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Sensory processing sensitivity in adult dental patients and its relation to perceived stress, cortisol, and serotonin secretion

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Sensory processing sensitivity (SPS) is a biologically determined trait that influences how individuals respond to external and internal stimuli. A high level of SPS is characterized by three factors: increased emotional reactivity, heightened sensitivity to subtle stimuli, and greater susceptibility to overstimulation, all of which may impact well-being and health. This study examined the relationships between SPS, perceived stress, affect, and biochemical responses in adult dental patients (*N* = 157) on the day of a routine dental visit. Biochemical measures included morning cortisol and serotonin secretion (saliva samples), and cortisol concentration accumulated in recent months (hair sample). Perceived stress and negative and positive affect were assessed while patients waited for a dental procedure. The correlation analysis revealed that higher SPS level was associated with elevated hair cortisol and more negative affect. Cluster analyses tested SPS and its factors independently, revealing that individuals with higher SPS had higher cortisol levels in saliva and hair samples, as well as greater perceived stress and negative affect. Salivary serotonin levels showed varied relationships with different SPS factors, indicating the need to analyze SPS as a multidimensional construct. The results indicate that increased hair and salivary cortisol may be considered as biomarkers of SPS. In the context of patient-centered care, considering SPS levels may contribute to enhanced motivation for regular dental visits and improved treatment adherence.

Keywords Sensory processing sensitivity, Stress, Cortisol, Serotonin, Dental treatment

Sensory processing sensitivity (SPS) is a biologically determined trait that influences how individuals respond to external and internal stimuli[1–4]. SPS is linked to the central nervous system's activity and is an interchangeable term for 'neurosensitivity'[5,6] or 'environmental sensitivity'[2]. In psychological literature, individual dispositions linked to SPS traits have a long history and constitute the basis for temperament research and theory[7]. Highly sensitive individuals are more likely to experience heightened emotional reactivity and may be more prone to stress, anxiety, depression, and health complaints[8–10]. Some dimensions of SPS (e.g., emotional reactivity, overstimulation) overlap with anxiety and neuroticism, but recent studies suggest that SPS may influence stress and somatic symptoms independently of neuroticism[9]. SPS may also be associated with positive experiences, such as greater sensitivity to aesthetic impressions and deeper processing of stimuli[4,10,11], potentially enhancing life satisfaction in supportive environments[2,9]. This suggests the distinctiveness of the SPS construct from anxiety and neuroticism.

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SPS is characterized by heightened responsiveness to stimuli[1], which can be observed at physiological, emotional, cognitive, and behavioral levels[8]. Studies have shown that highly sensitive individuals display greater brain activity in areas related to empathy, memory, self-awareness, and self-other processing[12,13]. However, these individuals' reactions are strongly influenced by environmental context[6]. For example, their physiological responses to stress may vary depending on the overall context and the environmental characteristics[6,14,15]. Research suggests that over 30% of people may exhibit traits of high SPS, highlighting the relevance of this trait in the general population[3,10]. Further studies on SPS, particularly in adult clinical populations, could offer valuable insights into how this trait interacts with stress and mental and somatic health[9,10,16]. Understanding the relationship between SPS and stress is crucial as stress can mediate the impact of SPS on mental well-being[17]. Clinicians may benefit from recognizing the unique challenges faced by highly sensitive individuals, such as overstimulation, emotional regulation difficulties, and sensitivity to criticism[18], which could help improve interventions and mental health support for this group[4,9,11,12].

Dental visits are often stressful due to their multisensory nature[19], making this context particularly interesting for exploring SPS and its effects. For patients with dispositions of high SPS, facing medical procedures can be a great source of stress because they might be easily overwhelmed by excessive stimulation. For example, the sounds of dental instruments may cause discomfort or irritation as there are some overlapping symptoms between high SPS and misophonia[20]. Siev et al.[21] indicate that specific blood-injection-injury fears among people with dental anxiety are associated with anxiety sensitivity and disgust sensitivity. Studies show that app. 12–15% of adults suffer from dental anxiety, which leads to avoiding or delaying visits to the dentist, thus possibly resulting in increased caries, tooth loss, and serious health problems[22,23]. Current research on adult dental patients in the context of SPS is very limited[24–26]. Eger et al.[24] found that soldiers with severe periodontitis had significantly higher levels of overstimulation tendency compared to those with milder symptoms, highlighting the link between SPS and dental anxiety. Significant associations between sensory sensitivity and dental anxiety were also confirmed by Ogawa et al.[25,26], who emphasized that knowledge of this relationship may be critical for managing dental anxiety and interventive programs. Below, we explore some biochemical and psychological aspects of stress and regulatory mechanisms, emphasizing their potential links with SPS among adult dental patients; on this basis, we formulate hypotheses for this study.

Heightened reactivity to stimuli activates the hypothalamic-pituitary-adrenal (HPA) axis, regulating cortisol release in response to stress. Cortisol, a key stress biomarker, is produced during the fight-or-flight response and in situations of uncontrollability and unpredictability, triggering physiological, emotional, and behavioral effects[27]. Research on a sample of children has shown that the relationship between cortisol and sensory sensitivity is complex, with different aspects of sensitivity linked to either higher or lower cortisol levels[28]. The consequences of increased cortisol are linked to stress, mental and somatic problems, e.g., depression, cardiovascular and metabolic disease, or inflammation[29]. Cortisol concentration may be assessed in blood, urine, saliva, and hair[30,31]. Hair cortisol remains a controversial research area, with potential publication bias arising from various factors that can influence hair samples[32]. However, some studies highlight the unique opportunity to assess long-term cortisol concentrations and the retrospective effects of chronic stress exposure through hair samples[30]. They also emphasize the significant potential of hair cortisol analysis in both clinical and scientific research to enhance patient care[33]. Only a few studies have directly analyzed the relationship between SPS and cortisol levels, focusing on salivary and hair samples in children[28,34].

The modulation of emotional responses to stress is linked to the serotonergic system[35]. In humans, serotonin (5-HT) is found in various biological fluids, including saliva, where it originates from both the central and peripheral nervous systems[36]. Given its role in mood, stress response, and coping behavior[37], salivary 5-HT can serve as an indicator of psychological states. Research suggests that salivary serotonin correlates with sensory processing, emotions, and social behaviors[38,39], and lower levels are linked to certain positive emotions and trait empathy[39]. This underscores serotonin's role in emotional regulation. Notably, salivary serotonin does not directly correlate with levels in peripheral tissues, such as platelets or the intestines, which contain 95% of the body's serotonin[40]. Rather than being produced by peripheral sources, serotonin in saliva is mainly the result of its release from nerve endings in the oral cavity and salivary glands, thus it does not reflect overall serotonin levels in the body[41,42]. Monitoring salivary serotonin offers a non-invasive method of assessing responses to stress-related stimuli, deepening our understanding of serotonin's role in mental health. Despite suggestions of a negative relationship between serotonin and SPS characteristics[43], no studies have yet been dedicated to analyzing the associations between level of salivary serotonin and specific dimensions of SPS.

Considering current findings and the still insufficient studies on biochemical correlates of SPS, we decided to research the potentially stressful situation of a dental visit. By focusing on cortisol and serotonin levels, we aim to gain deeper insights into how these biochemical markers contribute to sensory processing sensitivity and how these aspects are associated with perceived stress and affect during dental visits. According to previous findings[4,10,16], individuals with higher levels of sensory processing sensitivity should report higher levels of perceived stress. Based on the assumption that there are relationships between sensory processing sensitivity and psychological and biochemical indicators of stress, the following hypotheses were formulated:

H1: Individuals characterized by a higher level of sensory processing sensitivity will show higher levels of cortisol (both in hair and saliva).

H2: Individuals with higher levels of sensory processing sensitivity will show lower levels of serotonin in saliva.

H3: Individuals with higher levels of sensory processing sensitivity will show higher levels of negative affect while waiting for a dental procedure.

Deepening our understanding of the relationship between sensory processing sensitivity and experienced stress in a group of dental patients may lead to increased understanding and anticipation of how this specific situation is experienced in the context of healthcare. On the other hand, this knowledge may assist healthcare systems in planning suitable conditions and development of more effective interventions and personalized care strategies for highly sensitive individuals, thus improving their overall experience in healthcare settings.

Methods

Participants and procedure

One hundred fifty-seven adults (103 females, 54 men; mean age = 42.2 years; SD = 16.0 years) who were patients of a dental clinic participated in this study. Inclusion criteria: adult age, regular dental treatment, no hair dye in the last month. Exclusion criteria: adrenal disease, Cushing's disease, hyperthyroidism, depression, obesity, and taking steroids, oral contraceptives, amphetamines, spironolactone. During the follow-up visit, the patients underwent tooth scaling and/or carious cavity filling. More specialized and advanced procedures such as tooth extractions or root canal treatment were not performed.

The study procedure consisted of two stages. The first stage was the participant preparation. Patients who met the inclusion criteria and agreed to participate were informed about the study's purpose and given detailed instructions on how to collect saliva and hair samples. Each participant received a folder containing the *Highly Sensitive Person Scale* (HSPS), and three clearly marked envelopes – two for the saliva storage tubes and one for hair storage foil, along with detailed instructions on how to prepare for the test and collect saliva samples. Before the dental visit, participants were asked to complete the HSPS and were instructed to wash their hair with shampoo, not using conditioner, styling gel, or other hair cosmetics.

The second stage took place on the day of the dental visit. Participants were instructed to collect their saliva samples at home at 8.00 am, on an empty stomach, before teeth brushing. After rinsing the mouth with clean water for 1–5 s and 10 min waiting, they were asked to remove the swab from the Salivette® tube and insert the swab into the mouth for at least 2 min (without chewing). The swab was then placed back in the tube. This procedure was repeated twice: first for cortisol at 8.00 am and 15 min later for serotonin samples. The salivary samples were taken at the same time for all participants to minimize the effect of diurnal fluctuations in cortisol and serotonin levels[44,45].

The advantage of the Salivette® system lies in its easy and hygienic saliva collection process, which allows patients to collect their saliva independently at home without the need for medical personnel. Participants were provided with detailed instructions for collecting their saliva samples. This approach prioritized comfort during collection, taking place at home before visiting the dental office, rather than in the clinic, where the proximity of other patients might cause discomfort. The standardized conditions for saliva collection, guided by Salivette® instructions, ensured accurate and consistent sample collection across all participants. The Salivette® tube uses absorbent pads designed for optimal saliva collection. Two separate tubes ensure an adequate volume of saliva as some individuals may struggle to collect enough. Participants were instructed to store the collected saliva samples in a domestic refrigerator or at temperature protection until the appointment with the dentist.

At the clinic, further psychological measures of perceived stress and affect were performed in the waiting room just before the dental procedure. Hair samples were collected by a researcher using a disposable hair sampling kit, prepared in accordance with standard hair sampling guidelines[46,47]. The collection site was clean and free from external substances in the air that could exogenously contaminate the hair fibers. It is generally accepted that hair on the scalp grows at an average rate of 1 cm per month, with samples preferably taken near the scalp from the posterior vertex area as this region is associated with the least variability in growth rate. Hair was collected close to the scalp at the posterior vertex of the head, cut using small scissors. The sample for analysis consisted of approximately 50 mg of hair, roughly 150–200 strands. The collected hair samples were affixed to paper with tape and stored in a dry, airtight envelope at room temperature, protecting them from sunlight and moisture, following the procedure described by Wester and van Rossum[31]. Hair and saliva samples were transported from the dental clinic to medical diagnostics laboratory within 20 h of collection. Upon arrival, the saliva samples were immediately frozen at −80 °C until analysis.

This study was approved by the Commission on Ethics at Jagiellonian University and by the authorities of the dental clinic. The study was conducted voluntarily, in accordance with the recommendations of the Helsinki Declaration. All participants gave a written informed consent for participation in this study in accordance with the national legislation and the institutional requirements.

Questionnaires

The *Highly Sensitive Person Scale*(HSPS) by Aron and Aron[8]– researchers used the Polish version of this scale, created using a back translation procedure by Golonka and Gulla[10]. This 27-item self-report measure is designed to assess sensory-processing sensitivity. It consists of 3 subscales: *Emotional Reactivity*, *Sensing the Subtle* and *Overstimulation*. Items are rated on a 7-point scale, ranging from 1 (*not at all*) to 7 (*extremely*). The scale consistently shows good reliability among different samples, with Cronbach's alpha coefficient higher than 0.84[10,48].

The Polish version of the *Perceived Stress Scale*(PSS-10)[49,50] was administered in this study. It is a 10-item self-report questionnaire designed to assess the level of stress in one's life in the last month. Questions concern ways of coping, behaviors and subjective feelings in stressful situations. The Polish adaptation is a valid and reliable tool with Cronbach's alpha coefficient of 0.86 and stability after 4 weeks of 0.72[49].

The researchers used also the Polish adaptation of the *Positive and Negative Affect Schedule*(PANAS)[51,52]. This a 20- or 30-item (depending on the version) self-report questionnaire can be used to assess the severity of emotional states and relatively stable affective characteristics. Four versions are available: two of them (shorter, 20 item; longer, 30 item) regard current emotional states (S20 and S30). The other two versions concern relatively

stable affective characteristics (C20 and C30). Each version is a list of adjectives rated on a 5-point scale. Cronbach alpha coefficient across different versions ranges from 0.73 to 0.95. For the purpose of this study 20-item version analyzing emotional states was used[51].

Hair sample preparation for cortisol analysis

The hair samples were weighed, washed, and extracted with methanol, then finely chopped and ground. The presence of cortisol in the hair was analyzed using liquid chromatography-tandem mass spectrometry (LC-MS/MS). The hair analysis consists of four main stages[46,47]:

1. Decontamination: This step removes any exogenous contaminants from the hair structure and eliminates other unwanted substances. The decontamination process involves washing the hair samples with organic solvents or alternating between an organic solvent and an aqueous solution.
2. Homogenization: This process ensures sample uniformity by grinding the hair into smaller particles to facilitate subsequent stages of analysis. Homogenization is typically performed in a ball mill, which yields approximately 10–50 mg of ground hair.
3. Extraction: This step isolates the target substance from the hair fibers. The extraction is carried out by incubating the hair sample with an organic solvent (methanol). Methanol is commonly used for extraction as it is highly compatible with many medicinal substances.
4. Analysis: The extracted substance is analyzed using liquid chromatography coupled with mass spectrometry (LC-MS). This technique allows for precise identification and quantification of the target substance, such as cortisol, in the hair sample.

This process provides a reliable method of assessing cortisol levels in hair[46,47].

The collected hair samples were washed with propanol (three times) and homogenized using a bead mill homogenizer (Bead Mill Homogenizer, OMNI Int.; PerkinElmer Comp., USA). Two milliliters of methanol were added to the prepared samples, which were then left at room temperature for 24 h. Prior to centrifugation, the samples underwent ultrasonic extraction for 20 min. The centrifuged samples were filtered using an 80 g/m² filter, and the methanol was evaporated to dryness at 37 °C under a nitrogen atmosphere. The dry residue was dissolved in 30 µl of methanol containing the internal standard, cortisol-d3 (concentration = 5 µg/ml). The sample was placed in a chromatography vial and analyzed via LC-MS/MS.

The sample analysis was conducted using a Waters ACQUITY UPLC® H-Class liquid chromatograph system (Waters Corporation, Milford, MA, USA). Chromatographic separation was achieved using a Kinetex column (2.6 µm Biphenyl 100 Å, 100 × 2.1 mm; Phenomenex Companies Worldwide, Torrance, CA, USA), thermostatted at 40 °C. The mobile phases consisted of 0.1% aqueous formic acid solution (phase A) and methanol (phase B), with a mobile phase flow rate of 0.4 ml/min.

The sample analysis was conducted using a gradient program: 0–0.4 min, isocratic flow at 5.0% (B); 0.4–0.5 min, linear gradient from 5 to 50% (B); 0.5–1.9 min, isocratic flow at 50% (B); 1.9–2.0 min, linear gradient to 100.0% (B); 2.0–2.9 min, isocratic flow at 100.0% (B); 2.9–4.0 min, linear gradient from 100 to 5.0% (B); 4.0–5.0 min, isocratic separation at 5.0% (B). The injection volume was 2 µl, and the total run time for each sample was 5 min. The retention time for cortisol (COR; COR-d4) was 3.39 min.

For quantitative analysis, a Xevo TQ-S® mass spectrometer (Applied Biosystems MDS Sciex; Concord, ON, Canada) was used in electrospray ionization (ESI) mode with positive ionization. The ion source parameters were as follows: ion spray voltage (IS) at 5500 V; nebulizer gas (gas 1) at 30 psi; turbo gas (gas 2) at 20 psi; heated nebulizer temperature (TEM) at 300 °C; and curtain gas (CUR) at 30 psi. Quantitative assessment was performed in multiple reaction monitoring (MRM) mode. The ion pairs monitored were m/z = 363.11/120.92 for cortisol (COR) and m/z = 367.11/120.95 for cortisol-d4 (internal standard). Data were processed using MassLynx V4.2 software (Waters Corporation, Milford, MA, USA), and analyte concentrations were calculated relative to the internal standard using a response factor.

Preparation of saliva samples for cortisol analysis

After thawing the saliva samples at 37 °C, they were mixed and centrifuged at 3500×*g* for 10 min at room temperature. To 250 µl of the supernatant, 40 µl of the internal standard, cortisol-d3 (5 µg/ml), was added. The mixture was dissolved in 200 µl of 10% methanol and analyzed via LC-MS/MS following the previously described method.

Preparation of saliva samples for serotonin analysis

From the available methods for measuring serotonin (5-HT) levels in saliva, such as Enzyme-Linked Immunosorbent Assay (ELISA) and Radioimmunoassay, we selected the reference method, i.e., Liquid Chromatography-Mass Spectrometry (LC-MS/MS). The advantage of this method over the others lies in its high sensitivity and selectivity, as well as its ability to perform precise measurements without interference from other substances[53,54]. The use of LC-MS/MS for serotonin analysis ensures high-quality data with minimal external influences[55,56].

To 100 µl of the prepared saliva sample, 4 µl of the internal standard was added, containing a methanolic solution of the deuterated serotonin derivative (serotonin-d4: SER-d4) at a concentration of 500 µg/ml, followed by mixing for 10 s. The prepared sample was deproteinized by adding 100 µl of acetonitrile (1:1, v/v) and mixed for 30 s. The samples were centrifuged at 8,000 rpm for 10 min at 15 °C. 100 µl of the supernatant was placed into chromatography vials and subjected to chromatographic analysis.

Chromatographic separation was performed using a Waters ACQUITY UPLC® H-Class liquid chromatograph system (Waters Corporation, Milford, MA, USA). The samples were separated on a ZIC®-HILIC column (5 µm,

200 Å, 150 × 21.2 mm; Merck, Darmstadt, Germany) maintained at 40 °C in a thermostatted chamber. The mobile phases used were 0.1% aqueous formic acid solution (phase A) and 0.1% formic acid in acetonitrile (phase B), with a flow rate of 0.6 ml/min.

A gradient separation program was applied as follows: 0–−0.2 min, isocratic gradient at 5.0% (A); 0.2–1.5 min, linear gradient from 5 to 55% (A); 1.5–3.1 min, isocratic linear gradient at 55% (A); 3.1–4.5 min, linear gradient from 55.0 to 5.0% (A); 4.5–6 min, isocratic gradient at 5.0% (A). The injection volume onto the column was 4 µl, and the total run time for each sample was 6 min. The retention time for serotonin (SER; SER-d4) was 2.35 min.

Quantitative analysis was performed using a Xevo TQ-S® mass spectrometer (Applied Biosystems MDS Sciex; Concord, ON, Canada) in electrospray ionization (ESI) mode with positive ionization. The ion source parameters were set as follows: ion spray voltage (IS) at 5500 V; nebulizer gas (gas 1) at 30 psi; turbo gas (gas 2) at 20 psi; heated nebulizer temperature (TEM) at 550 °C; and curtain gas (CUR) at 30 psi. For quantitative assessment, the analysis was conducted in multiple reaction monitoring (MRM) mode. The monitored ion pairs were m/z = 177.0/119.0 for serotonin (SER) and m/z = 182.83/119.76 for serotonin-d4 (internal standard). The concentrations of the analytes were calculated using calibration curves prepared through linear regression analysis of peak area versus concentration.

Statistical analysis

Standard descriptive statistical methods were used for the calculation of means and standard deviations. All collected cortisol and serotonin results were normalized using natural logarithm transformations in Microsoft Excel. Statistical significance tests (Kolomogorow-Smirnov test for normality, linear regression, independent student t-test, and MANOVA) were performed using SPSS and Statgraphic Centurion 19. A significance level of 0.05 was used for all statistical analysis. When conducting the t-test, we calculated Cohen's d as a measure of effect size.

In the following step, correlation analysis was performed. Subsequently, the data were grouped using k-means clustering methods. K-means clustering is a supervised learning algorithm that aims to group various objects based on their attributes in k number of groups (clusters). The number of clusters (denoted as "k") is provided as the input. K points are chosen randomly from existing data as cluster centers, and each instance is calculated and assigned to its closest cluster center using a squared Euclidean distance metric. Each instance is grouped among clusters based on minimum Euclidean distances. The centroid (the mean for each cluster) is calculated and used as a new cluster center[57].

All analyses were conducted independently for both the general SPS score (SPS) and the three factors identified in the HSPS scale: Emotional Reactivity (SPS_ER), Sensing the Subtle (SPS_StS), and Overstimulation (SPS_Ovst)[10,58].

Results

Due to the non-normal distributions and significant skewness observed in the levels of cortisol in hair and saliva and serotonin in saliva, a logarithmic transformation was applied to these variables to normalize the data. Following the logarithmic transformation of the data, the Kolmogorov-Smirnov test indicated that the distribution of the variables did not significantly deviate from normality (hair cortisol, $p = 0.28$; saliva cortisol, $p = 0.29$; saliva serotonin, $p = 0{,}88$).

All statistical analyses between males ($n = 54$; 34.4%) and females ($n = 103$; 65.6%) were conducted using a two-tailed Student's t-test. Additionally, Cohen's d was employed to measure effect size. Significant differences were observed between male and female participants in terms of age, Sensory Processing Sensitivity (SPS), Emotional Reactivity (SPS_ER), Sensing the Subtle (SPS_StS), Overstimulation (SPS_OvSt), and perceived stress ($p < 0.05$). The effect size indicated a large and meaningful difference between males and females in age, SPS, SPS_StS, and SPS_OvSt. For SPS Factor I and perceived stress, the effect size fell within the medium range, still indicating practical significance. However, no significant differences were found in biochemical analysis, positive and negative affect, patient discomfort, pain assessment, and behavioral indicators (Table 1).

Table 1summarizes the results of biochemical indicators, psychological indicators of stress and general information taken from participants. It is worth noting the large standard deviation in hair cortisol levels. It was assumed that significant differences in the obtained results might occur due to numerous confounding factors reported in hair samples[32], which could not have been sufficiently controlled in this study.

Correlation analysis

A Pearson's correlation analysis of selected variables was conducted to examine linear correlations. Table 2 presents the correlations between hormonal and psychological stress variables. The level of hair cortisol showed a significant positive association with overall score of sensory processing sensitivity, tendency towards overstimulation (SPS_Ovst), and negative affect. However, all these correlations show weak associations. Furthermore, no associations were revealed between the level of cortisol and serotonin in saliva and any psychological measures, nor between the analyzed biochemical indicators (Table 2). Due to the absence of linear associations between most of the biochemical and psychological results, as well as the lack of a basis to assume predictive relationships, cluster analysis was subsequently performed to identify distinct groups within the data based on levels of biochemical indicators, as well as SPS scores.

K-means clustering

Three independent k-means clustering analyses were applied to the grouped individuals based on their cortisol and serotonin level in saliva as well as general index of individual sensitivity of sensory processing (SPS) and individual aspects of SPS: emotional reactivity (SPS_ER), sensitivity to nuances (SPS_StS) and tendency towards

	Male	Female	*p*	Size effect
N	54 (34.4%)	103 (65.6%)		
age	34.41 ± 13.76	46.23 ± 15.55	< **0.001**	0.79
hair cortisol [ug/g]	28.50 ± 72.20	89.9 ± 332.9	n.s	
saliva cortisol [ng/ml]	11.46 ± 12.14	10.19 ± 7.00	n.s	
saliva serotonin [ug/ml]	84.53 ± 22.20	83.16 ± 10.97	n.s	
ln (hair cortisol [ug/g])	1.92 ± 1.63	2.21 ± 2.10	n.s	
ln (saliva cortisol [ng/ml])	2.24 ± 0.52	2.16 ± 0.56	n.s	
ln (saliva serotonin [ug/ml])	4.41 ± 0.21	4.41 ± 0.14	n.s	
Sensory Processing Sensitivity	4.16 ± 0.67	4.73 ± 0.71	< **0.001**	0.81
SPS_Emotional Reactivity	4.15 ± 0.87	4.58 ± 0.93	**0.005**	0.47
SPS_Sensing the Subtle	4.61 ± 0.71	5.31 ± 0.66	< **0.001**	1.04
SPS_Overstimulation	3.75 ± 0.87	4.62 ± 1.01	< **0.001**	0.90
Perceived stress	16.35 ± 5.98	19.17 ± 6.05	**0.006**	0.47
Positive affect	28.24 ± 7.08	28.02 ± 6.54	n.s	
Negative affect	17.61 ± 5.98	18.46 ± 6.20	n.s	

Table 1. Demographic information, biochemical indicators, and psychological indicators of stress for study participants. The values signify mean ± standard deviation; *p* = probability value; n.s.= non-significant. The size effect was calculated using Cohen's test.

Variables	1.	2.	3.	4.	5.	6.	7.	8.	9.
1. ln (hair cortisol [ug/g])	-								
2. ln (saliva cortisol [ng/ml])	0.135	-							
3. ln (saliva serotonin [ug/ml])	−0.028	0.059	-						
4. Sensory processing sensitivity	**0.238****	0.084	0.031	-					
5. SPS_ER	0.158	−0.025	0.079	**0.886*****	-				
6. SPS_StS	0.099	−0.055	−0.140	**0.510*****	**0.279*****	-			
7. SPS_OvSt	**0.238****	0.136	0.006	**0.853*****	**0.664*****	**0.361*****	-		
8. Perceived stress	0.158	0.023	−0.069	**0.281*****	**0.369*****	−0.006	**0.184***	-	
9. Positive affect	0.003	0.060	−0.134	−0.064	−0.119	0.102	−0.097	**−0.219****	-
10. Negative affect	**0.162***	−0.025	−0.047	**0.246****	**0.315*****	0.047	**0.178***	**0.520*****	0.006

Table 2. Correlation coefficients and *p* for variables analyzed in the study. *Notes.* * - $p < 0.5$, ** - $p < 0.01$, *** - $p < 0.001$; SPS – Sensory Processing Sensitivity; ER – Emotional Reactivity; StS – Sensing the Subtle; OvSt - Overstimulation.

overstimulation (SPS_OvSt). Hair cortisol level was excluded from analysis due to its positive correlation with SPS and SPS_OvSt scores. This decision helps ensure the independence of variables and prevents potential confounding effects.

Sensory Processing Sensitivity (SPS)

Three variables were selected for cluster analysis: ln salivary cortisol, SPS (general index of individual sensitivity of sensory processing) and ln salivary serotonin. Based on the conducted analysis, two groups were identified (Fig. 1):

1) A group of more-sensitive individuals with higher cortisol levels in saliva ($n = 75$; 48%).
2) A group of less-sensitive individuals with lower cortisol levels in saliva ($n = 81$; 52%).

In the next stage, differences in the level of biochemical indicators and psychological variables between the identified groups based on the above cluster analysis were examined. The analysis was performed using the t-Student test (for unequal variances). The differences in variables in the low and high sensitivity groups of individuals are presented in Table 3.

Based on the comparison of the two clusters, it was observed that individuals with higher sensitivity are characterized by significantly higher levels of cortisol in hair and saliva (2.57 ± 2.19 vs. 1.68 ± 1.60 ln [µg/g]; 2.43 ± 0,52 vs. 1.97 ± 0,47 ln [ng/ml], respectively). However, no differences were found in the level of serotonin in saliva (4.41 ± 0.18 vs. 4.41 ± 0.15 ln [µg/ml]). Among the psychological stress indicators, the average values of SPS components Emotional Reactivity (5.03 ± 0.61 vs. 3.89 ± 0.84), Sensing the Subtle (5.36 ± 0.65 vs. 4.80 ± 0.75), and Overstimulation (5.07 ± 0.75 vs. 3.62 ± 0.77) were significantly higher in the high sensitivity group, as were the level of perceived stress (19.47 ± 5.51 vs. 17.07 ± 6.54) and negative affect (19.37 ± 6.66 vs. 17.10 ± 5.41).

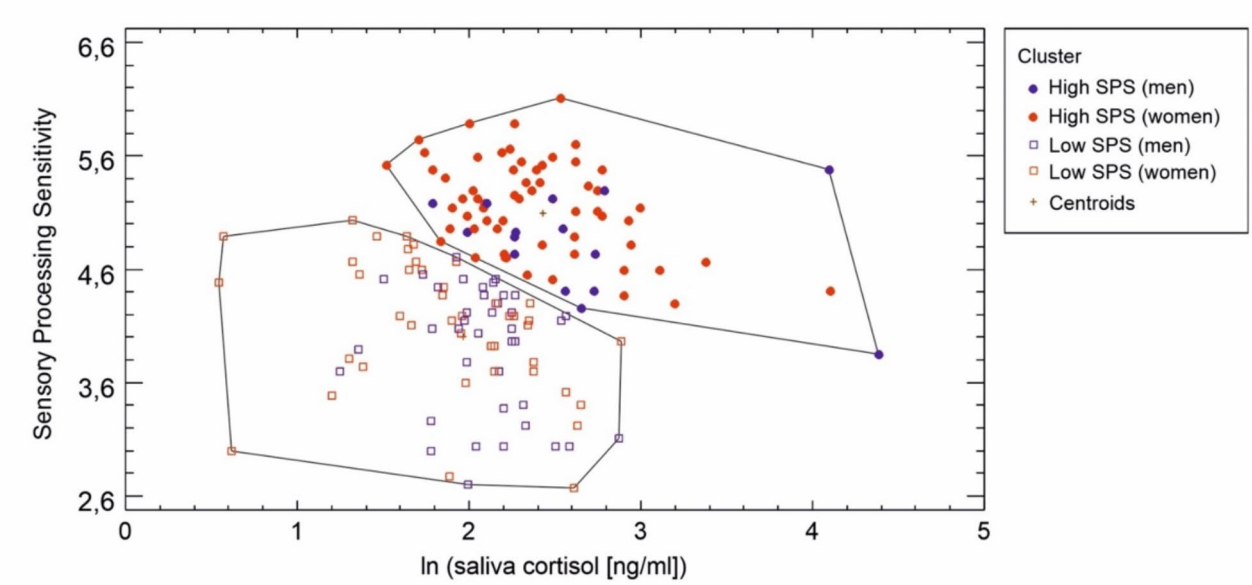

Fig. 1. Results of the k-means cluster analysis, demonstrating the formation of two distinct clusters. For each cluster, the mean values of Sensory Processing Sensitivity and the natural logarithm of saliva cortisol concentration [ng/ml] were calculated, representing the centroids. Within each cluster, participant gender is denoted: males are indicated in blue, and females in red.

	High SPS	Low SPS	*p*	size effect
N	75 (48%)	81 (52%)		
age	43.04 ± 16.44	41.20 ± 15.56	n.s.	
ln (hair cortisol [ug/g])	2.57 ± 2.19	1.68 ± 1.60	**0.005**	0.47
ln (saliva cortisol [ng/ml])	2.43 ± 0.52	1.97 ± 0.47	< **0.001**	0.94
ln (saliva serotonin [ug/ml])	4.41 ± 0.18	4.41 ± 0.15	n.s.	
SPS_Emotional Reactivity	5.03 ± 0.61	3.89 ± 0.84	< **0.001**	1.54
SPS_Sensing the Subtle	5.36 ± 0.65	4.80 ± 0.75	< **0.001**	0.80
SPS_Overstimulation	5.07 ± 0.75	3.62 ± 0.77	< **0.001**	1.90
Perceived stress	19.47 ± 5.51	17.07 ± 6.54	**0.014**	0.39
Positive affect	27.69 ± 6.40	28.47 ± 7.04	n.s	
Negative affect	19.37 ± 6.66	17.10 ± 5.41	**0.021**	0.38

Table 3. Results of t-student test for biochemical and psychological variables between low and high sensory Processing sensitivity groups. The values signify mean ± standard deviation; *p* = probability value, n.s.=non-significant. The size effect was calculated using Cohen's test. Note: SPS – Sensory Processing Sensitivity.

The effect size indicates a large (meaningful) difference between high and low SPS groups in ln saliva cortisol, Emotional Reactivity, Sensing the Subtle, and Overstimulation, and a medium effect (but still important) in ln hair cortisol, perceived stress, and negative affect (Table 3).

SPS: Emotional Reactivity (SPS_ER)

In the next step, a k-means clustering analysis was conducted to examine how the study group would be differentiated by features such as emotional reactivity of individual sensitivity of sensory processing (SPS_ER), ln saliva cortisol, and ln salivary serotonin. Based on the conducted analysis, two groups were identified (Fig. 2).

A comparison of the mean values of biochemical and psychological indicators between the identified groups was conducted using the Student's t-test for independent groups with unequal variances. The results of the Student's t-test are presented in Table 4. Group 1 is characterized by significantly higher levels of salivary cortisol (2.59 ± 0.44 vs. 1.86 ± 0.38 ln [ng/ml]), salivary serotonin (4.46 ± 0.18 vs. 4.37 ± 0.14 ln [ug/ml]), and higher levels of SPS_Overstimulation (4.51 ± 1.07 vs. 4.16 ± 1).

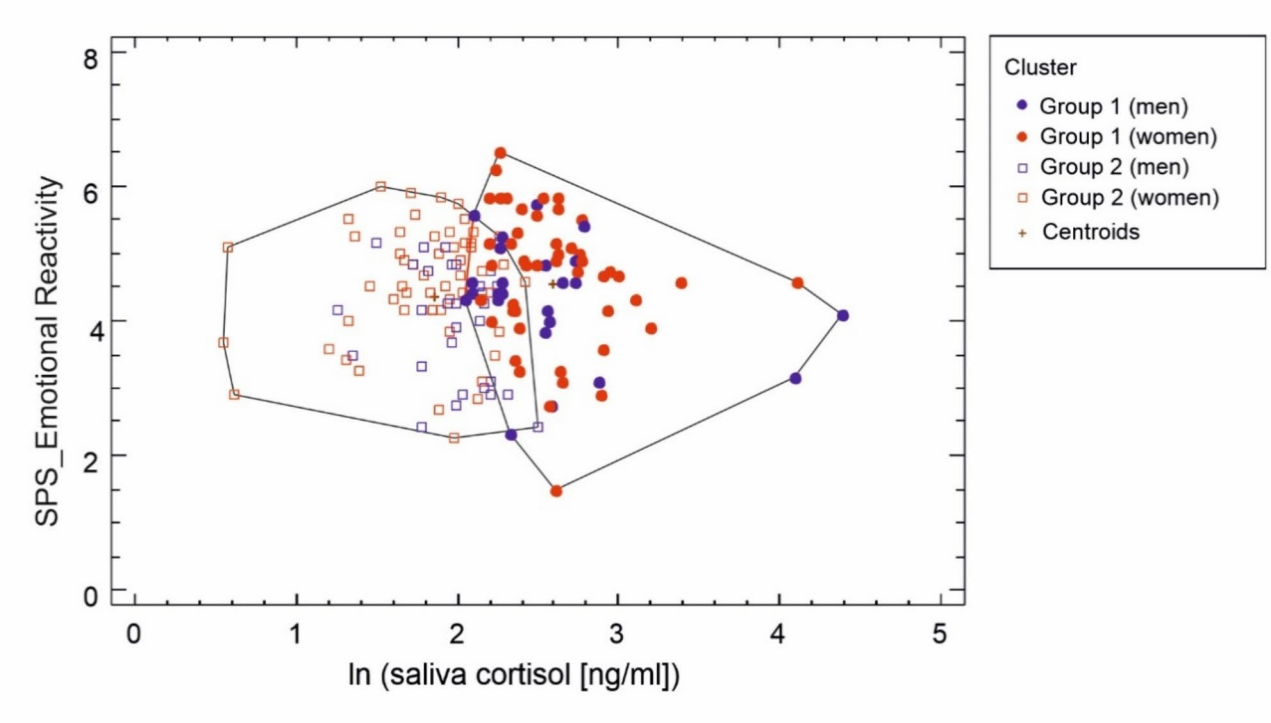

Fig. 2. Results of the k-means cluster analysis, demonstrating the formation of two distinct clusters. For each cluster, the mean values of Emotional Reactivity and the natural logarithm of saliva cortisol concentration [ng/ml] were calculated, representing the centroids. Within each cluster, participant gender is denoted: males are indicated in blue, and females in red.

Factor I	Group 1	Group 2	*p*	size effect
N	75 (48%)	81 (52%)		
age	40.97 ± 17.44	43.01 ± 14.66	n.s	
ln (hair cortisol [ug/g])	2.43 ± 2.01	1.84 ± 1.88	n.s	
ln (saliva cortisol [ng/ml])	2.59 ± 0.44	1.86 ± 0.38	**< 0.001**	1.804
ln (saliva serotonin [ug/ml])	4.46 ± 0.18	4.37 ± 0.14	**< 0.001**	0.558
Sensory Processing Sensitivity	4.65 ± 0.76	4.43 ± 0.73	n.s	
SPS_Emotional Reactivity	4.55 ± 0.96	4.34 ± 0.9	n.s	
SPS_Sensing the Subtle	5.04 ± 0.77	5.09 ± 0.74	n.s	
SPS_Overstimulation	4.51 ± 1.07	4.16 ± 1	**0.036**	0.341
Perceived stress	18.46 ± 6.13	18.02 ± 6.23	n.s	
Positive affect	28.01 ± 7.07	28.16 ± 6.47	n.s	
Negative affect	18.42 ± 6.69	18 ± 5.65	n.s	

Table 4. Results of t-student test for biochemical and psychological variables between two groups. The values signify mean ± standard deviation; *p* = probability value, n.s.=non-significant. The size effect was calculated using Cohen's test. Note: SPS – Sensory Processing Sensitivity.

SPS: Sensing the Subtle (SPS_StS)

K-means clustering analysis was conducted to examine how the study group would be differentiated by features such as Sensing the Subtle, ln saliva cortisol, and ln salivary serotonin. Based on the conducted analysis, two groups were identified (Fig. 3).

A comparison of the mean values of biochemical and psychological indicators between the identified groups was conducted using the Student's t-test for independent groups with unequal variances. The results of the Student's t-test are presented in Table 5. The group with high level of Sensing the Subtle is characterized by significantly lower level of salivary serotonin (4,35 ± 0,14 vs. 4,52 ± 0,16 ln [ug/ml]) and higher levels of general SPS (4.72 ± 0.68 vs. 4.19 ± 0.75), SPS Emotional Reactivity (4.55 ± 0.89 vs. 4.23 ± 0.97) and Overstimulation (4.54 ± 1.02 vs. 3.92 ± 0.99).

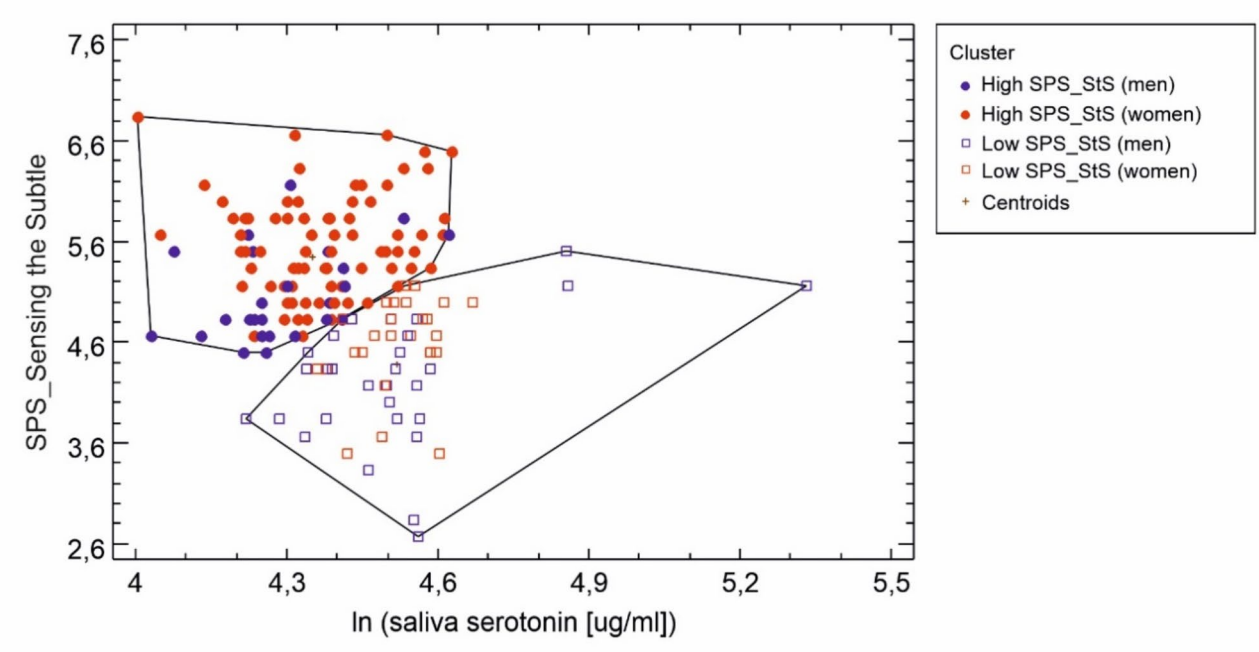

Fig. 3. Results of the k-means cluster analysis, demonstrating the formation of two distinct clusters. For each cluster, the mean values of SPS_StS and the natural logarithm of saliva serotonin concentration [ug/ml] were calculated, representing the centroids. Within each cluster, participant gender is denoted: males are indicated in blue, and females in red. SPS – Sensory Processing Sensitivity; StS – Sensing the Subtle.

Sensing the Subtle	High SPS_StS	Low SPS_StS	*p*	size effect
N	100 (64%)	56 (36%)		
age	42.62 ± 15.9	41.13 ± 16.17	n.s	
ln (hair cortisol [ug/g])	2.24 ± 2.02	1.88 ± 1.82	n.s	
ln (saliva cortisol [ng/ml])	2.17 ± 0.49	2.23 ± 0.64	n.s.	
ln (saliva serotonin [ug/ml])	4.35 ± 0.14	4.52 ± 0.16	< **0.001**	1.155
Sensory Processing Sensitivity	4.72 ± 0.68	4.19 ± 0.75	< **0.001**	0.748
SPS_Emotional Reactivity	4.55 ± 0.89	4.23 ± 0.97	**0.042**	0.351
SPS_Sensing the Subtle	5.45 ± 0.53	4.39 ± 0.59	< **0.001**	1.92
SPS_Overstimulation	4.54 ± 1.02	3.92 ± 0.99	< **0.001**	0.611
Perceived stress	18.27 ± 6.04	18.14 ± 6.44	n.s.	
Positive affect	28.79 ± 6.4	26.86 ± 7.17	n.s.	
Negative affect	18.31 ± 6.35	17.98 ± 5.76	n.s.	

Table 5. Results of t-student test for biochemical and psychological variables between two sensing the subtle (SPS_StS) groups. The values signify mean ± standard deviation; *p* = probability value, n.s.=non-significant. The size effect was calculated using Cohen's test. Note: SPS – Sensory Processing Sensitivity; StS – Sensing the Subtle.

SPS: Overstimulation (STS_OvSt)

For the k-means cluster analysis, three variables were selected: Overstimulation (SPS_OvSt), ln salivary cortisol, ln salivary serotonin. Based on the conducted analysis, two groups were identified (Fig. 4).

A comparison of groups for Overstimulation was conducted using the Student's t-test for independent groups with unequal variances. The results of the Student's t-test are presented in Table 6. The group with a high level of SPS_OvSt is characterized by significantly higher level of hair and salivary cortisol (2.59 ± 2.16 vs. 1.71 ± 1.67 ln [ug/g]; 2.45 ± 0.52 vs. 1.98 ± 0.47 ln [ng/ml], respectively), salivary serotonin (4.44 ± 0.16 vs. 4.39 ± 0.16 ln [ug/ml]), and higher levels of general SPS (5.05 ± 0.49 vs. 4.1 ± 0.65), SPS_ER (4.90 ± 0.70 vs. 4.05 ± 0.92) and SPS_StS (5.27 ± 0.76 vs. 4.90 ± 0.71).

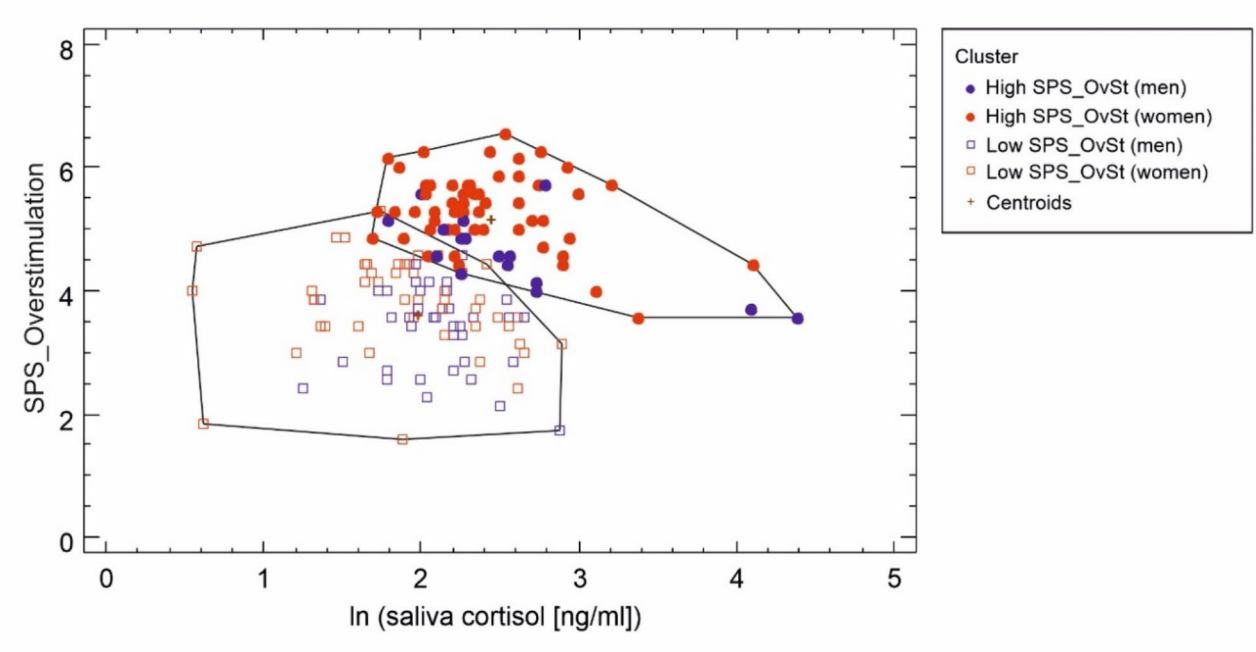

Fig. 4. Results of the k-means cluster analysis, demonstrating the formation of two distinct clusters. For each cluster, the mean values of Overstimulation (SPS_OvSt) and the natural logarithm of saliva cortisol concentration [ng/ml] were calculated, representing the centroids. Within each cluster, participant gender is denoted: males are indicated in blue, and females in red.

SPS_Overstimulation	High SPS_OvSt	Low SPS_OvSt	*p*	size effect
N	71 (48%)	85 (52%)		
age	44.28 ± 16.61	40.25 ± 15.26	n.s.	
ln (hair cortisol [ug/g])	2.59 ± 2.16	1.71 ± 1.67	**0.005**	0.463
ln (saliva cortisol [ng/ml])	2.45 ± 0.52	1.98 ± 0.47	**< 0.001**	0.947
ln (saliva serotonin [ug/ml])	4.44 ± 0.16	4.39 ± 0.16	**0.048**	0.321
Sensory Processing Sensitivity	5.05 ± 0.49	4.1 ± 0.65	**< 0.001**	1.625
SPS_Emotional Reactivity	4.9 ± 0.7	4.05 ± 0.92	**< 0.001**	1.037
SPS_Sensing the Subtle	5.27 ± 0.76	4.9 ± 0.71	**0.002**	0.508
SPS_Overstimulation	5.16 ± 0.66	3.61 ± 0.74	**< 0.001**	2.198
Perceived stress	19.03 ± 5.67	17.55 ± 6.51	n.s.	
Positive affect	28.04 ± 6.92	28.14 ± 6.61	n.s.	
Negative affect	19.17 ± 6.58	17.38 ± 5.64	n.s.	

Table 6. Results of t-student test for biochemical and psychological variables between two factor III groups. The values signify mean ± standard deviation; *p* = probability value, n.s.=non-significant. The size effect was calculated using Cohen's test. Note: SPS – Sensory Processing Sensitivity; OvSt – Overstimulation.

Discussion

The study aimed to investigate the relationship between biochemical and psychological indicators of stress among adult dental patients, with a focus on Sensory Processing Sensitivity (SPS) and its factors. The correlation analysis between psychological and biochemical measures revealed positive correlations between hair cortisol and sensory processing sensitivity, overstimulation and negative affect. No significant correlations were observed for salivary cortisol and salivary serotonin. The results were analyzed further by clustering individuals based on their SPS scores, SPS factors, cortisol and serotonin levels.

Cluster analysis based on SPS, salivary cortisol, and salivary serotonin identified two distinct groups: individuals with higher sensitivity and higher cortisol levels, and those with lower sensitivity and lower cortisol levels. Individuals in the high sensitivity group exhibited elevated levels of cortisol in both hair and saliva, suggesting a heightened physiological response to stress. This group also showed higher scores in all SPS factors, including Emotional Reactivity (SPS_ER), Sensing the Subtle (SPS_StS), Overstimulation (SPS_OvSt), as well as increased perceived stress and negative affect before dental procedures. However, the analysis based on the SPS

general score did not reveal associations between SPS and salivary serotonin, which is in line with Licht et al.'s findings[59]. The results of our study confirmed previous studies indicating that individuals with higher levels of sensory processing sensitivity report higher levels of perceived stress[4,10], additionally, our results suggest that:

Individuals characterized by a higher level of sensory processing sensitivity show higher levels of cortisol (both in hair and saliva cortisol).

Individuals with higher levels of sensory processing sensitivity show higher levels of negative affect while waiting for a dental procedure.

Thus, hypothesis H1 and H3 have been confirmed. Our results are in line with previous findings that indicated associations between SPS and dental anxiety[24–26]. In the light of these findings, it seems particularly important to consider possible strategies to manage patients' stress and prevent the vicious cycle described by Armfield et al.[22] in which a negative experience at a dental clinic may evoke fear that might lead to subsequent visits being postponed. Irregular dental care and delayed visits can lead to serious problems and symptom-driven treatment, often linked to pain and discomfort, which in turn may increase dental anxiety or phobia.

When examining the clusters formed based on Emotional Reactivity, two groups were observed with different neurohormonal responses: individuals with significantly higher and lower levels of salivary cortisol and serotonin. The group with higher cortisol and serotonin levels had also higher scores in Overstimulation. This interesting result could be considered inconsistent with hypothesis H2, which assumed lower serotonin levels in the high SPS group. However, regarding contradictory findings regarding the associations between SPS and serotonin secretion[43,59], we may take into account the multidimensionality of the SPS construct when interpreting these findings.

For Sensing the Subtle, the high sensitivity group was characterized by lower levels of salivary serotonin, higher overall SPS scores and higher scores in Emotional Reactivity and Overstimulation. Only analysis with Sensing the Subtle revealed distinct clusters that differentiated groups in serotonin level and scores in sensory sensitivity. The other factors and the overall SPS level were better differentiated by the cortisol level variable. This result partly supports hypothesis H2, thus leading to the following conclusion:

Individuals with higher levels of sensing the subtle show lower levels of serotonin in saliva.

In the analysis of Overstimulation (SPS_OvSt), the high sensitivity group showed significantly higher levels of cortisol in both hair and saliva, as well as higher levels of salivary serotonin. This group also had higher general SPS scores, SPS_ER and SPS_StS, indicating that individuals prone to overstimulation exhibit stronger neurohormonal responses and heightened sensitivity across multiple dimensions. Analyses based on SPS_ER and SPS_OvSt may be interpreted in line with greater reactivity to both positive and negative stimuli, as is often reported in highly sensitive individuals[4]. As Sperati et al.[60] point out, highly sensitive individuals may experience more challenges in negative environments, but also more benefits in positive ones, as compared to persons lower in SPS.

The cluster analysis based on different SPS factors indicates that exploring specific aspects of sensory processing sensitivity may bring different conclusions and supports the thesis regarding the complex characteristics of SPS [10,58]. This is in line with Corbett et al.'s[28]study, which indicated different outcomes between sensory sensitivity and morning cortisol, depending on which aspect of SPS is examined. In this analysis, Sensing the Subtle corresponds most to studies that associate SPS with a lower level of serotonin[43]. It may correspond to the results that indicate negative associations between salivary serotonin concentration and trait empathy, happiness[39], as well as current mood[61]. However, no associations were found between salivary serotonin levels and symptoms of depression and anxiety[61]. Importantly, in the high sensory sensitivity groups which were identified on Emotional Reactivity and Overstimulation factors, higher levels of salivary serotonin were observed. Thus, it is particularly significant to emphasize that salivary serotonin levels showed varied relationships with different SPS factors, indicating the need to analyze SPS as a multidimensional construct. On the other hand, only the general SPS score, which encompasses all tested factors (i.e., emotional reactivity, sensitivity to nuances, and tendency toward overstimulation), revealed differences associated with subjective psychological outcomes, such as perceived stress and negative affect. Therefore, analyzing the general SPS score also appears to be valuable.

The association between SPS and heightened reactivity is particularly relevant in the context of health care. Increased reactivity in highly sensitive individuals may result in stronger responses to both negative and positive factors associated with a dental visit[60]. It is important to note that various external stimuli lead to internal experiences, such as emotions and memories, which can influence attitudes toward the treatment process. These experiences may have further implications. For example, experiences during a dental visit – including those related to the procedure itself and interactions with medical staff – can impact how actively and systematically patients engage with future preventive and interventional procedures.

The findings underscore the importance of considering individual differences in sensitivity when assessing stress responses and suggest that heightened sensitivity is associated with increased physiological and psychological stress. This could be considered during a dental visit, offering substantial benefits for all dental patients, particularly for those with traits of high sensitivity. Referring directly to the dental context, Appukuttan[62] presents a literature review on possible strategies to help patients with excessive emotional response. Studies show that app. 12–15% of adults suffer from dental anxiety that leads to avoiding or delaying visits to the dentist, thus possibly resulting in increased caries, tooth loss, and serious health problems[22,23,63,64]. Understanding the dispositions and needs of patients with high sensory sensitivity could make it possible to offer solutions and interventions, such as sensory-adapted dental environments (SDE), good patient–dentist relationship and trust building, behavior-management techniques, relaxation techniques, guided imagery, distraction, enhancing control, or positive reinforcement[62].

Finally, we would like to point out the limitations of the study and some implications for future research. The study's quasi-experimental design allowed for natural conditions but lacked full control over the study variables. An ideal approach would have involved conducting the study in a controlled experimental setting, with better

control over sample collection and potential confounders. However, this could reduce external validity and limit the generalizability of the results to real-life situations. Additionally, the study could be repeated on a different day when no medical visit is planned in order to provide control measurements for comparison. Measurements at multiple time points to account for circadian fluctuations in cortisol and serotonin[47,65], as well as the use of alternative methods like blood or urine samples[30], could provide further insights. Including additional psychological measures would allow for a deeper focus on how patients evaluate various aspects of their medical visit. Qualitative research, such as interviews, could help identify factors that contribute to discomfort, anxiety, or fear, as well as those that promote a supportive environment and patients' well-being. Combining biochemical studies with in-depth psychological analysis could help improve healthcare by offering a deeper understanding of patients' experiences. Lastly, another important aspect of dental patients with high SPS should be emphasized: their discomfort, negative emotions, negative attitudes and behaviors, or more serious dental problems are all possible significant sources of stress for dentists. If we now change the perspective and consider that also about 30% of dentists may be highly sensitive persons, we may expect that not only patients experience problems. Planning an empathetic, patient-centered approach may result in not only greater comfort and better and more regular dental treatment, but also less stressful work for dentists, which may consequently improve all systems in dental medicine. The results refer to dental patients but may be universal in different contexts of medical care.

Data availability

The raw data supporting the conclusions of this article are available from the corresponding author (krystyna.golonka@uj.edu.pl) upon reasonable request.

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K.G., B.G., D.K., D.D., T.K., and W.K. contributed to the conception and design of the work. D.K. and D.D. conducted the research, data acquisition. W.K. and B.B. - conducted laboratory tests.K.G and B.C.-S. analysis of the data, data visualization and interpretation.All authors took part in drafting the work and/or revising it critically. All authors reviewed the manuscript.

Declarations

Competing interests
The authors declare no competing interests.

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