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Biological motion processing in schizophrenia – systematic review and meta-analysis.

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Abstract

Context: Patients with schizophrenia show impairments in processing of biological motion. This is especially important since deficits in domains of social cognition has been associated with functional outcome and everyday functioning in this population.

Objectives: We conducted a systematic review and meta-analysis of studies which have used point-light displays to present whole-body motion to patients with schizophrenia and healthy controls, to evaluate the magnitude of differences between these groups in biological motion processing.

Method: Firstly, relevant publications were identified by a systematic search of Google Scholar and PubMed databases. Secondly, we excluded non-relevant studies for the meta-analysis according to our exclusion criteria. Effect sizes were expressed as standardized mean difference (SMD).

Results: 15 papers reporting results of 14 different experiments with 571 patients and 482 controls were included in the meta-analysis. The results for the general biological motion perception analysis revealed that patients with schizophrenia (compared with healthy controls) present reduced biological motion processing capacity with the effect size (SMD) of 0.66 (95% CI, -0.79 to -0.54; $p < 0.001$). The results for the specific biological motion-based tasks were also statistically significant with SMD of 0.72 for Basic Biological Motion task (95% CI: -0.94 to -0.51; $p<0.001$) and SMD of 0.61 for Emotion in Biological Motion task, (95% CI: -0.79 to -0.43; $p<0.001$) respectively.

Conclusion: The findings from our meta-analysis highlight abnormalities in general and specific domains of biological motion perception in schizophrenia patients as compared with healthy controls.

Keywords: schizophrenia, biological motion, social cognition, meta-analysis, social perception, emotion recognition

Introduction

Processing of biological motion is one of the most basic abilities in a repertoire of human social cognitive skills. It has been emphasized, that recognition of visual biological motion is of equal importance as information coming from evolutionarily younger channels (namely face and speech perception) while inferring the identity and social role of the other person ("social perception") (Troje, 2013). Since the point-light methodology was first introduced by the Swedish psychologist Gunnar Johansson (1973), numerous studies have confirmed that healthy individuals can easily detect the actions of other human agents and extract multiple characteristics of the presented person, even if the display of the agent has been reduced to a few point-lights attached to the major joints of the human body ("point-light walker"; PLW).Preference for biological motion compared to non-biological motion and for more natural upright compared to upside-down displays of a PLW may be observed as early as in two-day old newborns (Simion et al., 2008). Furthermore, a fine tuning of the human visual system to process biological motion may be attributed to the specialized visual processing system for that type of stimuli, which encompasses superior temporal and frontal premotor areas and for which evidence was accumulated with lesion (Saygin, 2007), neuroimaging (Grosbras et al., 2012) and brain stimulation studies (Grossman et al., 2005).

Social cognitive deficits have become one of the primary focuses in schizophrenia research. This is due to a plethora of research linking domains of social cognition with functional outcome and everyday functioning of patients with schizophrenia (Fett et al., 2011). The significance of social cognitive deficits observed in patients has also been underlined by inclusion of social cognitive domains in MATRICS (Nuechterlein et al., 2008) and CNTRICS (Carter et al., 2009) initiatives, which aimed to provide standards for examination of cognitive deficits in patients with schizophrenia. Despite a great amount of attention being directed towards social cognitive deficits in schizophrenia (SCZ), no comprehensive meta-analysis of biological motion processing abilities in patients has been performed yet. This is surprising considering that biological motion is recognized as one of the two most prominent techniques to study processes associated with identification of social stimuli and their emotional value (Billeke and Aboitiz, 2013). Moreover, biological motion processing abilities are

perceived as one of the main hallmarks of social cognitive deficits in neurodevelopmental disorders (Pavlova et al., 2012). The potential for further development of biological motion tasks to study social cognitive and affective domains was discussed by the CNTRICS initiative (Carter et al., 2009) and examined by the multicenter NIMH-sponsored Social Cognition and Functioning in Schizophrenia study (SCAF; Green et al., 2013).

At the same time, no measure associated with a recognition of social information from whole-body motion was included in a meta-analysis of quantitative studies examining social cognitive domains in patients with schizophrenia (Savla et al., 2013). Moreover, some of the studies which have been included in the meta-analysis had reported the results on tasks examining biological motion processing in patients (Bigelow et al., 2006, Couture et al., 2010, Kern et al., 2013). Yet only social cognitive measures that were not based on PLWs were extracted for the meta-analytic proceedings by Savla et al. (2013). Thus, the average magnitude of differences that can be found between patients with schizophrenia and healthy individuals with respect to biological motion processing abilities has not been examined yet. This paper aims to fill this gap by providing a quantitative analysis of the results of the studies that used PLWs to study social cognitive abilities in patients with schizophrenia. Furthermore, we also calculate the effects for two tasks which are based on point-light displays and were used as part of the SCAF project (Green et al., 2013). The first of these tasks – Basic Biological Motion task (BBM) – measures the ability to distinguish biological from non-biological motion (Kim et al., 2005; Kern et al., 2013). BBM has been successfully used to study social perception both in patients with schizophrenia (Kim et al., 2005, 2011, 2013; Kern et al., 2013; Jahshan et al., 2015) and in patients with OCD (Kim et al., 2008). The second task - Emotion from the Biological Motion (EBM; Heberlein et al., 2004) - measures emotion recognition abilities and has been applied across multiple psychiatric populations. The participants' task is to recognize the emotional state of the point-light agent who is displayed walking across the screen in either a happy, sad, angry, fearful or neutral manner. The task was initially used to study emotion processing in neurological populations (Atkinson et al., 2007; Heberlein et al., 2004). Since then, it has been

applied in studies on emotion recognition in schizophrenia (Bigelow et al., 2006; Couture et al., 2010; Kern et al., 2013/Olbert et al., 2013; Vaskinn et al., 2016), major depressive disorder (Loi et al., 2009), Alzheimer's dementia (Henry et al., 2012), eating disorders (Lang et al., 2015) and autism (Couture et al., 2010).

We also aim to examine the association between biological motion processing and demographic, and clinical variables in patients. Finally, we aim to discuss the potential mechanisms that may impact the biological motion processing abilities in patients by systematically reviewing the existing literature on biological motion processing in schizophrenia.

Methods

Eligibility criteria for papers

The systematic review was planned and reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al. 2009; for PRISMA flowchart see Figure 1).To be included in the analyses, studies had to fulfill the following criteria: (a) report original research data of the behavioral task associated directly with recognition (recognise biological motion presented concurrently with non-biological motion; e.g. Kim et al., 2005), detection (detect the actions of the agent masked with visual noise-dots; e.g. Brittain et al., 2010) or extraction of social information (extract information regarding the emotions or intentions of the presented person; e.g. Vaskinn et al., 2016) presented with PLW gait displays; (b) report data from patients with schizophrenia or schizoaffective disorder; (c) include a healthy control group as a comparison group; (d) be published in peer-reviewed journals (conference abstracts and dissertations were excluded); (e) report results in English; (f) report results as means and standard deviations or statistical test values so that required effect size could be calculated.

Search strategies

The literature was searched using Google Scholar and PubMed databases for records from 1973 to 24 July 2016. Records of interest were identified by using the search terms: ("biological motion" OR "point-light displays") AND (schizo* OR psychosis). Furthermore, the search was supplemented by relevant papers found by reviewing the references provided in the identified articles. Finally, articles citing the source paper for Emotion in Biological Motion task (Heberlein et al., 2004) were reviewed to include papers not identified by previously mentioned search methods. In case of missing information, the authors of studies were contacted and additional data was added if the usable data have been received.

Study identification

Titles and abstracts of the papers indexed were screened for eligibility by the first author of the study (ŁO). If neither the title, nor the abstract of the text indicated any potential relevance for the meta-analysis or systematic review the paper was excluded from further investigation. Initial screening revealed 42 articles of interest. A significant portion of them were excluded on the basis of the criterion *a* (not reporting tasks based on the displays of PLW gait) (n=14). Although Tomlinson et al. (2006) used moving PLWs, animations were limited to the PLWs of the faces only and no gait was presented, thus we excluded this study from the analyses. Hashimoto et al.'s (2014) study employed a one-back task to ensure participants directed attention towards point-light stimuli, thus was not considered for further analyses due to the criterion *a.* Pilz (2013) and Hur et al. (2016) were excluded from further analyses on the basis of the criterion *b,* as only participants with schizotypal personality disorder or schizotypal traits were included in the studies. Five dissertations were excluded from further analyses due to the criterion *d.* One study was excluded due to not being published in English. Three studies reporting μ rhythm suppression in response to biological motion in schizophrenia (Minichino et al., 2016; Singh et al., 2011; 2016) were excluded due to the criterion *f* as no PLW-related task was presented.

Data extraction

Prior to analyses the following variables were extracted from each study: (1) study information (first author, year and country of origin), (2) characteristics of the clinical sample (number of participants, age, sex, inpatient/outpatient status, years of education), (3) characteristics of the control sample (number of participants, age, sex, years of education), (4) characteristics of the paradigm (type of study; description of the task, outcome variables, complexity of the PLW displays, length of PLW animations). These data can be found in Table 1. Additional clinical variables (type of the medication, CPZ equivalent, illness duration, symptomatology) were also extracted, if provided by the authors of the study.

In case of papers reporting results from overlapping samples (Brittain et al., 2010; 2012; Hastings et al., 2013) or reports including results of multiple experiments from the same sample (Kim et al., 2011; 2013; Kern et al., 2013; Matsumoto et al., 2015; Spencer et al., 2013) the outcome of the experiment with the most relevant data were included in the analysis. Secondary meta-analyses were based on the signal detection d-prime values for the Basic Biological Motion task (BBM; Kim et al., 2005) and percentages of correct responses in the Emotion in Biological Motion (EBM; Heberlein et al. 2004).

If more than one domain (recognition, detection, extraction) of biological motion perception was assessed in the same sample, the scores of the task which were the most comparable to the paradigms used across studies were selected for each domain and the mean weighted effect was used for the main analysis. For example, Kern et al. (2013) presented data from both the BBM and the EBM. Thus, the overall mean weighted effect observed in the tasks was included in the main analysis and is presented in Figure 2. At the same time the specific effects for d' from BBM and percentages of correct responses from EBM were used for secondary meta-analyses and are presented in Figure 3 and Figure 4, respectively.

Data analysis

From the extracted data we calculated the pooled effect size in the form of standardized mean differences (SMD). All analyses were performed using the Comprehensive Meta-Analysis Software (ver. 3) package (CMA; www.meta-analysis.com). Heterogeneity among study point estimates was assessed with Q statistics with magnitude of heterogeneity being evaluated with the I^2 index.

Publication bias was assessed with Begg's funnel plot and Egger's test. Fail-safe N for unpublished studies was also computed. To assess the robustness of the results, we performed sensitivity analyses by sequentially removing each study and rerunning the analysis.

Meta-regression was used to assess the effects of potential moderators. We included age (years), percent male, education (years in education) and inpatient status as potential moderating variables.

Results

Overall, 15 papers reporting results of 14 different experiments with 571 patients and 482 controls were included. All of the studies reported age (mean = 38,8 years old in both groups) and percent of males (SCZ: 67%; HC: 60%). Furthermore, all but one study reported years of education, with patients completing fewer years of education than controls (years of education: SCZ: 13,1 vs. HC:14,4). Most of the studies reported results from outpatients (n=8), four studies reported results from inpatients and two from mixed groups.

Less than half of the studies in a sample reported either type of the medication taken by the patients (k=6 no of patients=329: 82% treated with second generation antipsychotics; 11% - first generation antipsychotics; 2% combination of SGA and FGA; 5% - no medication) or CPZ equivalents (k=6; no of patients =149; mean: 477+/-343 mg). Illness duration was reported by 8 studies (mean duration 10,2+/-6,2 years). The analysis of the impact of the symptomatology on the biological motion processing was not possible due to the diversity of the measurement methods (PANSS, SAPS/SANS, BPRS) reported in the studies.

Both effect size models, fixed and random, were identical for the studies (T^2=0) therefore for the remainder of this paper, only results of the random effects model will be presented.

The results of the main meta-analysis revealed that schizophrenia (compared with healthy controls) present moderate to large deficits during biological motion processing (Figure 2). The overall mean effect size (SMD) was -0.66 (95% CI, -0.79 to -0.54; $p < 0.001$).

Similar effect sizes were observed for each of the specific tasks, which were considered during secondary meta-analyses.

A statistically significant SMD of -0.72 (95% CI: -0.94 to -0.51) was observed for the five studies which reported d-primes from Basic Biological Motion task, implying that patients are less capable of differentiating biological from non-biological motion. Similar results were observed for Emotion in Biological Motion task: a statistically significant SMD of -0.61, (95% CI: -0.79 to -0.43; $p<0.001$) was calculated on the basis of the six studies which reported correct response rates for patients and controls in EBM task (Figure 4).

Sensitivity analysis

Inspection of the funnel plot which is shown above (Figure 5), as well as the corresponding Egger's test (Intercept = -1.1 95% CI: -2.47 to 0.32; p=0.12) revealed no evidence for publication bias. If publication bias exists, the Begg's funnel plot is asymmetric and the Egger's test P value is <0.05. In this way, we assessed whether there was a tendency for selective publication of studies based on the nature and direction of their results. Furthermore, to ensure that the observed results are not due to the 'file-drawer' bias, we calculated the fail-safe N for missing studies that would bring the p-value to a non-significant threshold (p>0.05). Overall, 359 unpublished studies would have to be added to nullify the observed effects.

Finally, to ensure robustness of the results, we investigated if exclusion of any single study would affect the results of the meta-analysis. All of the effects computed after removal of a single study

were still statistically significant ($p<0.001$) and varied from SMD of -0.65; 95% CI: -0.78 to-0.52 (after removal of Matsumoto et al., 2015) to SMD of -0.71 95% CI: -0.84 to -0.58] (after removal of Henry et al., 2012).

Moderator analysis

Meta-regression found no effect for age (years), percent male, education (years in education) or inpatient status on biological motion processing in patients.

Discussion

This is the first meta-analysis that examined the abilities associated with biological motion processing in patients with schizophrenia in a domain specific way. Our results revealed that patients showed moderate to large deficits compared to healthy controls for all the tasks associated with biological motion processing (SMD=0.66 for overall analysis of biological motion processing, Basic Biological Motion task d=0.72; Emotion in Biological Motion task: d=0.61). We also ascertained that the observed results are not due to publication bias or the impact of any single study. Furthermore, these effects were not explained by potential moderating variables (age, percent male, education and inpatient status). Interestingly, between-group differences are of lower magnitude than those observed in studies which used full displays (static photos or dynamic videos of actors)of agents to study social perception (Hedges g=1.04; Savla et al., 2013) or emotion perception (g=0.89, Savla et al.; d=0.89, Kohler et al., 2010). Use of the biological motion displays reduces a number of potential confounding factors associated with cultural factors, ethnicity, or sympathy towards the agent, which may be influencing tests based on static pictures (e.g. PENN-ER40; Gur et al., 2002) or videoed scenes (e.g. TASIT; McDonald et al., 2003) of facial or full body displays. Thus, it may be suspected that reduction of the complexity of the stimuli may be beneficial in terms of patients' performance in social cognitive tasks.

Relationship with clinical and functional variables

The evidence for the relationship between biological motion processing and clinical symptoms of schizophrenia is limited, with studies showing either low correlation (Olbert et al., 2013) or lack thereof (Bigelow et al., 2006; Brittain et al., 2010; Kim et al., 2005; 2011 E1; 2011 E3; Okruszek et al., 2015; Vaskinn et al., 2016). There is, however, evidence for the relationship between biological motion processing capacity and patients' real-life social functioning (Kim et al., 2005). Both BBM and EBM performance correlates with functional capacity measured with real world role-play simulation tasks, but not questionnaire assessment methods (Olbert et al., 2013). The relationship between biological motion processing and functional outcome may be, however, mediated by the level of social cognitive abilities in patients (Brittain et al., 2010).

Relationship with perceptual and social cognitive abilities

While initial report suggested dissociation between impaired biological motion processing and within-the-norm global-form task performance in patients (Kim et al. 2005), later studies established an association between biological motion processing and lower-level visual abilities (namely visual masking (Brittain et al., 2010), non-biological motion processing (Brittain et al., 2010; Kim et al., 2013; Spencer et al., 2013)). Furthermore, performance in both BBM and EBM tasks correlates with general cognition measured by the MATRICS battery (Olbert et al., 2013).

Furthermore, biological motion processing may be associated with a wide range of social cognitive abilities in schizophrenia. Both biological motion detection (Brittain et al., 2010) and recognition of specific emotions conveyed by PLWs (Brittain et al., 2013) are associated with a performance in a Half-PONSS, which a standard task for measurement of social perception (Ambady et al., 1995). Also facial emotion identification ability was linked to patients' performance in BBM and EBM (Olbert et al., 2013), as well as to recognition of specific actions of two agents presented with point-light motion (Okruszek et al., 2015). Finally, complex social cognitive abilities, including mentalizing (Kim et al., 2013) and empathic accuracy (Olbert et al., 2013) may also be connected to biological motion

processing in patients. A relationship between self-reported affective, but not cognitive, empathy and biological motion detection was also observed (Matsumoto et al., 2015).

Neurobiology of biological motion perception in schizophrenia

The event-related fMRI study which used BBM found a decreased BOLD-response modulation to biological vs. scrambled motion in patients compared to controls in the posterior superior temporal sulcus (Kim et al., 2011) and frontal regions (right ventral premotor cortex and left inferior frontal gyrus; Kim et al., 2014). Furthermore, an ERP study which used BBM observed reduced Late Positive Potential modulation for biological vs. scrambled motion in patients (Jahshan et al., 2015). Interestingly, Hashimoto et al. (2014) used a block design to present biological motion and scrambled motion during a fMRI session and observed no differences in pSTS activity between patients and controls. At the same time, reduced modulation of activity in the left medial prefrontal cortex, left supramarginal gyrus, precuneus, cuneus and middle cingulate was found in patients (Hashimoto et al., 2014). Moreover, reduced μ rhythm suppression (Singh et al., 2011) and abnormalities in eye-movement patterns (Matsumoto et al., 2015) were also reported among neurophysiological findings on biological motion processing in schizophrenia.

Conclusion

In conclusion, we found that patients with schizophrenia show moderate to large deficits in biological motion processing, which are not moderated by demographic variables and show little correlation to symptoms in patients with schizophrenia. However, biological motion processing was found to be associated with both lower-level visual deficits, and with a wide range of higher order social cognitive functions in patients with schizophrenia. While biological motion displays are usually perceived as a tool to study low-level perceptual deficits, it can be also used to study higher-level processes associated with emotion recognition (Vaskinn et al., 2016) or intention attribution (Okruszek et al., 2015). Here we found a similar magnitude of deficits, regardless of the type of social information extracted from biological motion. The mechanisms associated with biological motion perception are,

ontogenetically and phylogenetically, one of the most archaic forms of social cognition (Troje, 2013). Thus, while speculatively, it may be suggested that aberrant visual processing of biological motion cues may be one of the mechanisms that underlie abnormal social cognitive development trajectories in patients with schizophrenia. While no studies examined the biological motion processing in relatives of patients with schizophrenia, abnormalities associated in biological motion processing have been documented in patients with schizophrenia spectrum disorders (Hur et al., 2016), thus the role of the biological motion processing as a potential endophenotype of schizophrenia should be further examined. Furthermore, while the neural mechanisms associated with biological motion processing are still unclear, there is a strong rationale to believe that the pSTS dysfunction may be critical for the abnormal processing of social information in schizophrenia (Kim et al., 2011). Thus, the potential role of this cortical region as a target of noninvasive brain stimulation interventions to improve social cognition in patients should be further explored.

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Legend of tables and figures

Table:

Table 1. Description of the studies included in the meta-analysis.

Figures:

Figure 1. PRISMA Flow Diagram

Figure 2. Meta-Analysis of General Biological Motion Processing in schizophrenia vs healthy controls.

Figure 3. Meta-Analysis of Basic Biological Motion Processing in schizophrenia vs. healthy controls.

Figure 4. Meta-Analysis of Emotions in Biological Motion Processing in schizophrenia vs. healthy controls.

Figure 5. Funnel plot of standard error by Fisher's Z from meta-analyses of biological motion processing in schizophrenia patients vs. healthy controls.