

Sensory processing sensitivity and axonal microarchitecture: Identifying brain structural characteristics for behavior

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30 **Abstract**

31 Previously, researchers used functional MRI to identify regional brain activations associated with
32 sensory processing sensitivity (SPS), a proposed normal phenotype trait. To further validate SPS as a
33 behavioral entity, to characterize it anatomically, and to test the usefulness in psychology of
34 methodologies that assess axonal properties, the present study correlated SPS proxy questionnaire
35 scores (adjusted for neuroticism) with diffusion tensor imaging measures. Participants (n=408) from
36 the Young Adult Human Connectome Project that are free of neurologic and psychiatric disorders were
37 investigated. We computed mean diffusivity (MD), radial diffusivity (RD), axial diffusivity (AD) and
38 fractional anisotropy (FA). A voxelwise, exploratory analysis showed that MD and RD correlated
39 positively with SPS proxy scores in the right and left subcallosal and anterior ventral cingulum bundle,
40 and the right forceps minor of the corpus callosum (peak Cohen's D effect size = 0.269). Further
41 analyses showed correlations throughout the entire right and left ventromedial prefrontal cortex,
42 including the superior longitudinal fasciculus, inferior fronto-occipital fasciculus, uncinate and arcuate
43 fasciculus. These prefrontal regions are generally involved in emotion, reward and social processing.
44 FA was negatively correlated with SPS proxy scores in white matter of the right
45 premotor/motor/somatosensory/supramarginal gyrus regions, which are associated with empathy,
46 theory of mind, primary and secondary somatosensory processing. Region of interest (ROI) analysis,
47 based-on previous fMRI results and Freesurfer atlas-defined areas, showed small effect sizes, (+0.151
48 to -0.165) in white matter of the precuneus and inferior frontal gyrus. Other ROI effects were found in
49 regions of the dorsal and ventral visual pathways and primary auditory cortex. The results reveal that
50 in a large, diverse group of participants axonal microarchitectural differences can be identified with
51 SPS traits that are subtle and in the range of typical behavior. The results suggest that the heightened
52 sensory processing in people who show SPS may be influenced by the microstructure of white matter
53 in specific neocortical regions. Although previous fMRI studies had identified most of these general
54 neocortical regions, the DTI results put a new focus on brain areas related to attention and cognitive
55 flexibility, empathy, emotion and low-level sensory processing, as in the primary sensory cortex.
56 Psychological trait characterization may benefit from diffusion tensor imaging methodology by
57 identifying influential brain systems for traits.

58 **1. Introduction**

59 **1.1 Sensory processing sensitivity (SPS)**

60 Sensory processing sensitivity (SPS) (Aron and Aron, 1997) is proposed to be a normal phenotype trait
61 observable as a high degree of environmental sensitivity (Pluess, 2015). It is unrelated to sensory
62 processing disorder. Heritability explains about 42% of the variance in twin studies (Assary et al.,
63 2020). The trait is present in about 20% of the population (Lionetti et al., 2018); the estimated number
64 varies from 15% (Kagan, 1997) to 30% (Pluess et al., 2018). A similar proportion is found in many
65 other species, suggesting the presence of two major survival strategies (Wolf et al., 2008): (1) SPS: A
66 high level of attention to environmental stimuli and observing carefully before acting and (2) a normal
67 level of attention to the environment and thus being the first to act. High attention to the environment
68 appears only in a minority of a population because this high sensitivity benefits an individual only if
69 the majority of members of the species lack it (negative frequency dependence).

70 In humans this increased sensitivity compared to the general population is hypothesized to result from
71 a greater depth of processing of sensory input, e.g. using many cognitive tags (Aron et al., 2012; Aron
72 and Aron, 1997). Lockart et. al. (Lockhart et al., 1976) suggested that memory is enhanced by
73 processing information to deeper cognitive levels by using a letter, word, word in context, or word
74 abstracted from many contexts, a concept important to educational methodology (Leow, 2018). This
75 type of processing, using semantics or many contexts to remember a visual stimulus, is thought to
76 enhance awareness of subtle stimuli and increase emotional responsiveness to stimuli in people with
77 SPS. The emotional responsiveness may in turn act as a motivator for the depth of processing
78 (Baumeister et al., 2007).

79 Research on SPS is growing, for a review see (Greven et al., 2019). For example, research using fMRI
80 found SPS was associated with significantly greater activation in brain areas involved in higher-order
81 visual processing, which is more evidence for greater depth of processing in SPS compared to the
82 general population. However, there are many open questions, especially about neuroanatomical
83 correlates. There has been no previous research that investigates microstructural changes using
84 diffusion tensor imaging or similar techniques.

85 SPS does not appear to be a disorder, given the percentages in the population, its presence in many
86 species, and its functionality as a successful survival strategy. In a review comparing fMRI studies of
87 SPS (Acevedo et al., 2018), autism spectrum disorder, schizophrenia, and post-traumatic stress
88 disorder, the authors conclude that SPS engages brain regions differently from these disorders, namely
89 those that are involved in reward processing, memory, physiological homoeostasis, self-other
90 processing, empathy, and awareness. However, SPS can be related to disorders in that it leads to greater

91 susceptibility to environmental influences (Belsky and Pluess, 2009). For example, adults high on SPS
92 scores who report difficult childhoods are more prone to depression, anxiety, and shyness (Aron et al.,
93 2005); however, young children who exhibit SPS and had especially good childhood environments
94 performed well on measures of social and academic competence (Pluess and Belsky, 2010), while those
95 with worse environments fared poorly.

96 The trait also has been shown to lead to greater positive outcomes following interventions (Nocentini
97 et al., 2018; Pluess and Boniwell, 2015), again suggesting that scores on the measure are correlated
98 with greater susceptibility to environmental influences. For example, a study (Karam et al., 2019) of
99 Syrian refugee children suggests that high-SPS scorers' previous experience with family trauma
100 (abuse, neglect, etc.) appeared to prepare them to be less affected by war trauma, while those with
101 positive family histories reported more trauma from similar war-related events, again suggesting a
102 survival strategy of noticing more rather than simply needing a positive childhood to adjust well to any
103 circumstance. Differential susceptibility makes the sample in the present study particularly valuable
104 given that participants were screened to avoid those with psychological disorders, that axonal
105 microstructural differences possibly due to a seriously problematic past would not confound our results.

106 1.2 The Young Adult- Human Connectome Project

107 The dataset of the Young Adult Human Connectome Project (YA-HCP) offered a large group to
108 analyze for a normal psychological variable and any relationship it might have to axonal
109 microarchitectural measures. This open data cohort includes high quality imaging data and an extensive
110 range of data analysis options. There is also extensive psychological testing for each participant.

111 1.3 Proxy scale used to measure SPS

112 The questionnaire measure for SPS used in previous studies is called the HSP or Highly Sensitive
113 Person Scale (Aron and Aron, 1997). The YA-HCP testing does not include the HSP Scale and it was
114 not feasible to re-contact participants to administer it. However, the YA-HCP dataset does include a
115 substantial number of multi-item self-report personality measures. Thus, it was possible to identify a
116 subset of items in the YA-HCP dataset that could serve as a proxy measure. As described in the
117 Methods, we developed and validated in other groups a 17-item proxy scale. We call this scale that
118 measures SPS in the present report the neuroticism-adjusted residual proxy HSP scale, or Proxy HSP
119 Scale.

120 1.4 Microstructural characteristics: Diffusion Tensor Imaging

121 Microstructural characteristics associated with SPS would be another strong piece of evidence that it
122 is a significant, reliable psychological trait. Also, identification of brain regional effects contributes to

123 better understanding of SPS functional systems. Thus, we used diffusion tensor imaging (DTI) to
124 identify any possible axonal microstructural characteristics for SPS. We captured measures from mean
125 diffusivity (MD), radial diffusivity (RD), axial diffusivity (AD) and fractional anisotropy (FA). First,
126 we used an exploratory voxelwise analysis for the whole brain. In addition, we used fMRI data from
127 previous studies to carry out a region of interest (ROI) analysis.

128 **1.5 Previous fMRI studies**

129 Several fMRI studies helped to validate SPS as a psychological trait affecting sensory processing by
130 finding correlations between the standard self-report measure of SPS and neurophysiological events
131 during a variety of perceptual tasks. These studies provided the locations for the ROI analysis. The first
132 study used a task of perceiving subtle differences in neutral landscapes (Jagiellowicz et al., 2011).
133 When detecting minor (vs major) changes in the landscape, high scores on the standard HSP Scale
134 were associated with greater activation in brain areas involved in higher-order visual processing: left
135 occipitotemporal, bilateral temporal, and medial and posterior parietal regions.

136 Another fMRI study looked at culturally influenced visual perception (Hedden et al., 2008). The
137 researchers gave 10 European-Americans and 10 East-Asians a visuospatial task that was either context
138 independent (judging the length of a line independent of a surrounding box, the absolute condition,
139 typically harder for Asians) or context dependent (judging the length of a line while paying attention
140 to the box, the relative condition, typically harder for Americans). Each group exhibited greater
141 activation for the culturally non-preferred task in frontal and parietal regions associated with greater
142 effort in attention and working memory. In the two cultural groups, the HSP Scale scores moderated
143 the brain activations such that neither cultural group with high HSP scores showed greater activation
144 on their culturally more difficult task (Aron et al., 2010). The data suggest that the high-SPS
145 participants were processing both the relative and absolute conditions, unaffected by their culture, by
146 paying close attention to details of the stimulus.

147 Another fMRI study used visual stimuli that were photos of familiar or unfamiliar faces with happy,
148 neutral, or sad expressions (Acevedo et al., 2014). Across all conditions standard HSP scores were
149 associated with increased brain activation of regions involved in attention and action planning (in the
150 cingulate and premotor area (PMA). For happy- and sad-face conditions, SPS was associated with
151 activation of brain regions involved in self-awareness, integration of sensory information, empathy,
152 and action planning (e.g., cingulate, insula, inferior frontal gyrus [IFG], middle temporal gyrus [MTG],
153 and premotor area [PMA]).

154 Finally, SPS individuals showed substantial differences compared to others in brain activation in
155 response to emotional (versus neutral) images (nonsocial visual International Affective Picture System
156 images; (Acevedo et al., 2017)). Standard HSP scores were associated with neural activations in the
157 temporal/parietal area and areas that process emotional memory, learning, awareness, reflective
158 thinking, and integration of information. There were similar results in the same study for an SPS x
159 Quality of Childhood Parenting (QCP) interaction. For positive stimuli, SPS showed significant
160 correlations with activation in subcortical areas involved in reward processing, self-other integration
161 (insula and IFG), calm (PAG), and satiation (subcallosal AC). These were stronger with increasing
162 QCP. For negative stimuli, the SPS x QCP interaction showed significant activation in the amygdala
163 and prefrontal cortex (PFC) involved in emotion and self-control.
164 Overall, these fMRI studies show that SPS is associated with greater activation in multiple brain areas
165 when processing subtle visual differences in neutral stimuli as well as stimuli evoking emotion or
166 empathy and personally relevant social stimuli. The ROIs for this study were in areas whose activation
167 was correlated with SPS under these conditions.

168 1.6 Study aims

169 We undertook this study to further validate and contribute to the broad understanding of SPS as an
170 innate trait associated with a high level of perceptual attention. This trait accounts for a broadly-defined
171 attentional survival strategy: high-level attention to detail. In the present research, we correlated HSP
172 proxy questionnaire scores with DTI measures to assess any axonal microarchitecture measures
173 associated with SPS, particularly in brain areas that might be related to primary and secondary
174 perceptual processes. Importantly, we also wanted to determine if a subtle behavioral trait such as SPS
175 could be detected using DTI. The results suggest that the heightened sensory processing in people with
176 the SPS trait may be influenced by the anatomical microstructure of white matter in specific neocortical
177 regions. Although previous fMRI studies had identified most of these general neocortical regions, the
178 DTI-based results put a new focus on attention and flexibility, low-level primary sensory processing,
179 empathy, emotion and depth of processing. Psychological trait characterization may benefit from
180 diffusion tensor imaging methodology by identifying influential brain systems for the trait.

181 2 Methods

182 2.1 Participants

183 We used data from the Young Adult Human Connectome Project (YA-HCP) WU-Minn-Oxford
184 consortium S500 release (Essen et al., 2012; Glasser et al., 2013), from which we used data of 408
185 subjects (243 females and 165 males) and self-report questionnaire data. Age of the subjects was

186 between 22 and 36 years (mean age for females: 29.2 years, standard deviation: 3.4 years; mean age
187 for males: 28.9 years, standard deviation: 3.6 years); ethnicity: 66.18 % White/European ancestry,
188 20.59% African-American, 7.84% Latino, 1.96% Asian or Nat. Hawaiian or other Pacific, 1.96% not
189 reported, 1.47% more than one. The participants were free of documented psychiatric or neurological
190 disorders.

191 **2.2 Assessment of sensory processing sensitivity**

192 The YA-HCP does not include the standard HSP scale for SPS, but does include multiple psychological
193 measures. Therefore, we systematically identified and tested a subset of items in the HCP dataset that
194 could serve as a proxy measure. First, the authors of the standard measure, the Highly Sensitive Person
195 (HSP) Scale (Aron and Aron, 1997) examined the various self-report measures in the YA-HCP data,
196 which are based on the NIH Toolbox, and selected 55 candidate items to assess SPS. We administered
197 the 55 candidate items along with the standard HSP Scale (in counterbalanced order) to a sample of
198 401 mTurk workers (crowd sourcing marketplace for questionnaires; see Amazon Mechanical Turk,
199 mturk.com). Of these 401, 19 failed one or more of four attention checks and 1 gave identical responses
200 (all 1s or all 7s) to all the items in three of the main scales. The remaining sample of 381 included 174
201 women, 206 men, and 1 who did not indicate gender; mean age was 35.88 (SD = 11.23); 72%
202 White/European ancestry, 8% African-American, 8% Asian, 7% Latino; 5% other.

203 We randomly divided the mTurk sample's data into three groups, with the constraint of equal
204 percentages of each gender in each group: Group 1, n=181, Groups 2 and 3, n=100 each. There were
205 no significant differences in age or ethnicity between subgroups. In Group 1, we correlated each
206 candidate item with the standard HSP Scale. Using those results, we explored several different subsets
207 of the 55 items, checking each subset both for overall correlation with the HSP Scale and internal
208 validity, and we identified a potentially optimal subset. Next, we administered this subset to Group 2
209 and made further adjustments, then tested this further adjusted version in Group 3 and also tested the
210 reliability of this set of items in the overall HCP sample.

211 The resulting scale consisted of 17 items (see Table 1). In our mTurk sample of 381, the correlation of
212 this 17-item measure with the standard HSP scale was 0.79; adjusting for reliabilities (0.93 for the HSP
213 Scale, 0.79 for the 17-item proxy) yielded a deattenuated correlation of 0.89. This indicates that the
214 17-item subset is strongly parallel to the standard HSP Scale, and thus an appropriate measure of SPS.
215 The alpha for these 17 items in the YA-HCP dataset was 0.62, which we considered marginally
216 adequate, especially given that these items were taken from separate, not contiguous, scales in the YA-
217 HCP dataset that measure using diverse response types. By contrast, in the mTurk sample the items

218 from these scales were all administered close to each other. This only marginally adequate reliability
219 does mildly undermine the strength of analyses, suggesting that some failures to find significant results
220 may be due to the low reliability, although significant results obtained in spite of this are likely to be
221 especially robust and may underestimate the actual effect size.

222 Finally, to control for negative affect, we further adjusted HSP scores. Typically, there is a substantial
223 correlation between HSP scale scores and negative affectivity or neuroticism. Thus, it is standard
224 practice to partial out scores on a measure of negative affect in SPS studies. We did so in the present
225 study by creating standardized residuals of the proxy HSP Scale using mean NEO Neuroticism Scale
226 scores from the sample. Thus, we computed neuroticism-score-adjusted studentized residuals, using a
227 standard model in the statistical program SPSS, which shows HSP scores in terms of a standard
228 deviation having negative and positive values. These scores were used to analyze the data and examples
229 are shown in the graph in Figure 1.

230 2.3 Imaging data & processing

231 We used the minimally processed diffusion magnetic resonance images (dMRI) (Sotiropoulos et al.,
232 2013), resulting in 90 diffusion-weighted images (DWIs) and 9 non-DWIs available for each
233 participant with b-value of 1000 s/mm². ExploreDTI version 4.8.6. (Leemans et al., 2009) and the
234 REKINDLE (Tax et al., 2015) tensor estimation approach was used to calculate the voxelwise
235 eigenvalues and eigenvectors. FA, MD, AD and RD maps were calculated from the fitted tensor model
236 and warped to the MNI template. We also corrected for the gradient nonlinearities in the diffusion-
237 weighted gradients (Bammer et al., 2003; Mesri et al., 2019), by using the voxelwise pattern of b-
238 values and gradient direction during tensor estimation. The mean FA mask was calculated using all
239 subjects and thresholded at FA > 0.2 to identify a white matter mask to limit the spatial extent of the
240 statistical tests. Computations were performed on a Dell multi-core parallel processing system with 72
241 Intel Xeon E7-8870 v3 @2.10Ghz dual cores with 1 TB RAM.

242 2.4 Statistical tests

243 To investigate the correlation between the SPS scores and diffusion measures (FA, MD, AD, and RD),
244 we used the nonparametric t-test via Permutation Analysis of Linear Models (PALM) (Eklund et al.,
245 2016; Holmes et al., 1996; Nichols and Holmes, 2003; Winkler et al., 2014) with 10000 iterations.
246 Significance was determined at $p_{\text{corr}} < 0.05$ using family-wise error rate (FWER) adjustment to correct
247 for multiple comparisons, which corrected for multiple contrasts and modalities as well (Winkler et al.,
248 2016b). Threshold-Free Cluster Enhancement (TFCE) (Smith and Nichols, 2009) was used to amplify
249 p-values. Calculation speed was accelerated using the tail approximation (Winkler et al., 2016a).

250 Because a large number of subjects can produce highly statistically significant results for small effects,
251 Cohen's D effect sizes were calculated and are the statistic we emphasize. FWER-corrected p-value
252 maps were fed into the FSL tool automated atlas query (*autoaq*) to facilitate the anatomical
253 interpretation of the statistically significant voxels.

254 In a separate analysis, the voxelwise effect size maps were thresholded at Cohen's D > 0.1, regardless
255 of the associated p-values, and the largest connected component (cluster) was selected using the
256 *bwconncomp* MATLAB function. Exploring the non-trivial effect sizes may provide additional
257 information regarding the spatial extent of the HSP scale – DTI metric relationship.

258 **2.5 Region of Interest Analysis**

259 In addition, we performed region of interest (ROI) analysis for primary sensory processing areas and
260 areas associated with emotion processing based on previous data (Acevedo et al., 2017, 2014; Aron et
261 al., 2010; Jagiellowicz et al., 2011). White matter ROIs were defined by the FreeSurfer (FS) 'wmparc'
262 atlas. Thus, the ROIs used larger areas than those detected in previous fMRI studies, which may dilute
263 any smaller regional significant effect. For example, previous studies found functional activations in
264 the angular gyrus, temporoparietal junction and supramarginal gyrus that are all within the "inferior
265 parietal" ROI region. Thus, we report the findings for some potentially diluted ROIs with P values
266 >0.05, because these were planned comparisons and hypothesis-driven. The ROIs tested were white
267 matter right and left: bankssts, caudal anterior cingulate, cuneus, entorhinal, fusiform, inferior parietal,
268 inferior temporal, lateral occipital, lateral orbitofrontal, middle temporal, paracentral, parsopercularis,
269 pericalcarine, postcentral, precuneus, superior parietal, transverse temporal (primary auditory), and
270 insula.

271 ROI-based statistical testing was performed similarly to the voxelwise tests for all regional mean DTI
272 metrics. PALM was utilized along with 10000 iterations with FWER adjustment and tail
273 approximation. Furthermore, regional volume has been demonstrated to influence DTI estimates (Vos
274 et al., 2011). Therefore, the ROI volume was considered as a co-variate of no-interest.

275 **3. Results**

276 **3.1 Range of HSP Scores and diffusivity values**

277 The raw HSP proxy questionnaire scores ranged from 1.71 to 3.82 (1 to 5, possible scores). HSP proxy
278 residual scores, which are standard deviations from the mean, were used for the analyses and they
279 ranged from -2.31 to +3.75 at the maximum effect size voxel (see Figure 1). The score range allowed
280 an adequate sampling of HSP/SPS trait intensities. Based on approximate cutoffs from (Lionetti et al.,
281 2018) latent class analysis of a large sample using the standard HSP scale, and adjusting their cutoff

282 for mean and SD in the Proxy scale, a score of 2.97 or greater was considered to reflect the HSP trait
283 as influential in everyday life. Sixteen percent (n=65) of our participants showed this range of scores,
284 a population prevalence estimated by other studies of HSP. Thus, a relatively small but statistically
285 adequate number of our participants would be considered a highly sensitive person, leading to small
286 effect sizes. Mean diffusivity ranged from $5-10 \times 10^{-4} \text{ mm}^2/\text{s}$, values found in normal, healthy brains
287 (Lebel et al., 2008).

288 **3.2 HSP proxy scores correlated with brain axon microarchitecture measures**

289 **3.2.1 Whole brain, exploratory analysis**

290 We found positive correlations between HSP-proxy scores and MD within the ventromedial cingulate,
291 ventromedial and ventrolateral prefrontal cortex. The largest effects were in the right anterior/ventral
292 subcallosal cingulum bundle, extending into the forceps minor of the corpus callosum (peak Cohen's
293 D = 0.269, P = 0.018). Fig. 1 shows the MD-HSP relationship at the peak effect size (MNI coordinates
294 X:12, Y:44, Z: -10). Other MD effects were in the left anterior-ventral subcallosal cingulum bundle
295 (Cohen's D=0.243, p =0.028). Fig. 2/A visualizes the voxelwise results from all comparisons on the
296 brain template, while Table 2 lists the regions, MNI coordinates, p-values and effect sizes.

297 There was also a positive correlation for RD in regions overlapping the MD effects in the right
298 anterior/ventral cingulum bundle and forceps minor of the corpus callosum (Cohen's D=0.170;
299 p=0.041) and in a second region of the cingulum bundle (Left, Cohen's D=0.228; p=0.033 Right,
300 Cohen's D=0.232; p=0.032; Table 2; Fig. 2/A).

301 Connected voxels showed a continuous band in the ventral cingulate and ventromedial prefrontal white
302 matter from the posterior genu of the corpus callosum and radiation of the straight gyrus to the frontal
303 pole, including the superior longitudinal fasciculus, inferior fronto-occipital fasciculus, uncinate and
304 arcuate fasciculus as shown in Fig. 2/B. Furthermore, these results extended into the ventrolateral
305 prefrontal cortex. White matter anatomical findings were near gray matter functional activations found
306 previously in SPS subjects reacting to emotional stimuli (Acevedo et al., 2017) and to a romantic
307 partner's emotional facial expression as shown in (Acevedo et al., 2014).

308 We also found a negative correlation between HSP-proxy scores and FA (Cohen's D=-0.181; p=0.042)
309 in the right premotor cortex area in the region of the origin of the corticospinal tract (Fig 2/A).

310 Connected voxels covered a large area that included white matter in the region of the dorsomedial
311 prefrontal cortex, premotor cortex, precentral gyrus (motor cortex), post central gyrus (somatosensory
312 cortex), and supramarginal gyrus (somatosensory association cortex) in the parietal lobe (Fig. 2/B, 3).

313 Fig. 3 shows the 3D render of the FA cluster, after thresholding only for effect size. This cluster was

314 near gray matter functional activations observed previously in SPS subjects reacting to a romantic
315 partner's emotional facial expression as shown in Acevedo et al. (2014) (Acevedo et al., 2014) (Fig.
316 2A/B).

317 **3.2.2 Region of interest analysis**

318 Region of interest analyses showed statistically significant positive RD and negative FA correlations
319 with neuroticism-adjusted HSP-proxy scores in two areas. Figs. 4 and 5 show the ROI analysis results,
320 while Table 3 shows the numerical summary. RD was positively correlated with scores in the left
321 precuneus (Cohen's D=0.1509, p=0.04; Fig. 4/C) and marginally on the right (Cohen's D=0.143,
322 p=0.06, Fig. 4 B/C). FA was negatively correlated with scores in the right parsopercularis/inferior
323 frontal gyrus (Cohen's D=-0.165, p=0.02).

324 We report other areas at $p>0.05$, because they are primary visual sensory or higher order sensory
325 processing areas that were activated in previous fMRI studies: the primary visual cortex (right lateral
326 occipital area, RD: Cohen's D=0.14, p=0.07, see Table 3; Fig. 4A/B), the right fusiform gyrus (MD;
327 Cohen's D=0.137, p=0.08, see Table 3; Fig. 4A/C), the right bank of the superior temporal gyrus (FA;
328 Cohen's D=-0.147, p=0.06; see Table 3; Fig. 4/A), and the inferior parietal cortex that includes the
329 angular gyrus, temporoparietal junction and supramarginal gyrus (FA Cohen's D: -0.136, p=0.08; Fig.
330 4/A). These areas (Fig. 4/A) are part of the "ventral visual stream" that identifies "what" in the visual
331 field and the "dorsal visual stream" that identifies "where" in the visual field (Milner and Goodale,
332 2008; Ungerleider and Haxby, 1994). Functional activations of these regions were seen in SPS
333 individuals during a visual discrimination task (Acevedo et al., 2017, 2012; Aron et al., 2010;
334 Jagiellowicz et al., 2011). Finally, MD was positively correlated with HSP-proxy scores in the right
335 transverse temporal/primary auditory cortex (Cohen's D=0.143, p=0.06; Fig. 4/A) and on the left
336 (Cohen's D=0.131, p=0.09).

337 **4. Discussion**

338 **4.1 Overview**

339 This study established an anatomical correlate in the white matter of the brain for SPS individuals:
340 those with the highest neuroticism-adjusted HSP proxy scores showed the greatest RD, FA and MD
341 effects in several neocortical areas compared to those with the lowest HSP scores (not highly sensitive).
342 Whole-brain, exploratory effects were greatest in brain regions involved in (a) higher-order emotion
343 and reward processing: the ventromedial prefrontal cortex; and (b) in regions involved in empathy,
344 self-other processing, attention and flexible coding of the environment: the premotor cortex and
345 supramarginal gyrus. Compared to whole brain results, smaller ROI effects were also seen in self-other

346 processing areas (IFG, precuneus, fusiform, angular gyrus), higher order visual processing regions of
347 the ventral and dorsal pathways (precuneus, inferior parietal, temporoparietal junction, STSb), and
348 primary sensory processing areas such as the lateral occipital and transverse temporal (primary)
349 auditory cortex.

350 All of these results are consistent with behavioral observations for SPS, which include sensory
351 sensitivity, a tendency to be overwhelmed by sensory stimuli, and more attention to emotional and
352 visual details of stimuli than others who do not show these traits (Aron et al., 2012; Aron and Aron,
353 1997). The localization of the higher-order visual processing effects is also consistent with the previous
354 studies, as reviewed in the Introduction, that used functional MRI to assess details of visual scenes and
355 emotional reactions in highly sensitive people (Acevedo et al., 2017, 2014; Jagiellowicz et al., 2011).
356 Thus, regional *functional* effects previously described were confirmed by microstructural effects. In
357 addition, this is the first study to suggest involvement of primary sensory processing areas in the cortex,
358 such as the visual and auditory cortex. The study also highlights the premotor cortex, with its
359 connections to the supramarginal gyrus and attention functions. Somatosensory as well as
360 environmental stimuli like vision are new possible highlights. Further, the study suggests a novel focus
361 on the functions of the ventromedial prefrontal cortex. Finally, this is one of few studies to show small
362 DTI anatomical effects within axonal tracts for normal-range behavioral traits, in this case sensory
363 processing. Other studies have investigated neurologically normal subjects for DTI effects, mostly
364 using the “big five” personality traits (Xu and Potenza, 2012), but these traits overlap very little with
365 the HSP Scale, other than with neuroticism (which is controlled for in this study). In this study of a
366 normal trait, the results indicate novel behavior-related brain regions to explore in future studies.

367 4.2 Ventromedial prefrontal cortex

368 The largest effects were in white matter of the ventromedial and ventrolateral prefrontal cortex (De La
369 Vega et al., 2016), on both right and left sides, but with more voxels on the right. These tracts connect
370 major limbic system components: the hippocampus/peri-hippocampal cortex and amygdala to the
371 medial prefrontal cortex. The subcallosal cingulum area, functionally connected with the ventromedial
372 and ventrolateral prefrontal cortex (Dunlop et al., 2017) is known for its influence on mood, especially
373 depression (Dunlop et al., 2017; Mayberg et al., 2013). The cingulum is also structurally connected to
374 several of the ROIs that were correlated with HSP-proxy scores in this study: the precuneus, bank of
375 the superior temporal sulcus, and supramarginal gyrus (Bathelt et al., 2019).

376 The ventromedial and lateral prefrontal cortex areas are described by (Hiser and Koenigs, 2018) as
377 having three broad domains of psychological function: Decision making based on reward and value

378 (Sescousse et al., 2013); generation and regulation of negative emotions; and, social cognition, such as
379 facial recognition, theory of mind, and processing self-relevant information. These of course interact
380 strongly, especially given the social nature of humans, as in the function of the vmPFC in making moral
381 decisions (Cameron et al., 2018) or in the “intuitive feeling of rightness” that guides decision making,
382 often social in nature, as a function of memory retrieval (Hebscher and Gilboa, 2016).
383 The major results in the vmPFC in this study, as well as in the preceding fMRI studies (Acevedo et al.,
384 2017, 2014), point to perhaps the most important aspect of SPS, which is “depth of processing” (Aron
385 et al., 2012). The term is based on cognitive conceptualizations of levels or processing, with the idea
386 that processing to deeper levels with more detailed cognitive contexts leads to better memory and better
387 learning overall (Leow, 2018; Lockhart et al., 1976). The hypothesized evolutionary development of
388 depth of processing in SPS is based on a computer simulation demonstrating that unusual responsivity
389 to the environment will evolve when there are enough payoffs for an individual difference in noticing
390 details, as long as most individuals do not notice these details (Wolf et al., 2008). (If all individuals
391 did, there would be no special benefit.) That is, SPS is considered fundamentally an individual
392 difference in “depth of processing” through careful observation of situation/time A in order to compare
393 those details in memory to situation/time B and gain any potential benefits others miss. Individuals
394 without the trait are thought not to process A as carefully, a strategy which is often equally or more
395 effective, since B may bear no resemblance to A or there may be little reward in noticing any
396 resemblances.
397 This type of careful processing relies on emotional motivation, the desire for rewards, such as winning,
398 and the desire to avoid fear-related stimuli, such as losing (Baumeister et al., 2007). Hence
399 understanding SPS as fundamentally about depth of processing for decision making based on reward
400 value and social value is consistent with the significant differences that were found in the vmPFC, with
401 its close connections to emotion-related memory processing areas such as the hippocampus and
402 amygdala. Memory enhanced by motivation is, again, key to SPS, and specific activations occur for
403 those high in SPS when processing emotional stimuli. For example, Acevedo et al (Acevedo et al.,
404 2017) found in their comparison of responses to positive and negative stimuli that there were
405 considerable differences in regional brain activation for high and low SPS in the vmPFC, in the same
406 areas where microstructural differences were found in this study (Fig. 2), and in regions that mediate
407 memory, attention, awareness, and reflective thinking.

408 **Theory of Mind**

409 In a meta-analytic review of the Theory of Mind, (Mar, 2011) highlighted a core mentalizing network:
410 the mPFC, precuneus, bilateral pSTS, bilateral angular gyri, and the right IFG. These structures showed
411 microstructural differences associated with SPS in this study, notably the mPFC, right IFG, precuneus,
412 the bank of the STS and angular gyrus region. Second, this mentalizing network overlaps with the
413 narrative comprehension network in a number of areas, including the mPFC, bilateral pSTS/TPJ,
414 precuneus, and possibly the right IFG, again areas implicated by this study. Theory of Mind is central
415 to the core concept of SPS, in that this survival strategy would require more reflection on another's
416 behavior in order to accurately see from their perspective and correctly attribute to them their
417 motivations and intentions.

418 **4.3 Premotor cortex, attention and somatosensory processing**

419 Finally, regarding the extensive cluster from the left premotor cortex to the post-central somatosensory
420 and supramarginal gyrus, it could be expected that the arc of axonal effects we found in sensory
421 processing areas from posterior to anterior (Figs. 2B, 4A and 5A) would include the premotor cortex,
422 where the hypothesized deep processing associated with SPS would result in the preparation for action.
423 This potential somatosensory/posterior parietal/premotor cortex involvement in SPS is a novel
424 contribution to its understanding and may be helpful in future studies.

425 The importance of this broad premotor area continues to evolve (Rizzolatti et al., 1987). Rizzolatti et
426 al. suggested a theory of attention focused on this area, presenting evidence that the premotor areas
427 were the source of attention rather than a separate attention-directing mechanism. That is, attention is
428 turned to a stimulus within the premotor area, so that attention consists of nothing more than
429 preparation for a motor activity (e.g., an eye movement towards a stimulus deemed important or
430 auditory areas preparing for a sound). Although refinements and extensions (Wollenberg et al., 2018)
431 have occurred, this view of attention is still tenable, according to experiments by (Schubotz and Von
432 Cramon, 2003).

433 Schubotz and Cramon distinguished the left premotor cortex, correlated in our study with SPS, as
434 associated with nonspatial tasks and rapid acquisition of new motor sequences. Overall, evidence
435 regarding the premotor area suggests “environmental features do not have to remind us of specific
436 actions or movements to induce premotor activation on a more or less conscious level. Rather, features
437 are represented in a highly fragmented format that allows for instant recombination and very flexible
438 coding of any currently attended environment” (p. 126). (Schubotz, 2007) presented considerable

439 evidence that the premotor area (along with most of the areas in the brain associated with SPS) helps
440 in the prediction of events.

441 Further, a mean diffusivity study by (Takeuchi et al., 2019) found that an area including the premotor
442 cortex plays a major role in emotional salience and empathy. This area was also activated in the
443 (Acevedo et al., 2014) fMRI study finding empathy for happy and distressed partners and strangers.

444 Attention, flexible coding, prediction, somatosensory processing and empathy all fit with the theory
445 that SPS involves attending to subtle stimuli that may be relevant for survival and predicting those
446 environmental details that what will be relevant in future environments. Overall, these whole brain,
447 exploratory analyses provide a picture that is consistent with behavior associated with SPS.

448 **4.4 ROI results**

449 The particular ROIs with clear statistical significance were the left precuneus (RD, Cohen's D =
450 +0.151, p=0.04), part of the dorsal visual stream, and the right parsopercularis/IFG (FA, Cohen's D =
451 0.165, p=.02), associated with empathy. For the precuneus, the other side was marginally significant
452 (p=0.06), while for the IFG, the same side was marginally significant for RD as well (Cohen's D =
453 0.137, p=0.07). Also, the transverse temporal gyrus/primary auditory cortex (A1), part of the dorsal
454 auditory stream was marginally statistically significant (MD, Cohen's D 0.143, p=0.06).

455 As for the precuneus, fMRI studies (Cavanna and Trimble, 2006) of healthy subjects suggest it plays
456 a major role in visuo-spatial imagery, episodic memory retrieval, and self-processing tasks, such as the
457 experience of agency and taking the first-person perspective. All of these activities are more prominent
458 in those high in SPS, and the precuneus was another area often correlated with SPS in fMRI studies.

459 There is also an hypothesized role for the precuneus in consciousness itself (Cavanna, 2007), along
460 with areas nearby in the posteromedial parietal cortex. It is especially active during the conscious
461 resting state, but is deactivated when consciousness decreases (e.g., sleep, anesthesia, Alzheimer's).

462 Indeed, it has been proposed that it is part of a larger network that correlates with self-consciousness,
463 as it engages in self-related mental representations, self-reflection, and autobiographical memory
464 retrieval. Meditation, which creates states of restful alertness, is associated with microstructural
465 differences in the precuneus in practitioners compared to controls (Avvenuti et al., 2020; Shao et al.,
466 2016). Without suggesting that SPS somehow results in more consciousness, it may well demonstrate
467 an internal tendency for more awareness and integration of diverse aspects of inner and outer
468 experience. Although the insula was not a factor in this study, it has a similar role in the brain and was
469 found to be more active in the fMRI studies of SPS already cited, and has also sometimes been
470 described as the “seat of consciousness” (Craig, 2009).

471 The right parsopercularis/IFG region was negatively associated with HSP proxy scores and FA
472 (p=0.02), and positively associated with RD (p=0.07). IFG functions may be particularly important to
473 recognize in further studies. In an fMRI study, the IFG region was positively associated with HSP
474 scores during positive emotion conditions while looking at a spouse or stranger (Acevedo et al., 2014).
475 It has been identified with a mirror neuron system (Iacoboni et al., 1999; Jabbi and Keysers, 2008; Van
476 Overwalle and Baetens, 2009) that responds to the movements of others, and may facilitate the
477 understanding of others' intentions and feeling of empathy. We previously suggested that this system's
478 activation is consistent with HSPs' bias toward noticing positive expressions in others and high
479 empathy (Acevedo et al., 2014).
480 Some of the ROI effects are along the dorsal and ventral visual/auditory pathways, which is especially
481 noteworthy as they are, again, what one would expect given that the hypothesized fundamental
482 characteristics of the SPS trait are depth of processing of sensory experiences and awareness of
483 subtleties. These pathways are described as identifying the "what" (ventral stream) and "where" (dorsal
484 stream) of what is seen and heard, taking sensory experience beyond its initial input (Milner and
485 Goodale, 2008). The ventral stream in particular is associated with object recognition and form
486 representation, the "what," and is strongly connected to the medial temporal lobe, which stores long
487 term memories; the limbic system, which controls emotions; and joins with the dorsal stream, which
488 identifies the "where." The dorsal stream is said to guide actions and recognize where objects are in
489 space. It stretches from the primary visual cortex in the occipital lobe into the parietal lobe. It contains
490 a detailed map of the visual field and serves to detect and analyze movements. Thus, it commences
491 with purely visual functions, ending with spatial awareness at its termination. As with the ventral
492 stream, processing of sensory input along the dorsal stream becomes "deeper" or more elaborate. It
493 ends up contributing to recognizing spatial relations, body image, and physical coordination. Again, as
494 SPS has been described, the trait is not characterized by better initial sensory perception, better hearing
495 or eyesight, but by more complete processing of what is perceived along these two visual/auditory
496 pathways. However, the potential involvement of primary visual, auditory and somatosensory areas
497 suggested in this study leads to other questions for study of the most basic sensory detection and
498 discrimination functions of these areas that may impact the higher-order processing regions.
499 The A1 cortex that we included as a ROI for this study is thought to operate very early in the recognition
500 of sounds. For example, a study by (Warrier et al., 2009) found that non-Mandarin-speaking subjects
501 who could successfully form an association between Mandarin Chinese "pitch patterns" and word
502 meaning were found to have transverse temporal gyri (A1) with larger volume than subjects who had
503 difficulty learning these associations. Successful completion of the task also was associated with a

504 greater concentration of white matter in the left A1 of the subject. In general, larger transverse temporal
505 gyri seemed to be associated with more efficient processing of speech-related cues, which could aid
506 the learning and perceiving of new speech sounds. The A1 cortex is also associated with inner speech,
507 what (Hurlburt et al., 2016) might be considered a more advanced level of processing, but still
508 preceding speech production. Although to date there are no studies of auditory functioning associated
509 with SPS, it would seem to be a fruitful area for future research.

510 The superior temporal sulcus (STS bank, $p=0.06$) is seen primarily as an area for higher visual
511 processing. (Hein and Knight, 2008), in a review of carefully selected fMRI studies, concluded that the
512 majority of findings implicate the STS in broader tasks involving theory of mind, audiovisual
513 integration, motion processing, speech processing, and face processing. They conclude that rather than
514 trying to pinpoint where in the STS these occur, it is best to view the function of the STS as varying
515 according to the nature of network coactivations with different regions in the frontal cortex and medial
516 temporal lobe during a particular task. This view is more in keeping with the notion that the same brain
517 region can support different cognitive operations depending on task-dependent network connections,
518 emphasizing the important role of network connectivity analysis in neuroimaging. It is consistent with
519 current hypotheses about SPS that those high in SPS would show greater microstructural differences
520 in an area associated with diverse types of processing (motion, speech, face, audiovisual) as well as
521 theory of mind.

522 **4.5 Microstructural differences: the physiological impact of positive MD/RA and negative FA 523 correlations**

524 The physiological impact of positive MD/RA and negative FA correlations is unclear (Soares et al.,
525 2013). The findings in this study are smaller than those seen in previous studies of disease progression
526 or aging (Nir et al., 2013; Voineskos et al., 2012). There is no neurological or behavioral pathology in
527 the group that we studied. The psychological traits measured are subtle and part of the normal range of
528 human behavior. Thus, the effects are part of a normal variability in the population, but may be markers
529 of slight anatomical differences in axon size and organization, perhaps impacting the speed of
530 communication among regions (Horowitz et al., 2015).

531 This study joins others that have looked at microstructural correlates of normal individual differences,
532 such as personality traits (Xu and Potenza, 2012) and cognitive abilities (Bathelt et al., 2019). Since
533 such phenotypic differences can be caused by multiple genetic and environmental effects, looking for
534 common microstructure may be another useful way to identify such differences.

535 **4.6 Limitations**

536 A limitation of the study is its reliance on a proxy measure of SPS. Few questions in the YA-HCP
537 questionnaire dataset addressed sensory processing directly. However, the proxy measure was found
538 in independent samples to have a strong correlation with the standard measure ($r=0.79$; $r=0.89$
539 adjusting for reliabilities). Future aims of research more generally will be to replicate these findings
540 and to examine the relation of SPS to DTI in younger and older age groups and in other populations.

541 **5. Conclusions**

542 This is the first study to investigate the relation of SPS to neural anatomical measures using DTI. The
543 study employed a relatively large sample of young healthy individuals, and it has identified several
544 brain systems that may be critical to fully understanding the SPS trait, such as parietal/premotor
545 connections. The study has also confirmed the involvement of several brain systems and areas
546 previously correlated with SPS in fMRI studies, such as those for empathy and higher-order visual
547 scene processing. Future research should focus on primary visual and auditory processing; higher-order
548 somatosensory processing; attention flexibility and reward value processing. Also, the development of
549 a proxy measure allows future research to examine the relation of SPS to other variables in the large
550 YA-HCP sample, such as various genetic, functional imaging, and self-report data. Finally, DTI may
551 be a valuable and fairly straightforward approach for future psychological and anatomical studies of
552 normal individual differences because the scan can be acquired quickly and is often included in the
553 usual battery of clinical scans.

554 **6. Conflict of interest**

555 The authors declare that the research was conducted in the absence of any commercial or financial
556 relationships that could be construed as a potential conflict of interest.

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560 **8. Data statement**

561 All data are available at <https://db.humanconnectome.org>.

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Sensory Processing Sensitivity and Axonal Microarchitecture

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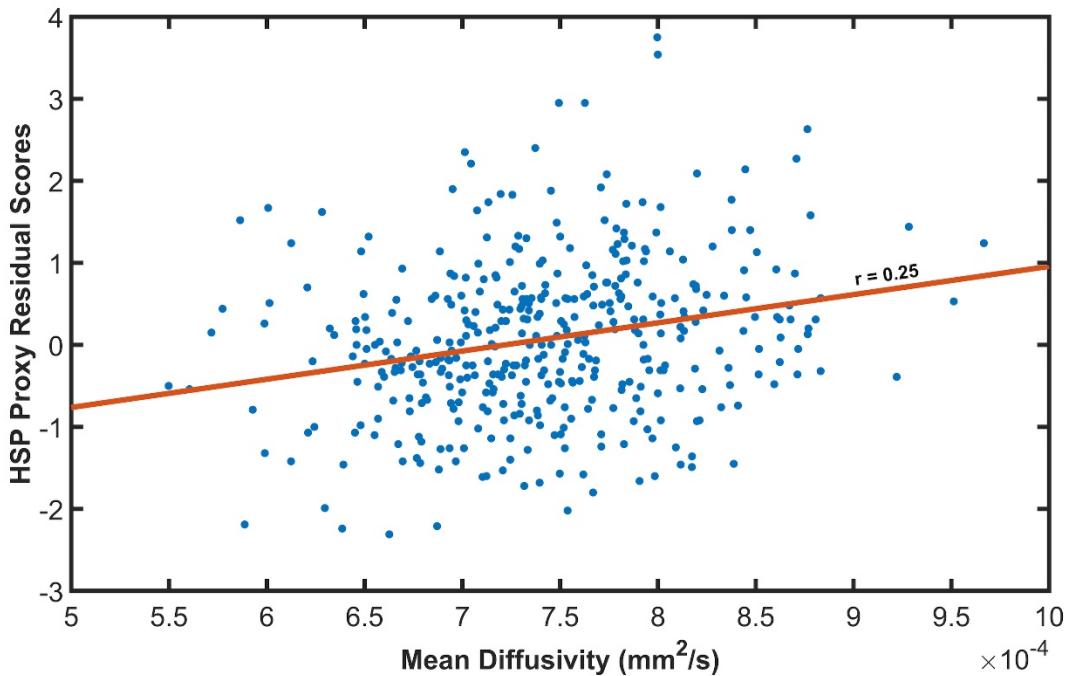
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Figures



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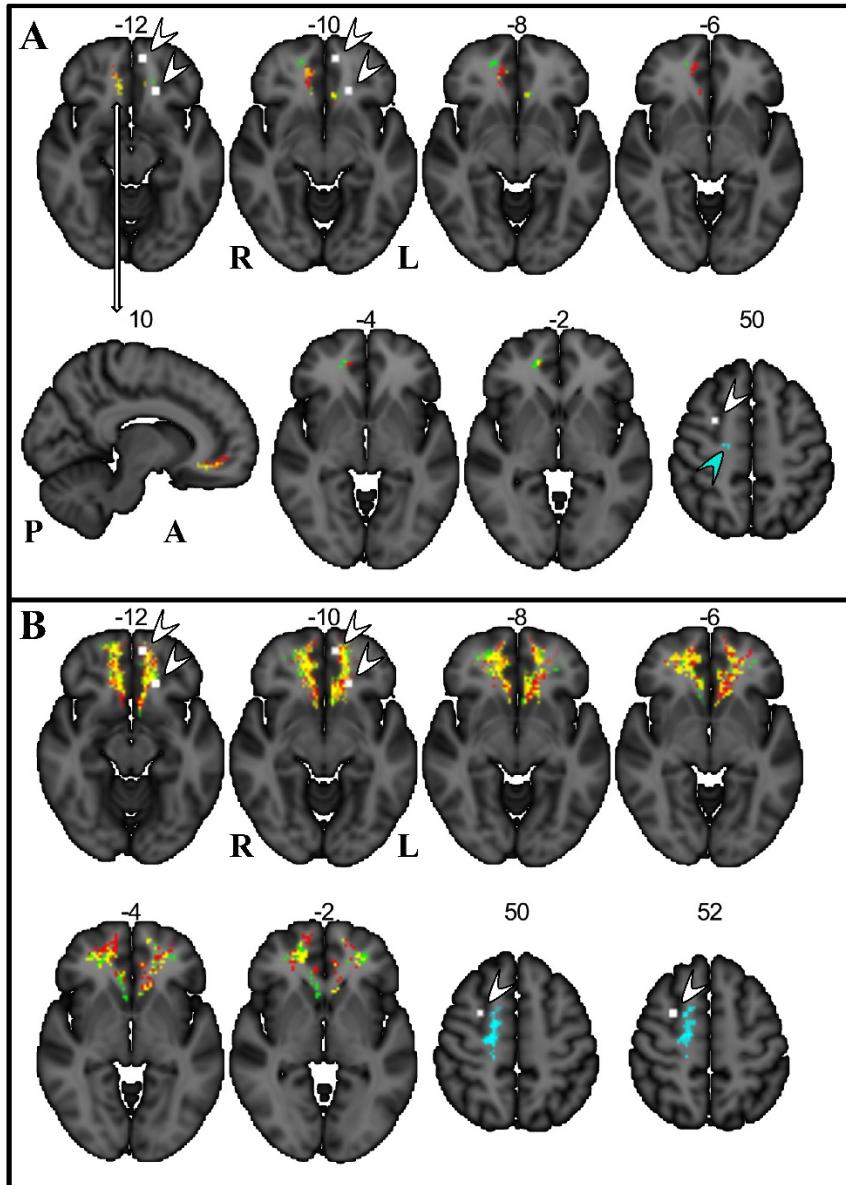
Figure 1

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Mean diffusivity correlation with HSP residual score (standard deviations from the mean) in a voxel in the right medial prefrontal cortex, within the cingulum bundle (MNI: 12, 44, -10; see Fig. 2). This voxel showed the highest Cohen's D effect size for the whole brain analysis (0.27; $t=5.24$).



783

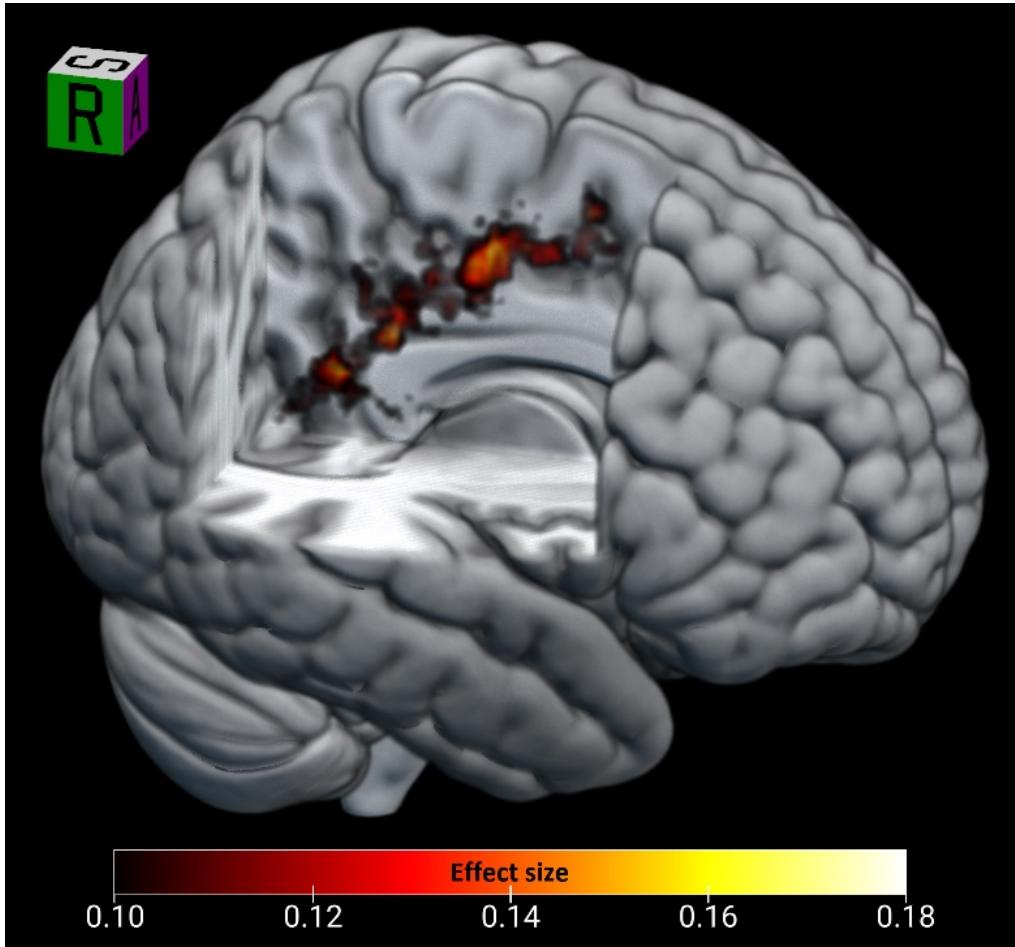
784 Figure 2

785 Voxelwise results presented in MNI stereotaxic space on axial and sagittal sections.

786 A. Voxels in color show statistically significant correlations with HSP proxy questionnaire scores.
787 They are located in the ventromedial prefrontal cortex, mostly on the right, within the forceps minor
788 of the corpus callosum and the subcallosal cingulum bundle. The correlated voxels extend about 10
789 mm axially and about 25 mm antero-posteriorly. Significant voxels are also on the left, mostly in the
790 subcallosal area. B. Colors show largest voxel clusters above Cohen's D effect size of 0.10 without
791 considering statistical significance (see Methods).

792

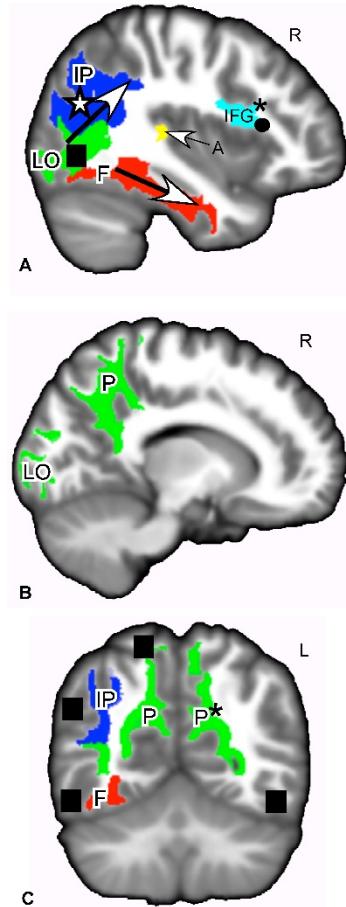
793 Red: positive correlation with MD (mean diffusivity); Green: positive correlation with RD (radial
794 diffusivity); Yellow: the overlap of MD and RD; Blue and blue arrow: negative correlation with FA
795 (fractional anisotropy); White voxels and white arrows: locations of fMRI activations that correlated
796 with HSP questionnaire scores in a previous study when participants viewed a romantic partner and a
797 stranger, happy or sad (Acevedo et al., 2014).



798
799

800 Figure 3

801 3D render of the largest FA cluster (negatively correlated with HSP score). The cluster extends from
802 the premotor cortex through the primary motor and somatosensory cortex into the supramarginal gyrus.



803

804 Figure 4.
805 White matter regions of interest where MD, RD or FA showed positive or negative correlations with
806 HSP proxy questionnaire scores.

807 A. Sagittal slice through ROIs that showed a correlation between HSP-proxy scores and DTI
808 measures. These ROIs are white matter of the ventral pathway for visual processing (LO,F
809 bottom arrow), dorsal pathway for visual processing (IP, top arrow), primary auditory
810 processing (A), and empathic responses (IFG).
811 B. Sagittal slice through regions that showed a positive correlation between RD and the HSP-
812 proxy scores. The ROIs are white matter of the ventral and dorsal visual pathways (LO, P).
813 C. Coronal slice through white matter regions involved in the ventral and dorsal visual pathway
814 (F,IP,P) that showed correlations between questionnaire scores and MD, RD and FA. These
815 regions are connected to gray matter areas associated with SPS (■)

816 Red: MD positive correlation; Green: RD positive correlation; Yellow: MD+RD positive correlations;
817 Dark Blue: FA negative correlation; Light Blue: FA negative+RD positive correlation.

818 * p<0.05. Otherwise, p values ranged from 0.06-0.09. Effect sizes -0.165 to + 0.151. See Table 3.

819

820 Shape symbols indicate where previous fMRI and behavioral studies of SPS found activations
821 implicating heightened sensory processing, empathy, attention and self-other processing.

822



823 Jagiellowicz et al., 2010

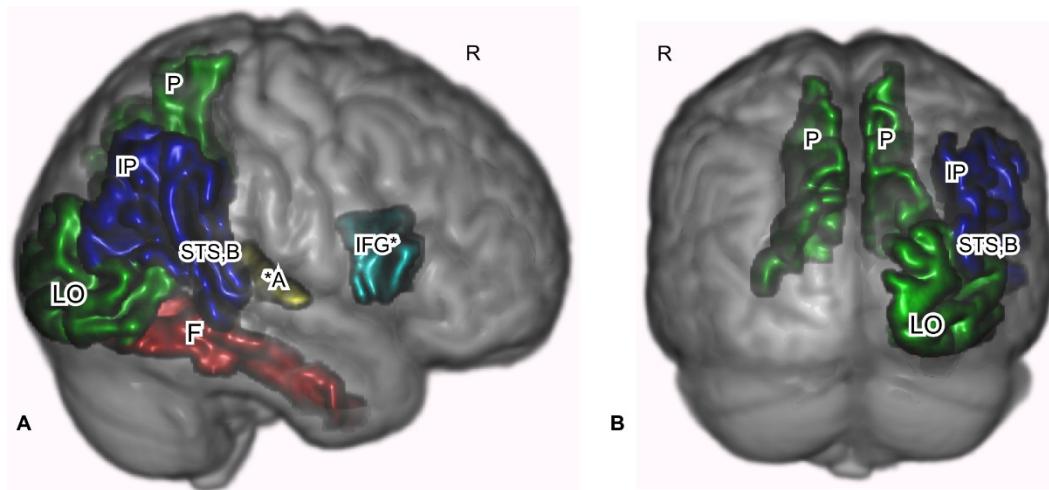


824 Acevedo et al., 2014, 2017

● Acevedo et al., 2014

825 Abbreviations: A, primary auditory cortex. F, fusiform. IFG, inferior frontal gyrus. IP= Inferior
826 parietal/angular gyrus/temporoparietal junction/supramarginal gyrus. LO, lateral occipital area. P,
precuneus. MD, mean diffusivity. RD, radial diffusivity. FA, fractional anisotropy.

827



828

829

830 Figure 5

831 Primary sensory, higher order sensory processing and cognitive processing regions were identified as
832 correlated with the HSP proxy scores. Freesurfer-based ROIs are shown for white matter where
833 Cohen's D effect size was -0.147 to +0.151, rendered in 3D on a template brain. Areas include the
834 general path of the dorsal and ventral visual pathways. A. Sagittal view of the right side. B. Posterior
835 view.

836

837 Red: MD positive correlation with HSP proxy questionnaire scores. Green: RD positive correlation.
838 Blue: FA negative correlation. Gold: MD and RD positive correlation. Aquamarine in IFG: RD and
839 FA correlations. * $p < 0.05$. Otherwise, p values were 0.06-0.09. See Table 3.

840

841 Abbreviations: A, primary auditory cortex. F, fusiform. IFG, inferior frontal gyrus. IP, inferior parietal
842 including angular gyrus/temporoparietal junction/supramarginal gyrus. LO, lateral occipital cortex. P,
843 precuneus. STS,B- bank of the superior temporal sulcus. MD, mean diffusivity. RD, radial diffusivity.
844 FA, fractional anisotropy.

845

846 Table 1: The HSP-Proxy Scale (17 items) Developed From Questions in the NIH Toolbox Used for
847 the Human Connectome Project.

848

849 From the NIH Toolbox Loneliness (Ages 18+) – Fixed Form

850 In the past month how often (from 1=never to 5=Always)

851 1. Act like my problems aren't that important [Soc 276]*

852 2. Criticize the way I do things [Soc264]

853 From the NIH Toolbox Emotion Anger-Affect (Ages 18+) – Fixed Form.

854 In the past 7 days (from 1=never to 5=Always)

855 3. I was irritated more than people knew [Anger31]

856 4. I felt annoyed [Anger50]

857 From the NIH Toolbox Fear (Ages 18+) – Item Bank

858 In the past 7 days (from 1=never to 5=Always)

859 5. I felt uneasy [Anxiety62]

860 From the NIH Toolbox Self-Efficacy (Ages 18+) – Item Bank/Fixed Form

861 ...how true is it of you in general (from 1=never to 5=Very Often)

862 6. If I am in trouble, I can think of a solution [GSE09]

863 From the NIH Toolbox Perceived stress (Ages 18+) – Item Bank/Fixed Form

864 In the past month... (from 1=never to 5=Very Often)

865 7. How often have you been upset because of something that happened unexpectedly? [SC001]

866 8. How often have you felt nervous and "stressed"? [SC003]

867 From the NEO-FFI-R (McCrae & Costa, 2004), included in the NIH Toolbox

868 ...circle the response which best describes your opinion of yourself (from SD Strongly disagree—
869 definitely false to SA Strongly agree—definitely true; for analyses, coded 1 to 5]

870 9. I am not a worrier [NEORAW_01_Num, reverse coded]

871 10. I enjoy concentrating on a fantasy or daydream and exploring all its possibilities, letting it grow
872 and develop [NEORAW_03_Num]

873 11. When I'm under lots of stress, I sometimes feel like I'm going to pieces[NEORAW_11_Num]

874 12. I am intrigued by the patterns I find in art and nature [NEORAW_13_Num]

875 13. I often feel tense and jittery [NEORAW_21_Num]

876 14. I often get angry at the way people treat me [NEORAW_36_Num]

877 15. I experience a wide range of emotions or feelings [NEORAW_38_Num]

878 16. When I read a poem or view art, I sometimes feel a wave of excitement[NEORAW_43_Num]

879 17. Poetry has little or no effect on me [NEORAW_23_Num, reverse coded]

880

881

882 *Note: codes in brackets are codes used for items in NIH Tool Box data sets

883

Sensory Processing Sensitivity and Axonal Microarchitecture

884 Table 2. Whole brain exploratory analysis. Brain white matter areas showed positive and negative
 885 correlations between diffusion tensor imaging measures and proxy HSP scores for Sensory Processing
 886 Sensitivity. X/Y/Z denotes the MNI coordinates for the peak voxel within the cluster. Effect size is
 887 defined as Cohen's D.
 888

Brain Region	x	y	z	# of Voxels	p-value	Peak effect size
<i>MD, Positive Correlation: ventromedial prefrontal cortex/ Cingulate cortex:</i>						
Anterior/Ventral Subcallosal Cingulum Bundle and Forceps minor of corpus callosum	12	44	-10	58	0.018	0.269
Anterior/Ventral Cingulum Bundle	-6	26	-10	7	0.028	0.243
<i>RD, Positive Correlation: ventromedial and lateral prefrontal cortex</i>						
Anterior/Ventral Subcallosal Cingulum Bundle and Forceps minor of corpus callosum	10	36	-12	29	0.041	0.170
Anterior/Ventral Cingulum Bundle	-6	26	-10	3	0.033	0.228
Anterior/Ventral Cingulum Bundle	18	48	0	21	0.032	0.232
<i>FA, Negative correlation; motor/premotor cortical region</i>						
Premotor area	22	-14	52	6	0.042	-0.181

889

Sensory Processing Sensitivity and Axonal Microarchitecture

890 Table 3. Region of Interest analysis. White matter areas with Cohen Effect Sizes >0.1 and p values
891 at statistically significant, or marginally significant values.
892

White Matter Regions	Side	MD		RD		FA	
		Effect size	P-value	Effect size	P-value	Effect size	P-value
Inferior Frontal Gyrus/Parsopercularis	R			0.137	0.07	-0.165	0.02
	L						
Precuneus	R			0.143	0.06		
	L			0.151	0.04		
Superior Temporal Sulcus, Bank	R					-0.147	0.06
	L						
Transverse Temporal/Auditory	R	0.143	0.06	0.131	0.09		
Lateral Occipital	R			0.140	0.07		
	L						
Fusiform	R	0.137	0.08				
Inferior Parietal (angular gyrus, temporoparietal junction, supramarginal gyrus)	R					-0.136	0.08
	L						

893