The Neuroanatomy of Poststroke Subjective Sensory Hypersensitivity

Hella Thielen, MS, Nora Tuts, MS,* Christophe Lafosse, PhD,† and Céline Raymond Gillebert, PhD*‡*

Background: Although subjective sensory hypersensitivity is prevalent after stroke, it is rarely recognized by health care providers, and its neural mechanisms are largely unknown.

Objective: To investigate the neuroanatomy of poststroke subjective sensory hypersensitivity as well as the sensory modalities in which subjective sensory hypersensitivity can occur by conducting both a systematic literature review and a multiple case study of patients with subjective sensory hypersensitivity.

Method: For the systematic review, we searched three databases (Web of Science, PubMed, and Scopus) for empirical articles discussing the neuroanatomy of poststroke subjective sensory hypersensitivity in humans. We assessed the methodological quality of the included studies using the case reports critical appraisal tool and summarized the results using a qualitative synthesis. For the multiple case study, we administered a patient-friendly sensory sensitivity questionnaire to three individuals with a subacute right-hemispheric stroke and a matched control group and delineated brain lesions on a clinical brain scan.

Results: Our systematic literature search resulted in four studies (describing eight stroke patients), all of which linked poststroke subjective sensory hypersensitivity to insular lesions. The results of our multiple case study indicated that all three stroke patients reported an atypically high sensitivity to different sensory modalities. These patients' lesions overlapped with the right anterior insula, the claustrum, and the Rolandic operculum.

Conclusion: Both our systematic literature review and our multiple case study provide preliminary evidence for a role of the insula in poststroke subjective sensory hypersensitivity and suggest that poststroke subjective sensory hypersensitivity can occur in different sensory modalities.

Received for publication April 8, 2022; accepted November 9, 2022.

From the *Department of Brain and Cognition, Leuven Brain Institute, KU Leuven, Leuven, Belgium; †RevArte Rehabilitation Hospital, Edegem, Belgium; and ‡TRACE, Centre for Translational Psychological Research, KU Leuven—Hospital East–Limbourgh, Genk, Belgium.

C.L. and C.R.G. contributed equally.

Supported in part by the Research Foundation Flanders (Fonds Wetenschappelijk Onderzoek, FWO) (G0H7718N [C.R.G.], 11G1120N [H.T.]).

The authors declare no conflicts of interest.

Correspondence: Céline Raymond Gillebert, PhD, Tiensestraat 102, P.O. Box 3711, Leuven 3000, Belgium (email: celine.gillebert@kuleuven.be).

Key Words: sensory sensitivity, sensory hypersensitivity, stroke, insula, sensory overload

(*Cogn Behav Neurol* 2023;36:68–84)

fMRI = functional magnetic resonance imaging. **OCS–NL** = Oxford Cognitive Screen (Dutch version).

The human brain is constantly bombarded with both external and internal sensory stimuli. To reach our goals in such a rich sensory environment, we must efficiently register and modulate this sensory stimulation and adapt our behavior to continuous changes therein. Humans show large interindividual differences in their self-reported responsiveness to sensory stimuli. Some individuals display an underresponsiveness to sensory stimuli that manifests itself as being underwhelmed by sensory stimuli (ie, hyposensitive); others display an overresponsiveness, causing them to become easily overwhelmed by sensory stimuli (ie, hypersensitive).

Subjective Sensory Hypersensitivity

Subjective sensory hypersensitivity to nonnociceptive sensory stimuli is prevalent in the neurotypical population (Greven et al, 2019) as well as in individuals with chronic pain (eg, fibromyalgia) (López-Solà et al, 2014) and those with different neurologic (eg, Tourette syndrome, mild traumatic brain injury) (Callahan et al, 2018; Isaacs and Riordan, 2020; Laborey et al, 2014), psychiatric (eg, schizophrenia) (Landon et al, 2016), and neurodevelopmental disorders (eg, autism spectrum disorder, Williams syndrome, attention deficits disorder) (Bijlenga et al, 2017; Glod et al, 2020; Tavassoli et al, 2014). Subjective (self-reported) sensory hypersensitivity is known to reduce one's quality of life: It has been related to social isolation (Callahan and Lim, 2018; Landon et al, 2012), reduced mental health (eg, higher negative affect and depression) (ie, Smith, 2003; Stansfeld and Shipley, 2015), reduced physical health (eg, sleep disturbances and fatigue) (Elliott et al, 2018; Hallberg et al, 2005; Landon et al, 2012), and difficulties carrying out activities of leisure (Callahan and Lim, 2018; Hallberg et al, 2005). Contrary to the high clinical relevance of subjective sensory hypersensitivity, its neural mechanisms remain unclear (Ward, 2019).

Previous research on the neural mechanisms of subjective sensory hypersensitivity in neurotypical and clinical populations relied mainly on functional magnetic resonance imaging (fMRI). These studies related subjective sensory hypersensitivity to functional abnormalities in different brain areas, including the sensory cortices (eg, Green et al, 2015; López-Solà et al, 2014); insula (eg, López-Solà et al, 2014); thalamus (eg, Acevedo et al, 2018); and limbic structures, such as the amygdala and the hippocampus (eg, Acevedo et al, 2018; Green et al, 2015). However, these studies varied greatly in their methodology (ie, they studied different sensory modalities using different fMRI designs) and their population of interest (ie, they studied neurotypical adults and different clinical populations with different comorbid symptomatology), making it difficult to interpret the variability in the reported functional neuroanatomy.

In addition, given that fMRI provides only correlational information, it does not allow researchers to make causal inferences about brain–behavior relationships. Brain regions may indeed show task-related activation due to their anatomical or functional connection to another brain region required for the function underlying the task. In contrast, lesion studies allow researchers to identify brain regions that are crucial for performing a specific cognitive function (Adolphs, 2016; Rorden and Karnath, 2004).

Subjective Sensory Hypersensitivity and Acquired Brain Injury

Several studies have suggested a relationship between subjective sensory hypersensitivity and acquired brain injury (eg, Alwawi et al, 2020; Callahan and Storzbach, 2019; Shepherd et al, 2020). After an acquired brain injury, some individuals report a change in their sensory sensitivity, resulting in an increased sensitivity to sensory stimuli (ie, subjective sensory hypersensitivity). For example, these individuals (a) report feeling overwhelmed in crowded environments, (b) detest bright sunlight, or (c) feel the need to isolate themselves from sensory stimuli (Alwawi et al, 2020).

Previous studies have reported a subjective sensory hypersensitivity to sound in 44% of 341 individuals with mild traumatic brain injury (Shepherd et al, 2021) and a subjective sensory hypersensitivity to light in 51% of 86 individuals with mild to severe traumatic brain injury (Goodrich et al, 2014; for more details, see Thielen et al, 2022). Subjective sensory hypersensitivity after brain injury has been associated with longer recovery times and mental health difficulties (Callahan et al, 2018; O'Kane et al, 2014; Shepherd et al, 2021).

Subjective Sensory Hypersensitivity and Lesion Neuroanatomy

To date, the behavioral and neural mechanisms underlying subjective sensory hypersensitivity remain largely unknown. Although some researchers have proposed that subjective sensory hypersensitivity is related to reduced information processing or altered sensory thresholds (eg, Chang et al, 2007; Schrupp et al, 2009; Shepherd et al, 2019), the available evidence is only correlational. Further research is needed to conceptualize subjective sensory hypersensitivity into a biopsychosocial model. Studying subjective sensory hypersensitivity in individuals with brain injury in relation to lesion neuroanatomy can help us uncover its neural basis.

When recruiting participants for lesion studies, de Haan and Karnath (2018) recommend including individuals with focal lesions such as those induced by stroke because the full extent of more diffuse damage (eg, diffuse axonal injury) cannot be detected using clinical brain scans. However, research on poststroke subjective sensory hypersensitivity is rare (Thielen et al, 2022). To our knowledge, the study by Chung and Song (2016) is the only study that has investigated the prevalence of poststroke subjective sensory hypersensitivity in a large stroke sample. The authors reported that 18% of 240 stroke patients experienced heightened subjective sensory sensitivity compared with neurotypical controls (ie, 18% of stroke patients scored above the 84th percentile that was based on the data of neurotypical controls).

The results reported by Chung and Song (2016) suggest that poststroke subjective sensory hypersensitivity is prevalent in stroke patients. However, the authors did not make inferences about the neuroanatomy of poststroke subjective sensory hypersensitivity, nor did they disclose whether poststroke subjective sensory hypersensitivity was modality specific rather than present across multiple modalities. Furthermore, it was unclear if all of the individuals in the sample reported a change in their sensory sensitivity from pre- to poststroke or whether they had already experienced subjective sensory hypersensitivity before their stroke (because this symptom is also prevalent in the neurotypical population).

To characterize the properties of poststroke subjective sensory hypersensitivity and identify its neuroanatomy, we first conducted a systematic literature review according to PRISMA (Preferred Items for Systematic Reviews and Meta-Analyses; Moher et al, 2009) guidelines. We focused on studies investigating poststroke subjective sensory hypersensitivity in relation to the lesion neuroanatomy and assessed the sensory modalities in which poststroke subjective sensory hypersensitivity was reported. Second, we complemented the systematic literature review with a multiple case study discussing three stroke cases with subjective sensory hypersensitivity.

LITERATURE REVIEW

Method

We searched the Web of Science, PubMed, and Scopus databases from their inception through January 31, 2022 using a search string including different synonyms for stroke as well as terms relating to sensory sensitivity or sensory intensity. The full search string was (stroke OR "subarachnoidal he$morrhage" OR "brain he$morrhage" OR "brain infarction" OR "cerebral infarction" OR "cerebral he$morrhage" OR "intracranial

he$morrhage") AND ("sensory *sens*" OR "sensory processing disorder" OR phonophobia OR photophobia OR osmophobia OR hyperacusis OR *sensitivit* NEAR/2 [light OR visual OR auditory OR sound OR noise OR touch OR tactile OR smell OR olfactory OR gustatory OR temperature OR taste OR vestibular] OR intensity NEAR/2 [light OR visual OR auditory OR sound OR noise OR touch OR tactile OR smell OR olfactory OR gustatory OR temperature OR taste OR vestibular]).

Articles were included if they discussed the lesion neuroanatomy (ie, the location of the lesion based on a CT or MRI scan) of subjective sensory hypersensitivity to environmental stimuli in individuals who had experienced a stroke. Only empirical studies were included; review articles and book chapters were excluded. Furthermore, articles were excluded if they were not written in English, if the studied population did not include individuals who had experienced a stroke, if they consisted of solely animal research, or if they studied poststroke sensory hyposensitivity (eg, in the context of peripheral dysfunction, hemiplegia, or hemianopia).

Articles regarding pain were only included if they studied poststroke pain. More specifically, articles about chronic migraine increasing the risk of stroke incidence were excluded, as were articles on pain describing photo- or phonophobia solely during migraine episodes or describing tactile hypersensitivity or temperature allodynia limited to the painful body part.

Two reviewers (H.T. and N.T.) independently reviewed the abstracts from the various databases for their relevance using the above-described in- and exclusion criteria (which were set before abstract screening). A third reviewer (C.R.G.) was consulted in case of disagreement.

Figure 1 displays a study flow diagram of the literature review based on the PRISMA guidelines. We identified 462 records through database searching. After excluding duplicates, we screened 368 articles. From these articles, 13 articles fulfilled the inclusion criteria.

From the 13 articles, we extracted the demographic characteristics (ie, title, authors, year of publication, journal), the characteristics of the studied stroke sample (ie, sample size, age and sex of stroke sample, type of stroke, time since injury), the sensory modalities that were studied, and the results of the analysis relating poststroke subjective sensory hypersensitivity to lesion neuroanatomy. Based on the data extraction, we had to exclude nine articles: One did not study subjective sensory hypersensitivity (Bonan et al, 2015), one studied subjective sensory hypersensitivity after acquired brain injury but did not provide results that were specific to the included individuals with stroke (Berthold-Lindstedt et al, 2017), one studied tactile hyposensitivity in hemiplegic limbs (Aikio et al, 2021), one studied temperature allodynia limited to painful body parts (Klit et al, 2011), one studied photophobia during a migraine episode with comorbid hemianopia (Tanev et al, 2021), three did not mention the neuroanatomy of poststroke subjective sensory hypersensitivity specifically (Alwawi et al, 2020; Carlsson et al, 2004, 2009), and one studied auditory illusions (palinacousis and paracusis) (Fukutake and Hattori, 1998).

Because the included articles consisted of single or multiple case studies, H.T. and N.T. used a case reports critical appraisal tool (Moola et al, 2020) to assess the methodological quality of each study. This tool includes eight criteria, of which five were applicable to our review.

We used qualitative synthesis to summarize the results on poststroke subjective sensory hypersensitivity. In alignment with our research aims, we focused on lesion location and sensory modalities. The data collection forms and the study protocol are available via https://doi.org/10.6084/m9.figshare.18096365.

Results

We identified four case reports (total of eight patients) about poststroke subjective sensory hypersensitivity through the systematic review (Table 1). The quality of the included reports is presented in Table 2: Two reports did not provide a detailed account of the patients' medical background. All four case reports linked insular lesions to poststroke subjective sensory hypersensitivity in one or two sensory modalities: auditory hypersensitivity (Boucher et al, 2015), visual hypersensitivity (Cantone et al, 2019), olfactory hypersensitivity (Mak et al, 2005), and gustatory hypersensitivity (Mak et al, 2005; Pritchard et al, 1999). However, the two patients discussed by Boucher et al (2015) reported a comorbid tactile or olfactory hypersensitivity, and the patient discussed by Mak et al (2005) reported a comorbid hypersensitivity to environmental temperature.

MULTIPLE CASE STUDY

Method

Participants

Stroke Patients. Stroke patients who were admitted to the RevArte Rehabilitation Hospital in Edegem, Belgium, in June through October 2018 and whose medical files mentioned poststroke subjective sensory hypersensitivity were recruited to participate in this study after referral by a clinical neuropsychologist. If a patient complained of sensory hypersensitivity to their clinical neuropsychologist during an intake, neuropsychological assessment, or neuropsychological rehabilitation, a description of their subjective sensory hypersensitivity was added to the medical file. Patients who were unable to provide informed consent, or who had a formal diagnosis of autism spectrum disorder, attention deficit hyperactivity disorder, schizophrenia, or posttraumatic stress disorder were excluded from the study. No exclusion was made based on stroke type, lesion location, cognitive profile, or time since stroke.

Of the 59 stroke patients who were admitted to the RevArte Rehabilitation Hospital during the stated time period, three patients were referred for our study. All three patients fulfilled the in- and exclusion criteria, consented to take part in the study, and reported that Flemish was their dominant language. Each of the stroke patients reported having intact hearing and vision and no epilepsy.

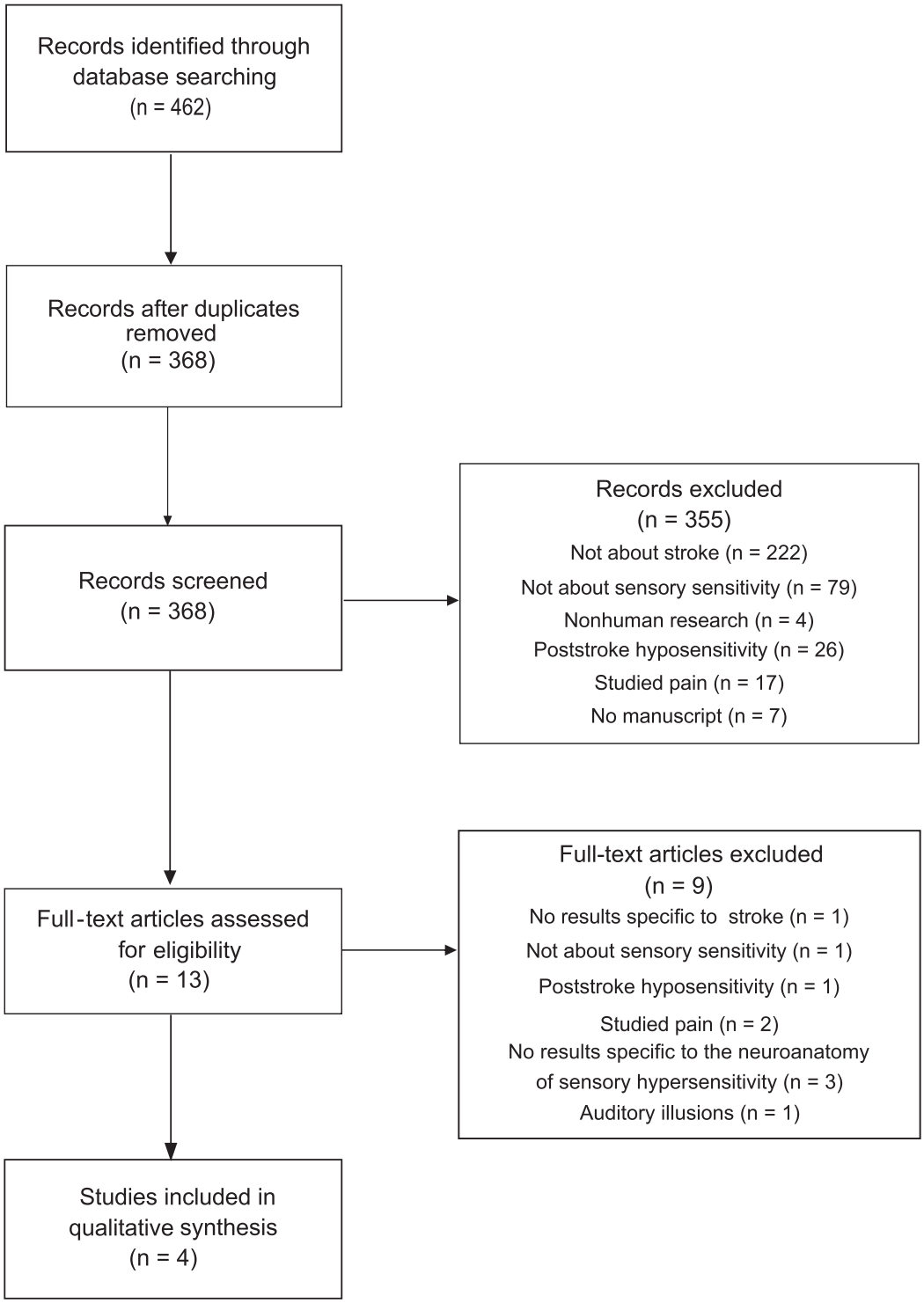

FIGURE 1. PRISMA flow diagram of the systematic literature review. **PRISMA** = Preferred Items for Systematic Reviews and Meta-Analyses.

The sex, age, and years of completed education (starting from the age of 6 years) of each patient were recorded (Table 3). Figure 2 shows lesion maps for each patient as well as a lesion overlap for the three patients combined.

Control Group. Because demographic characteristics such as sex and age are associated with subjective sensory sensitivity (eg, Benham, 2006; Ueno et al, 2019), we matched a control group based on sex, age, and education

TABLE 1. Overview of Studies Relating Poststroke Sensory Hypersensitivity to Lesion Neuroanatomy Based on a Systematic Literature Review

Reference	Case Descriptions	Stroke Type	Assessment of Subjective Sensory Hypersensitivity	Studied Sensory Modality	Lesioned Hemisphere	Lesion Location Based on MRI or CT Scan	Results
Pritchard et al (1999)	*Case 1 (G.B.)*: Age: 52 Sex: Female Months since stroke: 18	*Case 1 (G.B.)*: Unknown	Self-reported intensities of gustatory stimuli	Gustatory	*Case 1 (G.B.)*: Right	*Case 1 (G.B)*: Right rostral insula; frontal, parietal, and temporal opercula; and putamen	Three stroke cases (G.B., M.L., and P.G.) reported lower taste intensities on the ipsilesional versus the contralesional side of the tongue. Case M.K. showed no taste intensity differences between the ipsilesional and contralesional side of the tongue.
	Case 2 (M.L.): Age: 56 Sex: Female Months since stroke: 6	*Case 2 (M.L.)*: Subarachnoid hemorrhage			*Case 2 (M.L.)*: Left	*Case 2 (M.L.)*: Left posterior and rostral insula, left parietal and temporal lobes, as well as the left putamen and internal capsule	
	Case 3 (P.G.): Age: 65 Sex: Male Months since stroke: 2	*Case 3 (P.G.)*: Unknown			*Case 3 (P.G)*: Left	*Case 3 (P.G)*: Left rostral insula, orbitofrontal cortex, caudate nucleus, putamen, and internal capsule	
	Case 4 (M.K.): Age: 61 Sex: Female Months since stroke: 8	*Case 4 (M.K.)*: Ischemic stroke			*Case 4 (M.K)*: Left	*Case 4 (M.K.)*: Left posterior insula, parietal lobe, putamen, and internal capsule; signs of global atrophy	
Mak et al (2005)	Age: 70 Sex: Male Months since stroke: 13 (follow-up at 18 months)	Ischemic stroke	Rating of the intensity of gustatory and olfactory stimuli	Olfactory and gustatory	Left	Left posterior insula	Increased intensity rating of olfactory and gustatory stimuli, especially when stimuli were presented to the contralesional nostril or the contralesional side of the tongue
Boucher et al (2015)	*Case 1*: Age: 29 Sex: Female Months since stroke: 16	*Case 1*: Ischemic stroke	Hearing Sensitivity Questionnaire, loudness discomfort task	Auditory	*Case 1*: Left	*Case 1*: Left posterior insula	Self-reported auditory hypersensitivity and heightened loudness discomfort as compared to a matched control group
	Case 2: Age: 40 Sex: Female Months since stroke: 52	*Case 2*: Stroke type is unknown			*Case 2*: Right	*Case 2*: Right insula	
Cantone et al (2019)	Age: 62 Sex: Male Months since stroke: Unknown	Ischemic stroke	Subjective description	Visual (specific to curved, multicolored lines, or tangles)	Right	Right temporal-insula; periventricular white matter damage	Facial expression of fear and disgust, with a neurovegetative reaction and horripilation in response to visual stimuli

The two patients discussed by Boucher et al (2015) reported a comorbid tactile or olfactory hypersensitivity, and the patient discussed by Mak et al (2005) reported a comorbid hypersensitivity to environmental temperature.

TABLE 2. Critical Appraisal of the Included Studies

Article	1	2	3	4	5
Pritchard et al (1999)	+	−	+	+	+
Mak et al (2005)	+	+	+	+	+
Boucher et al (2015)	+	−	+	+	+
Cantone et al (2019)	+	+	+	+	+

The critical appraisal criteria (based on Moola et al, 2020): a clear description of the (1) patient's demographic characteristics, (2) patient's history presented as a time line, (3) current clinical condition, (4) diagnostic tests or assessment methods, and (5) case report takeaway lessons.

level to each of the three cases. To this end, we recruited 19 neurotypical volunteers from a participant database of adults who had previously participated in research. Exclusion criteria were a formal diagnosis of autism spectrum disorder, attention deficit hyperactivity disorder, schizophrenia, or posttraumatic stress disorder, or a probable history of neurologic disease. We excluded one control participant because of a probable history of mild traumatic brain injury. The in- and exclusion criteria were set before data collection.

Two neurotypical control groups were formed: one consisting of females and the other of males (in order to match to the sex of the different cases). To compare the age and years of education of the cases to the mean age and mean years of education of the matched control group, we followed the recommendations of Crawford and Garthwaite (2002) for significance testing. The age of each case did not differ significantly from the mean age of its respective control group (Case #1: $t = 0.6$, $P = 0.3$; Case #2: $t = 1$, $P = 0.2$; Case #3: $t = 0.9$, $P = 0.2$). The completed years of education of the cases also did not differ significantly from the mean years of education of their respective control group (Case #1: $t = -1.6$, $P = 0.07$; Cases #2 and #3: $t = -0.5$, $P = 0.3$).

This study was approved by the ethical committee of the GZA Hospitals (application number: 180606MASTER) and the social and societal ethics committee of the KU Leuven (application number: G- 2019031604). Informed consent was obtained in accordance with the World Medical Association Declaration of Helsinki.

Assessments

Sensory Sensitivity Questionnaire. To date, there is no validated sensory sensitivity questionnaire that is adapted to stroke patients and that assesses all sensory modalities (for an overview of the diagnostic tools that are used to assess subjective sensory sensitivity after acquired brain injury, see Thielen et al, 2022). Therefore, in order to systematically assess poststroke subjective sensory sensitivity across different modalities (ie, multisensory, visual, auditory, tactile, olfactory, gustatory, environmental temperature, vestibular sensitivity, and pain), we developed a new, patient-friendly sensory sensitivity questionnaire.

Our sensory sensitivity questionnaire consists of two parts. The first part contains 83 multiple-choice items assessing subjective sensory sensitivity across several modalities. Because it is unclear what the underlying behavioral mechanisms of subjective sensory hypersensitivity after brain injury are, we asked experts (ie, clinical neuropsychologists from the neuropsychology department at the RevArte Rehabilitation Hospital) to identify items from existing sensory sensitivity questionnaires that match the experience of subjective sensory hypersensitivity in stroke patients and to add items if they felt that certain experiences were lacking.

We included some items from the English versions of the Highly Sensitive Person Scale (Aron and Aron, 1997), the Sensory Hypersensitivity Scale (Dixon et al, 2016), and the Sensory Perception Quotient (Tavassoli et al, 2014) and had them translated to Dutch using back translation by two independent translators. Additionally, we included items based on the Dutch versions of the Adolescent/Adult Sensory Profile (Brown and Dunn, 2002; Rietman, 2007) and the Glasgow Sensory Questionnaire (Kuiper et al, 2019; Robertson and Simmons, 2013). Example items are provided in Table 4.

TABLE 3. Characteristics of the Study Participants

	Stroke Patients			Controls	
Characteristic	Case #1	Case #2	Case #3	Matched Control Group Case #1	Matched Control Group Cases #2 and #3
N	1	1	1	10	9
Sex	Female	Male	Male	Female	Male
Age (years)	67	72	71	60 ± 11	60 ± 11
Years of education	12	12	12	15 ± 2	14 ± 4
Time since stroke (months)	6†	2	3		
Type of stroke	Ischemic	Ischemic	Ischemic		
Lesion location	Right hemisphere	Right hemisphere	Right hemisphere		

Values are presented as M ± SD unless noted otherwise.

†Case #1 had a previous infarction with a lesion in the right temporal–occipital region (visible on slices $z = -12$ in Figure 2). For this infarction, Case #1 did not receive rehabilitation, and the medical file did not mention motor or cognitive deficits related to this infarction.

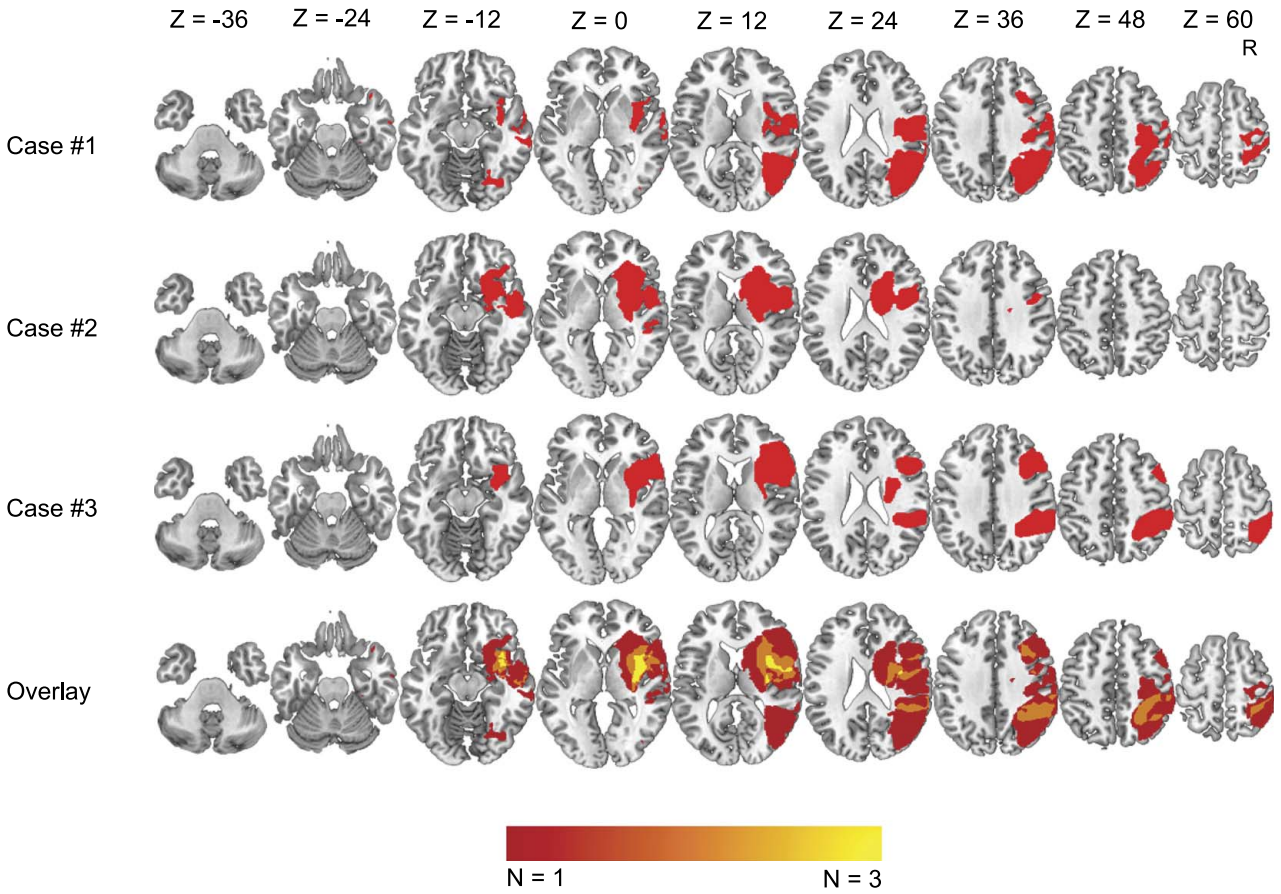

FIGURE 2. Lesion maps of the individual lesions of each stroke patient, and a lesion overlay plot projected on axial slices of the T1-weighted Ch2 template MRI from the Montreal Neurological Institute. Lesions were delineated on clinical fluid-attenuated inversion recovery scans for Cases #1 and #2 using the Clusterize toolbox (de Haan et al, 2015). Due to lower quality of the clinical CT scan from Case #3, we manually delineated his lesion following the procedure outlined by Biesbroek et al (2019). Normalization of CT and MR scans was performed using the Clinical Toolbox (Rorden et al, 2012) under SPM12. Montreal Neurological Institute coordinates of each transverse section (*z* axis) are provided. Lesion maps were overlaid on a normalized canonical image (ch2better-template) available in the MRICron software using the neurologic convention. The color scale indicates the number of cases having a lesion in this voxel. Lesion overlap across the three cases was found in the right anterior insula, the claustrum, and the Rolandic operculum.

Our sensory sensitivity questionnaire included multiple modalities assessing visual, auditory, tactile, olfactory, gustatory, environmental temperature, vestibular, and pain sensitivity. Items that could represent a sensitivity to multiple sensory stimuli across different modalities that are presented simultaneously (ie, "I get irritated when there is a lot going on around me") were included to form the multisensory sensitivity subscale. Per modality, we assessed if the stroke patients experienced a change in their sensory sensitivity from pre- to poststroke.

In order to prevent acquiescence bias—the tendency to agree with all items without it reflecting the responder's actual opinion—we included four items that were reverse coded. Each item could be answered using a 5-point Likert scale (*almost never*, *seldom*, *sometimes*, *frequently*, and *almost always*). Completion of the first part of the questionnaire resulted in a total sensory sensitivity score as well as modality-specific sensitivity scores.

The second part of the questionnaire contains 10 open-ended questions that assess whether the stroke patients experienced a change in their sensory sensitivity from pre- to poststroke and provide a detailed description of the changes in sensory sensitivity that they experienced. These items were also used to acquire data on the impact of subjective sensory hypersensitivity on their daily functioning (ie, "Do you feel sensory hypersensitivity has impacted your life? In what manner?"). Completion of the entire questionnaire took ~20 minutes.

Oxford Cognitive Screen. To screen cognition, we used version A of the Dutch version of the Oxford Cognitive Screen (OCS–NL; Huygelier et al, 2020). The OCS–NL is a short neuropsychological battery that uses 11 tasks to assess impairment in five cognitive domains (ie, attention, memory, language, praxis, and numeracy). Additionally, the OCS–NL includes a clinical confrontation test to assess visual field deficits. A detailed

TABLE 4. Example Items of the Sensory Sensitivity Questionnaire per Sensory Modality

Sensory Modality	Example Item
Multisensory	I get easily overwhelmed by strong sensory stimuli.
Visual	I am sensitive to bright light.
Auditory	I get overwhelmed by loud sounds.
Tactile	I cut the labels from my clothes.
Olfactory	I have a strong sense of smell.
Gustatory	I do not eat food with a strong taste (eg: very spicy, sour, or sweet food).
Environmental temperature	I get overwhelmed when I feel too hot or too cold.
Vestibular	I avoid elevators and/or escalators because I do not like the movement.
Pain	I can handle a large amount of pain.

description of the 11 tasks and the cutoff values for each task can be found in Huygelier et al (2020). The OCS–NL can be completed within 20 minutes.

Structural Anamnesis. To assess each patient's match to the in- and exclusion criteria, we conducted a structural anamnesis consisting of questions regarding their medical background. Additional questions regarding lesion location and time since stroke were answered by studying the stroke patients' medical files.

Procedure

Stroke Patients. We collected the stroke patients' data at the RevARte Rehabilitation Hospital in a quiet room without distraction. After acquiring written informed consent, patients completed the sensory sensitivity questionnaire and the OCS–NL. The session ended with the structural anamnesis interview and debriefing, during which we answered the patients' questions. Participation consisted of one session that lasted maximally 1½ hours. Sufficient breaks were offered during the session to promote feasibility. It was possible to split participation into two sessions if needed.

Control Group. After acquiring informed consent, we sent the neurotypical adults the link to an online version of the sensory sensitivity questionnaire. We also asked these individuals (a) for basic demographic information (sex, age, and education level), (b) if they had a probable history of neurologic or psychiatric disease, and (c) if they had a formal diagnosis of autism spectrum disorder or attention deficit hyperactivity disorder. Participation consisted of a single online session that lasted maximally 25 minutes.

Data Availability

The data set that was acquired and analyzed during the current study is available via https://doi.org/10.6084/m9.figshare.14140988.v2.

Statistical Analysis

To compare the raw scores of the three cases to those of their matched control group, we ran three different analyses. First, because sensory sensitivity is a continuous trait, and neurotypical adults can also be hypersensitive (Greven et al, 2019; Kuiper et al, 2019), we considered percentile scores. We assessed the point estimate of the percentage of the control population that would score lower than each stroke patient (ie, the estimated population percentile of the stroke case) following the recommendations of Crawford and Garthwaite (2002) using the software package Singlims_ES. The t statistic described by these authors allows the raw score of a patient to be compared to that of a matched control group. In addition, the statistic computes an estimate of the effect size and an estimate of the percentage of the control population that would obtain a score lower than that of each stroke patient (as well as the 95% confidence limits) (Crawford et al, 2010). This statistical method is suitable even in very small control samples (ie, $n = 5$) (Crawford and Howell, 1998).

Second, we assessed the point and interval estimates of the effect size of the difference between the raw score of the patient and the mean sensory sensitivity score of the matched control group (as described by Crawford et al, 2010). Crawford et al (2010) recommend focusing on the effect size in case-control design because it is not dependent on sample size (in contrast to significance testing) (see also, Sullivan and Feinn, 2012). We considered an effect size ≥ 2 to indicate exceptionally high sensory sensitivity (based on the recommendation of Hendriks et al, 2020). If the raw score of the stroke patient was $\geq$95th percentile and the point estimate of the effect size was ≥ 2, we considered the patient to be hypersensitive (similar to Kuiper et al, 2019).

Last, we compared the raw scores of each patient to the mean sensory sensitivity score of the matched control group. Because we were interested in hypersensitivity (instead of both hypo- and hypersensitivity), the reported P values are one-tailed. To correct for multiple comparisons, we used the adjustment method proposed by Benjamini and Hochberg (1995). No analyses were preregistered before data collection.

Results

Sensory Sensitivity Questionnaire

Case #1. Case #1 reported a poststroke change in her sensitivity to visual, auditory, olfactory, environmental temperature, and pain stimuli (Table 5). In an attempt to cope with her subjective heightened visual sensitivity to bright lights and flashing or moving images, she reported wearing sunglasses while watching television. In the days following her stroke, Case #1 had an intense hypersensitivity to smell, which has since normalized. During sensory overload, Case #1 expressed feeling tired, nauseated, and anxious. Due to her perceived hypersensitivity to background chatter, Case #1 did not attend social gatherings, causing her to feel socially isolated.

Regarding visual, environmental temperature, pain, and general sensory sensitivity (the Total score on the sensory sensitivity questionnaire), Case #1's raw scores on the questionnaire were indicative of subjective sensory hypersensitivity because her estimated percentiles

TABLE 5. Stroke Patients' Answers on the Open-ended Questions of the Sensory Sensitivity Questionnaire

Sensory Modality	Case #1	Case #2	Case #3
Did you experience a change in your sensitivity to sensory stimuli from pre- to poststroke?	Yes	Yes	Yes
Multisensory stimuli	No	Yes	No
Visual stimuli	Yes	No	No
Auditory stimuli	Yes	No	Yes
Tactile stimuli	No	No	No
Olfactory stimuli	Yes	Yes	No
Gustatory stimuli	No	No	No
Environmental temperature	Yes	Yes	No
Vestibular stimuli	No	Yes	No
Pain	Yes	Yes	Yes
Detailed descriptions of experienced sensory hypersensitivity and its impact on daily life	"After my stroke, I had to start wearing sunglasses while watching television because of my hypersensitivity to the bright light of the television screen and the flashing images on the screen." "Since my stroke, I started disliking everyday noises (eg, the sound from the television or a group of people who are talking)." "My sense of smell had heightened extremely in the first few days after my stroke. This has improved after the first week." "I do not tolerate warmer temperatures (eg, a room where the heating is on) as well as before my stroke. Just a small increase in temperature causes me to feel overwhelmed. I do not like when my husband turns on the heating in our house, even when it is cold outside." "It has become much harder for me to ignore pain. I have the feeling that I am much more sensitive for pain. I experience pain more intensely as compared to before my stroke." "When I am surrounded by a lot of sensory stimuli, I feel tired, nauseous, and anxious." "I avoid social gatherings."	"I feel extremely overwhelmed when I am in situations where there is visual and auditory stimulation (eg, when I have to listen to my therapist during my physical therapy while there is also a radio playing in the background and a lot of people moving around me). I never experienced this before my stroke." "I hate being in the presence of people who wear perfume, even when they do not wear a lot of perfume. I am also more sensitive to the smell of soaps or detergent as compared to before my stroke." "After my stroke, I started noticing small changes in environmental temperature. I often feel like it is too warm in certain rooms while my family members and other patients are not bothered by the temperature." "When I sit in a moving elevator or wheelchair, I feel very uncomfortable. The feeling of those movements is terrible." "I need time alone to recover from the sensory stimulation that I get throughout the day. So I ask my visitors to visit me very shortly or not as often as I would like. I get less and less social contact."	"I get my physical therapy in a special room where there are no other people or other noises. Due to my hypersensitivity to noises, it is impossible for me to practice or eat in the same room as other patients." "My family wanted to take me to the hospital cafeteria to drink a coffee. After 15 minutes, I had to leave my family behind to go back to my room to recover from the overload of sounds that I experienced. My family was very surprised because before my stroke, I loved going to cafes." "I find it much harder than before my stroke to ignore low levels of pain." "When I am surrounded by a lot of noise, I feel very nervous and stressed. It feels very uncomfortable" "I try to avoid situations where there is a lot of noise."

were ≥95th percentile and the point estimates of the effect sizes were ≥2 (Figure 3A and Table 6). Case #1's general sensory sensitivity score was significantly higher than the mean general sensory sensitivity score of her matched control group (n = 10).

When looking at the sensory modalities separately, Case #1 scored significantly higher on the items assessing visual, environmental temperature, and pain sensitivity compared with the mean score per sensory modality of her matched control group (Figure 3A). These differences were no longer significant after adjustment for multiple comparisons using the adjustment method of Benjamini and Hochberg (1995). Details of the statistical test values and the 95% CIs of the estimates are provided in Table 6.

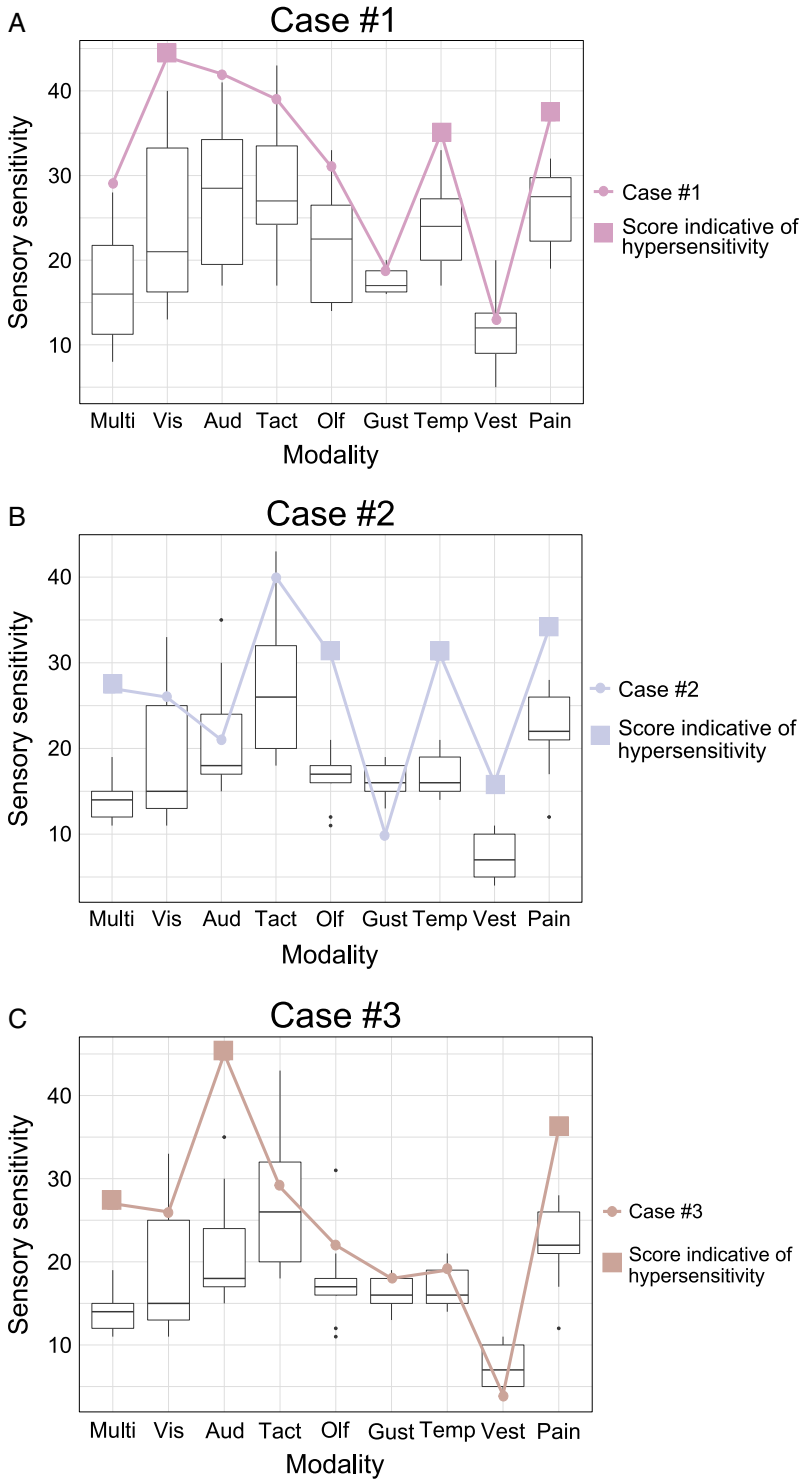

FIGURE 3. Stroke patients' scores on the sensory sensitivity questionnaire compared with the scores of their respective matched control group. The boxplots represent the distribution of the scores of the neurotypical controls. The lines visualize the scores of the stroke patients. The squares indicate scores of which the patient's estimated percentile is ≥95th percentile and effect size is ≥2. **Aud** = auditory. **Gust** = gustatory. **Multi** = multisensory. **Olf** = olfactory. **Tact** = tactile. **Temp** = environmental temperature. **Vest** = vestibular. **Vis** = visual.

TABLE 6. Scores on the Sensory Sensitivity Questionnaire of the Stroke Patients Compared to Scores From Their Respective Matched Control Group

	Controls (n = 10)			Estimated Percentile		Estimated Effect Size (Z_{cc})		Significance Test		
Scale	M	SD	Case Score	Point	95% CI	Point	95% CI	*t*	*P*	Adj. *P*
Case #1										
Multisensory	17	7	29	94	78; 100	1.8	0.8; 2.8	1.7	0.1	0.11
Visual	24	10	44	95	81; 100	2.0	0.9; 3.1	1.9	0.046*	0.1
Auditory	28	9	42	93	75; 100	1.7	0.7; 2.6	1.6	0.1	0.1
Tactile	30	9	39	84	62; 97	1.1	0.3; 1.9	1.1	0.2	0.2
Olfactory	22	7	31	89	68; 99	1.4	0.5; 2.2	1.3	0.1	0.2
Gustatory	18	1	19	83	60; 96	1.0	0.2; 1.8	1.0	0.2	0.2
Environmental temperature	24	5	35	95	81; 100	2.0	0.9; 3.1	1.9	0.045*	0.1
Vestibular	11	4	13	63	39; 84	0.4	−0.3; 1	0.3	0.4	0.4
Pain	26	4	37	98	88; 100	2.4	1.2; 3.7	2.3	0.02*	0.1
Total score	199	43	289	96	83; 100	2.1	1.0; 3.2	2.0	0.04*	0.1
	Controls (n = 9)									
Case #2										
Multisensory	15	5	27	97	85; 100	2.3	1.0; 3.6	2.2	0.03*	.1
Visual	19	8	26	81	56; 96	1.0	0.1; 1.8	0.9	0.2	0.2
Auditory	22	7	21	47	23; 72	−0.1	−0.7; 0.6	−0.1	0.5	0.5
Tactile	27	8	40	91	71; 99	1.6	0.6; 2.6	1.5	0.1	0.1
Olfactory	18	6	31	97	84; 100	2.3	1.0; 3.5	2.2	0.03*	0.1
Gustatory	16	2	10	1	0; 8	−3.0	−4.6; −1.4	−2.9	0.01*	0.1
Environmental temperature	17	2	31	100	100; 100	6.0	3.0; 8.9	5.7	0.0002***	0.007*
Vestibular	7	3	16	99	94; 100	3.3	1.6; 5	3.1	0.007**	0.1
Pain	22	5	34	97	86; 100	2.4	1.1; 3.8	2.3	0.03*	0.1
Total score	162	26	236	99	91; 100	2.9	1.3; 4.4	2.7	0.01*	0.1
	Controls (n = 9)									
Case #3										
Multisensory	15	5	27	97	85; 100	2.3	1.0; 3.6	2.2	0.03*	0.1
Visual	19	8	26	81	56; 96	1.0	0.1; 1.8	0.9	0.2	0.2
Auditory	22	7	45	99	95; 100	3.4	1.6; 5.2	3.2	0.006**	0.1
Tactile	27	8	29	59	34; 82	0.3	−0.4; 0.9	0.2	0.4	0.4
Olfactory	18	6	22	74	49; 93	0.7	0; 1.4	0.7	0.3	0.3
Gustatory	16	2	18	80	55; 96	0.9	0.1; 1.7	0.9	0.2	0.2
Environmental temperature	17	2	19	80	55; 96	0.9	0.1; 1.7	0.9	0.2	0.2
Vestibular	7	3	4	14	2; 38	−1.2	−2.1.; −0.3	−1.1	0.1	0.2
Pain	22	5	36	99	90; 100	2.8	1.3; 4.3	2.7	0.01*	0.1
Total score	162	26	226	98	87; 100	2.5	1.1; 3.8	2.4	0.02*	0.1

P values were adjusted for multiple comparisons using the adjustment method of Benjamini and Hochberg (1995).
*Significant at $P < 0.05$.
**Significant at $P < 0.01$.
***Significant at $P < 0.001$.

Case #2. Case #2 reported a poststroke change in his sensitivity to multisensory (especially the combination of visual and auditory stimuli), olfactory, environmental temperature, vestibular (eg, when standing or sitting in a moving elevator), and pain stimuli (Table 5). He had difficulty concentrating in the presence of irrelevant visual or auditory stimuli. At moments of sensory overload, Case #2 described feeling tired and uneasy, as well as having the urge to seek out privacy. As with Case #1, Case #2 had less social contact as a result of his sensory hypersensitivity.

Regarding multisensory, olfactory, environmental temperature, vestibular, pain, and general sensory sensitivity, Case #2's raw scores on the questionnaire were indicative of subjective sensory hypersensitivity because his estimated percentiles were ≥95th percentile and the

point estimates of the effect sizes were ≥2 (Figure 3B and Table 6). Case #2's general sensory sensitivity score was significantly higher than the mean general sensory sensitivity score of his matched control group (n = 9).

When looking at the sensory modalities separately, Case #2 scored significantly higher on the items assessing multisensory, olfactory, environmental temperature, vestibular, and pain sensitivity compared with the mean score per sensory modality of his matched control group. Case #2 scored significantly lower on his gustatory sensitivity compared with his matched control group. However, he did not report poststroke changes in his gustatory sensitivity. Except for sensitivity to environmental temperature, these differences were no longer significant after adjustment for multiple comparisons using the adjustment method of Benjamini and Hochberg (1995). Details of the statistical test values and the 95% CIs of the estimates are provided in Table 6.

Case #3. Case #3 reported a poststroke change in his sensitivity to auditory and pain stimuli (Table 5). He reported especially high distractibility as a result of auditory stimulation. When overloaded by sensory stimuli, Case #3 described getting a severe headache and feeling anxious.

Regarding multisensory, auditory, pain, and general sensory sensitivity, Case #3's raw scores were indicative of subjective sensory hypersensitivity because his estimated percentiles were ≥95th percentile and the point estimates of the effect sizes were ≥2 (Figure 3C and Table 6). Case #3's general sensory sensitivity score was significantly higher than the mean general sensory sensitivity score of his matched control group (n = 9).

When looking at the sensory modalities separately, Case #3 scored significantly higher on the items assessing multisensory, auditory, and pain sensitivity compared with the mean score per sensory modality of the matched control group. The differences between Case #3's raw scores and the mean scores of the matched control group were no longer significant after adjustment for multiple comparisons using the adjustment method of Benjamini and Hochberg (1995). Details of the statistical test values and the 95% CIs of the estimates are provided in Table 6.

Oxford Cognitive Screen

Table 7 provides an overview of the stroke patients' performance on the OCS–NL. Scores indicating an atypical score based on the cutoff values specified by Huygelier and colleagues (2020) are presented in bold. The stroke patients performed near ceiling level on the tasks regarding language, praxis, and memory. Cases #1 and #2 showed an impairment on one of the numeracy tasks. All three stroke patients showed an impaired score on the broken hearts cancellation task, which assesses selective attention.

For two of the patients, performance on the OCS–NL may have been disrupted by their sensory sensitivity. Case #1 could not complete the broken hearts cancellation task because she reported feeling overwhelmed by the large number of items on the page. Case #2 had difficulty completing the executive set-switching task because he reported finding it hard to ignore the distractors during the baseline condition. In contrast to what is expected based on the cognitive demands of the different conditions within the executive task (with the set-switching condition being more cognitively demanding than the baseline conditions), Case #2 performed better on the set-switching condition than the baseline condition due to high distractibility during the baseline condition.

TABLE 7. Stroke Patients' Performance on the Oxford Cognitive Screen (Dutch Version)

Task	Range of Possible Scores	Case #1	Case #2	Case #3
Language				
Picture naming	0–4	4	4	3
Semantics	0–3	3	3	3
Sentence reading	0–15	15	15	15
Numeracy				
Number writing	0–3	3	**2**	3
Calculations	0–4	**2**	3	4
Praxis				
Meaningless gesture imitation	0–12	11	12	12
Memory				
Orientation	0–4	4	4	4
Verbal memory: free recall and recognition	0–4	4	3	4
Episodic memory: recognition	0–4	4	3	4
Attention				
Broken hearts cancellation				
Total amount of targets	0–50	**14†**	**35**	**23**
Object asymmetry	−50, 50	**5**	0	**1**
Space asymmetry	−20, 20	**12**	−2	0
Set-switching	−12, 12	**4**	**−2**	3

Scores that indicate impaired functioning (based on the cutoff values specified by Huygelier et al (2020) are presented in bold.

†The broken hearts cancellation task was discontinued due to experiences of sensory overload.

Structural Anamnesis

None of the cases (or their medical files) reported having a neurologic, psychiatric, or other medical condition that could explain their subjective sensory hypersensitivity.

DISCUSSION

Literature Review

Our literature review on poststroke subjective sensory hypersensitivity identified four case reports that

linked insular lesions to subjective sensory hypersensitivity in one or two sensory modalities (Table 1). It is noteworthy that only four studies could be identified by our systematic search of the available literature, which indicates the lack of scientific attention for the neuroanatomy of poststroke subjective sensory hypersensitivity. This lack of scientific attention clearly contrasts with the clinical impact of these symptoms reported by the stroke patients in our multiple case study (Table 5) and the prevalence mentioned by Chung and Song (2016).

Of the four case reports, Mak and colleagues (2005) focused on olfactory and gustatory hypersensitivity, Boucher and colleagues (2015) focused on auditory hypersensitivity, and Cantone et al (2019) focused on visual hypersensitivity (ie, poststroke feelings of fear and disgust in response to complex visual stimuli). However, close reading of the cases showed evidence for multimodal hypersensitivity after insular damage. For example, even though Boucher and colleagues (2015) focused on poststroke hyperacusis, their two cases also reported being hypersensitive to other sensory modalities (ie, comorbid tactile and olfactory hypersensitivity), and the case discussed by Mak and colleagues (2005) reported a comorbid poststroke change in his sensitivity to environmental temperature in addition to olfactory and gustatory hypersensitivity.

The results reported by Pritchard et al (1999) are more difficult to interpret. They compared self-reported taste intensity between the ipsilesional and contralesional side of the tongue for different taste stimuli. Three of their four patients with insular lesions reported a lower taste intensity when taste stimuli were applied to the ipsilesional side of the tongue compared with taste stimuli applied to the contralesional side of the tongue. The authors interpreted this finding as evidence for an ipsilesional taste deficit after insular damage. However, these results could also indicate a hypersensitivity to taste on the contralesional side of the tongue (similar to Mak et al, 2005; Table 1).

From the article by Pritchard and colleagues (1999), we can only deduce difference ratings (ie, ipilesional rating vs contralesional rating); absolute intensity ratings for each hemibody separately are not included, thereby complicating interpretation of the results.

Overall, our literature review suggests that poststroke subjective sensory hypersensitivity can extend across several sensory modalities (visual, auditory, olfactory, gustatory), although it remains unclear in the aforementioned studies whether poststroke sensory hypersensitivity was uni- or multimodal within one patient.

Multiple Case Study

Regarding this remaining uncertainty, we used a multiple case design to extend the results of the previous case studies (Boucher et al, 2015; Cantone et al, 2019; Mak et al, 2005) (Table 1) by presenting three cases with subjective poststroke multimodal hypersensitivity. Our sensory sensitivity questionnaire showed that the subjective sensitivity of these three stroke patients could indeed be considered hypersensitive as compared to the self-reported sensitivity of their respective matched control group. In our study, Case #1 was found to be hypersensitive to visual, environmental temperature, and pain stimuli; Case #2 was found to be hypersensitive to multisensory, olfactory, environmental temperature, vestibular, and pain stimuli; and Case #3 was found to be hypersensitive to multisensory, auditory, and pain stimuli.

The modalities in which the patients experienced subjective sensory hypersensitivity were variable, suggesting that poststroke subjective sensory hypersensitivity is a complex, idiosyncratic symptomatology. Due to their subjective sensory hypersensitivity, the stroke patients reported reduced quality of life across several life domains (ie, social contact, mental, and physical well-being), thereby emphasizing the clinical importance of diagnosing poststroke subjective sensory hypersensitivity.

The lesions of the three stroke patients overlapped in the right anterior insula, the claustrum, and the Rolandic operculum. An association between insular damage and poststroke subjective sensory hypersensitivity is supported by previous case studies (Table 1). Although the previous studies focused mostly on unimodal subjective sensory hypersensitivity, we provide preliminary evidence for multimodal subjective sensory hypersensitivity after an insular lesion as well as self-reported heightened interoception (eg, subjective sensory hypersensitivity to pain; reported by all three cases).

The Role of the Insula in Subjective Sensory Hypersensitivity

The role of the insula in the subjective interpretation of multimodal sensory stimuli is complemented by fMRI data. Hyperactivation of the insula in response to sensory stimuli has been linked to subjective sensory hypersensitivity in individuals with fibromyalgia (López-Solà et al, 2014; for a meta-analysis, see Dehghan et al, 2016). Additionally, insula abnormalities have been mentioned in other clinical populations with abnormal sensory processing such as individuals with mild traumatic brain injury (Li et al, 2020), autism spectrum disorder (Di Martino et al, 2014), schizophrenia (Wylie and Tregellas, 2010), Tourette syndrome (Cavanna et al, 2017), or attention deficit disorder (Lopez-Larson et al, 2012). However, because stroke leads to both structural damage and impaired functionality due to diaschisis or disconnection, the neural mechanisms of subjective sensory hypersensitivity might include disruption of a larger neural network instead of focal damage to a specific structure.

Two recent reviews (Greven et al, 2019; Ward, 2019) proposed large-scale brain networks as neural markers of subjective sensory hypersensitivity, with a strong emphasis on the salience network. The insula is an important hub of the salience network and is often coactivated with the rest of the network (Menon and Uddin, 2010). Because the salience network is involved in the detection of relevant sensory input as well as attentional filtering of irrelevant

input (Menon, 2015), it is indeed plausible that disruption of this network can lead to subjective sensory hypersensitivity, especially when multiple regions of the network are compromised. Functional salience network abnormalities (not solely limited to the insula) have previously been linked to subjective sensory hypersensitivity in children with autism spectrum disorder (Green et al, 2016). It remains unclear if structural damage to other hubs of the salience network (not encompassing the insula) can also result in subjective sensory hypersensitivity.

All three patients that we studied sustained right-hemispheric damage, which could suggest an association between right insular damage and subjective sensory hypersensitivity. Indeed, previous fMRI research associated functional abnormalities in the right insula to subjective sensory hypersensitivity in individuals with chronic pain (ie, fibromyalgia) (Harte et al, 2016; López-Solà et al, 2014). However, it remains unclear if there is a differential hemispheric contribution to subjective sensory hypersensitivity because several case studies have suggested that subjective sensory hypersensitivity is also present after a left insular lesion (Boucher et al, 2015; Mak et al, 2005; Pritchard et al, 1999). Furthermore, all three of our patients had sustained an ischemic stroke, and just one of the cases described in Table 1 had sustained a hemorrhagic stroke. Although overrepresentation of ischemic stroke (vs hemorrhagic stroke) in the case studies could suggest an association between ischemic stroke and subjective sensory hypersensitivity, these results may just reflect the difference in prevalence between ischemic and hemorrhagic strokes (eg, Krishnamurthi et al, 2015). Furthermore, the stroke type of three of the cases identified by the systematic review was unclear, thereby limiting our available data on the relationship between stroke type and subjective sensory hypersensitivity. As such, further research is needed to investigate the prevalence of subjective sensory hypersensitivity after ischemic and hemorrhagic stroke, respectively, as well as how stroke type might relate to the underlying neuroanatomy.

Given that brain damage does not respect the boundaries of neuroanatomical structures, it is possible that damage to structures or white matter tracts that are adjacent to the insula belong to the neural underpinnings of subjective sensory hypersensitivity. A possibility is the insular–claustrum region (including the external and extreme capsule). Due to proximity and shared vascularization of these two structures, it is hard for fMRI and lesion studies to distinguish between them (Crick and Koch, 2005). Therefore, previous research focusing on the involvement of the insula in subjective sensory hypersensitivity might reflect involvement of the entire insular–claustrum region.

The claustrum, a neglected region, is known to support the processing and integration of multimodal sensory information (Crick and Koch, 2005; Reser and Picard, 2020), and claustrum lesions have been shown to result in sensory abnormalities (Maximov et al, 2018). A recent rodent study (Qadir et al, 2018) showed that the claustrum is involved in the detection of salient stimuli and is bidirectionally connected to important hubs of the salience network (eg, the anterior cingulate cortex). Damage to white matter tracts that are adjacent to the insula and the claustrum, and that connect these two regions (eg, the extreme capsule) or connect these regions to other cortical regions (eg, the external capsule), might increase vulnerability for poststroke subjective sensory hypersensitivity. This hypothesis is supported by studies reporting external capsule abnormalities in clinical populations with sensory processing disorders, such as individuals with mild traumatic brain injury (Narayana et al, 2014) and those with chronic pain (Lieberman et al, 2014). Further research allowing for investigation of the relationship between neuroanatomy and poststroke subjective sensory hypersensitivity with high structural resolution is needed.

Last, Haroutounian et al (2018) suggested that tactile hypersensitivity in the context of central poststroke pain originates from a maladaptive sensitization of central neurons to peripheral input, causing non-nociceptive input to cross a nociceptive threshold (that it would not cross under normal circumstances). It would be interesting to study if a similar interaction between the central and peripheral nervous systems can be found for poststroke subjective hypersensitivity to other sensory modalities as well as without comorbid pain.

A Relationship Between Subjective Sensory Hypersensitivity and Selective Attention

It must be noted that our three stroke patients all presented with both poststroke subjective sensory hypersensitivity and indications of selective attention impairments. In Cases #1 and #2, subjective sensory hypersensitivity hindered cognitive functioning during the attention-based tasks of the OCS–NL, and performance on these tasks was impaired in all three stroke patients.

A relationship between attention and subjective sensory hypersensitivity has previously been proposed in the neurotypical population and in other clinical groups (eg, autism spectrum disorder, attention deficit hyperactivity disorder, schizophrenia) (Marco et al, 2011; Micoulaud-Franchi et al, 2015; Panagiotidi et al, 2018). The described link between subjective sensory hypersensitivity and insular lesions might reflect this relationship between attention and subjective sensory hypersensitivity because the salience network is involved in attentional filtering (Menon, 2015). Poststroke subjective sensory hypersensitivity might be indicative of underlying selective attention difficulties, which would explain why patients report the most intense impairments when encountering multimodal stimuli, and that the impacted sensory modality is idiosyncratic and possibly arbitrary (Thielen and Gillebert, 2019).

Because we used only paper-and-pencil tasks to screen for deficits in selective attention, subtle attentional impairments may have been missed. Previous research has indeed shown that computer-based attentional testing is more sensitive to these subtle attention deficits (Bonato et al, 2013; Gillebert et al, 2011). Further research in-

cluding a comprehensive neuropsychological assessment (preferably including computerized attentional testing) is needed to determine if attention impairments are indeed part of the behavioral mechanisms of subjective sensory hypersensitivity.

Study Limitations

A limitation of the review process was that a gray literature search was not conducted, which could have led to recent emerging research being neglected. Our case study also had limitations, one of which was the small sample size. A larger control sample matched in sex, age, and education level to each case would have been preferable. Furthermore, we studied stroke patients with subjective sensory hypersensitivity in the subacute stage after stroke (ie, minimally 2 months after stroke), which limits our understanding of the relationship between lesion location and subjective symptoms because of the influence of functional reorganization. All three of our stroke patients had a right-hemispheric lesion, thereby biasing our results toward a right-hemispheric dominance for subjective sensory hypersensitivity. We recommend that future studies include patients with left, right, and bilateral strokes in order to expand our knowledge of hemispheric contribution to subjective sensory hypersensitivity.

Last, because isolated insula lesions are rare, and the insula is commonly damaged after middle cerebral arteries strokes due to its location and vasculature (Caviness et al, 2002), the suggested relationship between the insula and poststroke subjective sensory hypersensitivity might merely reflect differential vulnerability. For future research, we suggest using a technique that can study the relationship between structural lesions and subjective sensory hypersensitivity at a small structural scale while controlling for lesion volume. For instance, voxel-based lesion symptom mapping can be used to investigate the relationship between structural lesions and subjective sensory hypersensitivity at the level of an individual voxel (Mirman et al, 2018; Rorden et al, 2007; Varjacic et al, 2018), thereby allowing us to determine which brain regions are crucial for poststroke alteration in sensory sensitivity and to predict behavioral deficits from lesion location without having to a priori exclude patients based on the presence or absence of a certain behavioral deficit.

In this study, we included patients based on a report of subjective sensory hypersensitivity in their medical files, which caused a sampling bias where patients with a higher symptom severity or greater introspective and communicative abilities had a larger chance to be included in the study. Voxel-based lesion symptom mapping could provide a better understanding of the neural mechanisms of poststroke subjective sensory hypersensitivity by comparing the lesion location of patients with and without poststroke subjective sensory hypersensitivity in a larger stroke sample. Voxel-based lesion symptom mapping has previously been used successfully in stroke patients to examine the neuroanatomy of a variety of cognitive functions, including attention and executive functions (Varjacic et al, 2018). This promising technique could help us to determine which regions play a role in poststroke subjective sensory hypersensitivity.

CONCLUSION

By presenting three cases of poststroke subjective sensory hypersensitivity, we hope to raise awareness for the clinical importance of recognizing multimodal poststroke hypersensitivity as a possible consequence of stroke as well as to outline some of the outstanding questions surrounding the neuroanatomy of these subjective symptoms. Gaining more insight on the neural basis of poststroke subjective sensory hypersensitivity as well as its behavioral mechanisms will be of high importance for adequate diagnosis and rehabilitation of these symptoms.

To date, it remains unclear if poststroke subjective sensory hypersensitivity reflects an abnormal affective interpretation of sensory stimuli (ie, the perceived unpleasantness or perceived intensity), attentional difficulties (ie, poorer selective attention, high distractibility), or abnormal bottom-up processing of sensory stimuli (ie, abnormal sensory thresholds). Systematic research on subjective sensory hypersensitivity and its behavioral and neural mechanisms in a heterogenous stroke sample can provide further answers to these outstanding questions.

ACKNOWLEDGMENTS

The authors thank Jo Verhaegen, MS, Nathalie Vaes, PhD, Sophie Huybrechts, MS, Sabine Bruynseraede, MS, Marijke Bernaerts, MS, and Lara Stroobants, MS, of the RevArte Rehabilitation Hospital for their expert advice on the construction of the sensory sensitivity questionnaire as well as their referral of suitable stroke patients.

REFERENCES

Acevedo B, Aron E, Pospos S, et al. 2018. The functional highly sensitive brain: a review of the brain circuits underlying sensory processing sensitivity and seemingly related disorders. *Philos Trans R Soc Lond B Biol Sci*. 373:20170161. doi:10.1098/rstb.2017.0161

Adolphs R. 2016. Human lesion studies in the 21st century. *Neuron*. 90: 1151–1153. doi:10.1016/j.neuron.2016.05.014.Human

Aikio R, Laaksonen K, Sairanen V, et al. 2021. CMC is more than a measure of corticospinal tract integrity in acute stroke patients. *Neuroimage Clin*. 32:102818. doi:10.1016/j.nicl.2021.102818

Alwawi DA, Dean E, Heldstab A, et al. 2020. A qualitative study of stroke survivors' experience of sensory changes. *Can J Occup Ther*. 87:298–306. doi:10.1177/0008417420941975

Aron EN, Aron A. 1997. Sensory-processing sensitivity and its relation to introversion and emotionality. *J Pers Soc Psychol*. 73:345–368. doi:10.1037/0022-3514.73.2.345

Benham G. 2006. The highly sensitive person: stress and physical symptom reports. *Pers Individ Differ*. 40:1433–1440. doi:10.1016/j.paid.2005.11.021

Benjamini Y, Hochberg Y. 1995. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J R Stat Soc Series B Stat Methodol*. 57:289–300. doi:10.111/J.2517-6161.1995.TB02031.X

Berthold-Lindstedt M, Ygge J, Borg K. 2017. Visual dysfunction is underestimated in patients with acquired brain injury. *J Rehabil Med*. 49:327–332. doi:10.2340/16501977-2218

Biesbroek JM, Kuijf HJ, Weaver NA, et al. 2019. Brain infarct segmentation and registration on MRI or CT for lesion-symptom mapping. *J Vis Exp. 2019 Sep 25:151*. doi:10.3791/59653

Bijlenga D, Tjon-Ka-Jie JYM, Schuijers F, et al. 2017. Atypical sensory profiles as core features of adult ADHD, irrespective of autistic symptoms. *Eur Psychiatry*. 43:51–57. doi:10.1016/j.eurpsy.2017.02.481

Bonan IV, Gaillard F, Tasseel Ponche S, et al. 2015. Early post-stroke period: a privileged time for sensory re-weighting? *J Rehabil Med*. 47: 516–522. doi:10.2340/16501977-1968

Bonato M, Priftis K, Umiltà C, et al. 2013. Computer-based attention-demanding testing unveils severe neglect in apparently intact patients. *Behav Neurol*. 26:179–181. doi:10.3233/ben-2012-129005

Boucher O, Turgeon C, Champoux S, et al. 2015. Hyperacusis following unilateral damage to the insular cortex: a three-case report. *Brain Res*. 1606:102–112. doi:10.1016/j.brainres.2015.02.030

Brown CE, Dunn W. 2002. *Adolescent/Adult Sensory Profile*. New York, New York: Psychological.

Callahan ML, Lim MM. 2018. Sensory sensitivity in TBI: implications for chronic disability. *Curr Neurol Neurosci Rep*. 18:56. doi:10.1007/1910-018-0867-x

Callahan ML, Storzbach D. 2019. Sensory sensitivity and posttraumatic stress disorder in blast exposed veterans with mild traumatic brain injury. *Appl Neuropsychol Adult*. 26:365–373. doi:10.1080/23279095.2018.1433179

Callahan ML, Binder LM, O'Neil ME, et al. 2018. Sensory sensitivity in Operation Enduring Freedom/Operation Iraqi Freedom veterans with and without blast exposure and mild traumatic brain injury. *Appl Neuropsychol Adult*. 25:126–136. doi:10.1080/23279095.2016.1261867

Cantone M, Lanza G, Bella R, et al. 2019. Fear and disgust: case report of two uncommon emotional disturbances evoked by visual disperceptions after a right temporal–insular stroke. *BMC Neurol*. 19:193. doi:10.1186/2883-019-1417-0

Carlsson GE, Möller A, Blomstrand C. 2009. Managing an everyday life of uncertainty—a qualitative study of coping in persons with mild stroke. *Disabil Rehabil*. 31:773–782. doi:10.1080/09638280802638857

Carlsson GE, Möller A, Blomstrand C. 2004. A qualitative study of the consequences of "hidden dysfunctions" one year after a mild stroke in persons <75 years. *Disabil Rehabil*. 26:1373–1380. doi:10.1080/09638280400000211

Cavanna AE, Black KJ, Hallett M, et al. 2017. Neurobiology of the premonitory urge in Tourette's syndrome: pathophysiology and treatment implications. *J Neuropsychiatry Clin Neurosci*. 29:95–104. doi:10.1176/appi.neuropsych.16070141

Caviness VS, Makris N, Montinaro E, et al. 2002. Anatomy of stroke, part I: an MRI-based topographic and volumetric system of analysis. *Stroke*. 33:2549–2556. doi:10.1161/01.STR.0000036083.90045.08

Chang TTL, Ciuffreda KJ, Kapoor N. 2007. Critical flicker frequency and related symptoms in mild traumatic brain injury. *Brain Inj*. 21: 1055–1062. doi:10.1080/02699050701591437

Chung SM, Song BK. 2016. Evaluation of sensory processing abilities following stroke using the Adolescent/Adult Sensory Profile: implications for individualized intervention. *J Phys Ther Sci*. 28: 2852–2856. doi:10.1589/jpts.28.2852

Crawford JR, Garthwaite PH. 2002. Investigation of the single case in neuropsychology: confidence limits on the abnormality of test scores and test score differences. *Neuropsychologia*. 40:1196–1208. doi:10.1016/S0028-3932(01)00224-X

Crawford JR, Howell DC. 1998. Comparing an individual's test score against norms derived from small samples. *Clin Neuropsychol*. 12: 482–486. doi:10.1076/clin.12.4.482.7241

Crawford JR, Garthwaite PH, Porter S. 2010. Point and interval estimates of effect sizes for the case-controls design in neuropsychology: rationale, methods, implementations, and proposed reporting standards. *Cogn Neuropsychol*. 27:245–260. doi:10.1080/02643294.2010.513967

Crick FC, Koch C. 2005. What is the function of the claustrum. *Philos Trans R Soc Lond B Biol Sci*. 360:1271–1279. doi:10.1098/rstb.2005.1661

de Haan B, Karnath HO. 2018. A hitchhiker's guide to lesion-behaviour mapping. *Neuropsychologia*. 115:5–16. doi:10.1016/j.neuropsychologia.2017.10.021

de Haan B, Clas P, Juenger H, et al. 2015. Fast semi-automated lesion demarcation in stroke. *Neuroimage Clin*. 9:69–74. doi:10.1016/j.nicl.2015.06.013

Dehghan M, Schmidt-Wilcke T, Pfleiderer B, et al. 2016. Coordinate-based (ALE) meta-analysis of brain activation in patients with fibromyalgia. *Hum Brain Mapp*. 37:1749–1758. doi:10.1002/hbm.23132

Di Martino A, Yan CG, Li Q, et al. 2014. The autism brain imaging data exchange: towards a large-scale evaluation of the intrinsic brain architecture in autism. *Mol Psychiatry*. 19:659–667. doi:10.1038/mp.2013.78

Dixon EA, Benham G, Sturgeon JA, et al. 2016. Development of the Sensory Hypersensitivity Scale (SHS): a self-report tool for assessing sensitivity to sensory stimuli. *J Behav Med*. 39:537–550. doi:10.1007/0865-016-9720-3

Elliott JE, Opel RA, Weymann KB, et al. 2018. Sleep disturbances in traumatic brain injury: associations with sensory sensitivity. *J Clin Sleep Med*. 14:1177–1186. doi:10.5664/jcsm.7220

Fukutake T, Hattori T. 1998. Auditory illusions caused by a small lesion in the right medial geniculate body. *Neurology*. 51:1469–1471. doi:10.1212/WNL.51.5.1469

Gillebert C, Mantini D, Thijs V, et al. 2011. Lesion evidence for the critical role of the intraparietal sulcus in spatial attention. *Brain*. 134: 1694–1709. doi:10.1093/brain/awr085

Glod M, Riby DM, Rodgers J. 2020. Sensory processing in Williams syndrome: a narrative review. *Rev J Autism Dev Disord*. 7:32–45. doi:10.1007/s40489-019-00174-x

Goodrich GL, Martinsen GL, Flyg HM, et al. 2014. Visual function, traumatic brain injury, and posttraumatic stress disorder. *JRRD*. 51: 547–558. doi:10.1682/JRRD.2013.02.0049

Green SA, Hernandez LM, Bookheimer SY, et al. 2016. Salience network connectivity in autism is related to brain and behavioral markers of sensory overresponsivity. *J Am Acad Child Adolesc Psychiatry*. 55:618–626.e1. doi:10.1016/j.jaac.2016.04.013

Green SA, Hernandez L, Tottenham N, et al. 2015. Neurobiology of sensory overresponsivity in youth with autism spectrum disorders. *JAMA Psychiatry*. 72:778–786. doi:10.1001/jamapsychiatry.2015.0737

Greven CU, Lionetti F, Booth C, et al. 2019. Sensory processing sensitivity in the context of environmental sensitivity: a critical review and development of research agenda. *Neurosci Biobehav Rev*. 98: 287–305. doi:10.1016/j.neubiorev.2019.01.009

Hallberg LRM, Hallberg U, Johansson M, et al. 2005. Daily living with hyperacusis due to head injury 1 year after a treatment programme at the hearing clinic. *Scand J Caring Sci*. 19:410–418. doi:10.1111/j.1471-6712.2005.00361.x

Haroutounian S, Ford AL, Frey K, et al. 2018. How central is central poststroke pain? The role of afferent input in poststroke neuropathic pain: a prospective, open-label pilot study. *Pain*. 159:1317–1324. doi:10.1097/j.pain.0000000000001213

Harte SE, Ichesco E, Hampson JP, et al. 2016. Pharmacologic attenuation of cross-modal sensory augmentation within the chronic pain insula. *Pain*. 157:1933–1945. doi:10.1097/j.pain.0000000000000593

Hendriks MPH, Mol BAW, Kessels RPC. 2020. Opinie: uniformiteit in de kwalitatieve beschrijving van scores op prestatietaken. *Tijdschrift voor Neuropsychologie*. 15:166–176.

Huygelier H, Schraepen B, Demeyere N, et al. 2020. The Dutch version of the Oxford Cognitive Screen (OCS–NL): normative data and their association with age and socio-economic status. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn*. 27:765–786. doi:10.1080/13825585.2019.1680598

Isaacs D, Riordan H. 2020. Sensory hypersensitivity in Tourette syndrome: a review. *Brain Dev*. 42:627–638. doi:10.1016/j.braindev.2020.06.003

Klit H, Finnerup NB, Andersen G, et al. 2011. Central poststroke pain: a population-based study. *Pain*. 152:818–824. doi:10.1016/j.pain.2010.12.030

Krishnamurthi RV, Moran AE, Feigin VL, et al. 2015. Stroke prevalence, mortality and disability-adjusted life years in adults aged 20–64 years in 1990–2013: data from the Global Burden of Disease 2013 Study. *Neuroepidemiology*. 45:190–202. doi:10.1159/000441098

Kuiper MW, Verhoeven EW, Geurts HM. 2019. The Dutch Glasgow Sensory Questionnaire: psychometric properties of an autism-specific sensory sensitivity measure. *Autism*. 23:922–932. doi:10.1177/1362361318788065

Laborey M, Masson F, Ribéreau-Gayon R, et al. 2014. Specificity of postconcussion symptoms at 3 months after mild traumatic brain injury: results from a comparative cohort study. *J Head Trauma Rehabil*. 29:28–36. doi:10.1097/HTR.0b013e318280f896

Landon J, Shepherd D, McGarry M, et al. 2016. When it's quiet, it's nice: noise sensitivity in schizophrenia. *Am J Psychiatr Rehabil*. 19: 122–135. doi:10.1080/15487768.2016.1162758

Landon J, Shepherd D, Stuart S, et al. 2012. Hearing every footstep: noise sensitivity in individuals following traumatic brain injury. *Neuropsychol Rehabil*. 22:391–407. doi:10.1080/09602011.2011.652496
Li F, Lu L, Chen H, et al. 2020. Neuroanatomical and functional alterations of insula in mild traumatic brain injury patients at the acute stage. *Brain Imaging Behav*. 14:907–916. doi:10.1007/1682-019-00053-3
Lieberman G, Shpaner M, Watts R, et al. 2014. White matter involvement in chronic musculoskeletal pain. *J Pain*. 15:1110–1119. doi:10.1016/j.jpain.2014.08.002
Lopez-Larson MP, King JB, Terry J, et al. 2012. Reduced insular volume in attention deficit hyperactivity disorder. *Psychiatry Res*. 204:32–39. doi:10.1016/j.pscychresns.2012.09.009
López-Solà M, Pujol J, Wager TD, et al. 2014. Altered functional magnetic resonance imaging responses to nonpainful sensory stimulation in fibromyalgia patients. *Arthritis Rheumatol*. 66: 3200–3209. doi:10.1002/art.38781
Mak YE, Simmons KB, Gitelman DR, et al. 2005. Taste and olfactory intensity perception changes following left insular stroke. *Behav Neurosci*. 119:1693–1700. doi:10.1037/0735-7044.119.6.1693
Marco EJ, Hinkley LBN, Hill SS, et al. 2011. Sensory processing in autism: a review of neurophysiologic findings. *Pediatr Res*. 69:48–54. doi:10.1203/PDR.0b013e3182130c54
Maximov GK, Hinova-Palova DV, Iliev AA, et al. 2018. Ischemic stroke of the left claustrum in a 55-year-old female: a case report. *Claustrum*. 3:1528135. doi:10.1080/20023294.2018.1528135
Menon V. 2015. Salience network. In: Toga AW, ed. *Brain Mapping: An Encyclopedic Reference*. Rockville, MD: Elsevier; 597–611. doi: 10.1016/B978-0-12-397025-1.00052-X
Menon V, Uddin LQ. 2010. Saliency, switching, attention and control: a network model of insula function. *Brain Struct Funct*. 214:655–667. doi:10.1007/s00429-010-0262-0
Micoulaud-Franchi JA, Lopez R, Vaillant F, et al. 2015. Perceptual abnormalities related to sensory gating deficit are core symptoms in adults with ADHD. *Psychiatry Res*. 230:357–363. doi:10.1016/j.psychres.2015.09.016
Mirman D, Landrigan JF, Kokolis S, et al. 2018. Corrections for multiple comparisons in voxel-based lesion-symptom mapping. *Neuropsychologia*. 115:112–123. doi:10.1016/j.neuropsychologia.2017.08.025
Moher D, Liberati A, Tetzlaff J, et al. 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ*. 339:b2535. doi:10.1136/bmj.b2535
Moola S, Munn Z, Tufanaru C, et al. 2020. Systematic reviews of etiology and risk. In: Aromataris E, Munn Z, eds. *JBI Manual for Evidence Synthesis*. Adelaide, Australia: JBI; 217–269. doi:10.46658/jbimes-20-08
Narayana PA, Yu X, Hasan KM, et al. 2014. Multi-modal MRI of mild traumatic brain injury. *Neuroimage Clin*. 7:87–97. doi:10.1016/j.nicl.2014.07.010
O'Kane JW, Spieker A, Levy MR, et al. 2014. Concussion among female middle-school soccer players. *JAMA Pediatr*. 168:258–264. doi:10.1001/jamapediatrics.2013.4518
Panagiotidi M, Overton PG, Stafford T. 2018. The relationship between ADHD traits and sensory sensitivity in the general population. *Compr Psychiatry*. 80:179–185. doi:10.1016/j.comppsych.2017.10.008
Pritchard TC, Macaluso DA, Eslinger PJ. 1999. Taste perception in patients with insular cortex lesions. *Behav Neurosci*. 113:663–671. doi:10.1037/0735-7044.113.4.663
Qadir H, Krimmel SR, Mu C, et al. 2018. Structural connectivity of the anterior cingulate cortex, claustrum, and the anterior insula of the mouse. *Front Neuroanat*. 12:100. doi:10.3389/fnana.2018.00100
Reser D, Picard F. 2020. Editorial: structure and function of the insula-claustrum region. *Front Neuroanat*. 14:14. doi:10.3389/fnana.2020.00014
Rietman A. 2007. *Adolescent/Adult Sensory Profile-NL Tieners en volwassenen 11 t/m 65+ jaar Handleiding*. Amsterdam, The Netherlands: Pearson Clinical & Talent Assessment.
Robertson AE, Simmons DR. 2013. The relationship between sensory sensitivity and autistic traits in the general population. *J Autism Dev Disord*. 43:775–784. doi:10.1007/0803-012-1608-7
Rorden C, Karnath HO. 2004. Using human brain lesions to infer function: a relic from a past era in the fMRI age. *Nat Rev Neurosci*. 5: 813–819. doi:10.1038/nrn1521
Rorden C, Karnath HO, Bonilha L. 2007. Improving lesion-symptom mapping. *J Cogn Neurosci*. 19:1081–1088. doi:10.1162/jocn.2007.19.7.1081
Rorden C, Bonilha L, Fridriksson J, et al. 2012. Age-specific CT and MRI templates for spatial normalization. *Neuroimage*. 61:957–965. doi:10.1016/j.neuroimage.2012.03.020
Schrupp LE, Ciuffreda KJ, Kapoor N. 2009. Foveal versus eccentric retinal critical flicker frequency in mild traumatic brain injury. *Optometry*. 80:642–650. doi:10.1016/j.optm.2009.04.097
Shepherd D, Heinonen-Guzejev M, Heikkilä K, et al. 2021. Sensitivity to noise following a mild traumatic brain injury: a longitudinal study. *J Head Trauma Rehabil*. 36:289–301. doi:10.1097/HTR.0000000000000645
Shepherd D, Landon J, Kalloor M, et al. 2020. The association between health-related quality of life and noise or light sensitivity in survivors of a mild traumatic brain injury. *Qual Life Res*. 29:665–672. doi:10.1007/1136-019-02346-y
Shepherd D, Landon J, Kalloor M, et al. 2019. Clinical correlates of noise sensitivity in patients with acute TBI. *Brain Inj*. 33:1050–1058. doi:10.1080/02699052.2019.1606443
Smith A. 2003. The concept of noise sensitivity: implications for noise control. *Noise Health*. 5:57–59.
Stansfeld SA, Shipley M. 2015. Noise sensitivity and future risk of illness and mortality. *Sci Total Environ*. 520:114–119. doi:10.1016/j.scitotenv.2015.03.053
Sullivan GM, Feinn R. 2012. Using effect size—or why the *p* value is not enough. *J Grad Med Edu*. 4:279–282. doi:10.4300/JGME-D-12-00156.1
Tanev KS, Federico LE, Sydnor VJ, et al. 2021. Neuropsychiatric symptoms in a occipito-temporal infarction with remarkable long-term functional recovery. *Cortex*. 137:205–214. doi:10.1016/j.cortex.2021.01.013
Tavassoli T, Hoekstra RA, Baron-Cohen S. 2014. The Sensory Perception Quotient (SPQ): development and validation of a new sensory questionnaire for adults with and without autism. *Mol Autism*. 5:29. doi:10.1186/2040-2392-5-29
Thielen H, Gillebert CR. 2019. Sensory sensitivity: Should we consider attention in addition to prediction? *Cogn Neurosci*. 10:158–160. doi:10.1080/17588928.2019.1593125
Thielen H, Tuts N, Welkenhuyzen L, et al. 2022. Sensory sensitivity after acquired brain injury: a systematic review. *J Neuropsychol*. 2022: 1–31. doi:10.1111/jnp.12284
Ueno Y, Takahashi A, Oshio A. 2019. Relationship between sensory-processing sensitivity and age in a large cross-sectional Japanese sample. *Heliyon*. 5:e02508. doi:10.1016/j.heliyon.2019.e02508
Varjacic A, Mantini D, Demeyere N, et al. 2018. Neural signatures of Trail Making Test performance: evidence from lesion-mapping and neuroimaging studies. *Neuropsychologia*. 115:78–87. doi:10.1016/j.neuropsychologia.2018.03.031
Ward J. 2019. Individual differences in sensory sensitivity: a synthesizing framework and evidence from normal variation and developmental conditions. *Cogn Neurosci*. 10:139–157. doi:10.1080/17588928.2018.1557131
Wylie KP, Tregellas JR. 2010. The role of the insula in schizophrenia. *Schizophr Res*. 123:93–104. doi:10.1016/j.schres.2010.08.027