Contents lists available at ScienceDirect







journal homepage: www.elsevier.com/locate/ynicl

Sharpened self-other distinction in attention deficit hyperactivity disorder

Rebecca Boehme^{a,d,*}, Morgan Frost Karlsson^a, Markus Heilig^{a,b,d}, Håkan Olausson^{a,c,d}, Andrea Johansson Capusan^{a,b}

^a Center for Social and Affective Neuroscience, Linköping University, Department of Biomedical and Clinical Sciences, 58185 Linköping, Sweden

^b Department of Psychiatry, Linköping University, 58185 Linköping, Sweden

^c Department of Clinical Neurophysiology, Linköping University Hospital, 58185 Linköping, Sweden

^d Center for Medical Imaging and Visualization, Linköping University, 58185 Linköping, Sweden

A R T I C L E I N F O	A B S T R A C T	
Keywords: ADHD Social touch Self-other-distinction Bodily self fMRI Rubber hand illusion	Introduction: Differentiation between self-produced tactile stimuli and touch by others is necessary for social interactions and for a coherent concept of "self". In attention-deficit-hyperactivity-disorder (ADHD), tactile hypersensitivity and social cognition problems are part of the symptomatology, but pathophysiological me- chanisms are largely unknown. Differentiation of self- and non-self- generated sensations might be key to un- derstand and develop novel strategies for managing hypersensitivity. Here, we compared the neural signatures of affective self- and other-touch between adults with ADHD and neurotypical controls (NC). <i>Methods:</i> Twenty-eight adult ADHD participants and 30 age- and gender-matched NC performed a self-other- touch-task during functional magnetic resonance imaging: they stroked their own arm, an object, or were stroked by the experimenter. In addition, tactile detection thresholds and rubber hand illusion (RHI) were measured. <i>Results:</i> ADHD participants had more autistic traits than NC and reported to engage less in interpersonal touch. They also reported to be more sensitive to tactile stimuli. Compared to NC, ADHD participants showed enhanced responses to both the self- and other-touch conditions: stronger deactivation during self-touch in the anterior and posterior insula, and increased activation during other-touch in primary somatosensory cortex. ADHD partici- pants had intact tactile detection thresholds, but were less susceptible to the RHI. <i>Conclusions:</i> Unaltered detection thresholds suggest that peripheral processing is intact, and that hypersensi- tivity might be driven by central mechanisms. This has clinical implications for managing somatosensory hy- persensitivity in ADHD. The more pronounced differentiation between self- and other-touch might indicate a clearer self-other-distinction. This is of interest regarding body ownership perception in both NC and ADHD, and possibly other psychiatric conditions with altered self-experiences, like schizophrenia. A sharper bound	

1. Introduction

Attention-deficit/hyperactivity disorder (ADHD) is characterized by inattention, impulsivity and hyperactivity. ADHD is typically diagnosed during childhood but often persists into adulthood. ADHD can negatively affect life outcomes in multiple areas, e.g. in social interaction, education and occupation (Faraone et al., 2015).

ADHD is associated with a higher prevalence of depression, anxiety, substance use disorder and autism spectrum disorder (ASD) (Garcia et al., 2012). In ASD, sensory abnormalities like hyper- and hyposensitivity have been described (Baron-Cohen et al., 2009). Much less is

known about sensory processing in ADHD. The few available studies in children point to a sensory processing dysfunction (Ghanizadeh, 2011; Shimizu et al., 2014; Yochman et al., 2004), which seems comparable to that of children with ASD (Little et al., 2018). In children with ADHD, about 50% have increased somatosensory reactivity in multiple sensory domains, compared to 20% in typically developing children (Lane et al., 2010). In adults with ADHD, auditory hypersensitivity is related to inattention severity (Micoulaud-Franchi et al., 2015) and increased pain sensitivity (Treister et al., 2015). Atypical sensory processing is not related to the amount of autism traits, but to self-reported ADHD symptoms (Bijlenga et al., 2017), indicating that sensory dysfunction

E-mail address: Rebecca.bohme@liu.se (R. Boehme).

https://doi.org/10.1016/j.nicl.2020.102317

Received 16 April 2020; Received in revised form 2 June 2020; Accepted 13 June 2020 Available online 16 June 2020

2213-1582/ © 2020 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/BY-NC-ND/4.0/).

^{*} Corresponding author at: Center for Social and Affective Neuroscience, The Department of Biomedical and Clinical Sciences, Linköping University, S-581 83 Linköping, Sweden.



Fig. 1. Recruitment process and drop-out of ADHD participants.

should be considered as a key symptom domain in ADHD. Even in the general population, ADHD traits relate to altered self-reported sensory sensitivity (Panagiotidi et al., 2018). Altogether, this suggests that sensory hypersensitivity plays an important role for attention deficits in ADHD.

Most studies on hypersensitivity in ADHD involve children and rely

on self-report or parent-report; few studies have tested hypersensitivity experimentally. Such studies suggest differences in tactile adaptation (Puts et al., 2017) and in physiological measures of recovery from a sensory challenge (Lane et al., 2010). While one study found higher tactile detection thresholds – possibly related to inattention – (Puts et al., 2017), another found no difference between children with ADHD

and typically developing controls (Parush et al., 1997). Abnormal tactile processing in ADHD might relate to cortical mechanisms involved in adaptation (Puts et al., 2017). Indeed, neural responses to somatosensory stimuli appear to be altered in ADHD: children with ADHD show larger somatosensory evoked cortical responses (Parush et al., 1997), and adults with ADHD show differences in cortical synchronization patterns in response to somatosensory stimuli (Dockstader et al., 2009).

Sensory processing problems relate to sleep and behavior problems in ADHD (Molagholamreza Tabasi et al., 2016; Shochat et al., 2009). Furthermore, tactile hypersensitivity can have far reaching consequences for affected people, from leisure activities (Engel-Yeger and Ziv-On, 2011) to food preferences (Nederkoorn et al., 2019, 2015). Considering the importance of social touch during development (McGlone et al., 2014), hypersensitivity to touch by others might relate to social problems in ADHD, as has been suggested for ASD (Carissa J (Cascio et al., 2018). However, somatosensory processing, especially social touch, has hardly been studied in the ADHD population, and particularly not in adults. Symptomatology, comorbidities and subtypes might differ between adults and children (Faraone et al., 2015, 2006; Moffitt et al., 2015). Therefore, we studied the processing of social touch stimuli in young adults with ADHD.

Adult ADHD participants and matched controls performed the selfother-touch-task previously established in neurotypical people (Boehme et al., 2019). Participants stroked their own arm (self-touch condition) or were stroked by the experimenter (other-touch condition). We used functional magnetic resonance imaging (fMRI) and psychophysics to measure behavioral and neurophysiological processing of self-touch and other-touch. Based on previously reported hypersensitivity problems, we hypothesized that the psychophysical test of ADHD participants would show lower detection thresholds for weak tactile stimuli.

With regard to fMRI, we hypothesized that ADHD participants would be more sensitive to non-self-generated sensations, accompanied by a sharper self-other-distinction. Our region of interest here was the insula, given studies showing that posterior insula activates in response to slow stroking social touch (Morrison et al., 2011; Olausson et al., 2008) and plays a role in body ownership (Tsakiris et al., 2007), while anterior insula has been implicated in integrating interoceptive signals (Kirsch et al., 2020), in the awareness of the own body (Craig, 2002, 2009; Karnath and Baier, 2010) and in tracking mismatches between predicted and actually perceived sensations (Allen et al., 2016).

A clearer self-other-distinction might in turn sharpen the experienced bodily self (Fotopoulou and Tsakiris, 2017; Gallagher, 2000; Gallagher and Meltzoff, 1996). A way to test the stability of one's own body are body ownership illusions, like the rubber hand illusion (RHI) (Tsakiris et al., 2006). Since we hypothesized that ADHD participants exhibit a clearer self-other-distinction, we expected them to be less susceptible to the RHI.

2. Methods and materials

The study consisted of two parts: the first part was a functional magnetic resonance imaging (fMRI) session and the second part included detection thresholds and rubber hand illusion (RHI).

2.1. Participants

Exclusion criteria for the neurotypical controls (NC) were any psychiatric disorder, alcohol or substance abuse, chronic pain, or any other major health concern as assessed during a structured telephone interview.

Clinically stable ADHD participants were recruited at their biannual routine checkup visit at the adult Psychiatric Clinic, at the Linköping University Hospital, Sweden. Exclusion criteria for the ADHD group were any severe acute psychiatric disorders (such as, but not exclusively, psychosis, bipolar disorder, severe obsessive–compulsive disorder), ASD, substance use disorder within the past year, chronic pain or any other major health concern. In total, 53 adults with ADHD expressed interest in the study. Of these, five could not be reached, four declined participation after detailed study description, six were excluded for reasons related to MR scanning (metal in the body, claustrophobia), one due to ASD diagnosis, and one's age was outside our target age range. Furthermore, seven participants did not show up for their appointment and one did not finish the fMRI task. The 24 persons not included had mean age 28.3 \pm 5.0 years, 12 females (Fig. 1).

Some individuals with ADHD who could not participate in the first part due to MRI contraindications were able to participate in the second part, resulting in two partially overlapping samples.

Functional imaging data were thus obtained from 28 adults with ADHD (25.7 ± 4.7 years old, 15 females). 30 neurotypical adults were recruited as age- and gender-matched controls (23.7 ± 3.6 years old, 16 females). After fMRI, the participants filled out the Social Touch Questionnaire (Wilhelm et al., 2001), the Autism Quotient (Baron-Cohen et al., 2001), and the Empathy Quotient (Baron-Cohen and Wheelwright, 2004).

The majority (23 of 28 [82%]) took stimulant medication, two had medication with atomoxetin, and two had no medication for ADHD. ADHD volunteers were asked to refrain from taking stimulant medication for 48 h prior to participation. Four individuals with ADHD were on medication with antidepressants (SSRI), which they continued during the experiment.

All fMRI participants were contacted and asked to participate in the study's second part. Threshold detection data was collected for 14 ADHD participants (26.7 \pm 5 years old, 5 female) and 15 NC (24.9 \pm 3 years old, 7 female), rubber hand illusion (RHI) data were obtained for 10 ADHD participants (24.1 \pm 4.5 years, 6 female) and 15 NC. These samples contained two newly recruited ADHD participants also took stimulant medication, from which they refrained for 48 h prior to the experiment. During phone contact for the second appointment, participants answered a questionnaire about their tactile sensitivity, based on the Sensory Perception Quotient (Tavassoli et al., 2014) and the Sensory Profile (Dunn, 1999; Dunn and Bennett, 2002).

The Linköping Regional Ethics Review Board approved the study (Dnr 2016/360-31, 2019-02318), and written informed consent was obtained after complete study description.

2.2. Self-other-touch task

Participants performed the self-other-touch task as described before (Boehme et al., 2019). In short, the task consists of three conditions: 1) self-touch, during which participants stroked their own left forearm with the right hand; 2) object-touch, where participants stroked a pillow with the right hand; 3) other-touch, where participants were stroked on the left forearm by the experimenter. Participants were instructed to perform slow, light stroking. Our main interest was the difference between self-touch and other-touch. The object-touch was a control for movement during self-touch.

2.3. fMRI

During fMRI, participants performed the touch task lying comfortably in a 3.0 Tesla Siemens scanner (Prisma, Siemens, Erlangen, Germany) with their left arm placed on their belly and the right arm propped up by pillows, to reduce the movement during self-touch.

The participants watched a computer screen through goggles, where they could read the task instruction and the cues for the upcoming trial. The cues were presented for three seconds (in Swedish): "Active, please stroke your arm"; "Active, please stroke the object"; "Passive, your arm will be stroked by the experimenter". When the text turned green, the participant was stimulated or had to perform the stimulation while the text was on the screen, i.e. during a period of twelve seconds. The experimenter was standing next to the scanner bore and received auditory

Table 1

Ch (TD)

Neurotypical controls and ADHD participant characteristics, AQ: autism quotient, EQ: empathy quotient, STQ: social touch questionnaire, m: mean, sd: standard deviation.

IWIKI		
	Neurotypical controls	ADHD
age (m, sd)	23.73 (3.61)	25.68 (4.73)
sex (N)	f: 16; m: 14	f: 15; m: 13
education level (N)	university: 25; high school:	university: 6; high
	1; no answer: 1	school: 17; no answer: 1
smoking (N)	yes: 0; no: 25; no answer: 2	yes: 5; no: 18
AQ (m, sd)	11.00 (6.38)	19.76 (6.74)
EQ (m, sd)	51.83 (13.38)	42.23 (11.24)
STQ (m, sd)	23.38 (11.07)	33.24 (13.73)
Tactile sensitivity (m,	43.29 (6.06)	50.75 (8.69)
sd)		
Detection Threshold		
	Neurotypical controls	ADHD
age (m, sd)	24.87 (3.02)	26.71 (5.01)
sex (N)	f: 7; m: 8	f: 6; m: 8
education level (N)	university: 15; high school:	university: 3; high
	0; no answer: 0	school: 8; no answer: 3
smoking (N)	yes: 0; no: 8; no answer: 7	yes: 3; no: 7; no answer: 4
AQ (m, sd)	13.71 (8.93)	18.10 (6.94)
EQ (m, sd)	47.86 (13.56)	42.36 (13.43)
STQ (m, sd)	28.00 (9.47)	26.95 (13.47)
Tactile sensitivity (m,	42.87 (4.99)	51.54 (10.99)
sd)		
RHI		
	Neurotypical controls	ADHD
age (m, sd)	24.86 (3.13)	27.30 (4.52)
sex (N)	f: 6; m: 8	f: 6; m: 4
education level (N)	university: 14; high school:	university: 2; high
	0; no answer: 0	school: 5; no answer: 3
smoking (N)	yes: 0; no: 8; no answer: 6	yes: 3; no: 4; no answer: 3
AQ (m, sd)	14.23 (9.08)	19.5 (8.87)
EQ (m, sd)	48.31 (14.01)	49.14 (12.62)
STQ (m, sd)	29.00 (9.76)	32.07 (15.73)
Tactile sensitivity (m,	42.93 (5.18)	50.67 (10.15)
sd)		

cues on when to perform the stroking action via headphones. In order to provide a comparable tactile stimulation during the self- and the othertouch condition, as our previous study evaluated using hand tracking, the experimenter watched the self-stroking motion that the participant was doing and mimicked it as closely as possible (Boehme et al., 2019). Each condition occurred 10 times with 12 s rest between each stroking block, resulting in a total length of 13 min.

A 12 channel head coil was used to acquire 801 T2-weighted echoplanar images (*EPI*) containing 48 multiband slices (TR = 1030 ms, TE = 30 ms, slice thickness 3 mm, matrix size 64*64, field of view 488*488 mm², in-plane voxel resolution 3 mm², flip angle = 63°). Functional MRI data were analyzed using statistical parametric mapping (SPM12, Wellcome Department of Imaging Neuroscience, London, UK; http://www.fil.ion.ucl.ac.uk/spm) in Matlab R2018b (The MathWorks, Natick, MA, USA). The following steps were performed: motion correction, co-registration of the mean *EPI* and the anatomical image, spatial normalization to the MNI T1 template, and segmentation of the T1 image using the unified segmentation approach (Ashburner and Friston, 2005). Finally, all images were spatially smoothed with an isotropic Gaussian kernel of 6 mm full width at half maximum.

For statistical analysis of the blood oxygen level dependent (BOLD) response, the general linear model approach was used as implemented in SPM12. Because of our short TR, the FAST-option (Corbin et al., 2018) was used, which increases autocorrelation modelling performance (Olszowy et al., 2019). Using a block-design, the conditions self, other, and object were convolved with the hemodynamic response function. Additional regressors of no interest were the cue phase, which included the motor preparation, and the period of one second after the active conditions, when subjects stopped their movement and put their

right arm back into a resting position. To account for movement associated variance, realignment parameters were included as regressors-ofno-interest. Because our paradigm might be prone to movement artifacts, we also included the first temporal derivative of motion parameters in x,y,z-directions plus an additional regressor censoring scans with more than 1 mm scan-to-scan movement (Boehme et al., 2017). In addition, we compared movement parameters between groups and found no significant difference (F(51,6) = 0.882, p = 0.52). Individual contrast images were taken to group-level analysis, where an ANOVA was used to compare conditions between groups. Family-wise-error correction at the voxel level was used to correct for multiple comparisons at the whole-brain level and for small volume correction based on our *a priori* regions of interest (ROI): the anterior and posterior insula. as the insula is implicated in the processing of affective touch (Morrison, 2016), and the awareness of feelings from the body and body ownership (Craig, 2011; Karnath and Baier, 2010).

2.4. Detection thresholds

Following our previous protocol (Boehme et al., 2019), detection thresholds were measured during the three touch conditions and during baseline (no stimulation) using von Frey monofilaments (Bioseb, USA/ Canada). The four conditions were randomized. Subjects sat comfortably, with eyes closed, resting their left, exposed arm on an armrest or a table in front of them. They were instructed to report when they felt the stimulation with the filament on the left forearm. During self-touch and other-touch this stimulation occurred in addition to the stroking on the same arm. The filaments were presented in an ascending-descending order (0.08–78.5 mN). The perceptual threshold was defined as the smallest filament that was detected in at least five out of 10 trials. Groups were compared using a repeated measures ANOVA in SPSS (IBM Corp.).

2.5. Rubber hand illusion

To induce a rubber hand illusion (RHI), participants were seated comfortably in front of a desk with the RHI set up. They placed their right arm below a small table and viewed the rubber hand next to their own arm through a window in the table. The rubber hand and the participant's hand were stroked simultaneously while the participant was watching the rubber hand. Three synchronous and 3 asynchronous (temporal and local mismatch) stroking trials were performed in a randomized order. After 1.5 min, the participant was asked to report, how much they felt that the rubber hand could be their own hand, by giving a number between 0 (not at all) and 10 (very much). Proprioceptive drift data was not collected because our set-up was too prone for using visual cues to guide the answer. Furthermore, proprioceptive drift may not reflect body ownership (Rohde et al., 2011). Groups were compared using t-tests in SPSS (IBM Corp.).

3. Results

3.1. Participant characteristics

ADHD participants (Table 1) displayed reduced social abilities: they had more autistic traits (T = 4.2, p < 0.001) and lower empathy scores (T = 2.6, p = 0.012). They also differed in touch-behavior: ADHD participants reported to enjoy interpersonal touch less (T = 2.8, p = 0.006) and displayed more tactile hypersensitivities (T = 3.6, p = 0.001).

In NC, the amount of autistic traits was negatively correlated to empathy scores (: r = -0.64, p < 0.001) and positively correlated to tactile hypersensitivities (r = 0.51, p = 0.02). We found no such associations in the ADHD group (AQ-EQ: r = -0.15, p = 0.48; AQ-sensitivity: r = -0.13, p = 0.61).



Fig. 2. Other-touch and self-touch in neurotypical controls (NC) and attention deficit hyperactivity disorder (ADHD) participants compared to baseline. A) Other-touch in NC, B) self-touch in NC, C) other-touch in ADHD, D) self-touch in ADHD. Positive BOLD signal in redyellow, negative BOLD signal in bluegreen, p < 0.05, FWE-corrected at the whole brain level, other-touch at [44 64], self-touch at [41 64]. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

3.2. BOLD signal related to self- and other-touch

We were interested in group differences in BOLD signal in response to self-touch and other-touch. There was no main group effect. Both groups showed a higher activation for other-touch than for self-touch in superior and middle temporal gyrus, amygdala, anterior cingulate gyrus, claustrum, prefrontal and cerebellar regions (Fig. 2, Tables S2 & S3). The whole-brain comparison of the other-touch condition revealed that ADHD participants showed a stronger activation in the right primary somatosensory cortex (Fig. 3A), while there was no difference for the whole-brain group comparison during self-touch.

With respect to our ROIs, anterior and posterior insula, we found a group*condition interaction (Fig. 3B). To understand this interaction better, we performed a *post-hoc* test comparing groups separately for self-touch and for other-touch. The interaction was mainly driven by the self-touch condition, during which ADHD participants showed a stronger deactivation than NC (Fig. 3C). There was no group difference in the insula ROIs during other-touch.

3.3. Detection threshold

To see if the ADHD group was more sensitive to tactile stimuli, we compared stimulus detection thresholds between groups for a tactile stimulus that occurred either alone or simultaneously with our three touch conditions. In NC we found a difference between the four conditions (baseline, self-touch, other-touch, object-touch) using a Kruskal–Wallis ($\chi 2(3) = 29.8$, P < 0.001, Fig. 4). A *post hoc* Wilcoxon signed-rank test showed that detection thresholds during self-touch, (baseline: Z = -3.4, P < 0.001; object: Z = -3.4, P < 0.001; object: Z = -3.4, P < 0.001), but not higher than during other-touch (Z = -0.25, P = 0.8). ADHD participants did not differ from NC in detection thresholds (repeated measures ANOVA: between subjects effect: F(1,24) = 0.5, p = 0.49) and there was no interaction between group and condition (F (1.85,44.36) = 0.92, p = 0.4).

3.4. Rubber hand illusion

NC reported to experience the illusion during synchronous stroking (mean rating = 7.6 \pm 1.8), but not during asynchronous stroking, which is considered a control condition (mean rating = 2.7 \pm 1.9). ADHD participants were less susceptible to the RHI during synchronous

stroking (mean rating ADHD = 5.1 ± 1.5 , T = 3.58, p = 0.002). There was no difference between groups during asynchronous stroking (mean rating ADHD = 3.4 ± 3 , T = 0.7, p = 0.48).

4. Discussion

This is, to our knowledge, the first study to investigate responses to social touch in adults with ADHD. We found a clearer difference between processing of self-touch and social (other) touch in ADHD and that the ADHD group was less susceptible to the RHI illusion. Both these findings might indicate a clearer self-body-boundary. Detection thresholds did not differ between groups. This finding suggests intact peripheral detection of tactile stimuli in ADHD, while central processing might be altered.

The suggestion of a sharper self-other-distinction in ADHD is based on two observations: a stronger deactivation in the insula during selftouch and a stronger activation in the primary somatosensory cortex during other-touch. The stronger deactivation during self-touch might be related to stronger predictions about the sensory consequences of own actions resulting in an increased attenuation of self-generated stimuli (Blakemore et al., 1998). Typically, the brain seems to attenuate the sensations arising from one's own actions, as they are behaviorally irrelevant. This is thought to work through an efference copy of the outgoing motor command, which predicts its sensory consequences (Von Helmholtz, 1867). This mechanism is important in detecting surprise, i.e. unpredicted sensations - which might indicate a threat (e.g. an injury) or a reward (e.g. a positive social interaction). The anterior insula has been implicated in this mechanism through ascending input from thalamus and bidirectional functional connectivity with the primary somatosensory cortex. Furthermore, anterior insula might compare actual sensations with predicted sensations, identify mismatches and direct attention/awareness (Allen et al., 2016; Menon and Uddin, 2010). In line with this, anterior insula activates when detecting surprising tactile events (Allen et al., 2016). In the present study, we examined the opposite effect: a highly predictable tactile sensation during self-touch. Deactivation of anterior insula in both groups might indicate that there is no mismatch between predicted and perceived tactile sensation. In ADHD, we observed increased insular deactivation only during this highly predictable event. Considering a possible sensory overload in ADHD, this could an overcompensation: a stronger suppression of stimuli that a person with ADHD is hypersensitive to - if they are predictable, like in the case of self-touch.



Fig. 3. Attention deficit hyperactivity disorder (ADHD) participants showed stronger activation of primary somatosensory cortex during other-touch compared to neurotypical controls (NC) and stronger deactivation of bilateral insula during self-touch. A) Activation during other-touch, whole brain analysis: ADHD > NC, [24-40 60], p < 0.05, FWEcorrected, t = 5.54; **B)** Group*Condition interaction, ROI analysis: p < 0.05 FWE-corrected for anterior insula left $[-38\ 14-14]$ F = 4.22.3, p = 0.001; right [38 10-16] F = 21.18, = 0.002, posterior left [-36-20 10] Р F = 21.74, p = 0.002; right [36 8-16] F = 16.35, p = 0.013; C) Deactivation during self-touch, ROI-analysis: ADHD > NC [-36 11-7], p < 0.005, FWE-corrected for ROIs (anterior insula left $[-36\ 14-14]$ t = 4.37; right [38 10–16] t = 4.53, posterior left [-36–20 8] t = 4.05; right [44 0-8] t = 3.74); B&C three sholded at p < 0.001, cluster size = 10 for illustration purposes.

Future studies should investigate developmental trajectories of sensory attenuation in ADHD (Martel et al., 2012; Moffitt et al., 2015).

An alternative interpretation could be that people with ADHD show stronger attenuation of self-produced stimuli because they experience a clearer bodily self with sharper boundaries, as has been suggested for people with ASD (Mul et al., 2019) – which could in turn lead to clearer efference-copy based predictions.

Our finding, of a heightened activation in the primary somatosensory cortex in response to other-touch, might relate to somatosensory hypersensitivity and alterations in social interaction behavior. This hypersensitivity to touch is in line with previous reports of sensory over-reactivity in ADHD (Lane et al., 2010; Micoulaud-Franchi et al., 2015; Panagiotidi et al., 2018), and strengthens the assumption that altered sensory processing – although not a core symptom according to diagnostic criteria – should be regarded as an important domain in

ADHD.

If touch by others is experienced as more intense by people with ADHD, they might not enjoy social touch as much and engage in it less, as indicated by results of the self-report questionnaire in our study. Considering the importance of social-touch during development (McGlone et al., 2014), tactile hypersensitivity could impact important social learning situations in early life. This might in turn lead to less social skills, and could be one of the mechanisms for the higher autistic traits and lower empathy scores observed in this ADHD sample and elsewhere (Molagholamreza Tabasi et al., 2016; Uekermann et al., 2010). Interestingly, although we found more autistic traits in participants with ADHD compared to NC, there were no associations between these traits in the ADHD group and atypical sensory processing. This replicates earlier findings (Bijlenga et al., 2017), indicating sensory dysregulation as a key feature of ADHD in adults that should be



Fig. 4. Attention deficit hyperactivity disorder (ADHD) participants did not differ from neurotypical controls (NC) with regard to their detection thresholds. Green: NC, blue: ADHD, plot indicates mean (bold line), median (dashed line), 95% confidence interval (inner box), one standard deviation (outer box) and individual data points. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

addressed as part of the clinical assessment.

Our results in ADHD are similar to previous findings in ASD, demonstrating a lower susceptibility to the RHI and other body illusions (Cascio et al., 2012; Paton et al., 2012). It is possible that a sharper distinction between self-generated and other-generated sensations might increase the perceived boundaries of the bodily self, thereby making its perception more stable and preventing body illusions. A possible alternative could be that ADHD participants did not experience the illusion because of attention deficits during the procedure.

A sharpened boundary of the bodily self could increase somatosensory sensitivity, if it becomes harder to integrate and adapt to sensations that are not self-generated. This may explain why people with ADHD may be preoccupied with behaviorally irrelevant somatosensory stimuli – like the tag of a shirt. If such a stimulus is constantly present and cannot be habituated to, it might be hard to focus on other tasks.

In contrast to our hypothesis, ADHD participants showed intact detection threshold for tactile stimuli for all conditions. This suggest that altered central processing of somatosensory stimuli might explain the reported hypersensitivity, i.e. individuals with ADHD do not actually perceive more/weaker stimuli but rather have difficulties attenuating percepts of irrelevant stimuli. Deficits in sensorimotor gating, i.e. the suppression of response to redundant stimuli, have been reported previously, e.g. for auditory stimuli (Holstein et al., 2013), however the picture in ADHD is complicated, since other studies reported enhanced habituation (McDiarmid et al., 2017). We found stronger activity of primary somatosensory cortex in response to other-touch, however dysfunctional gating/habituation might already occur at an earlier processing step, e.g. in the spinal cord or the thalamus, which is considered to play a crucial role in sensory gating (Boehme et al., 2019; McCormick and Bal, 1994) – or the insula as we discussed above.

These findings have implications for clinical management of the reported hypersensitivity. A relationship between attention deficits and problems in attenuating irrelevant stimuli has been described in self-reports (Micoulaud-Franchi et al., 2015) and on measurements of evoked potentials in adults with ADHD (Micoulaud-Franchi et al., 2019). Sensorimotor integration training is already part of the clinical approaches to manage hypersensitivity symptoms, especially in children (Banaschewski et al., 2001), but there are few studies on behavioral training and biofeedback, with contradictory results (Caye et al., 2019). Typical outcomes in evaluation of the efficacy of such training

focuses mostly on motor skills, hyperactivity and externalizing behavior. Our results suggest an additional focus on the ability to habituate to irrelevant sensations, which might positively affect core symptoms (attention and hyperactivity). A base for novel approaches in sensorimotor integration therapy can be found in the Bayesian brain hypothesis (Friston, 2010, 2012). Within this framework, hypersensitivity might be due to heightened prediction errors, which would interfere with the attenuation of irrelevant stimuli and could lead to deficits in attention control. Based on this, a possible training could be to improve somatosensory predictions. Novel developments in brain-machine interface could also offer promising approaches, like functional electrical stimulation, which could support the learning of habituation and attention control or improve sensorimotor prediction loops (Pisotta et al., 2015).

4.1. Limitations

Participants included in the ADHD group of this study were young, adults, stable on stimulant medication, with no significant medical or psychiatric comorbidities. The high prevalence of comorbidity of adult ADHD with substance use disorder and/or ASD (Faraone et al., 2015) may limit generalizability of our findings to adults with these conditions and warrants further studies involving ADHD subjects with relevant comorbid disorders. Furthermore, we only examined people with ADHD who had not taken stimulant medication for two days. We do not know how medication may alter tactile processing and it would be interesting to compare medicated and unmedicated states in a future study.

4.2. Conclusion

We demonstrated a larger difference between self-generated and other-generated touch in the adult ADHD population. While this increased differentiation is present at the cortical level, we did not find differences at a detection threshold task, suggesting intact basic somatosensory thresholds. We furthermore show a less flexible bodily self-percept in ADHD using RHI, which might be related to the sharper self-other-distinction. Future studies need to investigate how an increased differentiation between self-generated and other-generated stimuli impacts attention, bodily self-boundaries and social cognition – and how it changes with regard to age and medication status.

5. Funding

This work was supported by grants from the Swedish Medical Research Council, Sweden (2015-02684) to HO, and from Swedish Läkaresällskapet, Sweden (SLS-878101) and Lions Forskningsfond, Sweden (liu-2019-01191) to RB.

6. Disclosure

AJC has served as consultant and received speakers' fees from Indivior, Camurus and Lundbeck, all outside the scope of this work. MH has received personal fees from BrainsWay Technologies, Indivior, and Aelis Farma, and other income from Pfizer and Adial Pharmaceuticals, outside the scope of the submitted work. RB, MFK and HO have nothing to disclose.

CRediT authorship contribution statement

Rebecca Boehme: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Software, Supervision, Visualization, Writing - original draft, Writing - review & editing. **Morgan Frost Karlsson:** Data curation, Formal analysis, Investigation, Project administration, Writing - review & editing. **Markus Heilig:** Conceptualization, Resources, Supervision,

Validation, Writing - review & editing. Håkan Olausson: Conceptualization, Funding acquisition, Methodology, Resources, Supervision, Validation, Writing - review & editing. Andrea Johansson Capusan: Conceptualization, Formal analysis, Investigation, Project administration, Supervision, Validation, Visualization, Writing - review & editing.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https:// doi.org/10.1016/j.nicl.2020.102317.

References

- Allen, M., Fardo, F., Dietz, M.J., Hillebrandt, H., Friston, K.J., Rees, G., Roepstorff, A., 2016. Anterior insula coordinates hierarchical processing of tactile mismatch responses. Neuroimage 127, 34-43. https://doi.org/10.1016/j.neuroimage.2015.11. 030.
- Ashburner, J., Friston, K.J., 2005. Unified segmentation. Neuroimage 26 (3), 839-851. Banaschewski, T., Besmens, F., Zieger, H., Rothenberger, A., 2001. Evaluation of sensorimotor training in children with ADHD. Percept. Mot. Skills 92 (1), 137-149.
- Baron-Cohen, S., Ashwin, E., Ashwin, C., Tavassoli, T., Chakrabarti, B., 2009. Talent in autism: hyper-systemizing, hyper-attention to detail and sensory hypersensitivity. Philos. Trans. Royal Soc. B: Biol. Sci. 364 (1522), 1377–1383.
- Baron-Cohen, S., Wheelwright, S., 2004. The empathy quotient: an investigation of adults with Asperger syndrome or high functioning autism, and normal sex differences. J Autism Dev. Disord. 34 (2), 163-175.
- Baron-Cohen, S., Wheelwright, S., Skinner, R., Martin, J., Clubley, E., 2001. The autismspectrum quotient (AQ): evidence from asperger syndrome/high-functioning autism, malesand females, scientists and mathematicians. J. Autism Dev. Disord. 31 (1), 5-17.
- Bijlenga, D., Tjon-Ka-Jie, J., Schuijers, F., Kooij, J., 2017. Atypical sensory profiles as core features of adult ADHD, irrespective of autistic symptoms. Eur. Psychiatr. 43, 51–57. Blakemore, S.-J., Wolpert, D.M., Frith, C.D., 1998. Central cancellation of self-produced tickle sensation. Nat. Neurosci. 1 (7), 635–640.
- Boehme, R., Hauser, S., Gerling, G.J., Heilig, M., Olausson, H., 2019. Distinction of selfproduced touch and social touch at cortical and spinal cord levels. Proc. Natl. Acad. Sci. USA. https://doi.org/10.1073/pnas.1816278116.
- Boehme, R., Lorenz, R.C., Gleich, T., Romund, L., Pelz, P., Golde, S., Behr, J., 2017. Reversal learning strategy in adolescence is associated with prefrontal cortex activation. Eur. J. Neurosci. 45 (1), 129-137.
- Cascio, C.J., Foss-Feig, J.H., Burnette, C.P., Heacock, J.L., Cosby, A.A., 2012. The rubber hand illusion in children with autism spectrum disorders: delayed influence of combined tactile and visual input on proprioception. Autism 16 (4), 406-419. https://doi.org/10.1177/1362361311430404.
- Cascio, C.J., Moore, D., McGlone, F., 2018. Social touch and human development. Dev. Cogn. Neurosci.
- Caye, A., Swanson, J.M., Coghill, D., Rohde, L.A., 2019. Treatment strategies for ADHD: an evidence-based guide to select optimal treatment. Mol. Psychiatr. 24 (3), 390-408.
- Corbin, N., Todd, N., Friston, K.J., Callaghan, M.F., 2018. Accurate modeling of temporal correlations in rapidly sampled fMRI time series. Hum. Brain Mapp. 39 (10), 3884-3897
- Craig, A., 2011. Significance of the insula for the evolution of human awareness of feelings from the body. Ann. N. Y. Acad. Sci. 1225 (1), 72-82.
- Craig, A.D., 2002. How do you feel? Interoception: the sense of the physiological condition of the body. Nat. Rev. Neurosci. 3 (8), 655-666. https://doi.org/10.1038/ nrn894
- Craig, A.D., 2009. How do you feel-now? The anterior insula and human awareness. Nat. Rev. Neurosci. 10 (1), 59-70. https://doi.org/10.1038/nrn2555
- Dockstader, C., Gaetz, W., Cheyne, D., Tannock, R., 2009. Abnormal neural reactivity to unpredictable sensory events in attention-deficit/hyperactivity disorder. Biol. Psychiatr. 66 (4), 376-383.
- Dunn, W., 1999. Sensory Profile: User's Manual. Psychological Corporation, San Antonio, TX.
- Dunn, W., Bennett, D., 2002. Patterns of sensory processing in children with attention deficit hyperactivity disorder. OTJR: Occupation, Participation Heal. 22 (1), 4-15.
- Engel-Yeger, B., Ziv-On, D., 2011. The relationship between sensory processing difficulties and leisure activity preference of children with different types of ADHD. Res. Dev. Disabil. 32 (3), 1154–1162.
- Faraone, S.V., Asherson, P., Banaschewski, T., Biederman, J., Buitelaar, J.K., Ramos-Quiroga, J.A., Franke, B., 2015. Attention-deficit/hyperactivity disorder. Nat. Rev. Dis. Primers 1, 15020. https://doi.org/10.1038/nrdp.2015.20.
- Faraone, S.V., Biederman, J., Mick, E., 2006. The age-dependent decline of attention deficit hyperactivity disorder: a meta-analysis of follow-up studies. Psychol. Med. 36 (2), 159-165 S003329170500471X [pii] 10.1017/S003329170500471X.
- Fotopoulou, A., Tsakiris, M., 2017. Mentalizing homeostasis: The social origins of interoceptive inference. Neuropsychoanalysis 19 (1), 3-28.
- Friston, K., 2010. The free-energy principle: a unified brain theory? Nat. Rev. Neurosci. 11 (2), 127-138. https://doi.org/10.1038/nrn2787.
- Friston, K., 2012. The history of the future of the Bayesian brain. Neuroimage 62 (2), 1230-1233.

- Gallagher, S., 2000. Philosophical conceptions of the self: implications for cognitive science. Trends Cogn. Sci. 4 (1), 14-21.
- Gallagher, Shaun, Meltzoff, Andrew N., 1996. The earliest sense of self and others: Merleau-Ponty and recent developmental studies. Philos. Psychol. 9 (2), 211-233. https://doi.org/10.1080/09515089608573181.
- Garcia, C., Bau, C., Silva, K., Callegari-Jacques, S., Salgado, C., Fischer, A., Rohde, L., 2012. The burdened life of adults with ADHD: impairment beyond comorbidity. Eur. Psychiatr. 27 (5), 309-313.
- Ghanizadeh, A.J.P.I., 2011. Sensory processing problems in children with ADHD, a systematic review. 8(2): 89-94.
- Holstein, D.H., Vollenweider, F.X., Geyer, M.A., Csomor, P.A., Belser, N., Eich, D., 2013. Sensory and sensorimotor gating in adult attention-deficit/hyperactivity disorder (ADHD). Psychiatr. Res. 205 (1-2), 117-126.
- Karnath, H.O., Baier, B., 2010. Right insula for our sense of limb ownership and selfawareness of actions. Brain Struct. Funct. 214 (5-6), 411-417. https://doi.org/10. 1007/s00429-010-0250-4.
- Kirsch, L.P., Besharati, S., Papadaki, C., Crucianelli, L., Bertagnoli, S., Ward, N., Fotopoulou, A., 2020. Damage to the right insula disrupts the perception of affective touch. Elife 9. https://doi.org/10.7554/eLife.47895.
- Lane, S.J., Reynolds, S., Thacker, L., 2010. Sensory over-responsivity and ADHD: Differentiating using electrodermal responses, cortisol, and anxiety. Front. Integr. Neurosci, 4, 8,
- Little, L.M., Dean, E., Tomchek, S., Dunn, W., 2018. Sensory processing patterns in autism, attention deficit hyperactivity disorder, and typical development. Phys. Occup. Ther. Pediatr. 38 (3), 243-254.
- Martel, M.M., von Eye, A., Nigg, J., 2012. Developmental differences in structure of attention-deficit/hyperactivity disorder (ADHD) between childhood and adulthood. Int. J. Behav. Dev. 36 (4), 279-292. https://doi.org/10.1177/0165025412444077.
- McCormick, D.A., Bal, T., 1994. Sensory gating mechanisms of the thalamus. Curr. Opin. Neurobiol. 4 (4), 550-556. https://doi.org/10.1016/0959-4388(94)90056-6.
- McDiarmid, T.A., Bernardos, A.C., Rankin, C.H., 2017. Habituation is altered in neuropsychiatric disorders-a comprehensive review with recommendations for experimental design and analysis. Neurosci. Biobehav. Rev. 80, 286-305.
- McGlone, F., Wessberg, J., Olausson, H., 2014. Discriminative and affective touch: sensing and feeling. Neuron 82 (4), 737-755. https://doi.org/10.1016/j.neuron.2014. 05.001.
- Menon, V., Uddin, L.Q., 2010. Saliency, switching, attention and control: a network model of insula function. Brain Struct. Funct. 214 (5-6), 655-667. https://doi.org/ 10.1007/s00429-010-0262-0.
- Micoulaud-Franchi, J.-A., Lopez, R., Cermolacce, M., Vaillant, F., Péri, P., Bover, L., Philip, P., 2019. Sensory gating capacity and attentional function in adults with ADHD: a preliminary neurophysiological and neuropsychological study. J. Attention Disord. 23 (10), 1199-1209.
- Micoulaud-Franchi, J.-A., Lopez, R., Vaillant, F., Richieri, R., El-Kaim, A., Bioulac, S., Lancon, C., 2015. Perceptual abnormalities related to sensory gating deficit are core symptoms in adults with ADHD. Psychiatr. Res. 230 (2), 357-363.
- Moffitt, T.E., Houts, R., Asherson, P., Belsky, D.W., Corcoran, D.L., Hammerle, M., Caspi, A., 2015. Is adult ADHD a childhood-onset neurodevelopmental disorder? Evidence from a four-decade longitudinal cohort study. Am. J. Psychiatr. 172 (10), 967-977. https://doi.org/10.1176/appi.ajp.2015.14101266.
- Molagholamreza Tabasi, F., Aliabadi, F., Alizade Zarei, M., Qorbani, M., Rostami, R., 2016. Survey of behavioral problems and sensory processing in children with attention deficit/hyperactivity disorder. Iran. Rehab. J. 14 (1), 63-68.
- Morrison, I., 2016. ALE meta-analysis reveals dissociable networks for affective and discriminative aspects of touch. Wiley-Blackwell.
- Morrison, I., Bjornsdotter, M., Olausson, H., 2011. Vicarious responses to social touch in posterior insular cortex are tuned to pleasant caressing speeds. J. Neurosci. 31 (26), 9554-9562. https://doi.org/10.1523/JNEUROSCI.0397-11.2011.
- Mul, C.-L., Cardini, F., Stagg, S.D., Sadeghi Esfahlani, S., Kiourtsoglou, D., Cardellicchio, P., Aspell, J.E., 2019. Altered bodily self-consciousness and peripersonal space in autism. Autism 1362361319838950.
- Nederkoorn, C., Houben, K., Havermans, R.C., 2019. Taste the texture. The relation between subjective tactile sensitivity, mouthfeel and picky eating in young adults. Appetite 136, 58-61.
- Nederkoorn, C., Jansen, A., Havermans, R.C., 2015. Feel your food. The influence of tactile sensitivity on picky eating in children. Appetite 84, 7-10.
- Olausson, H.W., Cole, J., Vallbo, A., McGlone, F., Elam, M., Kramer, H.H., Bushnell, M.C., 2008. Unmyelinated tactile afferents have opposite effects on insular and somatosensory cortical processing. Neurosci. Lett. 436 (2), 128-132. https://doi.org/10. 1016/j.neulet.2008.03.015.
- Olszowy, W., Aston, J., Rua, C., Williams, G.B., 2019. Accurate autocorrelation modeling substantially improves fMRI reliability. Nat. Commun. 10 (1), 1220.
- Panagiotidi, M., Overton, P.G., Stafford, T., 2018. The relationship between ADHD traits and sensory sensitivity in the general population. Compr. Psychiatr. 80, 179-185.
- Parush, S., Sohmer, H., Steinberg, A., Kaitz, M., 1997. Somatosensory functioning in children with attention deficit hyperactivity disorder. Dev. Med. Child Neurol. 39 (7), 464-468
- Paton, B., Hohwy, J., Enticott, P.G., 2012. The rubber hand illusion reveals proprioceptive and sensorimotor differences in autism spectrum disorders. J. Autism Dev. Disord. 42 (9), 1870-1883.
- Pisotta, I., Perruchoud, D., Ionta, S., 2015. Hand-in-hand advances in biomedical engineering and sensorimotor restoration. J. Neurosci. Methods 246, 22-29.
- Puts, N.A., Harris, A.D., Mikkelsen, M., Tommerdahl, M., Edden, R.A., Mostofsky, S.H., 2017. Altered tactile sensitivity in children with attention-deficit hyperactivity disorder. J. Neurophysiol. 118 (5), 2568-2578.
- Rohde, M., Di Luca, M., Ernst, M.O., 2011. The rubber hand illusion: feeling of ownership

and proprioceptive drift do not go hand in hand. PLoS ONE 6 (6), e21659.

- Shimizu, V.T., Bueno, O.F., Miranda, M.C., 2014. Sensory processing abilities of children with ADHD. Braz. J. Phys. Ther. 18 (4), 343–352.
- Shochat, T., Tzischinsky, O., Engel-Yeger, B., 2009. Sensory hypersensitivity as a contributing factor in the relation between sleep and behavioral disorders in normal schoolchildren. Behav. Sleep Med. 7 (1), 53–62.
- Tavassoli, T., Hoekstra, R.A., 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 (1), 29.
- Treister, R., Eisenberg, E., Demeter, N., Pud, D., 2015. Alterations in pain response are partially reversed by methylphenidate (Ritalin) in adults with attention deficit hyperactivity disorder (ADHD). Pain Pract. 15 (1), 4–11.
- Tsakiris, M., Hesse, M.D., Boy, C., Haggard, P., Fink, G.R., 2007. Neural signatures of body ownership: a sensory network for bodily self-consciousness. Cereb. Cortex 17

(10), 2235–2244.

- Tsakiris, M., Hesse, M.D., Boy, C., Haggard, P., Fink, G.R.J.C.C., 2006. Neural signatures of body ownership: a sensory network for bodily self-consciousness. 17(10): 2235–2244.
- Uekermann, J., Kraemer, M., Abdel-Hamid, M., Schimmelmann, B.G., Hebebrand, J., Daum, I., Kis, B., 2010. Social cognition in attention-deficit hyperactivity disorder (ADHD). Neurosci. Biobehav. Rev. 34 (5), 734–743.
- Von Helmholtz, H., 1867. Handbuch der physiologischen Optik, vol. 9, Voss. Wilhelm, F.H., Kochar, A.S., Roth, W.T., Gross, J.J., 2001. Social anxiety and response to touch: incongruence between self-evaluative and physiological reactions. Biol. Psychol. 58 (3), 181–202.
- Yochman, A., Parush, S., Ornoy, A., 2004. Responses of preschool children with and without ADHD to sensory events in daily life. Am. J. Occup. Ther. 58 (3), 294–302.