Journal of the Academy of Consultation-Liaison Psychiatry 2025:66:389–400

Original Research Article

Hallucinations and Related Perceptual Phenomena in Systemic Lupus Erythematosus and Inflammatory Arthritis: A Cross-sectional Mixed-Methods Study

Arjoon Arunasalam, M.Sc., Thomas A. Pollak, M.R.C.Psych., Ph.D., Avni Varshney, M.Sc., James A. Bourgeois, O.D., M.D., David D'Cruz, M.D., Guy Leschziner, M.D., Ph.D., Mervi Pitkanen, M.R.C. Psych., M.D., Alessandra Bortoluzzi, M.D., Ph.D., Lucy Calderwood, B.A., Kaira Naidu, M.Sc., Elaine Dunbar, L.L.B., Laura Andreoli, M.D., Ph.D., Martha Piper, M.Sc., Sydnae Taylor, M.Phil., Melanie Sloan, Ph.D.

Background: *The INSPIRE (Investigating Neuropsychiatric Symptom Prevalence and Impact in Rheumatology Patient Experiences) research project explored neuropsychiatric symptoms associated with Systemic Autoimmune Rheumatic Diseases (SARDs), identifying hallucinatory experiences as lesser known but impactful symptoms. Following consultations with clinicians and patients, areas of focus included the prevalence, sensory modalities, insight, timings, and emotional valence of hallucinations in SARDs. Our previous research shows that hallucinations and related perceptual phenomena often go unreported and unrecognised in clinical settings with SARD patients.* **Objective:** *This study analyses and compares hallucination experiences in patients with systemic lupus erythematosus (SLE) and inflammatory arthritis (IA). We evaluated prevalence, modalities, insight, emotional valence, and timings of hallucinations.* **Methods:** *Quantitative data from cross-sectional surveys ($n = 1022$) and qualitative data from interviews were integrated using mixed methods. Quantitative data are presented descriptively and comparatively (using Pearson's χ^2 tests), and qualitative data were analyzed thematically.* **Results:** *SLE patients reported a greater lifetime prevalence of hallucinations than IA patients, with significant differences in visual (12% vs 6%), olfactory (11% vs 6%), tactile (11% vs 5%), and presence (10% vs 3%) modalities (all $P < 0.005$). Auditory hallucinations were not significantly more frequent in SLE (8%) than IA (5%) ($P = 0.071$). Consistent lack of insight into hallucinations was rare (11% of SLE and 4% of IA patients). SLE patients were significantly more likely to experience hallucinations in contexts unrelated to periods of sleep transition than IA patients ($P = 0.020$). Recognizing hallucinations as SARD symptoms helped patients develop positive coping mechanisms and reduced distress. However, fear of clinician judgment, stigma, and misdiagnoses discouraged reporting.* **Conclusions:** *The higher prevalence in*

Received March 11, 2025; revised April 25, 2025; accepted May 12, 2025.
From the Institute of Psychiatry, Psychology and Neuroscience (A.A., T.A.P, A.V., M.P.), King's College London, and South London and Maudsley NHS Foundation Trust, London, UK; Department of Psychiatry and Behavioral Sciences (J.B.), University of California, Davis Medical Center, Sacramento, CA; The Louise Coote Lupus Unit (D.D.), Guy's and St Thomas' Hospitals NHS Foundation Trust, London, UK; Department of Neurology (G.L.), Guy's and St Thomas' Hospitals NHS Foundation Trust, London, UK; Rheumatology Unit (A.B.), Department of Medical Sciences, University of Ferrara and Azienda Ospedaliero-Universitaria S. Anna, Ferrara, Italy; Patient and Public Partners (L.C., E.D.); Department of Public Health and Primary Care Unit (K.N., M.P., S.T., M.S.), University of Cambridge, Cambridge, UK; Unit of Rheumatology and Clinical Immunology (L.A.), ASST Spedali Civili, Brescia, Italy; Department of Clinical and Experimental Sciences (L.A.), University of Brescia, Brescia, Italy; Danish Centre for Expertise in Rheumatology (CeViG) (L.A.), Danish Hospital for Rheumatic Diseases, Sønderborg, Denmark; Institute for Regional Health (L.A.), Southern Danish University, Odense, Denmark; Faculty of Medicine and Health Sciences (M.S.), University of East Anglia, Norwich, England. Send correspondence and reprint requests to Arjoon Arunasalam, MSc, Institute of Psychiatry, Psychology and Neuroscience, King's College London, and South London and Maudsley NHS Foundation Trust, 16 De Crespigny Park, London SE5 8AB, UK; e-mail: arjoon.arunasalam@kcl.ac.uk

SLE likely reflects its greater direct impact of SLE (compared to IA) on the brain. Hallucinatory experiences in SARDs aligned more closely with neurological diseases than primary psychotic disorders. Understanding the varying modalities and contexts of hallucinations as potential direct effects of SLE could improve attribution, treatment, and coping strategies, while reducing stigma and fostering open communication between patients and clinicians.

(Journal of the Academy of Consultation-Liaison Psychiatry 2025; 66:389–400)

Key words: systemic lupus erythematosus, inflammatory arthritis, rheumatoid arthritis, hallucinations, patient-clinician interactions, mixed methods.

INTRODUCTION

Systemic autoimmune rheumatic diseases (SARDs), including systemic lupus erythematosus (SLE) and inflammatory arthritis (IA), involve immune dysregulation that can cause multi-organ damage and significantly impact quality of life.[1] Neuropsychiatric symptoms (NPS) in SARDs are particularly difficult to diagnose and treat, with inadequate reporting in clinical settings leading to underestimation of their prevalence.[2] NPS range from anxiety to psychosis, yet hallucinations and related perceptual phenomena remain underexplored.[3] Our previous work also highlights the challenge of attributing these symptoms to the direct effect of the disease on the brain.[4] This study investigates and compares their prevalence and phenomenology in SLE and rheumatoid arthritis (RA)/IA patients. As the IA cohort primarily consists of RA patients, we refer to it as RA/IA. Throughout this paper, "hallucinations" encompasses related perceptual phenomena, with distinctions made where necessary.

Hallucinations are perceptions of objects or events in the *absence* of corresponding external stimuli, encompassing all sensory modalities such as visual, auditory, olfactory, tactile, and gustatory.[3,5] Visual hallucinations are typically classified into *formed* hallucinations (e.g., detailed, nonveridical images) and *unformed* hallucinations (e.g., seeing lights flash). Illusions are visual misperceptions of actual existing stimuli (e.g., seeing "a person" when the actual stimulus is an animal).[3] Sensed presence or presence hallucinations, which pertain to a "feeling of someone nearby" without any corresponding external stimulus, are also documented in patients with primary neuropsychiatric disease.[5,6] Hallucinations are also reported in the general population, with one study suggesting that up to 80.1% of people will experience hallucinations in their lifetime.[3] However, exact mechanisms associated with hallucinations continue to intrigue researchers, prompting calls to unify models for a holistic understanding.[7]

Our previous research found a higher lifetime prevalence of hallucinations in SLE (15%) than RA/IA (7%) ($P < 0.01$).[2] This may be due to direct central nervous system (CNS) involvement in SLE, where autoantibodies and inflammatory cytokines disrupt neural function,[8] and/or to hallucinations as a side effect of immunomodulators, such as corticosteroids.[9–11] Insight into experiences of CNS symptoms often develops independently of general disease awareness, complicating SARD management. During active disease phases, neurological impairments may reduce recognition of hallucinations as "unreal,"[12] while limited awareness of NPS among clinicians and patients contributes to underreporting.[4] The emotional impact of hallucinations varies widely, from distressing to moderately pleasant, depending on content and context.[3,5,12,13]

This study aimed to explore and characterize hallucination prevalence, modalities, timing, emotional valence, and insight in SLE and RA/IA patients using mixed methods to assess differences in presentation and experience. By systematically comparing these patient- and clinician-voiced dimensions, we sought to generate novel insights into the phenomenology of hallucinations in SLE and RA/IA, laying groundwork for future hypothesis-driven research.

MATERIALS AND METHODS

The INSPIRE Project

This study is part of the INSPIRE (Investigating Neuropsychiatric Symptom Prevalence and Impact in Rheumatology Patient Experiences) project, a series of mixed-method studies identified by patient groups, researchers, and clinicians (neurologists, rheumatologists,

psychiatrists) as key to understanding the prevalence, impact, and reporting of NPS in SARDs.

Quantitative and qualitative methods were integrated throughout to maximize their complementary strengths.[14] The research is guided by both moderate realist and constructivist approaches, with strong emphasis on participant involvement through member checking and representation of diverse perspectives. Ultimately, INSPIRE seeks to amplify the voices of patients and clinicians, enhance understanding of NPS, and support better, more inclusive clinical care.

Further details on methodology, including descriptions of modalities, recruitment, data analysis, and adherence to STROBE and COREQ (Consolidated criteria for reporting qualitative research) guidelines,[15] are available in Supplementary Data S1 (*Rheumatology online*).[2]

Participants and Design

The survey was initially piloted with patients to assess the suitability and ease of completion. The final pretested surveys were made available between July 2022 and September 2022 (patients) or November 2022 (clinicians) internationally on the online platform Qualtrics, via social media, patient support groups, and professional networks. Participants were invited to be interviewed after completing the survey.

Three experienced medical researchers conducted semi-structured interviews with participants who were purposively selected to represent a diverse range of sociodemographic backgrounds (e.g., ethnicity, gender, age, time since diagnosis) and experiences, by using the survey data and open-ended responses. The duration of these interviews ranged from 28 minutes to over 3 hours.

Inclusion Criteria

Inclusion criteria included being 18 years old and over and reporting a SARD(s) confirmed in clinical correspondence. Any SARD groups with $n > 50$ participants who had experienced hallucinations and related perceptual phenomena in visual, auditory, tactile, olfactory, and presence modalities were included in this sub-study (SLE and RA/IA).

Materials

No single validated measure adequately captured the full range of hallucinations and perceptual phenomena in SARDs. The Psycho-Sensory hAllucinations Scale[16], for example, lacks coverage of "morphing" illusions and tactile hallucinations, both reported in our sample. Psychosis-focused tools also prioritize auditory hallucinations and symptom severity in primary psychiatric disorders, making them less applicable to chronic autoimmune diseases. To address this gap, our research team (patients, clinicians, and researchers) codeveloped bespoke survey questions (see Appendix A). Lay terminology and examples were standardized to minimize interpretative differences, following discussions with patients and the study neuropsychiatrist (TAP) (see Supplementary Material S1).[3]

Analyses

Quantitative data reported were derived solely from patients' self-reports in the bespoke survey. Pearson χ^2 tests were used to investigate the differences in the prevalence of reported aspects of hallucinations. SLE and RA/IA groups were selected for comparison as these subjects with SARDs had a suitable number of participants reporting hallucinations for meaningful statistical comparison ($n > 50$), and due to the prevailing clinician viewpoint that SLE patients would have more NPS than RA/IA patients that are attributable to the direct effects of the SLE on the brain.

The qualitative analysis incorporated data from open-ended survey questions and in-depth semi-structured interviews, following Braun and Clarke's thematic analysis framework.[17,18] This includes: (1) immersion in the data; (2) developing a coding (categorization) scheme and coding; (3) combining participant extracts for each code; and (4) generating themes directly from the data using the codes, and with input on interpretation from the multidisciplinary study team. AA performed the initial coding while TAP, AV, and MS confirmed the codes were representative of the data. To address threats to validity, emergent findings were tested and refined using additional data, qualitative and quantitative results were triangulated, and conflicting views were thoroughly discussed. Adopting a constructionist qualitative paradigm[19] ensured that the resulting themes were co-created by the study team and participants.

RESULTS

Demographics

A total of 1022 participants were surveyed (n = 566 SLE patients and n = 456 RA/IA patients), of which 34

agreed to be interviewed (n = 29 SLE patients and n = 9 RA/IA patients). The survey sample was predominantly female (93.35%) (Table 1). The RA/IA group was predominantly older with 42.6% aged 60 years and above, compared to 24.2% of SLE patients. The SLE group had greater geographical and racial diversity than the RA/IA group with more Black (3.4% vs. 0.4%), Asian (6.4% vs. 1.1%), and mixed-race (3.2% vs. 1.1%) representation.

Following the process of thematic analysis, five main themes were identified:

- Varied presentations of hallucinations.
- Positive coping mechanisms through symptom labelling.
- Spectrum of emotional valence that affects reporting of symptom.
- Hallucinations during sleep transition.
- Clinicians' reliance on a comorbid psychiatric illness to explain hallucinations.

TABLE 1. Demographics of survey respondents in SLE and RA/IA groups

Characteristics	SLE patients (n = 566)		RA/IA patients (n = 456)	
Age (y)	N	%	N	%
18-30	39	6.9%	15	3.3%
30-39	90	15.9%	38	8.3%
40-49	129	22.8%	72	15.8%
50-59	170	30.0%	137	30.0%
60-69	11	17.8%	149	32.7%
70+	36	6.4%	45	9.9%
Prefer not to say	1	0.2%	-	-
Gender				
Female	535	94.5%	419	91.9%
Male	30	5.3%	35	7.7%
Non-binary	-	-	1	0.2%
Other/Undisclosed	1	0.2%	1	0.2%
Country/region				
England	375	66.3%	349	76.5%
Scotland	44	7.8%	39	8.6%
Wales	31	5.5%	28	6.1%
N. Ireland or Republic of Ireland	15	2.7%	5	1.1%
US or Canada	12	2.1%	24	5.3%
Europe	63	11.1%	9	2.0%
Asia	14	2.5%	-	-
Africa	3	0.5%	-	-
South America	2	0.4%	-	-
Australia or New Zealand	4	0.7%	2	0.4%
Other/Undisclosed	3	0.6%	-	-
Ethnicity				
White	486	85.9%	439	96.3%
Asian	36	6.4%	5	1.1%
Black	19	3.4%	2	0.4%
Mixed	18	3.2%	5	1.1%
Other/Undisclosed	5	0.9%	5	1.1%

Theme 1: Varied Presentations of Hallucinations

There was a statistically significant difference in the proportion of respondents that experienced hallucinations between the groups. SLE patients (n = 117/566) were more likely to report hallucinations in one or more modalities than RA/IA patients (n = 56/456), X^2 (1, N = 1022) = 12.644, $P < 0.001$. Post-hoc analysis (Figure 1A) revealed that SLE patients were also more likely than RA/IA patients to experience hallucinations in visual [X^2 (1, N = 1022) = 9.400, P = 0.002], olfactory [X^2 (1, N = 1022) = 7.864, P = 0.005], tactile [X^2 (1, N = 1022) = 9.187, P = 0.002], and presence [X^2 (1, N = 1022) = 17.724, $P < 0.001$] modalities, but no statistical difference was found in the auditory modality [X^2 (1, N = 1022) = 3.260, P = 0.071]. We also broke down visual phenomena for comparison (Figure 1B), namely visual distortions [X^2 (1, N = 1022) = 2.759, P = 0.097] and a phenomenon we term as "morphing" [X^2 (1, N = 1022) = 2.216, P = 0.137]. Although there were no statistical differences between SLE and RA/IA, the prevalence was lower than formed visual hallucinations [X^2 (1, N = 1022) = 8.530, P = 0.003] which was significant.

Participants described hallucinations occurring across various sensory modalities, highlighting the complex and multifaceted nature of these phenomena. These could occur simultaneously (e.g., seeing, hearing, and smelling a hallucinated person) or involve different modalities during different episodes (Figure 2):

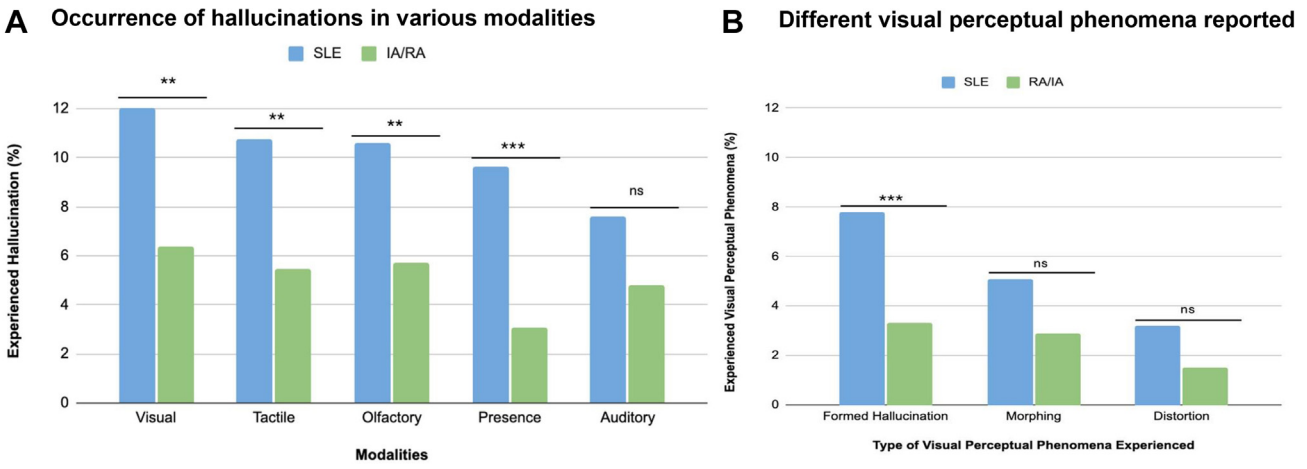
> "*I see high contrast, then see snow/rain/sleet across my vision, I smell smoke, manure or bleach that isn't there, tactile hallucinations of crawling on skin, auditory hallucinations of the same music, noises that aren't there.*" (PT 0034, SLE, Scotland)

Visual hallucinations and related perceptual phenomena varied widely among participants. Some reported *unformed* images such as moving shadows, while others experienced *formed* hallucinations. These often included animals and, more rarely, people:

> *"I tend to see animals at nighttime when I am trying to sleep; things like guinea pigs sat in the lamp shade, rats running along my curtains"* (PT 0920, SLE, England)

Several participants described seeing objects transform or "morph" into entirely different entities,

FIGURE 1. Comparison of Percentage (%) of SLE and RA/IA Patients Who Reported Experiencing Hallucinations in Visual, Auditory, Olfactory, Tactile, and Presence Modalities, With Detailed Breakdown of Visual Phenomena



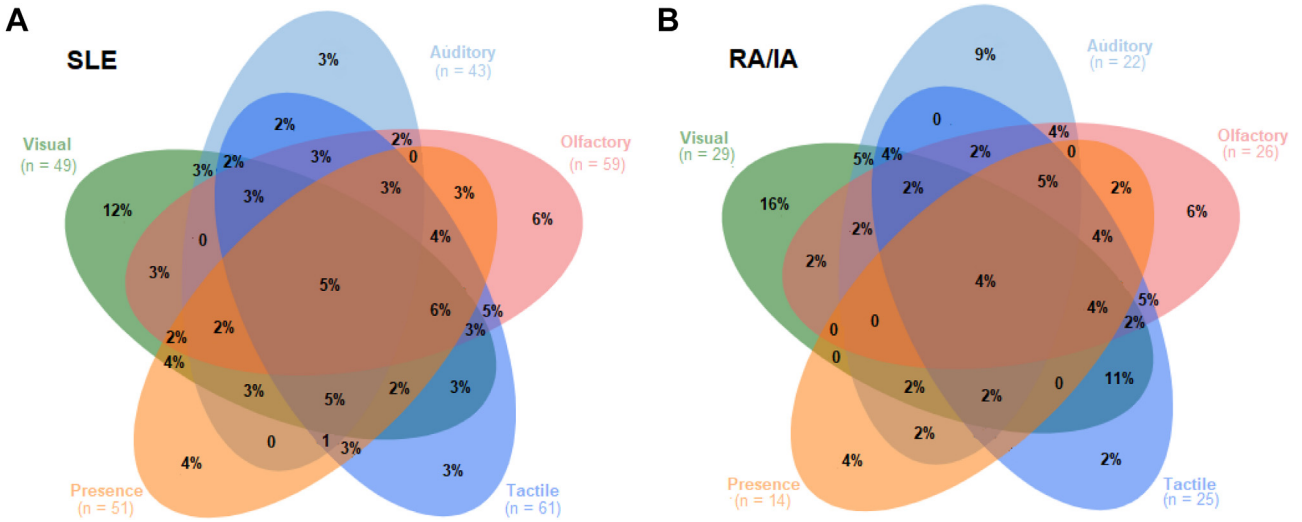
Comparisons in these figures are based on all SLE and RA/IA respondents, not just those that reported experiencing hallucinations. *A:* Visual hallucinations and other visual perceptual phenomena combined. *B:* Visual hallucinations and other visual perceptual phenomena independent. Significance levels of <0.001 are denoted as (***), <0.01 as (**), and <0.05 as (*). Non-significant results are denoted as (ns). RA/IA = rheumatoid arthritis/inflammatory arthritis; SLE = systemic lupus erythematosus.

illustrating the dynamic nature of these visual experiences:

> "*I often see objects being something that they are not … a shoe in the house being a bird. This lasts a few seconds.*" (PT 0069, SLE, England)

An interesting finding regarding these "morphing" phenomena was several patients describing how the disconfirmatory use of another sense (usually touch) would allow for more rapid transition of the morphed object back to reality.

FIGURE 2. Combinations of Lifetime Hallucination Modalities That Participants Reported Across SLE and RA/IA Groups, Respectively



Frequency (n) is reported where percentage of participants is less than 1%. These figures show lifetime prevalence of modalities. Whether the hallucinations occurred in different modalities simultaneously was not controlled for. SLE patients (left) were more likely to experience hallucinations in more than one modality than RA/IA patients (right) (72% vs 63%). Both groups show the highest overlaps among visual, tactile, and olfactory modalities, but the SLE group demonstrated a broader range of experiences.

Auditory hallucinations encompassed a range of experiences, from hearing indistinct conversations and background music to more detailed and disruptive noises. These auditory phenomena could be intermittent or continuous, significantly impacting the individual's ability to focus and function in daily activities.

Participants also reported olfactory hallucinations, such as smelling foul odors like decay, smoke, or something burning. These olfactory experiences could occur independently or alongside gustatory hallucinations, where individuals reported tasting unusual or unpleasant flavors. Although less common, pleasant tastes or smells were also reported.

Tactile hallucinations involved sensations of being pushed, touched, or experiencing specific sensations like insects crawling on the skin (formication). These physical sensations could be particularly distressing, as they often felt very real to the individuals experiencing them. Some participants reported presence hallucinations usually involving a feeling that someone else was in the room with them, or the sensation of being watched, especially while falling asleep.

Theme 2: Positive Coping Mechanisms through Symptom Labelling

Labelling hallucinations as CNS symptoms of rheumatologic disease itself, or as a side-effect of medication, often helped patients develop positive coping mechanisms. Many patients (and reportedly their clinicians) initially perceived their hallucinations as unrelated to the rheumatologic illness, which can prevent them from seeking help. Recognizing hallucinations as part of their SARD, often through repeated episodes, provided substantial relief and understanding.

The importance of clinicians understanding the potential direct relationship with the SARD or comorbid disease was frequently highlighted in terms of reassuring patients that hallucinations were not related to a comorbid primary psychotic disorder, and they were not "going mad," even if no intervention for the symptoms was offered:

> *"It was a relief to have an explanation as I was beginning to question my sanity, but nothing was really done about the symptoms."* (PT 0383, SLE, England)

Moreover, understanding that hallucinations are part of their rheumatologic disease enabled patients to develop specific coping strategies. One patient with lupus described a saying used to manage their symptoms though flares:

> *"It's been happening for so long, that when it does occur, I have a pre-prepared reassuring statement to utter to myself: 'It's not real, you're in a middle of a flare. It's lupus. You're not going mad'. Makes no difference but as I don't know what else to do, I fervently maintain this mantra."* (PT 0730, SLE, England)

Sharing experiences with other patients and formal support groups also played a crucial role in reducing stigma around the topic of hallucinations, helping patients to learn coping strategies from others who face similar challenges and fostering a sense of community and support.

Self-reported insight was higher among patients with IA/RA than SLE although the differences were not significant (X^2 (1, N = 172) = 0.269, P = 0.874) (Figure 3A). Forty percent of IA/RA patients experiencing hallucinations always had insights that they were not real, compared to 29.9% of SLE patients. Only 3.6% of IA/RA and 11.1% of SLE patients reported never having insight.

Theme 3: Spectrum of Emotional Valence That Affects Reporting of Symptoms

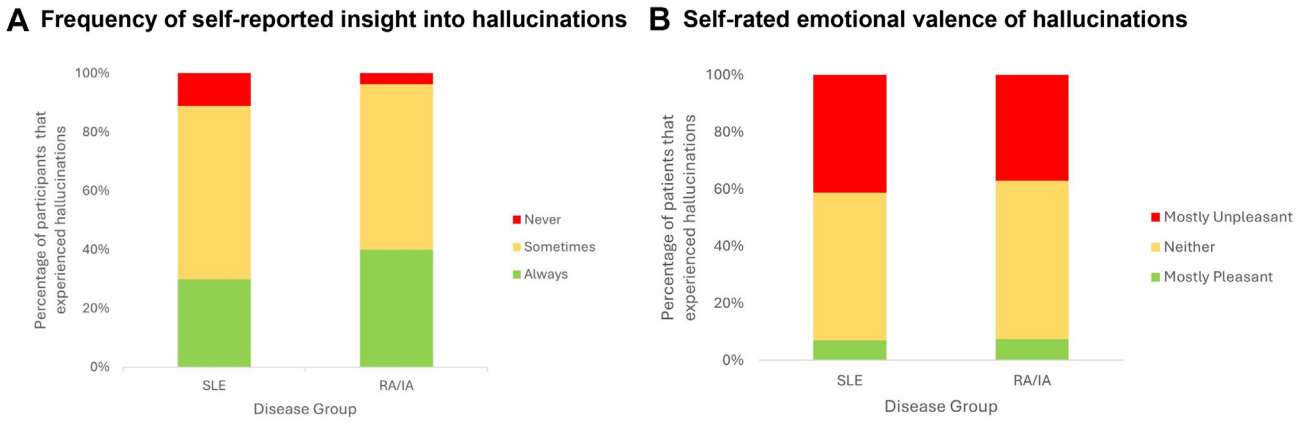
Hallucinations varied greatly in terms of their emotional valence, ranging from unpleasant, through neutral, to pleasant (Figure 3B). For many patients, hallucinations evoked feelings of helplessness and fear, making the experience highly unpleasant and impactful on the patient's mental health and daily functioning, regardless of the content and level of insight:

> *"I feel like I am losing my mind; I know that what I am experiencing is not and cannot be real but I have no control over stopping it."* (PT 0346, SLE, England)

Similar levels of classifying their hallucinations as "mostly unpleasant" was reflected in the SLE and RA/IA groups (41.2% and 37.0%, respectively). However, more than half of the survey respondents reported experiencing a neutral level of pleasantness (51.8% and 55.6% in the same groups, respectively).

Emotional valence can influence the decision to report or even discuss hallucinations colloquially. This extended further to "pleasant" hallucinations which were least reported (7.0% in SLE and 7.4% in RA/IA) and can be positive or even enjoyable.

FIGURE 3. Reported Insight and Emotional Valence of Hallucinations in SLE and RA/IA Groups



Comparisons in these figures are based on SLE and RA/IA respondents that experienced hallucinations.

> *"I felt fine, really happy to accept what I was seeing and feeling."* (PT 1434, RA/IA, England)

Quantitative data (Figure 3B) show the distribution of self-reported emotional valence of hallucinations among patients with SLE and those with RA/IA. Statistical analysis indicates no significant difference between the two groups in terms of experiencing mostly pleasant, neutral, or unpleasant hallucinations, X^2 (1, N = 172) = 0.269, P = 0.874.

Theme 4: Hallucinations During Sleep Transition

Hallucinations that occurred during sleep transitions could be particularly distressing and confusing for patients. These experiences often blurred the boundaries between reality and sleeping/dreaming mental activity, making it difficult for individuals to process and understand what they were experiencing.

> "*When the hallucinations started, they were exclusively at night, similar to night terrors. I still have them to this day, where I wake up and am completely awake for the hallucination but cannot process that what I am seeing isn't real.*" (PT 0862, SLE, England)

This indicates that hallucinations can be vivid and persist even after the individual is fully awake, suggesting a significant overlap between sleep and wakefulness. There is an added element of imprecision due to not knowing whether the hallucinator is still dreaming due to the abrupt disruption of sleep that might influence the levels of insight they have into the hallucination. Another patient recounted:

> *"One morning I woke and my whole body was paralysed, and I could see a cage over my bed."* (PT 1063, RA/IA, England)

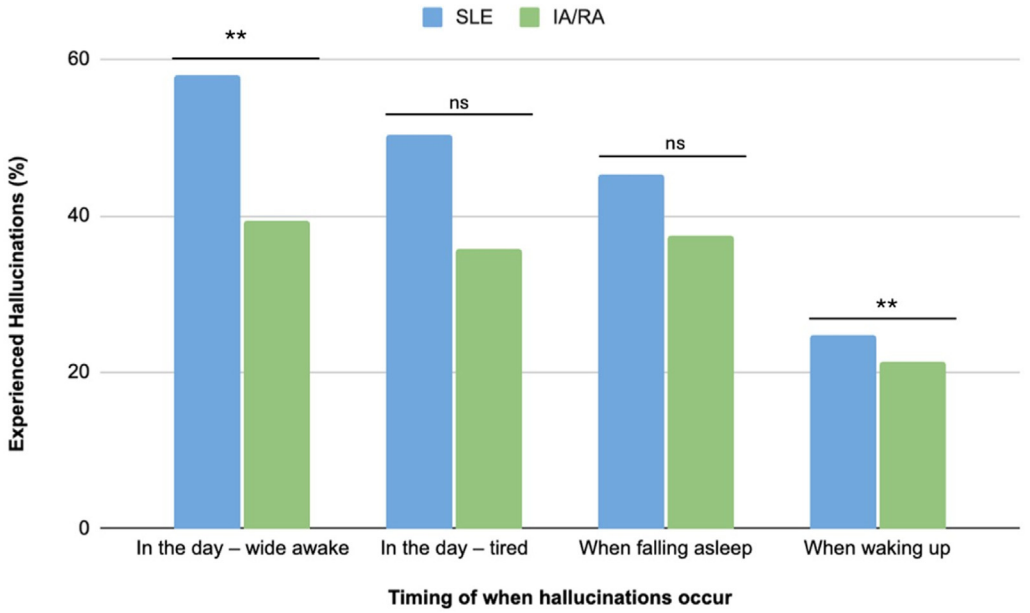
This description aligns with *hypnopompic* hallucinations, which occur upon waking and can be accompanied by sleep paralysis, a condition where the individual is temporarily unable to move or speak while transitioning between rapid eye movement sleep and wakefulness. The opposite occurs in *hypnogogic* hallucinations, which occur upon entering sleep. Several participants had considered the association of their general health with their sleep-related hallucinations:

> *"I often think it happens when I'm tired and feeling ill."* (PT 0181, RA/IA, England)

This suggests that factors like severe sleep restriction, extreme fatigue, and related symptoms can exacerbate these experiences, possibly by disrupting normal sleep patterns and increasing the likelihood of experiencing hallucinations during sleep transitions.

The data in Figure 4 further supports these narratives, showing the distribution of hallucinations during different times of the day between patient groups. The statistical analysis indicates no significant difference between the groups in hypnopompic [X^2 (1, N = 173) = 0.236, P = 0.637], hypnogogic [X^2 (1, N = 173) = 0.941, P = 0.332], or hallucinations during the day when feeling tired [X^2 (1, N = 173) = 3.304,

FIGURE 4. Comparison of Timings of When Participants Report Experiencing Hallucinations Between SLE and RA/IA Patient Group



Comparisons in this figure are based on SLE and RA/IA respondents who reported experiencing hallucinations. Significance levels of <0.001 are denoted as (***), <0.01 as (**), and <0.05 as (*). Non-significant results are denoted as (ns).

$P = 0.069$]. However, a significant difference was noted in experiencing hallucinations in contexts unrelated to sleep, with SLE patients more likely to report such experiences, X^2 (1, $N = 173$) = 5.382, $P = 0.020$.

Theme 5: Clinicians' Reliance on Comorbid Psychiatric Illness to Explain Hallucinations

Many patients discussed refraining from reporting their hallucinatory experiences to clinicians due to fear of being "judged" (PT 0679, SLE, England), stigmatized, and misdiagnosed:

> *"I only told my psychologist about these things; I've never told a medical doctor because they love to tell me I am crazy, not sick."* (PT 1159, SLE, Republic of Ireland)

This sentiment reflects a widespread concern among patients that their physically attributable CNS SARD symptoms might be dismissed as "purely psychological," leading to a reluctance to seek medical advice. The apprehension of being marked as "mentally unstable" because of hallucinations or other psychiatric symptoms prevented some individuals from discussing their symptoms openly, potentially delaying appropriate diagnosis and treatment:

> *"Don't tell anyone because once it's on your notes, that's all you will ever be diagnosed with. Even if you had cancer the specialist would say it's depression!"* (PT 1464, SLE, England)

These views and experiences were not infrequent and underscore the long-term consequences of stigma in medical records, where initial misdiagnoses can overshadow future medical evaluations and treatments, leading to mistrust in the healthcare system. However, a contrasting experience highlights the positive outcomes of integrated care:

> *"Initially I was sectioned as they thought I was mentally ill with psychosis, but my rheumatologist requested a brain scan, and they saw it was lupus. The psychiatrist and rheumatologist worked well together to make me better."* (PT 0448, SLE, England)

Although this was one of the rarer cases where objective evidence assisted with establishing an SLE diagnosis, this case demonstrates the value of interdisciplinary collaboration in achieving accurate diagnoses

and effective treatments, potentially overcoming initial mislabelling.

DISCUSSION

This study demonstrated significantly higher reported prevalences of lifetime hallucinations in all modalities, aside from auditory, among patients with SLE than among those with RA/IA. There was no single or combination of sensory modalities identified that had a much greater prevalence than others and could thus be labelled a "typical SARD hallucinatory experience." This underscores the need for individualized approaches in managing NPS in SARD patients and suggests that no straightforward phenomenological "signature" of SARD-related hallucinations will be forthcoming to apply to all patients.

A novel finding was in the description of some visual perceptual phenomena that the study team, including patients who had experienced these episodes, labelled as "morphing." This was the illusion of observing a veridical percept visually transform, taking on a full, detailed appearance of another non-veridical percept. From interviews, we ascertained that these experiences were longer in duration than common fleeting illusions, and an external stimulus was often required to provoke the illusion. These might then resolve after receiving contradictory secondary sensory information pertaining to the originating stimulus (e.g., touching it), or after scrutinizing the illusion.

The high prevalence of tactile hallucinations could be contributed to by the presence of peripheral neuropathy and/or small fiber neuropathy, where neuropathic pain (i.e., "pins-and-needles" sensation) is common, especially if neuropathy affects the afferent division.[20] Auditory hallucinations, although highly prevalent in primary psychotic disorders (e.g., schizophrenia),[5,21] occurred relatively infrequently among patients in this study, differing from some prior research reliant on medical records[22] which may not have fully captured patient experiences due to high levels of underreporting.[4]

The overall character of our findings suggests that SARD hallucinatory experiences are more aligned with those more commonly seen in a neurological illness, although there are states of overlap between psychiatric and neurological causes.[5,23] For instance, in Parkinson's disease dementia, visual hallucinations occur in 22%-38%,[24] presence hallucinations in 36%,[25] and auditory hallucinations in 8%[23] of patients. This alignment suggests that the NPS in SARDs may stem more from neurological mechanisms than from those driving primary psychotic disorders. The lower prevalence of hallucinations in this study compared to general population estimates[3] could reflect sampling bias or differing definitions of hallucinations.

The identified high level of insight among the SLE and RA/IA patients contrasts with primary psychotic disorders like schizophrenia, where poor insight is common.[19] Patients' insight fluctuated with disease activity, often improving in remission when hallucinations were retrospectively recognized as unreal but temporarily lost during flare-ups.[4] When interpreting and attributing the causality of hallucinations, it is possible that the source may be the general level of inflammation associated with rheumatic disease, a focal lesion/effect on areas of the brain itself, and/or the direct effect of immunomodulators on the CNS.[9–11]

Immunomodulators have been associated with psychotic symptoms (such as hallucinations), and in general, high doses and rapidly escalated doses make this more likely. This relationship is best elaborated for corticosteroids, wherein daily doses of more than 40 mg of prednisone equivalents are more commonly associated with psychotic symptoms shortly after dose initiation/increases.[26] Ascertainment of these symptoms in the context of SARDs should therefore take the impact of immunomodulators into account. In addition, chronic systemic CNS illness invariably increases the risk of delirium, especially when there is an additional medical complication (e.g., infection, electrolyte disturbance). This awareness is essential for both patients and clinicians to attribute hallucinations as an NPS of SARDs or related treatments rather than a discrete, separate, and unrelated neuropsychiatric illness.

The pattern of reported emotional valence of hallucinations mirrored that in neurological diseases,[5] with most being "neutral," followed by "unpleasant," and "pleasant" being least common. Understanding this variability is crucial, as research suggests emotional valence significantly impacts well-being and quality of life.[27] Given the high proportion of neutral experiences, clinical intervention may not always be necessary.[28] Instead, psychoeducation and open dialogue with clinicians may suffice, as many patients in our study found reassurance through discussion.

It is important to note that the hypnagogic and hypnopompic hallucinations reported by our participants are also common in the general population.[3] Recent research into insight, metacognition,[19] and hypnagogic states[29] highlights the need for interdisciplinary approaches to better understand hallucinations. Combining cognitive psychology, psychiatry, neurology, neuroimaging, and patient narratives can enhance diagnostic precision, improve intervention strategies, and reduce misattribution in SARDs.

Hallucinations in SARDs rarely have objective biomarkers, meaning clinician-patient dialogue is essential for their identification. However, fear of misattribution, negative clinician judgment, and stigma act as barriers to disclosure. Clinicians should normalize these symptoms in SARDs, particularly SLE,[4] and encourage open discussion to foster better care and reduce distress.

Limitations include the relatively small sample size of RA/IA patients experiencing hallucinations and related perceptual phenomena (n = 56) and the high proportion of female (>90%) participants, which may limit the generalizability of the findings. However, the gender difference was expected due to both diseases being more common in men than in women. The high percentage of White participants, in RA/IA (>96%) compared to SLE (>85%), although expected given varying disease prevalence across ethnicities, may have influenced comparative results. In addition, the concept of insight varies culturally, with "naturalistic" explanations (e.g., disease) and "personalistic" explanations (e.g., karma, sin) both shaping how hallucinations and related symptoms are understood and reported.[30]

There is a high potential for sampling bias, as online recruitment may overrepresent individuals who are more digitally engaged and underrepresent those with limited internet access or online involvement. In addition, because we could not determine how many individuals viewed the survey invitation, we were unable to calculate a formal response rate, further limiting the generalizability of our findings.

Another limitation was the lack of a validated questionnaire specifically designed for SARD patients, as no existing measure sufficiently covered the diverse hallucinations and perceptual anomalies seen in these diseases. The bespoke survey was co-produced by patients, clinicians, and researchers to better capture these experiences, including rare phenomena like "morphing" illusions. However, it lacks external validation or against clinically administered or validated assessments, limiting comparability with other datasets.[3,5] Clinical interviews risk underrepresenting symptom prevalence and nuance in this population,[4] as they rely on patient disclosure within time-constrained clinical encounters. By cross-validating survey responses with patient interviews, we aimed to center participant perspectives and minimize stigma-related underreporting. Future studies should integrate both patient- and clinician-reported measures while addressing systemic barriers to symptom disclosure.

This study did not control for potential effects of immunomodulatory treatments, an important factor considering that many such therapies can significantly alter the immune response and, by extension, impact NPS[9–11] as discussed previously. This will be a focus of future INSPIRE outputs. Given emerging evidence of CNS involvement in RA/IA,[31] future comparisons with non-inflammatory diseases such as osteoarthritis could help disentangle the relative contributions of inflammation, autoimmunity, and neuropsychiatric vulnerability.

There are benefits to focus on longitudinal studies to track the progression of hallucinations and their correlation with disease activity in SLE and RA/IA. Exploring the underlying neurobiological mechanisms through advanced neuroimaging techniques may provide a deeper understanding of the pathophysiology of hallucinations in these conditions. A strength of this study is the multidisciplinary research team, full and equal involvement of patients, and integrating qualitative data. This offers richer insights into the personal and emotional dimensions of hallucinations, facilitating the development of more comprehensive diagnostic and treatment strategies.

CONCLUSIONS

This study provides valuable and novel understandings into the prevalence, modalities, insight, emotional valence, and timing of hallucinations and related perceptual phenomena in SLE and RA/IA patients. Compared to IA/RA, SLE patients experienced significantly higher prevalences of all modalities of hallucinations, aside from auditory, potentially reflecting the greater direct involvement of the brain in SLE. The hallucinatory experiences of both SARD groups

demonstrated more similarity with neurological diseases as opposed to primary psychotic disorders where auditory hallucinations are more common, and insight regarding hallucinations is more often lacking. Recognizing hallucinations in all modalities except auditory as prevalent and potentially a direct effect of SLE and other SARDs could improve attribution and treatment and increase positive coping mechanisms. Empathetic eliciting and normalization should increase patient trust and confidence in reporting these often distressing symptoms.

Disclosure: MS is funded by NIHR, The Lupus Trust, LUPUS UK, Vasculitis UK, and reports consultancy fees from Otoimmune. MP and ST are funded by The Lupus Trust. JAB has received speaking fees from Psychiatric Times and Oakstone and receives royalties from American Psychiatric Publishing, Springer International, Lippincott Williams & Wilkins, and Cambridge University Press; he also receives support from Abbott. LA has received consultancy fees/speaker fees from: Eli Lilly, Glaxo Smith Kline, Janssen, Novartis, UCB, and Werfen Group. DD'C reports grants from MRC, NIHR, LUPUS UK, and The Lupus Trust; consultancy/speaker fees from GSK, Eli Lilly, and UCB; and a leadership role on the board of APS support UK. TAP was supported by the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley National Health Service Foundation Trust and King's College London. TAP receives consulting fees from Arialys Inc. ST reports funding from LUPUS UK and Vasculitis UK. The remaining authors have declared no conflicts of interest. The views expressed are those of the study participants and/or author(s) and not necessarily those of the NHS, the funders, the NIHR, or the Department of Health and Social Care.

Funding: This work was supported by the The Lupus Trust (award number: G130831). The funders had no role in the study design, data collection, analysis, interpretation, or writing of this manuscript.

Ethical Approval: Ethical approval was obtained through the Cambridge Psychology Research Committee: PRE 2022.027. The overall INSPIRE protocol and statistical analysis plan (SAP) were pre-registered: https://osf.io/zrehm, and the SAP for this sub-study was pre-agreed with the study supervisors (MS and TAP) and lead author (AA) prior to AA accessing and analyzing the data.

Acknowledgments: We would like to express our great thanks to the many patients, clinicians, healthy friends, and SARD charity staff who contributed their time and expertise to the INSPIRE study. We would also like to thank the wider INSPIRE team patient, academic and clinician collaborators, and advisors.

References

1. Melo LF, Da-Silva SL: Neuropsychological assessment of cognitive disorders in patients with fibromyalgia, rheumatoid arthritis, and systemic lupus erythematosus. Rev Bras Reumatol 2012; 52:181–188
2. Sloan M, Andreoli L, Zandi MS, et al: Attribution of neuropsychiatric symptoms and prioritization of evidence in the diagnosis of neuropsychiatric lupus: mixed methods analysis of patient and clinician perspectives from the international INSPIRE study. Rheumatology 2024; 63:3471–3485
3. Linszen MM, de Boer JN, Schutte MJ, et al: Occurrence and phenomenology of hallucinations in the general population: a large online survey. Schizophrenia 2022; 8:41
4. Sloan M, Wincup C, Harwood R, et al: Prevalence and identification of neuropsychiatric symptoms in systemic autoimmune rheumatic diseases: an international mixed methods study. Rheumatology 2024; 63:1259–1272
5. Schutte MJ, Linszen MM, Marschall TM, et al: Hallucinations and other psychotic experiences across diagnoses: a comparison of phenomenological features. Psychiatry Res 2020; 292:113314
6. Lenka A, Pagonabarraga J, Pal PK, Bejr-Kasem H, Kulisvesky J: Minor hallucinations in Parkinson disease: a subtle symptom with major clinical implications. Neurology 2019; 93:259–266
7. Collerton D, Barnes J, Diederich NJ, et al: Understanding visual hallucinations: a new synthesis. Neurosci Biobehavioral Rev 2023; 150, 105208
8. Schwartz N, Stock AD, Putterman C: Neuropsychiatric lupus: new mechanistic insights and future treatment directions. Nat Rev Rheumatol 2019; 15:137–152
9. Justiz-Vaillant AA, Gopaul D, Soodeen S, et al: Neuropsychiatric systemic lupus erythematosus: molecules involved in its immunopathogenesis, clinical features, and treatment. Molecules 2024; 29:747
10. Huynh G, Reinert JP: Pharmacological management of steroid-induced psychosis: a review of patient cases. J Pharm Technology 2021; 37:120–126
11. Lane JC, Weaver J, Kostka K, et al: Risk of depression, suicide and psychosis with hydroxychloroquine treatment for rheumatoid arthritis: a multinational network cohort study. Rheumatology 2021; 60:3222–3234

12. D'Antonio F, Boccia M, Di Vita A, et al: Visual hallucinations in Lewy body disease: pathophysiological insights from phenomenology. J Neurol 2022; 269:3636–3652
13. Gao D, Gao X, Yang F, Wang Q: Neuroimmune crosstalk in rheumatoid arthritis. Int J Mol Sci 2022; 23:8158
14. Creswell JW, Clark VL: Designing and Conducting Mixed Methods Research. Thousand Oaks: Sage Publications; 2017
15. Tong A, Sainsbury P, Craig J: Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Health Care 2007; 19:349–357
16. De Chazeron I, Pereira B, Chereau-Boudet I, et al: Validation of a Psycho-Sensory hAllucinations Scale (PSAS) in schizophrenia and Parkinson's disease. Schizophr Res 2015; 161:269–276
17. Braun V, Clarke V: Thematic analysis. In: Cooper H, Camic PM, Long DL, Panter AT, Rindskopf D, Sher KJ, (eds) APA handbook of research methods in psychology, Vol. 2. Research designs: Quantitative, qualitative, neuropsychological, and biological. Washington, D.C: American Psychological Association; 2012. p. 57–71
18. Braun V, Clarke V: Reflecting on reflexive thematic analysis. Qual Res Sport Exerc Health 2019; 11:589–597
19. Davis BJ, Lysaker PH, Salyers MP, Minor KS: The insight paradox in schizophrenia: a meta-analysis of the relationship between clinical insight and quality of life. Schizophr Res 2020; 223:9–17
20. Galosi E, Pirone C, Ceccarelli F, et al: Clinical, histologic, and immunologic signatures of small fiber neuropathy in systemic lupus erythematosus. J Peripher Nervous Syst 2024; 29:315–328
21. Triola M, Cobo J, González-Rodríguez A, et al: Impact of delusions and hallucinations on clinical insight dimensions in schizophrenia spectrum disorders. Psychopathology 2024; 57:267–276
22. Abrol E, Coutinho E, Chou M, et al: Psychosis in systemic lupus erythematosus (SLE): 40-year experience of a specialist centre. Rheumatology 2021; 60:5620–5629
23. Llorca PM, Pereira B, Jardri R, et al: Hallucinations in schizophrenia and Parkinson's disease: an analysis of sensory modalities involved and the repercussion on patients. Sci Rep 2016; 6:38152
24. Fénelon G, Alves G: Epidemiology of psychosis in Parkinson's disease. J Neurol Sci 2010; 289:12–17
25. Fénelon G, Mahieux F, Huon R, Ziégler M: Hallucinations in Parkinson's disease: prevalence, phenomenology and risk factors. Brain 2000; 123:733–745
26. Dubovsky AN, Arvikar S, Stern TA, Axelrod L: The neuropsychiatric complications of glucocorticoid use: steroid psychosis revisited. Psychosomatics 2012; 53:103–115
27. Badcock JC, Brand R, Thomas N, Hayward M, Paulik G: Multimodal versus unimodal auditory hallucinations in clinical practice: clinical characteristics and treatment outcomes. Psychiatry Res 2021; 297:113754
28. Cox TM, ffytche DH: Negative outcome charles bonnet syndrome. Br J Ophthalmol 2014; 98:1236–1239
29. Ghibellini R, Meier B: Hypnagogic states are quite common: self-reported prevalence, modalities, and gender differences. Conscious Cogn 2023; 115:103582
30. Saravanan B, Jacob KS, Prince M, Bhugra D, David AS: Culture and insight revisited. Br J Psychiatry 2004; 184:107–109
31. Sağ S, Sağ MS, Tekeoğlu I, Kamanlı A, Nas K, Acar BA: Central nervous system involvement in rheumatoid arthritis: possible role of chronic inflammation and tnf blocker therapy. Acta Neurol Belgica 2020; 120:25–31