$, $p = 0.004$) and EK-60F ($r = 0.495$, $p < 0.001$) scores.

Higher UPDRS III scores were observed in the DEL_SCZ group ($p = 0.04$). EK-60F scores were significantly lower in the DEL_SCZ group ($p = 0.025$).

Table 1: Clinical and demographical characteristics of the sample.

Continuous variables	Mean ± SD
Age	24.9 ± 7
IQ	86.2 ± 16.5
UPDRS III	6.1 ± 9
TASIT EmRec	20.3 ± 4.2
EK-60F	60.4 ± 17.1
Categorical variables	*N* (%)
Gender	
Female	15 (26.8)
Male	41 (73.2)
Diagnosis	
DEL_SCZ	18 (32.1)
DEL	38 (67.9)

DEL = group of individuals with 22q11.2DS; DEL_SCZ = group of individuals with 22q11.2DS and psychosis; EK-60F = Ekman 60 Faces Test; IQ = intelligence quotient; SD = standard deviation; TASIT EmRec = The Awareness of Social Inference Test Emotion Recognition; UPDRS III = Unified Parkinson's Disease Rating Scale III.

Table 2: Statistical difference between the SCZ and noSCZ groups in behavioral scores.

	Group	*N*	Mean ± SD	*t*	*p*
UPDRS III	DEL_SCZ	18	9.7 ± 11.5	2.101	0.040*
	DEL	38	4.4 ± 7.2		
EK-60F	DEL_SCZ	16	52.6 ± 14.4	-2.308	0.025*
	DEL	34	64.1 ± 17.1		
TASIT EmRec	DEL_SCZ	18	19.3 ± 4.4	-1.304	0.198
	DEL	38	20.8 ± 4.1		

DEL = group of individuals with 22q11.2DS; DEL_SCZ = group of individuals with 22q11.2DS and psychosis; EK-60F = Ekman 60 Faces Test; IQ = intelligence quotient; *N* = number; SD = standard deviation; TASIT EmRec = The Awareness of Social Inference Test Emotion Recognition; UPDRS III = Unified Parkinson's Disease Rating Scale III.

In the whole sample, we found significant negative correlations between UPDRS III score and both TASIT EmRec ($r = -0.289$, $p = 0.031$) and EK-60F ($r = -0.387$, $p = 0.006$) scores (Figure 1). These results were confirmed also when adjusting for control variables; the negative correlation between UPDRS III and TASIT EmRec scores was still significant when adjusting for both CPZ Eq ($r = -0.370$, $p = 0.009$) and IQ ($r = -0.336$, $p = 0.018$). The same held for the negative correlation between UPDRS III and EK-60F scores ($r = -0.386$, $p = 0.006$ for CPZ Eq and $r = -0.355$, $p = 0.012$ for IQ).

Once dividing the sample according to psychiatric diagnosis, the significance of some of these results vanished. The abovementioned correlations indeed disappeared in the DEL_SCZ group (UPDRS III-TASIT EmRec, $p = 0.629$; UPDRS III-EK60F, $p = 0.933$) (Figure 1). On the contrary, a stronger negative correlation was observed between UPDRS III score and both TASIT EmRec ($r = -0.560$, $p < 0.001$) and EK60F ($r = -0.542$, $p < 0.001$) scores for the DEL group (Figure 1). These results remained significant when adjusting for CPZ Eq (UPDRS III–TASIT EmRec, $r = -0.590$, $p < 0.001$; UDPRS III–EK60F, $r = -0.540$, $p = 0.001$) or IQ (UPDRS III–TASIT EmRec, $r = -0.548$, $p < 0.001$; UDPRS III–EK60F, $r = -0.489$, $p = 0.004$) as control variables.

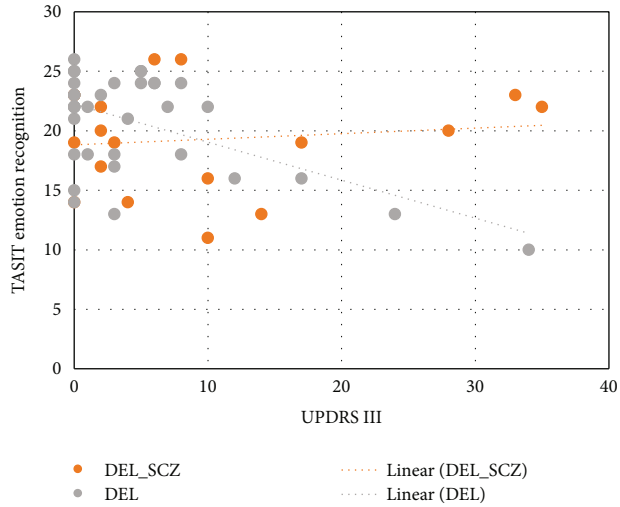

Figure 1: The negative correlation between UPDRS III and TASIT EmRec scores in the whole sample. DEL = group of individuals with 22q11.2DS; DEL_SCZ = group of individuals with 22q11.2DS and psychosis; TASIT EmRec = The Awareness of Social Inference Test Emotion Recognition; UPDRS III = Unified Parkinson's Disease Rating Scale III. The dotted line represents the correlation for the whole sample.

5. Discussion

The present study firstly aimed at investigating potential SC deficits in a population of individuals affected by 22q11.2DS, analysing patients' performance both on ToM and on FEE recognition tasks. Subsequently, we sought to investigate potential correlations between the ability in facial emotion recognition and the presence of early motor symptoms and signs of parkinsonism in individuals with 22q11.2DS who appear at higher genetic risk of developing neurodegenerative disorders [55]. Although evidence is accumulating about the presence of deficits in SC in patients with PD [30], to our knowledge this is the first study to investigate potential correlations between deficits in facial emotion recognition and motor symptoms and signs in a sample of patients with the 22q11.2DS by means of both static (EK-60F) and dynamic (TASIT EmRec) FEE assessments. Overall, people with 22q11.2DS showed an inverse correlation between their ability to recognize facial emotion expressions and the severity of their motor symptoms, as resulting from EK-60F, TASIT EmRec, and UPDRS III measurements. Indeed, in people with 22q11.2DS without psychotic symptoms, we observed a modulation between emotion recognition abilities and motor symptoms and signs, given that the better they performed on emotion recognition tasks, the less motor symptoms they showed. However, this correlation was not confirmed for individuals with 22q11.2DS associated with psychosis.

With respect to the first aim of the study, we employed both static and dynamic assessments of facial emotion recognition (EK-60F and TASIT EmRec) to investigate more reliably SC deficits in a group at genetic risk for developing movement disorders and EOPD. In patients with PD no significant differences between static and dynamic emotion recognition performances have been reported [56, 57], suggesting that their SC deficits are not modulated by contextual cues. Consistently with previous literature [58, 59], our findings confirmed specific deficits in facial emotion recognition and in ToM in people with 22q11.2DS. As expected, the general cognitive level showed a significant impact on the emotion recognition process of the recruited participants. Although Social Cognition and ToM have been previously described as particular and well-defined neurocognitive processes [2, 3, 9, 60], they seem to be influenced by neurodevelopment in general.

Once the sample has been divided based on psychopathological status, we observed that people with a diagnosis of psychosis showed worse motor symptoms, likely due to both their neuropsychiatric condition [61] and to the well-known side effects of pharmacological treatments they are exposed to [62].

With reference to the second aim, the negative correlation between motor symptoms and emotion recognition abilities in 22q11.2DS appeared to be modulated by psychiatric diagnosis, disappearing in patients with psychosis and increasing in strength in those without psychotic symptoms. Findings were confirmed even when adjusting for the general cognitive level (IQ) and the pharmacological status (CPZ Eq), suggesting that the interplay between social cognition and movement impairments would arise from specific neurobiological underpinnings, likely involving common circuits of neurotransmitters [63–68].

Patients with psychosis and the deletion syndrome showed the worst performances in both static and dynamic facial emotion recognition tasks, suggesting that their difficulties in social inference abilities would result both from neurobiological and neuropsychological factors. It is known that emotional face processing implies the activation of widespread brain networks including the fusiform gyrus, the inferior and middle occipital gyri, and the lingual gyrus among visual areas, the amygdala, the parahippocampal gyrus, the posterior cingulate cortex, the parietal lobule, the middle temporal gyrus, the insula, the medial frontal gyrus, the putamen, and the cerebellum [69]. Pathological conditions show abnormalities in the activation of these nuclei and the circuits connecting them; in paediatric bipolar disorder, hypoactivation in the fusiform gyrus is observed upon exposure to happy, sad, fearful, and angry faces [70]. In 22q11.2DS, the loss of normal face selectivity in the fusiform gyrus has been reported [71] and diffusion tensor imaging showed an increased fractional anisotropic diffusion in the white matter of the right amygdala to fusiform gyrus pathway [72]. All this makes the fusiform gyrus a region to target in future therapeutic approaches.

SC involves both ToM and empathy [73] which appear to be fundamental in structuring interpersonal relationships [74, 75]. Previous studies have found that in patients with PD, affective components of empathy and ToM appeared quite preserved compared to other social cognitive difficulties [76]. Furthermore, people with PD showed significant difficulties in understanding others' mental state and in describing others' emotional experiences compared to HCs [77], with impairments in cognitive components of ToM being more predictable than those in its affective components. Facial emotion recognition processes appear to be tightly linked to the ability of elaborating visual-spatial information [78, 79] while more complex social inference functions, like the ability in representing other's perspective or merging information derived from different contexts, are modulated by other executive domains [80]. Considering the connection between facial emotion recognition and executive functions as visuo-spatial perception, attention, memory, and language [81], the well-ascertained cognitive decline occurring in individuals with a diagnosis of PD, even at early stages [82, 83], may contribute to the progressive impairment in affective and cognitive ToM abilities. In addition, impairments in visuo-spatial processes have been directly associated with ToM deficits in people with PD [84]. On the other side, SC deficits are well documented in schizophrenia [85–87] and significant associations between a low neurocognitive level and deficits in social inference abilities and a greater severity of psychotic symptoms have been described [2, 6, 88, 89]. The extrapyramidal syndrome (EPS) has been associated with severity of psychopathology and cognitive impairments in people with schizophrenia and among extrapyramidal signs, parkinsonism correlated with more severe positive and negative symptoms [62]. This evidence is consistent with our findings about higher and more severe motor symptoms in patients with 22q11.2DS and psychosis. Moreover, EPS and parkinsonism have been associated with greater SC deficits in patients with schizophrenia [62], once again in line with our findings regarding a poorer performance in emotion recognition tasks of people with 22q11.2DS and psychotic symptoms. Individuals with this syndrome, who are at risk for psychosis, appear to share a common, genetically determined neurobiological vulnerability, involving both motor organisation and the emotion recognition process. Indeed, the 22q11.2DS is tightly associated with an increased risk of developing motor disorders [20, 23, 24, 90–96]; furthermore, people with this syndrome show higher impairments in SC abilities compared to the general population [58, 59]. It has been suggested that parkinsonism in schizophrenia does not directly impact on social inference process but is rather mediated by the severity of psychopathology and poor neurocognition [62]. Confirming this, our findings showed that patients with 22q11.2DS and psychosis displayed both worse motor signs and poorer performance on emotion recognition, regardless of the general cognitive level and pharmacotherapeutic status. Concerning the mechanism through which EPS and parkinsonism may affect neurocognition, pre-existing neural dysfunctions [97] and the impairment of specific motor abilities required in neurocognitive processes have been hypothesised to be responsible, as observed for patients with PD [98–100] and for patients with schizophrenia and EPS [101]. We may suppose that the genetic condition of people

with 22q11.2DS would predispose to movement disorders starting from a neurobiological vulnerability which likely concerns the dopaminergic pathways, which in turn are affected by neurodevelopmental abnormalities leading to the neuropathophysiology of psychosis [102].

Impairments in SC have been associated with poor quality of life (QoL) in people affected by PD [103–105] and in turn, poor QoL appears to significantly increase caregiver burden [106, 107]. These considerations seem to suggest that the relation between poor QoL and caregivers' burden may be mediated by SC deficits. For these reasons, we may suppose that in 22q11.2DS with PD, motor symptoms impact on SC abilities, impairing patients' QoL.

The main limitation of this study is the small size of the recruited group. However, 22q11.2DS is a rare syndrome with a low incidence, making it hard to recruit a significant number of individuals carrying this microdeletion. The presented findings are preliminary results and the employed statistical analysis was designed to avoid any significant bias. Another limitation is a potential recruitment bias, since we did not compare motor symptoms between 22q11.2DS and non-22q11.2DS PD. Furthermore, we had no general population group to compare with our groups; future studies will hopefully include such groups. We sought to investigate potential correlations between social inference abilities and motor symptoms in an aetiologically homogenous sample; further studies would contribute to confirm our findings by recruiting and comparing different genetic conditions.

6. Conclusions and Future Perspectives

In the present study we found that people with 22q11.2DS show significant impairments in social cognition processes, particularly regarding their facial emotion recognition abilities which are negatively correlated with the presence of motor symptoms. This modulation seems to disappear for patients with 22q11.2DS and psychotic symptoms, likely due to other factors contributing to impairments in emotion recognition capacities in the frame of psychosis. We may hypothesize that psychosis abolished this negative modulation by impairing the successful process of facial emotion recognition, but this is purely speculative given the dearth of data likely to support it; other future studies aimed at testing this hypothesis would be certainly valuable.

The 22q11.2DS represents a genetic condition involving a neurobiological vulnerability to SC deficits and motor disorders, affecting patients' quality of life. Our findings seem to confirm the reliability of such a biological model to study genetic vulnerability to neuropsychiatric diseases. 22q11.2DS provides the opportunity to investigate specific clinical and neurocognitive features which are neurobiologically determined and appear to be associated with the risk of developing schizophrenia and motor disorders. It would be useful to systematically assess both social cognition and motor features in these patients to better define suited intervention strategies aimed at motor rehabilitation and social skills training.

Data Availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Ethical Approval

The study adopted the Principles of Human Rights, as issued by the World Medical Association at the 18th WMA General Assembly, Helsinki, Finland, June 1964 and subsequently amended by the 64th WMA General Assembly, Fortaleza, Brazil, in October 2013 and received approval by the Ethics Committee of the Umberto I University Hospital, Rome, Italy. All patient and other participant data were anonymised. prot. n. 250/19 dated 7th March 2019 approved by the Ethics Committee of the Umberto I University Hospital, "Sapienza" University of Rome, Italy.

Conflicts of Interest

The authors declare no conflict of interests.

Authors' Contributions

TA, MFa, AB, and MFr designed the study. TA organised the work schedule and wrote the first draft. MFr cured the database and performed statistical analyses. CP, CDB, MFa, AP, AM and BM recruited assessed patients. TA, MFr, and GDK performed literature searches. MB and MP supervised the research programme. FDF led the research program. FDF and GDK supervised the writing. AB, TA, FDF, and GDK provided the final draft. All authors viewed and approved the final version of the manuscript.

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