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► To cite this version:

Andrew Laurin, Nicolas Ramoz, Aurély Ameller, Antoine Dereux, Julie Zajac, et al.. Self-consciousness impairments in schizophrenia with and without first rank symptoms using the moving rubber hand illusion. *Consciousness and Cognition*, 2021, 93 (6), pp.103154. 10.1016/j.concog.2021.103154. hal-04547873

HAL Id: hal-04547873

<https://hal.science/hal-04547873v1>

Submitted on 22 Jul 2024

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Self-consciousness impairments in schizophrenia with and without first rank symptoms using the moving rubber hand illusion

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1. Introduction

Schizophrenia is a mental disease with a lifetime prevalence between 0.5 to 1% (McGrath et al., 2008) and involves three different nosographic dimensions (disorganization, positive and negative symptoms) (American Psychiatric Association, 2013). In the middle of the 20th century, Kurt Schneider described a set of positive symptoms named first rank symptoms (FRS) (Schneider, 1959). These symptoms include: auditory hallucinations with the perception of several voices speaking between them or making comments about patient's actions or thoughts (conversing or commenting hallucinations), the feeling of patient's thoughts have been broadcast, withdrawn or inserted by an external force, and the delusion of actions or thoughts are controlled by an external agent. FRS seem to be very specific to schizophrenia (Soares-Weiser et al., 2015) and affect between 25% to 88% of people with schizophrenia (Nordgaard et al., 2008), but may also be present in mood disorders with psychotic symptoms such as manic states or severe depression with psychotic symptoms (Lake, 2012; Soares-Weiser et al., 2015). Self-consciousness disturbances are particularly important when schizophrenia is associated with FRS (Heinz et al., 2016 ; Nordgaard et al., 2020; Waters & Badcock, 2010). Indeed, patients with schizophrenia have difficulties to distinguish the self and the external world (Jeannerod, 2009; Ferroni et al., 2019) supported by sense of body ownership and agency impairments.

On one side, body ownership refers to the perceptual status of one's own body, making bodily sensations seem unique to oneself in order to allow self-other distinction (Tsakiris et al., 2007). Body ownership is based on a multisensorial integration to

26 constitute internal body representations (Braun et al., 2018; Tsakiris, Costantini, &
27 Haggard, 2008). Sense of body ownership would be based on the multisensory
28 integration of external and internal sensory information in order to constitute
29 immediate body representations that would be malleable and based on Bayesian
30 perceptual learning (online-representation, bottom-up mechanisms); once integrated,
31 immediate body representations would be compared to pre-existing mental body
32 representations that are stable and not very malleable in order to avoid the introduction
33 of non-bodily or non-humanoid shapes, or objects in an aberrant anatomical position,
34 into body representations (long-term-body-representation, top-down semantic
35 mechanisms) (Ehrsson, 2020; Litwin, 2020; Tsakiris, 2010). Sense of body ownership
36 therefore contributes to a sense of self, a developmental basis for a psychological
37 identity (Gallagher, 2000). Body ownership disturbances in schizophrenia may reflect
38 impairments in multisensorial integration (Costantini et al., 2020; Farrer & Franck,
39 2009; Peled et al., 2000; Peled et al., 2003; Prikken et al., 2018; Thakkar et al., 2011) also
40 called “perceptual incoherence” (Postmes et al., 2014).

41

42 On the other side, the sense of agency refers to the subjective experience of being
43 the initiator of one’s own voluntary actions (body agency) associated with the ability to
44 predict the consequences of these actions (external agency) (Hirjak et al., 2013; Pyasik
45 et al., 2019). Considering that thoughts are related to commands and motor
46 representations (Leisman et al., 2016), FRS probably reflect sense of agency
47 impairments in schizophrenia (Blakemore et al. , 2000; Koreki et al., 2019) e.g.
48 commentary or discussion hallucinations arise from the patient’s own system of
49 thought, but the patient no longer recognizes himself as the author of his thoughts and
50 attributes them to an external force, hence their xenopathic nature. Indeed, FRS may

51 derive from abnormalities related to an anticipatory model of consequences of one's
52 own action (Frith, 2012; Frith, Blakemore, & Wolpert, 2000) with an impaired ability to
53 attribute an action to its origin (Georgieff & Jeannerod, 1998). In healthy subjects,
54 efference copy mechanisms generated by voluntary motor commands are used to
55 predict sensory consequences of this action in order to decrease self-induced
56 perceptions to better focus on externally sensorial perceptions (Blakemore et al., 2000).
57 Patients with schizophrenia with FRS would have dysfunctional efference copy
58 mechanism associated with an impaired predictive processes (Graham-Schmidt et al.,
59 2016). The mismatch between motor predictions and sensory inputs in schizophrenia
60 (Ford & Mathalon, 2019; Pynn & DeSouza, 2013) would be at the origin of their
61 difficulties to distinguish self and external perceptions, therefore perceiving their
62 actions as having an external origin (Graham-Schmidt et al., 2018; Synofzik et al., 2010;
63 Voss et al., 2010).

64

65 Body ownership and agency constitute two dissociable aspects of the self-
66 consciousness (Gallagher, 2000; Kalckert & Ehrsson, 2012; Kalckert & Ehrsson, 2014;
67 Tsakiris, Schütz-Bosbach, & Gallagher, 2007) but they are also probably interacting
68 (additive model) (Caspar et al., 2015; Kalckert & Ehrsson, 2012; Kalckert & Ehrsson,
69 2014; Pia et al., 2016; Pyasik et al., 2018). Indeed, the sense of agency is supposed to
70 contribute to the sense of body ownership, with an integration of afferent signal from
71 the bodily movements, and the sense of body ownership seems to modulate the sense of
72 agency (Braun et al., 2018; Burin et al., 2015; Kalckert & Ehrsson, 2012; Tsakiris,
73 Prabhu, & Haggard, 2006) e.g. implicit measures of the sense of agency tend to appear
74 if the sense of body ownership is present (Pyasik et al., 2019). Nevertheless, their
75 reciprocity is still poorly understood (Burin et al., 2015). One of the most common way

76 to evaluate the body ownership is the rubber hand illusion (RHI) (Botvinick & Cohen,
77 1998) in which a synchronous visuo-tactile stimulation in anatomic congruence induce a
78 subjective embodiment of the fake model hand, associated with the feeling that the fake
79 model hand is our own hand (sense of body ownership). ~~However, the RHI does not~~
80 ~~allow the evaluation of the sense of agency.~~ However, in its original version, the RHI did
81 not evaluate the sense of agency. In 2012, Kalckert and Ehrsson (Kalckert & Ehrsson,
82 2012) have proposed the moving rubber hand illusion in which the induction of the
83 illusion is provided by voluntary movements (visuo-motor stimulations), that involve
84 intentions and motor predictions from efference copy mechanisms, allowing the
85 evaluation of both the sense of body ownership and agency. In anatomic congruence
86 among healthy subjects, this experimental paradigm showed that (i) synchronous
87 movements between the real hand and the model fake hand induced a sense of agency
88 and body ownership, with an embodiment of the fake model hand. In contrast, it showed
89 that (ii) asynchronous movements ~~broke up~~ abolished the sense of body ownership,
90 with a non-embodiment of the fake model hand, but did not disrupt the sense of agency
91 allowing a specific evaluation of the sense of agency, and that (iii) passive synchronous
92 movements ~~eliminated~~ abolished the sense of agency, but the sense of ownership tended
93 to persist allowing a specific evaluation of the sense of body ownership. Thus, the
94 authors conclude that the sense of agency is modulated by the sense of ownership
95 (Kalckert & Ehrsson, 2012; 2014). These results highlighted the dissociation and the
96 cooperation between the sense of body ownership and agency that are two components
97 of the self-consciousness in healthy subjects (Longo et al., 2008; Seghezzi et al., 2019). It
98 is important to note that experiences evaluating self-consciousness alterations can be
99 influenced by several factors such as sex (Longo et al., 2008) and the participant's
100 psychological state (Riemer et al., 2019). In the case of schizophrenia it is important to

101 consider not only positive symptoms (Prikken et al., 2018; Prikken et al., 2017) and
102 their duration (Nelson et al., 2012), but also the potential impact of antipsychotic
103 treatments (Peled et al., 2000; Peled et al., 2003) and negative symptoms such as
104 anhedonia (Ferri et al., 2014).

105

106 Considering self-consciousness disturbances in people with schizophrenia with
107 FRS, the present study aims to investigate their performances from the moving rubber
108 hand illusion compared to people with schizophrenia without FRS. Indeed, we
109 hypothesized that patients with FRS will have a smaller sense of agency compared to
110 patients without FRS when we include a temporal bias during a voluntary movement
111 (active synchronous versus active asynchronous condition). Moreover, to take account
112 potential cooperation between the sense of agency, isolated in asynchronous active
113 condition, and the sense of body ownership, isolated in synchronous passive condition,
114 the purpose of this study is also to investigate to analyze in an exploratory way their
115 associations under these two conditions to highlight specific cooperation in
116 schizophrenia with FRS compared to schizophrenia without FRS. We wanted to explore
117 the dissociation between the sense of agency and the sense of body ownership in
118 asynchronous active and synchronous passive conditions in patients with schizophrenia
119 in order to evaluate how is affected the sense of the agency when the sense of ownership
120 is perturbed by a temporal bias (asynchronous active condition) and how is affected the
121 sense of ownership when the sense of the agency is perturbed by a passive movement
122 (synchronous passive condition).

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125 **2. Materials and methods**

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2.1 Participants and clinical assessments

We included inpatients and outpatients from 18 to 65 year of age, all right-handed, with a diagnostic of schizophrenia confirmed by the Diagnostic Interview for Genetic Studies (DIGS) (Nurnberger et al., 1994), a semi-structured interview leading to socio-demographic characteristics as well as lifetime diagnoses (according to the classification criteria of the DSM-IV) for schizophrenia and other psychiatric disorders available in French. Psychotic symptomatology was assessed by the SAPS (Scale for the Assessment of Positive Symptoms) (Andreasen, 1984) and SANS (Scale for the Assessment of Negative Symptoms) (Andreasen, 1982). Seven items of the SAPS involve FRS (item 2: voices commenting, item 3: voices conversing, item 15: delusions of being controlled, item 16: delusions of mind reading, item 17: thought broadcasting, item 18: thought insertion, item 19: thought withdrawal). The FRS sub-score was obtained by summing the seven SAPS items that refer to the FRS described above (items 2, 3, 15 to 19). To be included in the group with FRS, participants should have at least two positive items involving FRS with a minimum score ≥ 2 for each item (Waters & Badcock, 2010). Participants with substance abuse disorder (except tobacco and caffeine) and left-handed were excluded. We included a total of fifty-six right-handed patients with schizophrenia: thirty-one with FRS (FRS+) and twenty-five without FRS (FRS-). All participants gave their written consent after given information about the process of the study. This study protocol was approved by a favorable opinion from the local Ethics Committee for the Protection of Persons.

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153 2.2. Experimental procedure

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156 << Insert Figure 1 about here >>

157

158 Participants performed the moving RHI according the descriptions of Kalckert
159 and Ehrsson ([Kalckert & Ehrsson, 2012; 2014](#)). Participants were seated comfortably in
160 front of a table with a wooden box (dimensions 35 x 25 x 15 cm) at 50 cm distance.
161 Participants placed their right hand inside the box with the palmar side in contact with
162 the base of the box (Figure 1). In this position, only the fake model hand above the box
163 was visible by participants. The real and the fake model hand were placed in a white
164 latex glove, and were connected by light stick set at the level of the index's distal
165 interphalangeal articulation. A black sheet was stretched between the participant's right
166 shoulder and the box to give an illusion of continuity between the participant and the
167 box. The experiment consisted of three conditions, with three trials per condition, and
168 all conditions were realized in anatomic congruence. The right model fake hand was
169 aligned with the right real hand of the participant, without rotation of the fake model
170 hand.

171

172 Presenting counterbalanced, the following three conditions were performed
173 (Figure 1): (i) active synchronous condition : index of the real and the fake model hand
174 were connected and moved (extension) in temporal synchrony at approximatively 1 Hz,
175 (ii) active asynchronous condition : index of the real and fake model hand were

176 disconnected and the experimenter moved the fake hand's index with a delay of
177 approximately 500 msec (movements of the false index and the participant index were
178 in opposition), (iii) passive synchronous condition : the experimenter moved the fake
179 hand's index at approximately 1 Hz while the real hand was relaxed in the box. The
180 experimenter was placed in front of the participants with a black sheet stretched
181 between his shoulder and the box in order to hide the manipulations. The experimenter
182 was present in all three conditions throughout the experiment. We have chosen these
183 three conditions in anatomical congruence to compare the impact of a temporal bias on
184 the sense of agency (active synchronous condition versus active asynchronous
185 condition) in patients suffering from schizophrenia with and without FRS. Moreover,
186 based on results in healthy subjects to compare the sense of agency alone with the sense
187 of body ownership alone (the dissociation between the sense of agency and the sense of
188 body ownership) (Kalckert & Ehrsson, 2012; 2014), we realized the synchronous
189 passive condition to exclude voluntary movements (asynchronous active condition
190 versus synchronous passive condition).

191

192 Each condition was composed of three trials of 60 seconds. After each condition
193 (active synchronous, active asynchronous, passive synchronous), participants had to fill
194 out the 16-statements questionnaire constructed by Kalckert and Erhsson (Kalckert &
195 Ehrsson, 2012; Longo et al., 2008) (Table 1). The statements were randomly ordered to
196 explore the subjective experience of the sense of agency and body ownership with a 7
197 point-Lickert scale ranging from “-3” (totally disagree) to “+3” (totally agree). The
198 questionnaire is composed of 4 statements to evaluate the sense of agency and 4
199 statements to evaluate the sense of ownership. After each three condition, we calculated
200 the mean scores obtained for each item (agency, control agency, body ownership,

201 control body ownership) before defining the median value obtained per group (FRS-
202 and FRS+). A median value $\geq +1$ confirm that participants had a subjective experience
203 of ownership or agency. The questionnaire also included 8 control statements (4
204 statements for agency control and 4 statements for ownership control) to check task
205 compliance and suggestibility. The ownership and agency statements scores were
206 compared to their respective control statements. A subjective experience of body
207 ownership or agency, evaluated by the scores obtained in the questionnaire, had to be
208 confirmed with a statistical difference with their scores in respective control ratings
209 (body ownership control and agency control). This difference helps to ensure that
210 patients have clearly distinguished and understood the experiences of agency and body
211 ownership without being influenced by the experimenter's suggestions, the presence of
212 patient opposition or a misunderstanding of sentences referring to the sense of agency
213 or body ownership.

214

215 << Insert Table 1 about here >>

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217

218 **2.3 Statistical analysis**

219

220

221 Categorical variables were summarized as frequencies and percentages and
222 continuous variables as means and standard deviations for clinical assessments and
223 demographic data. The RHI measures were summarized as means, standard errors,
224 standard deviations, first (Q1) and third (Q3) quartiles, medians with their 95%
225 confidence intervals (95% CI).

226 For between-group comparisons of clinical and demographic variables,
227 categorical data were analyzed using the chi-square (χ^2) test and the Mann-Whitney's
228 test were used to analyze quantitative data. We used the Wilcoxon signed-rank test for
229 intra-group analyses to compare agency and body ownership measures with their
230 respective control ratings in each three conditions. We used the one-way Kruskal-Wallis
231 ANOVA for intergroup comparisons of control sentences (agency control and ownership
232 control in each three conditions) after verifying the lack of normality in the distribution
233 of RHI measures by the Shapiro-Wilk test.

234 Spearman's rank correlations were calculated to analyze correlations between
235 agency and body ownership measures in active synchronous, active asynchronous and
236 passive conditions. The association between body ownership measures and agency
237 measures in passive synchronous and active asynchronous conditions were analyzed
238 through a multivariate linear regression to consider confusion factors (clinical and
239 demographic variables). Odds ratio (OR) with their 95% confidence intervals were
240 calculated for each characteristic included in the model. Results were considered
241 statistically significant at $p \leq 0.05$. Statistical analyses were performed with R version
242 4.0.1 (R Foundation for Statistical Computing, Vienna, Austria).

243 We conducted a priori power analysis using G*Power (Faul et al., 2007) [version
244 3.1] for these explanatory analyses. Considering the Mann-Witney test, for a large effect
245 (effect size: 0.8), 21 participants or more would be required in each group for a
246 significance level of 0.05 and 80% power.

247

248 **3. Results**

249

250

251 << Insert Table 2 about here >>

252

253 Socio-demographic and clinical data are shown in Table 2. Patients with FRS+
254 were significantly more frequently men compared to patients without FRS ($p = 0.021$).
255 Patients with or without FRS did not differ on age at inclusion, years of studies, age at
256 onset, illness' duration and treatment dose in chlorpromazine equivalent. As expected,
257 positive symptoms assessed with SAPS (including the seven items referring to FRS) and
258 FRS subscores were significantly higher in FRS+ compared to FRS- ($p < 0.0001$), and
259 negative symptoms assessed with SANS were significantly lower in FRS- compared to
260 FRS+ ($p = 0.007$).

261

262 << Insert Figure 2 about here >>

263

264 Subjective evaluations of ownership and agency from the RHI questionnaire, with
265 their control statements, are available in the supplementary material Table 1 with a
266 graphical representation (median values with their 95% CI) in the Figure 2. In the FRS+
267 group, after synchronous active movements, the ownership and agency statements were
268 rated significantly higher than ownership and agency control statements using Wilcoxon
269 signed-rank tests ($Z = -4.139$, $p < 0.0001$ and $Z = -4.540$, $p < 0.0001$, respectively). In
270 the FRS- group, after synchronous active movements, we also found the same significant
271 differences between ownership and ownership control statements ($Z = -3.776$, $p <$
272 0.0001) and between agency and agency control statements ($Z = -4.289$, $p < 0.0001$).
273 Using Spearman's rank correlations, we did not find an association between the sense of
274 ownership and the sense of agency in synchronous active condition in the FRS+ group (r
275 $= 0.336$, $p = 0.064$) nor in the FRS- group ($r = 0.197$, $p = 0.197$).

301 and agency measures in the active asynchronous condition in the FRS+ group (OR =
302 1.825, 95% CI = 1.402; 2.376, $p < 0.001$), but also in the FRS- group without statistical
303 difference between the two groups (OR = 0.806, 95% CI = 0.538; 1.208, $p = 0.288$)
304 (Table 3). We also found an association between body ownership measures in active
305 asynchronous condition and the treatments (OR = 1.001, 95% CI = 1; 1.002, $p = 0.017$).
306 In the passive condition, the analyses found a strong association between body
307 ownership and agency measures in the FRS+ group (OR = 2.04, 95% CI = 1.394; 2.986,
308 $p < 0.001$) but not in the FRS- group with a statistically significant difference between
309 the two groups (OR = 0.398, 95% CI = 0.219; 0.721, $p = 0.003$) (Table 4). The main
310 differences between the two groups were the SANS score, the SAPS score and the
311 male/female distribution. However, when added as covariates in a multivariate linear
312 regression, SANS / SAPS measures and the sex variable did not statistically correlate to
313 body ownership and agency measures.

314

315 << Insert Table 3 and 4 about here >>

316

317

318 **4. Discussion**

319

320

321 To our knowledge, this is the first study using the robust paradigm of the moving
322 RHI to compare and analyze the sense of ownership and agency in patients with
323 schizophrenia with FRS compared to patients with schizophrenia without FRS. Our
324 results are consistent with our hypothesis. Patients diagnosed with schizophrenia with
325 FRS are characterized by a deficit of agency in active asynchronous condition involving

326 efference copy. Moreover, our study showed that patients with schizophrenia associated
327 with FRS are also characterized by a strong association between ownership and agency
328 in active asynchronous and passive synchronous condition. With the pathological model
329 of schizophrenia with FRS, our findings highlight the potential bidirectional cooperation
330 between ownership and agency. In patients diagnosed with schizophrenia with FRS, the
331 lack of agency seems to induce a greater lack of ownership, and vice-versa. We thus
332 observed a non-dissociation between the sense of agency and ownership in patients
333 with schizophrenia with FRS compared to those without FRS. In practice, and based on
334 our results, we have hypothesized that the processing of sensory and motor information
335 that is sufficiently salient and clear is properly analyzed by patients with schizophrenia
336 to determine the origin of action (synchronous active condition). However, in the case of
337 less salient and more subtle information (asynchronous active condition with temporal
338 bias), patients suffering from schizophrenia with FRS seem to be less able to process this
339 information correctly to determine the origin of the action. This defect in the sense of
340 agency would then affect their sense of body ownership. According to our results, it is
341 this double deficit, which is bidirectional, that seems to characterize first rank
342 symptoms in schizophrenia.

343

344 As expected, both two groups had a sense of agency in active synchronous
345 condition. In a context of temporal congruence between the perception and the
346 movement, the high priority given to visual clues in schizophrenia ([Synofzik et al., 2010](#))
347 was sufficiently salient to induce a subjective sense of agency. In active asynchronous
348 condition, isolating the sense of agency, FRS+ had no sense of agency compared to FRS-
349 who tended to have a sense of agency. These results were expected considering previous
350 studies pointing the efference copy defects from voluntary movements as being the

351 origin of FRS (Franck et al., 2001, Pynn & DeSouza, 2013, Waters & Badcock, 2010). In
352 addition, we also see that the sense of agency in patients with schizophrenia with FRS
353 are more sensitive to temporal factors between the action and its external consequences
354 (temporal proximity) than those without FRS to determine the origin of the action
355 (Sandsten et al., 2020). Interestingly, in our study, the delay of 500 ms in the
356 asynchronous condition is sufficiently important to break up the sense of ownership in
357 the two groups, similarly to healthy people (Kalckert & Ehrsson, 2012 ; 2014), even
358 though some studies showed that participants with schizophrenia may have a longer
359 window of temporal binding (Graham et al., 2014, Klaver & Dijkerman, 2016). Moreover,
360 in experimental paradigms inserting temporal bias, people with schizophrenia tend to
361 attribute to themselves the perceived movements in a phenomenon named “over-
362 inclusive agency” (Franck et al., 2001; Louzolo, Kalckert, & Petrovic, 2015). This
363 phenomenon of over-inclusive agency in schizophrenia is still unclear but incompatible
364 with the Frith’s model, expecting a decrease of sense of agency, and seems to be the
365 consequence of a hypersalient processing of external sensory perceptions (Heinz &
366 Schlagenhauf, 2010; Synofzik et al. , 2010; Voss et al., 2010). With the moving RHI,
367 Louzolo and colleagues (2015) suspected in healthy subjects that “deficient motor
368 prediction may counteract the hypersalience of delusion process”. Our results are in the
369 same way and tend to confirm their hypothesis applied to schizophrenia. Indeed, the
370 FRS+ group, characterized by a deficient motor prediction, had no sense of agency in
371 active asynchronous condition including an absence of over-inclusive agency.

372

373 In passive synchronous condition, that isolates the sense of body ownership, both
374 groups had no sense of ownership. We assumed that efference copy mechanisms from
375 voluntary movements seem to be essential to generate a sense of ownership in people

376 with schizophrenia ([Burin et al., 2015](#), [Klaver & Dijkerman, 2016](#)). Considering
377 multisensorial integration impairments in schizophrenia ([Sandsten et al., 2020](#)), we
378 support the hypothesis that without efference copies from voluntary movements to
379 stabilized and generated the illusion, patients with schizophrenia could not generate a
380 sense of body ownership in passive condition. Through these results from active
381 asynchronous and passive synchronous conditions, we showed that sensory-motor
382 information is a key element of self-consciousness disorders in schizophrenia with FRS
383 common to the sense of agency and sense of body ownership ([Ardizzi et al., 2020](#)). In
384 addition, and interestingly, the FRS- group has significantly higher scores in the control
385 sentences than the FRS+ group. It therefore seems that the FRS+ group is better able to
386 distinguish self and others by better distinguishing semantic traps from control
387 sentences that focus on the author of actions and embodied objects.

388

389 We also found an association between ownership and agency in active
390 asynchronous condition and in passive synchronous condition in the FRS+ group, with a
391 non-dissociation between agency and body ownership. In the pathological model of
392 schizophrenia with FRS, our results highlight the bidirectional cooperation between
393 ownership and agency. In neuroimaging studies, FRS are associated and correlated to a
394 hyperactivity of some brain regions in the agency network (inferior parietal lobule,
395 frontal cortex, basal ganglia, insula) ([Farrer et al., 2004](#), [Franck et al., 2002](#), [Koreki et al.,](#)
396 [2019](#), [Spence et al., 1997](#)) that are also implicated in the multisensorial integration
397 processes for bodily self-consciousness ([Blanke, 2012](#), [Blanke et al., 2002](#)). Considering
398 dysconnectivity in schizophrenia ([Crow, 1998](#), [Koreki et al., 2019](#)), we hypothesized that
399 this specific cerebral hyperactivity in the agency network may also impact the
400 multisensorial integration in schizophrenia with FRS in an interactive model between

401 the sense of agency and the sense of body ownership (Seghezzi et al., 2019). In contrast,
402 the dissociation between agency and body ownership persisted in the FRS- group and
403 we showed that agency was modulated by the sense of ownership in active
404 asynchronous condition, as in healthy subjects (Kalckert & Ehrsson, 2012). Finally, our
405 analyses have shown that antipsychotic treatments could limit the phenomenon of non-
406 embodiment of the rubber hand in asynchronous active condition, which is an
407 interesting hypothesis for understanding antipsychotic treatments in schizophrenia
408 involving a stabilization of body mental representations. The question of the impact of
409 antipsychotic treatments on multisensory integration has been raised for a long time
410 (Peled et al., 2000; 2003). To date, no studies have been conducted on this subject and
411 should be investigated in more detail in future studies.

412

413 However, the present study has several limitations that should be mentioned.
414 First, laterality was a self-reported variable evaluated using one single question (left,
415 mixed or right-handedness). Participants were asked by the examiner to sit with their
416 hands on their thighs and asked to demonstrate their performance of writing. Second, in
417 absence of consensus in the literature, we used the arbitrary limit score with the
418 presence of two FRS to define the FRS+ group. However, Waters and Badcock (2010)
419 consider that recruitment based on the presence of at least two FRS provides a reliable
420 method of categorization to distinguish patients with FRS. Third, the induction of the
421 illusion in FRS- group in active synchronous condition (reference condition of illusion
422 induction) can be highly criticized, and calls for caution in interpreting the results in this
423 group, especially for body ownership ratings. Fourth, we considered only patients with
424 FRS during the experimental RHI. Some authors consider FRS as a trait phenomena
425 (Prikket et al., 2017) with a stability over time open to debate according to the different

426 conceptions of FRS (Heering et al., 2013). However, patients with and without FRS did
427 not differ in term of age or duration of illness in our study, and to confirm our
428 hypothesis, we chose to consider FRS as a state phenomena. Fifth, our study only
429 considered explicit self-questionnaire measures of the sense of body ownership and the
430 sense of agency. Implicit measures such as proprioceptive drift for the sense of body
431 ownership, and intentional binding or sensory attenuation for the sense of agency, were
432 not included in our work (Pyasik et al., 2018). However, there is now increasing
433 evidence that explicit and implicit measures each involve different and dissociable
434 neurocognitive processes (Gallagher et al., 2021; Pyasik et al., 2018). Future studies on
435 this topic may further our work by including implicit measures in patients with
436 schizophrenia with FRS. Finally, our study did not include a control group of healthy
437 subjects to compare the performance and associations found because we relied mainly
438 on the original results of Kalckert and Ehrsson's work on the subject (Kalckert &
439 Ehrsson, 2012; 2014). Moreover, the main objective of our study was to evaluate self-
440 consciousness impairments that characterize first rank symptoms in schizophrenia. It
441 seemed more interesting to us to take as a control group of patients suffering from
442 schizophrenia without first rank symptoms who had potentially the same
443 neurodevelopmental trajectory as patients suffering from schizophrenia with first rank
444 symptoms (age of the participants, age of onset and duration of the disease well
445 balanced between the two groups), with similar treatments, as many shared factors
446 which could influence the performance of the RHI. Taking a control group of patients
447 would have allowed us to limit the confounding factors compared to a control group of
448 healthy subjects which would not have provided relevant information, or biased
449 information, regarding our main objectives. Further studies might include control
450 subjects to evaluate if patients without FRS showed some self-consciousness deficit

451 compared to controls even if they are less marked than those found in patients with FRS.

452

453

454 **5. Conclusion**

455

456

457 This study, using an original moving RHI paradigm, confirms the existence of
458 specific alterations of the self-consciousness in schizophrenia with FRS characterized by
459 a lack of agency and a non-dissociation between the sense of agency and body
460 ownership compared to schizophrenia without FRS. Our work confirms that a better
461 understanding of self-consciousness alterations in schizophrenia is essential and may
462 open up interesting perspectives for treatments, particularly with regard to
463 neuromodulation techniques that could be used to reduce body-consciousness
464 disturbances by targeting specific brain areas involved in the sense of agency and the
465 sense of ownership.

466

467 **Conflicts of interest**

468 The authors declare that there is no conflict of interest.

469

470 **Acknowledgements**

471 Authors wish to thank “Le Congrès Français de Psychiatrie” (research grant) and “La
472 Fondation pour la Recherche Médicale” for their financial supports.

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484

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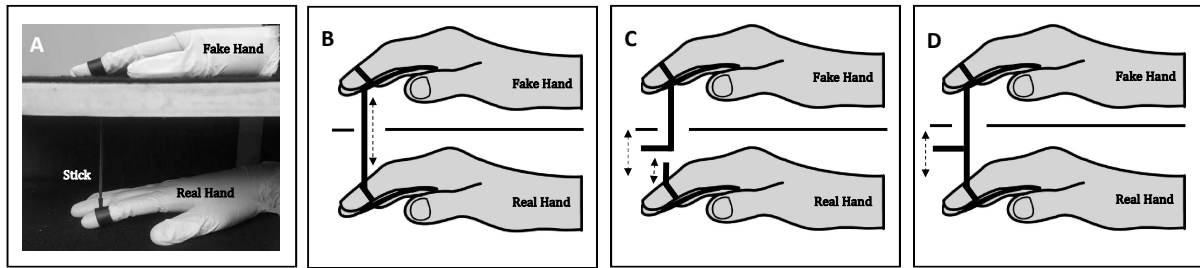


Figure 1: Picture of the moving rubber hand illusion (A) used in our study with illustrations of the three conditions realized : the synchronous active condition (B) where the index finger of the real hand and the fake hand are connected during the realization of the movements of the index finger of the real hand; the asynchronous active condition (C) where the index finger of the real hand and the index finger of the fake hand are disconnected, thus it is the experimenter who ensures the movements of the index finger of the fake hand with a delay of about 500 ms with respect to the movements of the index finger of the real hand; the synchronous passive condition (D) where the index finger of the real hand and the fake hand are connected but it is the experimenter who ensures the movements while the real hand remains passively held following the movements.

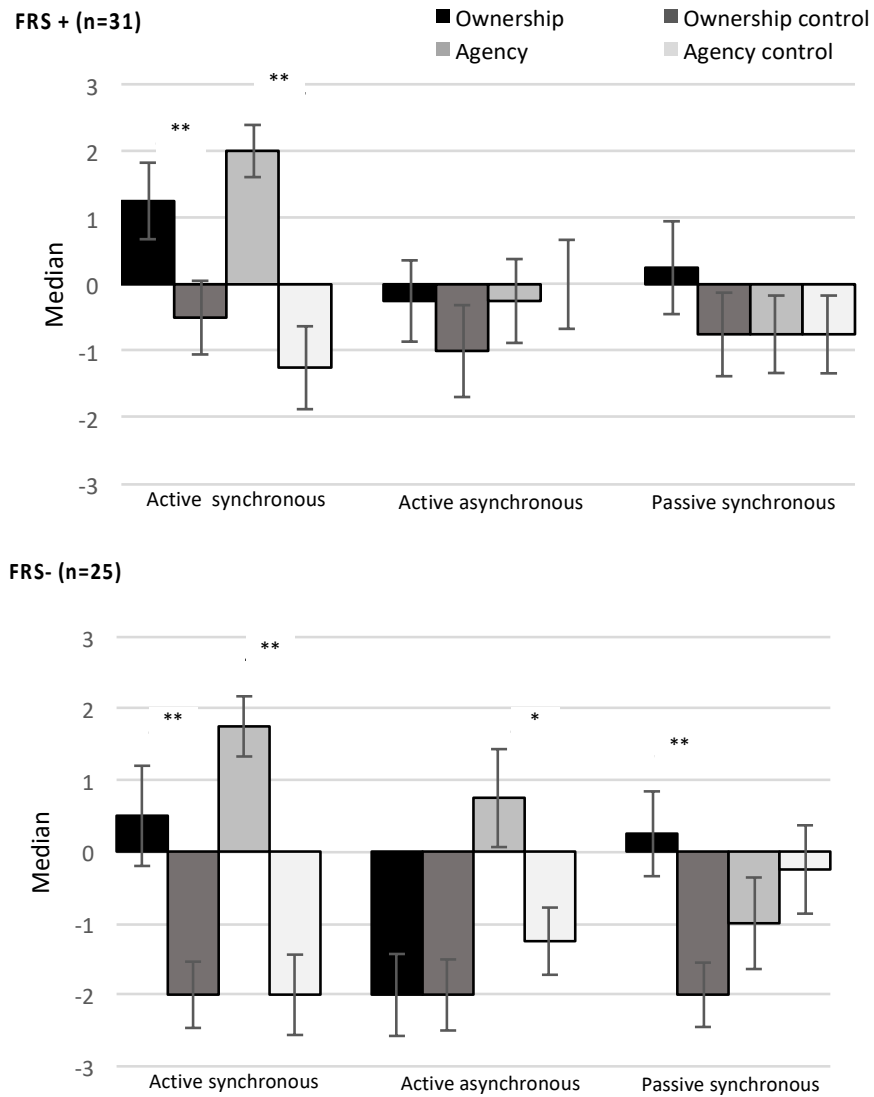


Figure 2: Results of the moving rubber hand illusion questionnaire. Data are median values with their 95% confident intervals in each three conditions. (*) indicates $p = 0.004$ and (**) indicates $p < 0.0001$ using the Wilcoxon signed-rank test. FRS+ = Schizophrenia with First Rank Symptoms. FRS- = Schizophrenia without First Rank Symptoms.

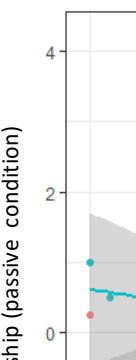
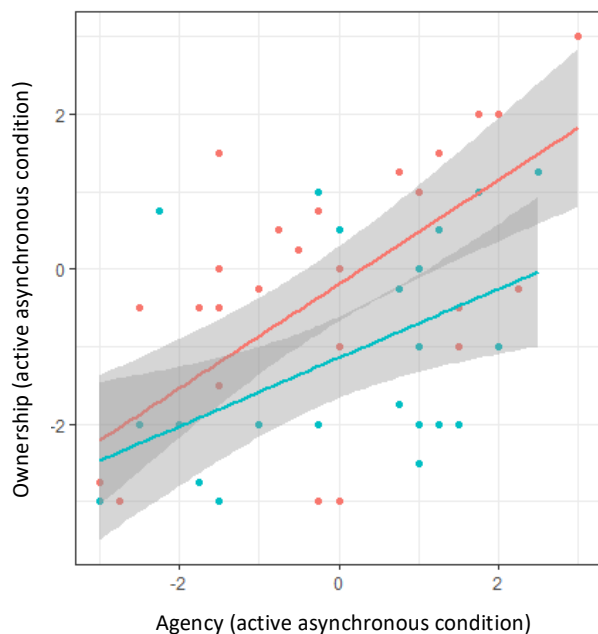


Figure 3: Correlations between ownership and agency ratings in active asynchronous condition (on the left) in the FRS+ group (in red) and in the FRS- group (in blue) (Spearman's rank correlations: $r = 0.646$, $p = 0.01$ and $r = 0.555$, $p = 0.004$ respectively). Correlations between ownership and agency in passive condition (on the right) in the FRS+ group (in red) (Spearman's rank correlation: $r = 0.583$, $p = 0.001$) but not in the FRS- group (in blue) (Spearman's rank correlation: $r = -0.169$, $p = 0.419$).

Category

Ownership	1. I felt as if I was looking at my own hand 2. I felt as if the rubber hand was part of my body 3. It seemed as if I were sensing the movement of my finger in the location where the rubber hand finger moved 4. I felt as if the rubber hand was my hand
Ownership control	5. I felt as if my real hand were turning rubbery 6. It seems as if I had more than one right hand 7. It appeared as if the rubber hand were drifting towards my real hand 8. It felt as if I had no longer a right hand, as if my right hand had disappeared
Agency	9. The rubber hand moved just like I wanted it to, as if it was obeying my will 10. I felt as if I was controlling the movements of the rubber hand 11. I felt as if I was causing the movement I saw
Agency control	12. Whenever I moved my finger I expected the rubber finger to move in the same way 13. I felt as if the rubber hand was controlling my will 14. I felt as if the rubber hand was controlling my movements 15. I could sense the movement from somewhere between my real hand and the rubber hand 16. It seemed as if the rubber hand had a will of its own

Table 1: The RHI questionnaire used in our study (extract from Kalckert & Ehrsson, 2012)

Table 2

	FRS+ (n=31)	FRS- (n=25)	Stat	p-values
Sex (% male)	23 (74.2%)	11 (44.0%)	$\chi^2 = 5.290$	0.021
Age (in years)	37.74 (10.46)	43.36 (12.12)	$z = -1.667$	0.096
Years of studies	8.42 (3.49)	8.84 (3.20)	$z = -0.588$	0.557
Age at onset of illness (in years)	21.94 (7.13)	29.04 (12.79)	$z = -1.652$	0.099
Total duration of illness (in years)	15.48 (7.45)	14.32 (7.79)	$z = -0.562$	0.574
CPZ-equivalent (in milligrams)	477.32 (459.51)	534.88 (523.98)	$z = -0.008$	0.993
SAPS	42.55 (18.22)	9.36 (10.74)	$z = -5.745$	< 0.0001
FRS score	14.94 (6.09)	0.48 (0.82)	$z = -6.501$	< 0.0001
SANS	32.23 (19.75)	19.24 (22.00)	$z = -2.698$	0.007

Data are n (%) or mean (SD); z = z value for Mann-Whitney U test; χ^2 = Chi-square test; FRS = First Rank Symptoms; CPZ = Chlorpromazine; SAPS = Scale for the Assessment of Positive Symptoms; SANS = Scale for the Assessment of Negative Symptoms.

Socio-demographic and clinical characteristics of the study sample

Table 3

Multivariate regression analysis used to identify variables associated with body ownership measures in active asynchronous condition in schizophrenia with first rank symptoms

	OR	95% CI lower	95% CI higher	p-value
Agency measures in active asynchronous condition	1.825	1.402	2.376	<0.001
Age	1.221	0.934	1.596	0.141
Sex	1.323	0.583	3.002	0.494
Age at onset of illness	0.824	0.629	1.079	0.156
Years of studies	0.941	0.841	1.052	0.277
Total duration of illness	0.804	0.610	1.060	0.118
CPZ-equivalent	1.001	1	1.002	0.017
SANS	1.006	0.989	1.024	0.462
SAPS	1	0.974	1.027	0.980
Diagnostic of schizophrenia without FRS	0.806	0.538	1.208	0.288

Abbreviations: FRS = First Rank Symptoms; CPZ = Chlorpromazine; SAPS = Scale for the Assessment of Positive Symptoms;

SANS = Scale for the Assessment of Negative Symptoms.

Table 4

Multivariate regression analysis used to identify variables associated with body ownership measures in passive condition in schizophrenia with first rank symptoms

	OR	95% CI lower	95% CI higher	p-value
Agency measures in passive condition	2.04	1.394	2.986	<0.001
Age	1.149	0.803	1.644	0.439
Sex	0.62	0.209	1.839	0.380
Age at onset of illness	0.881	0.614	1.264	0.484
Years of studies	0.936	0.810	1.081	0.358
Total duration of illness	0.887	0.614	1.281	0.513
CPZ-equivalent	1	0.999	1.001	0.766
SANS	0.992	0.969	1.016	0.518
SAPS	0.998	0.963	1.035	0.913
Diagnostic of schizophrenia without FRS	0.398	0.219	0.721	0.003

Abbreviations: FRS = First Rank Symptoms; CPZ = Chlorpromazine; SAPS = Scale for the Assessment of Positive Symptoms; SANS = Scale for the Assessment of Negative Symptoms.