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"Sensation seeking correlates with increased white and grey matter integrity of structures associated with visuospatial and decision-making processing in healthy adults"

"Correlazione tra sensation seeking e aumentata integrità della sostanza bianca e grigia in strutture associate alle funzioni visuo-spaziali e di decision-making in adulti sani"

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SUMMARY:

BACKGROUND

Sensory processing

Sensory perception is a neurobiological essential function that allows the interaction between the human body and the stimuli of the outer world, through the sensory receptors that convey the sensory information (visual, auditory, olfactory, taste, touch, movement and activity level) to the central nervous system.

The central nervous system is able to process and integrate the stimuli, which acquire meaning through its elaboration, called Sensory Processing, and then reflect on the individual's environmental responses. The features of Sensory Perception are its **concreteness**, its **involuntary** and its **time-space collocation**, and these are necessary for the proper reality examination.

The dynamic processing of **sensory input and experienced events** creates one's neurological organization and personality development (1). This means that an individual's sensory processing is going shape them in various elements, from their intellective and linguistic evolution to their temperament and personality.

On the other hand, Sensory Processing is itself determined by one's way of detecting, regulating, interpreting and responding to sensory stimuli (2), meaning, at first, a physiological component, that allows the perceiving process, and then a behavioural component, as a response to the stimulus. The former refers to the functioning of the nervous system and its structural changes (3), while the latter relates to one's ability to modulate reactions to stimuli in order to adapt to the environment (4).

It is Sensory Processing itself that, if properly functioning, enables adaptive and organized reactions to environmental demands, that may not occur whenever a subject has atypical patterns of sensory processing, which imply a detrimental influence on the individual's everyday life. (5)(2)

Depending on the **neurological threshold** for the sensory stimuli, meaning the lowest level needed by stimuli to activate a neuronal group, atypical sensory processing may be exteriorized in two opposite directions, which are **hypersensitivity** and **hyposensitivity** to sensory stimuli. Individuals with a low neurological threshold require low intensity stimuli to react, whereas a high neurological threshold implies higher intensity stimuli or a longer time to react to the same stimuli (2). **Hypersensitivity** can be defined as a tendency to have negative reactions to a sensory input that is generally thought to be inoffensive, such as noises and smells in a room or tactile sensitivity to certain fabrics, while **hyposensitivity** is considered to be a

reduced sensitivity to environmental stimuli, that can lead, for example, to inattention to injuries or excessive touching (6). These two conditions are not to be considered as separate phenomena, as they represent the extremes of the same continuum (7), and they can coexist in the same individual in different sensory systems (8).

Dunn's model of Sensory Processing

Winnie Dunn, an American occupational therapist, designed a model of sensory processing consisting in two axes that represent the neurological threshold of the individual, that can be high or low, and their **behavioural response**. Furthermore, for each neurological threshold there is an active or passive behavioural response strategy, where an active behavioural response is embodied by actions aimed at coping with the neurological threshold, whereas a passive behavioural response is represented by the lack of attempt to minimize or enhance the stimulation, although the latter does not meet the neurological threshold.

Based on these criteria and their relations, four orthogonal quadrants can be identified, representing four sensory profiles, that are pictured in Dunn's four quadrant model:

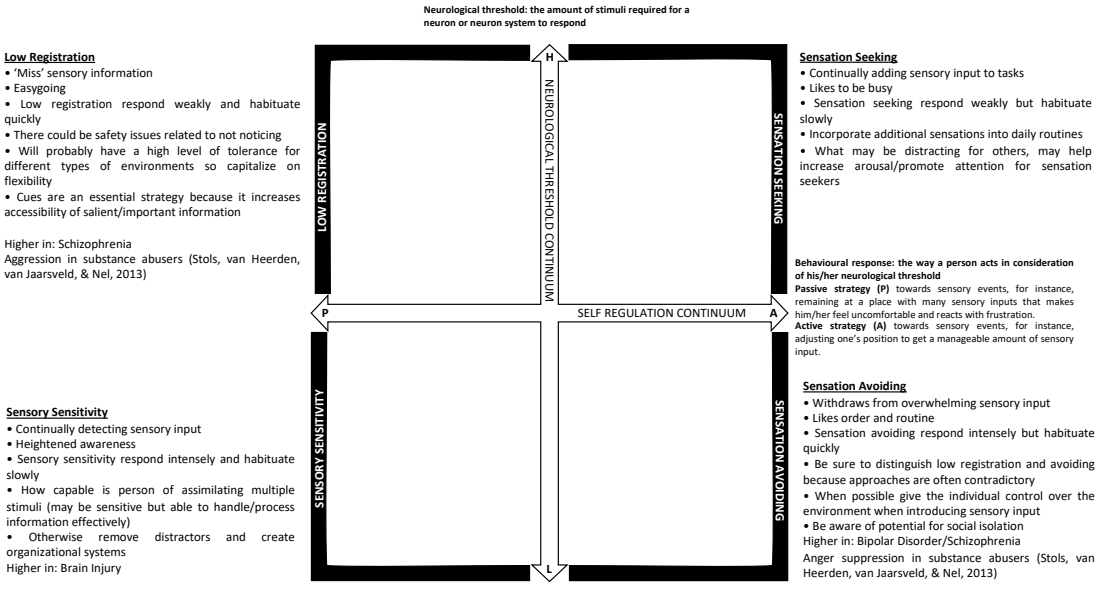

Figure 1. The Dunn's model of sensory profiles*. The axes of the neurological threshold and the behavioural response intersect creating four quadrants, that represent four different sensory profiles: low registration, sensation seeking, sensory sensitivity and sensation avoiding.*

The four sensory profiles identified by Dunn have specific characteristics, conferred by the different susceptibility to the sensory stimuli, having an impact on the individual's psychological functioning.

- **Low Registration** is characterized by a passive behavioural response and high neurological threshold, therefore the reaction to a stimulus will be slow or even absent, even though that can be strong or even damaging. This kind of behaviour can be interpreted as indifferent, sluggish or lacking of motivation and interest in the world and in relationships, however that is actually due to an absence of sensory reaction which implies the inability to recognise possibility for action (9). In the daily life that manifests as a defect in reacting to falls, injuries or extreme temperatures (10).
- **Sensation Seeking** represents high neurological threshold and active behavioural response, that lead to the active seek of high intensity stimuli in order to meet the high neurological threshold. Individuals with this sensory profile tend to engage in activities aimed at increasing sensory experience, such as excessive motor activity, seeking physical contact with items and people, and they also tend to quest for strong stimuli, such as spicy food or strong noises or exciting visuals (10). The resulting behaviour may be perceived as irresponsible, impatient and disrespectful, due to the lack of physical boundaries and their dangerous behaviour, aimed to boost their sensory experiences in order to make the sensory input cross their reaction threshold.
- **Sensory Sensitivity** is represented by low neurological threshold and a passive behavioural response, that causes a lack of action in stopping or reducing the stimuli causing discomfort. Those can cause intense sensory reactions, leading to feelings of tension, anxiety and nervousness and therefore aggressive and negative reactions, since the stimuli are perceived as intense, overwhelming and invasive (10).
- **Sensation Avoiding**, with low neurological threshold and active behavioural response, that lead to active avoidance of the sensory stimuli to decrease unpleasant experience, which is caused by intense sensory reaction to every sensory stimulus. Since these reactions generate/develop tension, anxiety and nervousness, they can be expressed by refraining from outdoor activities such as travelling, isolation and social withdrawal, in order to avoid overwhelming sensory input (9).

The Adolescent/Adult Sensory Profile (AASP)

This Sensory Profile tests is one of the few sensory processing tools available for adolescents (above 11 years) and adults, it is non-intrusive and easy to administer.

The AASP is a 60-item self-report psychometric assessment, developed by Dunn and Brown, that includes questions about each of the sensory processing categories (visual, auditory, touch, taste/smell, movement and a general category of sensory level). The AASP test is designed as a trait measure of sensory processing, evaluating through the questions the behavioural responses to everyday sensory experience for each category. The scoring system consists in a 5-point Linker scale, through which the participants indicate the intensity/frequency of their behavioural responses to sensory stimuli in everyday life, and each of the four quadrants, namely the sensory profiles, are represented by fifteen items that cover all the classes of stimuli (11).

The various items relate to the sensory processing categories:

- Taste/Smell processing items assess one's response to scents and tastes. (I often find dishes to be bland).
- Motion processing items assess responses to vestibular and proprioceptive stimuli (I am not sure to walk on stairs).
- Visual processing items assess the reaction to what one sees (I would rather go to places that are colourful and bright).
- Touch processing items measure the response to stimuli that touch the skin (I usually find fabrics to be too rough).
- Activity Level items assess the attitude to engagement in everyday activities (I am used to working on two or more tasks at the same time).
- Auditory processing items assess a person's reaction to what they hear. (I get distracted if there is any noise around).

Regarding the measurement of the Neurological Threshold Continuum:

- High Threshold items measure the need for higher intensity sensory stimuli, or even absence of response (I hum, whistle, sing or make other noises). This attribute identifies Low Registration and Sensation Seeking profiles.

Low Threshold items measure an individual's awareness or discomfort perceived towards sensory stimuli (I don't like strong tases mints). This attribute identifies Sensory Sensitivity and Sensation Avoiding profiles. Regarding the Behavioural Response and the Self-Regulation Continuum:

- Passive Behaviour items measure the tendency to respond according to one's neurological threshold (I don't notice when my name is called). This attribute identifies Sensation Seeking and Sensation Avoiding profiles.
- Active Behaviour items measure a person's tendency to act in order to make the stimulus meet their neurological threshold (When others get too close, I move away). This attribute identifies Sensation Seeking and Sensation Avoiding profiles.

Factor analysis allowed to derive the four features described on the AASP categories, and the results were consistent with the quadrant model's a priori hypothesis (9).

The limitation of the use of the AASP questionnaire in sensory profiling is owed to the difficulty of self-monitoring (12), but it is the best option to date to identify sensory profiles, and consequentially to help determine the sensory processing interindividual variabilities.

Association of sensory profiles with affective disorders

Sensory processing is the ability to register, modify and organize sensory information in order to adapt to environmental circumstances (13) (10), and the **extreme processing patterns,** that include hyper- or hyposensitivity to non-aversive stimuli, are to be considered sensory processing disorders since they interfere with function and participation in daily life (2,10). Hypersensitivity is generally referred as the main sensory processing disorder (SPD), since in this case daily sensory events are perceived as noxious (14), or harmless sensory input can trigger an exaggerated behavioural reaction. (15) (16), (17).

Hyposensitivity has been mainly related to depression and lower levels of arousal, whereas hypersensitivity has been primarily connected with anxiety and higher levels of attention and arousal (18,19). However, both hyper and hyposensitivity could possibly be linked to depression since they enhance negative emotionality (20).

The sensory processing patterns that are most associated with emotional disturbances are **sensory sensitivity, sensory avoiding and low registration,** that are correlated to high levels of anxiety, somatization, distress symptoms, interpersonal difficulties, ego weakness, thought distortion and poignancy (21). Extreme sensory processing patterns have also been reported as a stable feature that might be used to classify people with major affective disorder (22–24), although a single profile should not confer a unique vulnerability pattern associated with mental disorders.

The impairment in modulating emotional and behavioural responses that is caused by the extreme sensory processing patterns **can affect everyday situations** that involve sensory stimuli, that may be accompanied by fear, anxiety and discomfort (25), causing obstacles in the daily life functioning and leading to confinement from social events (26–29).

In particular, **sensory sensitivity and sensory avoiding** (and higher ability to register sensory input) could be predictors of depression and anxious/cyclothymic affective temperaments, whereas **low registration** could foretell anxious and irritable affective temperaments. On the other hand, decreased severity of depression and hyperthymic affective temperament are linked to **sensation seeking patterns** (22).

Higher quality of life in individuals with SPD is predicted by the development of coping strategies, and higher physical quality of life can be found in younger patients and in patterns with **lower sensory sensitivity** (23). The coping strategies are able to define an individual's response to complex environmental events and stressors by combining personality and temperamental elements with previous experiences and learning components.

In case where sensory patterns are extreme, responses to environmental stimuli may be emphasized or alternatively absent, based on the enhanced or reduced level of reactivity to the sensory input, and this may lead to an increased chance of developing anxiety or depression owed to different psychological expectations and maladaptive coping strategies, that are intended to equilibrate the imbalance caused by the deficit of integration of the sensory information (30).

Low registration implies a defect in identifying environmental inputs, therefore resulting in decreased emotional and behavioural reactivity to the environment (9), that may result in passiveness, lack of motivation and reduced emotional expression (30).

On the other hand sensation seeking may be a resilient trait (22,23), since individuals with this sensory profile are more likely to create a resilience-promoting environment as they fancy both physical and social interactions (31). Furthermore, lower levels of **sensory sensitivity** were linked to higher autistic traits, which included significant interpersonal difficulties and impaired social communication (32).

Evidence of lower tendency to pursue sensory input has been found in various clinical populations, such as neurodevelopmental (33,34), mood (10,17,22,35,36) or psychotic (37–39) disorders.

Indeed, autism spectrum disorder and ADHD are strongly predictive of alterations in two domains each of the ASSP, since autism appears to be connected **to Sensory Sensitivity** by genetics and to **Low Registration** and **Sensory Avoiding** by non-shared environmental factors (34).

There is also evidence that supports that hyposensitivity, meaning **Low Registration**, and hypersensitivity to sensory stimuli co-exist in adolescents with early-onset schizophrenia, with a correlation between negative symptoms and hyposensitivity, and between positive symptoms and hypersensitivity. This association is real even though there is no diagnosis of psychosis, but only schizotypal traits. Negative symptoms can be exacerbated in particular by Low Registration traits, defined by inefficient perception of social cues and information, since this can lead to the creation of dysfunctional beliefs such as self- stigmatisation (40). Positive symptoms are related to hypersensitivity, which is associated with the inability to strain irrelevant information, possibly resulting in abnormal cognitive-perceptual experience. As opposite to this, schizotypal traits are not found correlated with **Sensation seeking** (39). **Furthermore** increased predisposition to look for stronger sensory stimuli typical of **Sensation seeking** is reported to secure reduced symptomatology (41) such as physical anhedonia, which plays a role in proneness to schizophrenia (36), and higher quality of life (23).

Overall, literature concordantly reported results indicating the correlation between the sensation seeking profile and resilience to mental illnesses.

Current findings on the neurobiological substrate of sensory profile

Since SPDs have been found as transdiagnostic risk factors for various psychiatric disorders, the association between sensory processing patterns alterations and neurological structures has been studied through neuroimaging, and considering that magnetic resonance is the best tool to investigate neurological structure, various techniques of MRI have been exploited in order to evaluate grey and white matter structures and microstructures.

Task-based MRI allows to visualize which areas are activated by sensory stimuli, and a previous study indicated that multiple cortices were simultaneously activated by sensory stimuli, suggesting that those were involved in the process of integrating sensory stimuli (42,43). This implies that an important role in sensory processing is played by white matter, since white matter tracts, which are myelinated axonal fibers,

connect multiple cortices in the brain (44,45), such as primary sensory cortices, higher cortices, deep grey nuclei and brain stem (46).

Diffusion Tensor Imaging, on the other hand, allows to evaluate white matter microstructure, as it is sensitive to the diffusion process of water and other molecules. As a result, this method allows visualization of white matter microstructures in their maximum diffusivity direction, which is also aligned with their direction of orientation and their myelination, that function as barriers to the random flow of water molecules (49). The measurement of molecules' movement is on a micron scale, and is characterized by four diffusion parameters: fractional anisotropy (FA), axonal diffusivity (AD), radial diffusivity (RD), and mean diffusivity (MD); cell density, axons and myelin sheath, which are significant information about white matter tracts, are provided by these parameters (50).

The interindividual variability and the disorders in sensory processing could be partially due to the different white matter networks that come into being in every individual, and this ultimately reflects in each individual's behavioural response (47,48).

Regarding the healthy population, to our knowledge only one study explored the correlation among white matter tracts, using Diffusion Tensor Imaging, and sensory processing profiles, using the Adolescent/Adult Sensory Profile (AASP) questionnaire in a sample of 84 healthy young adults (42 females, 42 males) aged 24,5±4.7 (range: 19–39 years) (51).

More precisely, a positive correlation ($P<0,001$) was found, through the analysis of the AASP scores and the diffusion parameters, in the right Cingulum-Cingulate Gyrus bundle (CCG) and no other regions, in particular between AD and activity level, AD and sensory sensitivity, AD and sensation avoiding and MD and sensation avoiding. The analysis of the AASP subscores and diffusion parameters demonstrated positive correlations ($P<0,001$) in the right CCG, between AD and sensory sensitivity-activity level, AD and sensation avoiding-touch, MD and sensory sensitivity, and in the right uncinate fasciculus (UNC) between MD and sensory sensitivity-auditory. The study suggested that variability in CCG's and UNC's white matter microstructures may imply low neurological threshold for sensory stimuli. (51).

As observed by the authors, their results "should not be applied to other developmental stages", and they highlight the need for "more studies involving participants in other

development stages" in consideration of the young age of their sample and the maturational changes of the white matter during normal development.

Regarding variations of grey matter volume (GMV) related to sensory profiles, among literature there is only a study, by Yoshimura and colleagues, that examined 51 young, healthy volunteers (26 females) aged: 22.5±4.5 (range: 19-43 years), and reported a positive relationship was found between the GMV, in primary or secondary sensory areas for every modality, and sensory profile modality specific subscales, and between the left Dorsolateral Prefrontal Cortex volume and Sensory Sensitivity (12).

Aside from these two articles, most of the neuroimaging studies on sensory profiles consists of case-control studies on neurodevelopmental disorders. This led to highlighting the differences between children with a sensory processing disorder and typically developing ones, showing, for example, a decreased Fractional Anisotropy (FA) and increased Mean Diffusivity (MD) and Radial Diffusivity (RD) in particular in the Posterior Corpus Callosum, in the Posterior Corona Radiata and the Posterior Thalamic Radiations(47).

In a recent study, adults with autism spectrum disorder and Attention Deficit Hyperactivity Disorder (ADHD) manifested a significant correlation between Sensory Sensitivity scores and Radial Diffusivity values in the posterior portion of the Corpus Callosum (52).

It has been found an association between the sensation seeking trait and reward expectancy related activity in the left Ventrolateral Prefrontal Cortex and the Ventral Striatum (53).

The **left ventrolateral prefrontal cortex** is a region in the frontal lobe which is involved in numerous cognitive operations, involved in the response inhibition processes and goal directed response selection (54). The **ventral striatum,** which composes part of the striatum together with the putamen and the caudate, includes the Nucleus Accumbens, and connects different parts of the brain, in particular the limbic region (55).

Yet, further research is needed regarding the role of SPD in the physiopathology of mental disorders as expressed in a self-report questionnaire, since that reflects the patients' daily life, as well as in objective measures that provide possible explanations to underlying neural mechanisms that explain the un adaptive behaviours in everyday life (22).

Neuroimaging

Neuroimaging technologies existing nowadays can be classified into structural and functional neuroimaging techniques. Referring to structural neuroimaging techniques means computed tomography (CT), magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI), whereas functional neuroimaging techniques include positron emission tomography (PET), single photon emission computed tomography (SPECT) and functional magnetic resonance imaging (fMRI).

The modalities that were used in this study are standard neuroimaging, functional magnetic resonance imaging (fMRI) and diffusion-weighted magnetic resonance imaging (DTI).

Standard Neuroimaging

One of the most efficient and versatile imaging tools for evaluating brain tissue is Magnetic Resonance Imaging (MRI), leading us to investigate this technique as a potential objective evaluation method for sensory processing.

Specifically, MRI utilize a magnetic field to align protons in water molecules for creating anatomical images of the brain. For this reason, standard neuroimaging is used to verify the anatomy of the subjects, evaluating the cortical thickness and grey matter volume of ROI- structures.

This neuroimaging technique allows to reproduce two- or three-dimensional high-quality images of cerebral structures through magnetic fields and radio waves, thereby without the use of ionizing radiation or radioactive traces.

Magnetic resonance imaging produces images that reflect different physical properties, depending on the type of sequence that is being used. The most applied sequences in neuroimaging are the T1 and T2 weighted sequences, FLAIR, spin echo, inversion recovery, fast spin echo and gradient recovery.

In particular, to create a T1-weighted image, magnetization must recover before the signal is measured by changing the repetition time (TR). This image weighting is useful, for example, to evaluate the cerebral cortex. On the other hand, T2-weighted image are created when the magnetization decays before measuring the MRI signal, by changing the echo time (TE). This image weighting is useful for detecting water-rich tissues, such as the presence of edema and inflammation, revealing white matter lesions.

Functional Magnetic Resonance Imaging

The idea behind functional magnetic resonance imaging (fMRI) is to deduce brain activity by evaluating changes in cerebral circulation. Increased brain activity is accompanied by significantly elevated cerebral blood flow (CBF) (56). Many studies in the last decades, including the 130-years-old Roy-Sherrington hypothesis, characterized the relationship between brain activity and CBF, that is based on the increased demand for cerebral metabolism in response to neural activity, that leads to task-induced vasodilatation in the brain areas involved in the activity.

Functional MRI rely on the paramagnetic properties of oxygenated and deoxygenated haemoglobin to visualize images of changes in blood flow in brain areas associated with neural activity.

This technique has had a real impact on basic cognitive neuroscience research, since it can be employed to reveal brain structures and processes associated with perception, thought and action. Positron emission tomography (PET) has been largely replaced by f-MRI for the study of brain activation patterns, even though PET retains the significant advantage of being able to identify specific brain receptors associated to particular neurotransmitters through its ability to visualize radio-labelled receptor "ligands".

Diffusion Tensor Imaging

Diffusion Tensor Imaging is a diffusion-weighted RMI technique that allows to measure the diffusion process of water molecules in tissues. In neurological structures water moves in an anisotropic way, which means a directional way, in particular molecules will mainly move along the axis of the neural fiber, instead of random directions as described by Brownian motion.

For this reason, this method permits the evaluation of white matter microstructures in vivo in their maximum diffusivity direction, which is also aligned with their direction of orientation and their myelination, that function as barriers to the random flow of water molecules (49).

The measurement of molecules' movement is on a micron scale, and is characterized by four diffusion parameters:

- **Fractional anisotropy** (FA). Anisotropy occurs when the movement of water is no longer random, and there is directionality in the diffusion of water. FA quantifies the how strong the directionality of diffusivity of the local tract structure is, and it is highly sensitive to microstructural changes even though it

can be unspecific to the cause of change (57,58). Its maximum theoretical value is 1, and it corresponds to major white matter tracts, while lower values, which tend to zero in cerebrospinal fluid, are found in grey matter (58).

- **Axonal Diffusivity** (AD) is a diffusion parameter in the axonal direction (59–61), and it is sensitive to axonal disassembly and degeneration, increasing as the tortuosity of white matter tracts in the axonal direction decreases (59,60). In denotes tract-specific or timing specific changes in axonal morphology (59), increasing with brain maturation.
- **Radial Diffusivity** (RD), sensitive to changes in myelination (59,60), it increases in demyelination.
- **Mean Diffusivity** (MD) is the average diffusivity of the principal diffusivities in axonal direction and perpendicular to axons. Since it expresses the matter of water diffusion any given diffusion tensor, it quantifies cellular and membrane density (57) and depends on the size and integrity of the fibers (62). High MD is believed to represent fiber immaturity or a disease process such as necrosis or edema (57), therefore a deviation of it may be significant.

Cell density, axons and myelin sheath, which are significant information about white matter tracts, are provided by these parameters (50).

Diffusion MRI is suitable for the study of white matter development, as it can virtually extract individual tracts and produce parameters that might reflect alterations in the underlying neural micro-structure (myelination, axon density, fiber coherence), although it is limited by its lack of specificity and other methodological problems (59).

DTI information can be analysed through different methods, such as the ROI-based method, the VBM morphometry approach, the TBSS method and the DTI tractography.

The ROI-based analysis (ROI meaning Region of Interest) consists on focusing on brain areas that are previously selected as involved in the processes that are meant to be studied. This means that it can be hypothesis-driven, based on current knowledge of the neural substrates of various neurological functions or disfunctions.

The biggest limit of this method is that focusing on specific brain regions means leaving out other regions that may be involved in a certain condition, and because of this reason it is not an ideal technique for investigating for the first time the brain areas involved in a certain neurological condition (63).

The Voxel Based Morphometry (VBM) method allows a comprehensive analysis of the brain, although, regarding the interpretability of the results from this approach, the content of each voxel can be imprecise, carrying data that can be ambiguous due to local misalignment. Nevertheless, by accurate validation and interpretation, this method can lead to valid conclusions (64).

Tract-Based Spatial Statistics (TBSS) is a method arranged to carry out statistical testing of diffusion parameters' data alleviating the alignment problems. This is achieved through the use of an initial approximate nonlinear registration, followed by the projection onto an alignment-invariant tract representation, which is an estimation of a "group mean FA skeleton" (58).

This represents the centres of all fibre bundles, or collection of white matter neurons all with a similar anatomical pathway, that are statistically common to subjects involved in the study.

As a result, with TBSS analysis the spatial smoothing is not needed, unlike in voxel-wise statistics, preventing distortion of the results due to smoothing. TBSS thus allows DTI data to be compared between groups of individuals in an automated and reliable way (63).

DTI tractography is a qualitative method that allows visualization of white matter tracts, facilitating the study of connectivity and continuity of neural pathways. It works on an a priori hypothesis, identifying a "pixel of interest" on the structural map from which a line is propagated along the fiber orientation determined by V1, allowing virtual reconstruction of white matter fiber bundles and their microstructural properties. Since DTI tractography is only qualitative, it only graphically illustrates the directionality of fiber pathways, without being fully anatomically realistic, due to the fact that.it is often an estimation based on a tractography algorithm(63).

AIM OF THE STUDY:

Available literature reported the need to fill the lack of knowledge regarding the neuroradiological correlates of sensory profiles in healthy adults. So, we aimed to examine the MRI correlates of sensory profiles in a sample of typically developed adult individuals with different techniques: structural T1, DTI and resting-state functional MRI (rs-fMRI).

Methods

Participants and Demographics

Thirty-four females and twenty-three males (mean age ± standard deviation (SD) = 32.7 ± 9.3), typically developing right-handed subjects, participated in this study.

Our study was approved by the Ethical Committee of IRCCS Ospedale Policlinico San Martino, and all subjects provided informed consent for participation in the study, after receiving a comprehensive explanation of study procedures and goals.

Inclusion criteria were:

- Age greater than 18 years.
- Willingness to participate in the study.
- Spoken language: Italian.

Exclusion criteria were:

- History of psychiatric disorders.
- First-degree familiarity for psychiatric disorders.
- Presence of severe neurological and medical illnesses (e.g., Parkinson disease, vascular diseases, cancer).
- Current alcohol and substance abuse (during the previous three months).
- Inability to undergo an MRI examination (e.g., metal implants, claustrophobia).

In addition, the medical staff of the Psychiatric Unit of the IRCCS Ospedale Policlinico San Martino collected sociodemographic data and medical and psychiatric status information.

MESUREMENTS:

Every participant to the study has completed the Adolescent/Adult Sensory Profile (AASP) and has undergone MRI examination with three different MRI techniques: structural T1, Diffusion Tensor Imaging (DTI) and resting state functional MRI (rs-fMRI).

The Adolescent/Adult Sensory Profile (AASP)

In order to assess the sensory processing patters of the participants to the study, they responded to the AASP test, a 60-items self-report test, designed as a trait measure of sensory processing, evaluating through the questions the behavioural responses to everyday sensory experience for each category. The participants were asked to indicate the frequency of their behavioural responses to sensory experiences in daily life, and

scoring system consists in a 5-point Linker scale, and each of the four quadrants, namely the sensory profiles, are represented by fifteen items that cover all the classes of stimuli (11). Norms exist for different age groups.

Statistical analysis

Statistical analysis was performed using R software.

Mri recording

We used a 1.5-T GE scanner with a standard head coil. Foam pads were used to reduce head motion and scanner noise.

Three-dimensional T1-weighted anatomical images were acquired in a sagittal orientation employing a 3D-SPGR sequence (TR/TE=11.5/5 ms, IR=500 ms, flip angle=8 degree, FOV=25.6 cm) with a resolution in-plane of 256x256 and slice thickness of 1 mm. Diffusion tensor imaging was acquired with a pure axial single-shot echo-planar imaging sequence. The diffusion sensitizing gradients were applied along 60 non-collinear directions (b=1000 s/mm2), together with 5 acquisitions without diffusion weighting (b=0).

Fifty-five contiguous axial slices were acquired with a slice thickness of 2.5 mm without a gap. The acquisition parameters were as follows: TR/TE=13750/93 ms; image matrix=128x128; FOV=24 cm; NEX=1.

Functional MRI (fMRI) scanning was carried out in the dark, with participants instructed to keep their eyes closed, relax, and move as little as possible. Functional images were collected using a gradient **Echo Planar Imaging (EPI)** sequence sensitive to Blood-Oxygen-Level Dependent (**BOLD**) contrast (TR/TE = 2000/30 ms, flip angle = 90, FOV = 24 cm). Whole-brain volumes were acquired in 33 contiguous 4-mm-thick transverse slices, with a 1-mm gap and 3.75 x 3.75 mm2 in-plane resolution. For each participant, fMRI scanning lasted 5 min and acquired a total of 150 scans.

Mri processing

In this study, we aimed at correlating the four sensory profiles to all the MRI sequences we recorded.

We run **correlation analysis** with anatomical, resting state, and diffusion data at the whole-brain level in a first stage analysis.

From anatomical data, we investigated cortical thickness and voxel-based morphometry.

From EPI recording at rest, we run a within-network melodic analysis and an FSLNets one.

We run a preliminary TBSS analysis from diffusion data to define which tracts to reconstruct with tractography and then calculate their mean metrics. In a second stage analysis, since we found that only the sensation seeking profile was correlated with our whole brain data (precisely DTI one), we ran a correlation analysis between such sensory dimension and ROI-based structural values.

Anatomical data

3D T1-weighted MRI scans were converted to NIFTI format and resliced from sagittal to axial orientation. They were visually inspected, and their origin was set in correspondence with the anterior commissure.

The following processes were then carried out with the Computational Analysis Toolbox (CAT, version 12.6) within SPM12 using MATLAB (version 2017b).

All images were normalized using an affine followed by non-linear registration, corrected for bias field inhomogeneity, and then segmented into GM, WM, and CSF components (66). The Diffeomorphic Anatomic Registration Through Exponentiated Lie (DARTEL) algebra algorithm normalizes the segmented scans into a standard MNI space (67) using six iterations.

Compared to the conventional algorithm, the DARTEL approach can provide more precise spatial normalization to the template(68)). We performed a non-linear deformation on the normalized segmented images with the CAT12 toolbox as part of the modulation step. This modulation provides a comparison of the absolute amounts of tissue corrected for individual differences in brain size(69). All segmented, modulated, and normalized GM and WM images were smoothed using 8-mm full width-half-maximum (FWHM) Gaussian smoothing. Cortical thickness (CT) was evaluated according to the projection-based thickness (PBT) method (70).

The surface extraction pipeline used topology correction, spherical mapping (71), estimation of local surface complexity, and local gyrification (72). Finally, cortex surfaces were smoothed (FWHM=15mm) and resampled to a 32k mesh compatible with the Human Connectome Project (HCP). Individual values of mean white (Vwm) and gray matter (Vgm) volumes were calculated in each ROI of the Neuromorphometrics atlas (labeled data provided by Neuromorphometrics Inc. Mean CT values (mCT) within the ROIs defined in the a2000s atlas included in CAT were also calculated. In a parallel pipeline, following the canonical FSL anatomical one, the

axial-reoriented T1 images underwent bias field correction, skull-stripping, and non-linear co-registration to the standard MNI template. The resulting transformations were later used to normalize DTI and rs-fMRI data.

Diffusion data

Individual pre-processing

The diffusion-weighted data were skull-stripped using the Brain Extraction Tool implemented in

FSLv6.0 and then corrected for distortions caused by eddy currents and movements. The diffusion tensor (DT) was estimated on a voxel-by-voxel basis using the DTIfit toolbox, part of the FMRIB Diffusion Toolbox within FSL, to obtain fractional anisotropy (FA), mean (MD), axial (AD), and radial (RD) diffusivities maps, the latter obtained by averaging L2 and L3 images. A bedpost processing was done on eddy-current corrected images to allow probabilistic tractography analysis later.

Exploratory TBSS analysis

An exploratory Tract-Based Spatial Statistics (TBSS) was performed on the whole group. Individual FA images of all subjects were non-linearly registered to a standard fractional anisotropy template. We did not create a study-specific skeleton template, but we non-linearly reported each subject's fractional anisotropy map to the **FMRIB58 skeleton** (parameter –T in the tbss_3_postreg script). This was done to segment our results with the XTRACT atlas better, as later described. The same operations were subsequently applied to the individual mean, axial, and radial diffusivity images using the previously calculated transformation. Voxelwise cross-subject statistics were then applied to these data.

TBSS Results segmentation

To understand which tracts the TBSS significant voxels belonged to and which tract percentage extent they covered, significant maps resulting from TBSS analysis were segmented according to the tracts defined in the XTRACT atlas. To do this, we first created a skeletonized version of each XTRACT's tract in the standard space by masking the FMRIB58 skeleton with each volume of the xtract-tract-atlases-maxprob5-1mm image.

The number of voxels composing each skeletonized XTRACT atlas tracts was calculated. Then, we masked TBSS results with each of these skeletonized tracts, and we calculated the number of significant voxels belonging to each of these tracts and

their coverage percentage (the number of voxels divided by the number of voxels composing each tract *100).

Mean FA (and other metrics scores) values of the significant skeleton voxels within each subject tract were correlated to the SP score of interest to exclude any outlier subject. The corpus callosum region, not present in the XTRACT atlas, was obtained from the "Atlas of Human Brain Connections".

Tractography of tracts of interest

In those tracts where more than 10% of the voxels were significant, an automated XTRACT tractography analysis, using its default settings, was performed in the native space of each subject. Mean tract values, were calculated, averaging all the voxels belonging to each tract.

Individual mean values within corpus callosum were calculated in the FMRIB58 space considering all the 31704 voxels of such tract.

Resting-state functional connectivity data:

A well-established analysis *pipeline*, tested on both children(73,74) and adults (75–77) (75–77) was run on the present data. Here, we first run a within-network functional connectivity analysis of DMN.

Then, a seed-based functional connectivity analysis was run from those DMN clusters whose connectivity was modulated by AASP subscale scores.

Pre-processing

Pre-processing was performed using FEAT (78) and included:

- removal of the first four volumes to allow for signal equilibration.
- head movement correction by volume realignment to the middle volume using MCFLIRT.
- Global 4D mean intensity normalization.
- Spatial smoothing (5 mm FWHM).

We then applied ICA-AROMA (Independent Component Analysis-based Automatic Removal Of Motion Artifacts;16) to identify independent components (ICs) representing motion-related artifacts. This method calculates a set of spatial and temporal discriminative features and accordingly exploits a classification procedure to identify ICs representing motion artifacts. Specifically, these features evaluate the spatial overlaps of each component with the brain and cerebral spinal fluid (CSF) edges, the frequency content and the temporal correlation with realignment parameters

of the IC time series. Finally, ICs classified as motion-related were removed from the fMRI dataset by means of linear regression. The resulting fMRI dataset was then high-pass filtered (cut-off frequency of .01 Hz), and the mean values of the BOLD signal in both liquor and white matter were regressed from the data.

Statistical analysis

Regardless of the specific implementation of either FSL or SPM software, the same General Linear Model was tested; the four factors of each sensory profile set and subjects' age and gender were used as regressors. Contrasts evaluated each factor's positive and negative correlation, correcting for the two latter values.

Anatomical data

Cortical thickness and VBM analysis were performed with the multiple regression model of SPM using default parameters. Moreover, the ROI values (Vwm, Vgm, and mCT) previously calculated were exported, and their relation with sensory profiles scores was analysed in R software using either parametric or non-parametric (respectively, whether both measures were normally distributed or not) partial correlations, correcting for either age and gender. We reported only those significant correlations ($p<0.05$) that had an R-value over 0.3.

DTI data

For TBSS group analysis, two general linear models were designed, each composed of the four regressors of each sensory profile set (SP1 and SP2) and both age and gender subject information. All values were demeaned. Correlation between DTI metrics and SP parameters was carried out with non-parametric permutation tests (5000 permutations) and output maps were threshold-free cluster enhancement (TFCE) corrected using a significance threshold of $p < 0.05$. Mean DTI metrics on individual tracts obtained through tractography (or on FMRIB58 space template in the corpus callosum case) were correlated with the SP scores using Pearson correlation analysis (after having verified their normality through the Shapiro-Wilk test.

Melodic analysis

To assess correlations between within networks connectivity and sensory profiles parameters, pre-processed images for each participant were temporally concatenated to create a single 4D dataset. This fMRI dataset was then decomposed into ICs with a free estimation of the number of components using MELODIC (Multivariate Exploratory Linear Optimized Decomposition into Independent Components, (80). To

identify the participant-specific temporal dynamics and spatial maps associated with each individuated RSN, a dual regression analysis was applied (81). This method implies:

- The use of the selected group-IC spatial maps in a linear model fit (spatial regression) against the single participant fMRI dataset, resulting in matrices describing the temporal dynamics for each IC and participant.
- The use of these time-course matrices, which are entered into a linear model fit (temporal regression) against the associated fMRI dataset to estimate participant-specific spatial maps.

After the dual regression, spatial maps of all the participants were grouped into a single 4D file for each RSN of interest. Candidate RSNs of interest were selected by visual inspection based on previous literature (82).

Within-RSN connectivity differences were carried out with non-parametric permutation tests (5000 permutations), and analyses were restricted within the spatial RSN of interest using binary masks obtained by thresholding the corresponding Z map image ($Z > 2.3$). Output maps were threshold-free cluster enhancement (TFCE) corrected using a significance threshold of $p < 0.05$.

RESULTS

Sociodemographic characteristics

Thirty-four females and twenty-three males (mean age ± standard deviation (SD) = 32.7±9.3 years), typically developing right-handed subjects, participated in this study. **Table 1** depicts the sociodemographic characteristics of the sample as measured by the ranges, mean, and SD scores.

Questionnaires analysis

No significant age and gender difference was found in the participant's mean AASP subscale scores. **Table 1** depicts the number and percentage of subjects with scores under, above and in the normal range, for each sensory pattern.

Table 1 Sociodemographic characteristics and sensory profiles quadrant distribution of the sample

Variable	**Mean**	**SD**	**Range**	
Number (N)	57			
Age	32.7	9.3	20-59	
Gender, female (male)	34 (23)			
Race, Caucasian	57			
Dominant hand (right)	57			
BMI Kg/m^2	23.2	2.1	17.8-27.7	
Full scale IQ	102	13	87-132	
Sensory Profile		**N**	**%**	**Range**
Low registration	Under norm	15	26.3	15-23
	Norm	32	56.1	24-35
	Above norm	10	17.5	36-75
Sensation Seeking	Under norm	19	33.3	15-42
	Norm	35	61.4	43-56
	Above norm	3	5.3	57-75
Sensory sensitivity	Under norm	10	17.5	15-25
	Norm	36	63.2	26-41
	Above norm	11	19.3	42-75
Sensation Avoiding	Under norm	6	10.5	15-26
	Norm	40	70.2	27-41
	Above norm	11	19.3	42-75

TBSS analysis

Analysis of FA and RD revealed a significant connection to a sensory profile, in particular they were found respectively positively and negatively correlated to the sensation seeking profile in a total of 9408 and 12443 voxels. On the contrary, the analysis of MD and AD did not reveal any significant correlation with any sensory profile. The results are displayed in **Fig 2.**

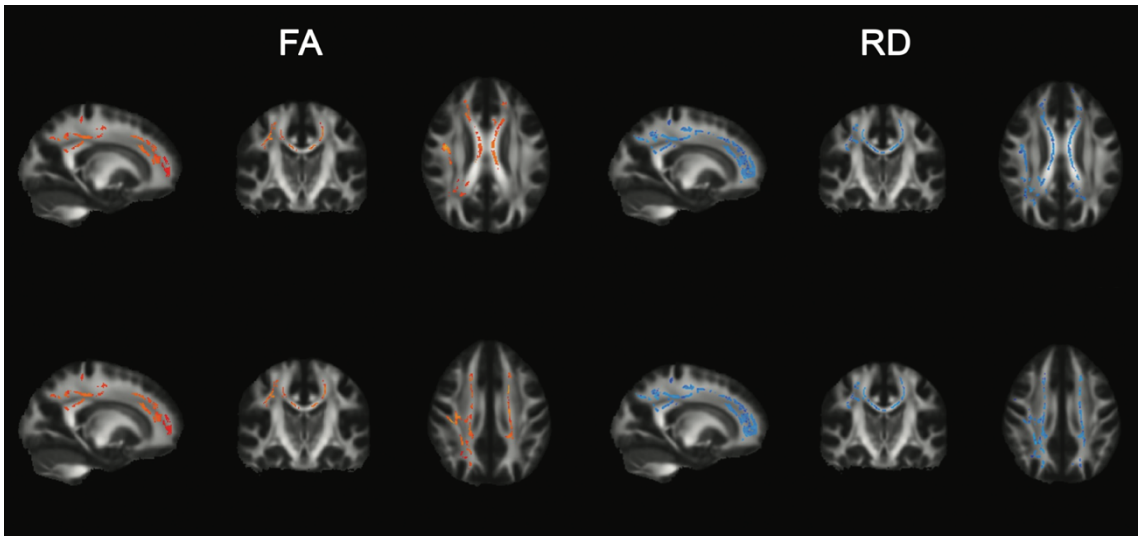

Figure 2: TBSS results. Positive (left) and negative (right) correlation between SP_STS, FA and RD.

Segmentation of TBSS results with XTRACT atlas

We segmented both FA and RD significant TBSS maps with each XTRAT tract's skeletonized version and found that 15 and 17 tracts had a fraction (higher than 10%) of their voxels' values, respectively FA and RD, correlated with the SP_STS score. The coverage percentages within each of these tracts are summarized in table 2.

Table 2 Correlations between sensation seeking and DTI metrics: FA (left) and RD (right) of whole-brain TBSS and XTRACT based analyses. cov %: percentage of voxels within each XTRACT tract that TBSS analysis found significantly correlated with sensation seeking. Correlation between sensation seeking and significant voxels of TBSS (tbss-R and tbss-P). Correlation between sensation seeking and all voxels of each XTRACT's tract (Xtract-R and Xtract-P). R= regression coefficient, p=statistical significance, n.s.= not significant.

	FA					**RD**				
	TBSS			**xTract**		**TBSS**			**xTract**	
tract	**cov %**	**R**	**P**	**R**	**p**	**cov %**	**R**	**p**	**R**	**p**
af_r	13.1	0.51	<.0001	0.23	0.093	12.9	-0.37	0.0041	-0.23	0.1
atr_l	12.2	0.5	<.0001	0.31	0.021	17.6	-0.49	<.0001	-0.36	0.008
atr_r	13.3	0.54	<.0001	0.3	0.029	13.7	-0.5	<.0001	-0.36	0.007
cbd_l	25.7	0.45	<.001	0.41	0.0018	22.4	-0.45	<.001	-0.33	0.016
cbp_l	45.0	0.3	0.024	n.s.	n.s.	11.4	-0.31	0.017	n.s.	n.s
cst_r	--	--	--	--	--	11.3	-0.46	<.001	-0.34	0.012
fa_l	10.1	0.38	0.0035	0.28	0.042	12.4	-0.42	0.0011	n.s.	n.s.
fa_r	10.8	0.43	<.001	0.28	0.041	12.4	-0.45	<.001	n.s.	n.s.
fmi	27.4	0.49	<.0001	0.29	0.036	43.1	-0.47	<.001	n.s.	n.s.
mdlf_r	10.5	0.47	<.001	0.34	0.013	10.7	-0.46	<.001	-0.35	0.008
or_r	14	0.38	0.0033	0.37	0.0066	13.7	-0.41	0.0016	-0.28	0.04
slf1_l	13.1	0.44	<.001	0.33	0.013	18.3	-0.42	0.001	-0.31	0.025
slf1_r	15.6	0.5	<.0001	0.3	0.025	28.7	-0.43	<.001	n.s.	n.s.
slf2_r	24.3	0.56	<.0001	0.35	0.01	24.3	-0.46	<.001	-0.34	0.012
slf3_r	12.6	0.53	<.0001	n.s	n.s	--	--	--	--	--
cc	19.9	0.55	<.0001	0.41	0.003	27	-0.52	<.0001	-0.38	0.011
uf_l	--	--	--	--	--	15.2	-0.4	0.0021	-0.26	0.011
str_r	--	--	--	--	--	10.4	-0.4	0.0019	-0.25	0.013

Abbreviations: af, Arcuate Fasciculus; **atr**, Anterior Thalamic Radiation; **cc**, Corpus Callosum; **cbd**, Cingulum subsection: Dorsal; **cbp** Cingulum subsection: Peri-genual; **cst**, Corticospinal Tract; **fa**, Frontal Aslant Tract; **fmi**, Forceps Minor; **mdlf**, Middle Longitudinal Fasciculus; **or**, Optic Radiation; **slf**, Superior Longitudinal Fasciculus; **str**, Superior Thalamic Radiation; **uf**, Uncinate Fasciculus.

Pearson correlation analysis allowed to confirm the correlation between DTI metrics FA and RD and sensation seeking.

These tracts were reconstructed in each subject's native space through the automated XTRACT tractography analysis (corpus callosum is not present in the XTRACT), and

we calculated their mean FA and RD and correlated it with SP_STS, and the results are summarized in the columns XTRACT-R and XTRACT-P.

Other Whole- brain analysis

No significant correlation was revealed using whole-brain VBM and CT analysis between any voxel/vertices and any sensory profile. After dual-regression analysis, the same occurred analysing within network connectivity.

Second stage (anatomical) analysis

We thus focused our attention on the sensation seeking profile, looking for its correlation with ROI-based structural metrics. In none of the ROIs of Neuromorpohmetric atlas, the white matter volumes correlated with it. Instead, its grey matter volumes related positively in the left and right parahippocampal cortex (PHC) and the right precentral gyrus, inferior temporal gyrus, and cuneal cortex. Values are summarized in Table 2 and displayed in Figure 3.

Table 3 Correlations between sensation seeking and grey matter volumes (left) and cortical thickness (right) in five and three ROIs, respectively, belonging to the Neuromorphmetrics and a2000s atlases. R= regression coefficient, p=statistical significance.

GM VOLUMES	**R**	**p**	**CT**	**R**	**P**
L PHC	0.35	0.008	L IFG	0.33	0.014
R PHC	0.41	0.0018	L Postcentral gyrus	0.32	0.016
R Precentral gyrus	0.32	0.017	R Postcentral gyrus	0.38	0.004
R ITG	0.35	0.0079			
R Cuneal cortex	0.3	0.023			

Abbreviations: IFG , inferior frontal gyrus**; ITG,** inferior temporal gyrus**; L,** left**; PHC,** parahippocampal cortex**, R,** right

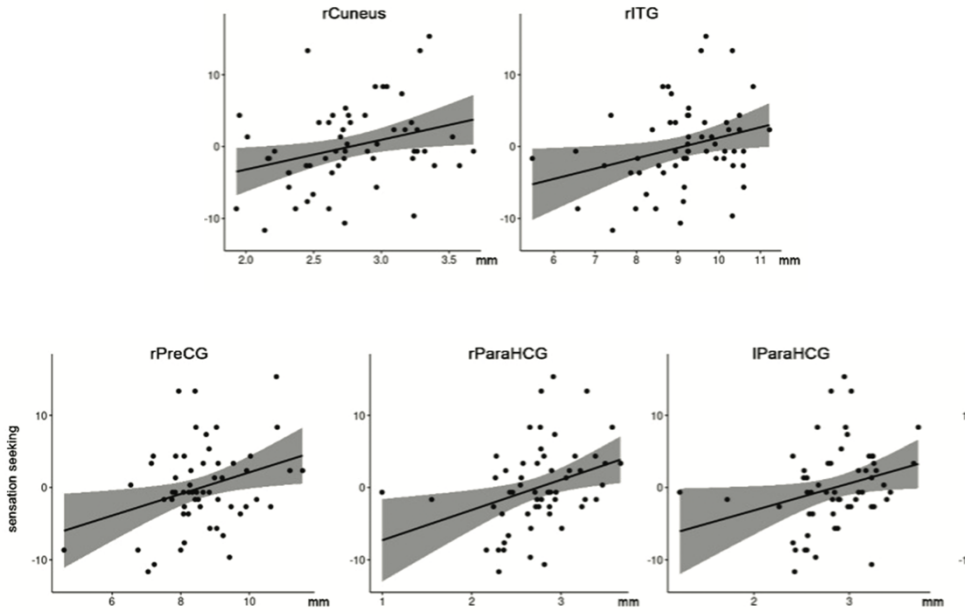

Figure 3: Correlations between sensation seeking and grey matter volumes in 5ROI of Neuromorphometric atlas.

Cortical thickness mean values within the a2000s atlas positively correlated with sensation seeking profiles in the right and left postcentral cortex and left inferior frontal gyrus. Values are summarized in Table 3 and displayed in Figure 4.

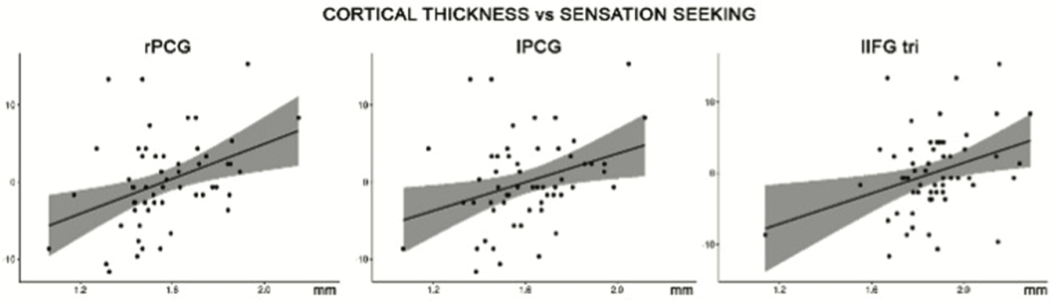

Figure 4: Correlations between Sensation Seeking and cortical thickness in three ROI of s2000s atlas

Rs-fMRI analysis

The rs-fMRI analyses did not show any significant correlation between any resting-state network and any AASP subscale.

DISCUSSION:

To the best of our knowledge, this is the first study evaluating, in a sample of healthy young adults, the relationship between sensory processing patterns and structural measures obtained from the three primary MRI sequences used in brain research: the anatomical T1, the Echo-Planar Imaging (EPI) at rest and the Diffusion Tensor Imaging (DTI).

The study's preliminary results showed a strong correlation between ASSP Sensation Seeking subscale score and several white matter tracts involved in **visuospatial sensory processing** and **affective regulation**. More precisely, we found a positive and a negative correlation with FA and RD in optic radiation (OR), superior longitudinal fasciculus (SLF), arcuate fasciculus (AF), anterior thalamic radiation (ATR), corpus callosum (CC), cingulate cortex and the cingulum bundle (CB).

Instead, we did not find any significant correlation between other AASP dimensions and whole-brain structural data (VBM and cortical thickness) or within network functional connectivity (FC) indices.

When we explored the partial correlation between sensation seeking and structural metrics within the ROIs of a well- known atlas, we found a correlation in grey matter volumes and cortical thickness in a few of those ROIs.

Tracts with enhanced white matter integrity among sensation seekers are transdiagnostically associated to major psychiatric disorders vulnerability

Our results highlight the correlation between higher white matter integrity in multisensory and affective brain regions with sensation seeking scores. Notably, available literature suggests a linkage between these tracts' reduced white matter integrity and the expression of severe mental illnesses like schizophrenia (SZ), bipolar disorder (BD), and major depressive disorder (MDD).

The optic radiation

The optic radiation is a white tract implicated in low-level simple visual processing. It runs from the lateral geniculate nucleus to the primary visual cortex in the occipital lobe (83).

Functionally, the optic radiation conveys visual inputs mainly from the magnocellular and parvocellular pathways, which project the visual dorsal and the ventral streams (84).

The superior longitudinal and the arcuate fasciculi (SLF e AF)

The superior longitudinal fasciculus (SLF) and the arcuate fasciculus (AF), considered in the past as a single structure, are distinct white matter tracts with different functions (85).

The SFL is a vast tract whose primary function is to connect frontal and parietal lobes and, to a lesser extent, temporal cortex (86). Anatomically, the SLF comprises three subcomponents (SLF I, II, and III) (85).

The SLF I runs from the medial and dorsal parietal cortices to the dorsal and medial frontal cortices; the SLF II conveys information from the angular gyrus in the inferior parietal cortex to the dorsolateral frontal cortex; the SLF III connects the parietal supramarginal gyrus to the ventral premotor and prefrontal areas (87).

On the other hand, the AF runs from the auditory area to the middle and inferior frontal gyri (87).

SLF I and SLF II integrate sensory information and motor planning, subserving visuospatial attention and complex motor functions (88). AF, SLF II, and SLF III are involved in auditory and language processing in the dominant hemisphere and spatial processing in the right non-dominant hemisphere (89); moreover, AF and SLF III are implicated in the prediction of others' emotional states based on facial expression, eye gaze, and other cues (87).

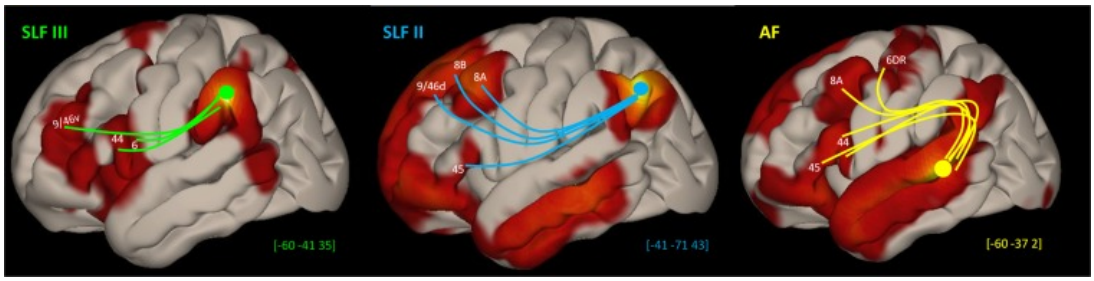

Figure 5 Seed-to-voxel resting state connectivity group results using 5 mm spheres as seeds. The supramarginal seed (green) was placed at MNI coordinates [x = −60, y = −41, z = 35], the angular seed (blue) at [x = −41, y = −71, z = 43], and the temporal seed (yellow) at [x = −60, y = −37, z = 2]. Significance threshold of p-uncorrected height of 0.001 and FDR corrected cluster-threshold of p = 0.05. Schematic representation of each tract and their frontal targets are displayed (89) .

The Anterior Thalamic Radiation (ATR)

The anterior thalamic radiation (ATR) fibers connect the mediodorsal thalamic nuclei with the prefrontal cortex (90) with minor projections directed to ventral periaqueductal grey and the temporomesial region (91), and the anterior thalamic nuclei and the anterior cingulate cortices (99).

The Corpus Callosum (CC)

The corpus callosum (CC) is the largest commissure of the human brain, which plays an essential role in the communication between the right and left hemispheres (93). The information flows through fibers distributed according to specific modalities: the anterior fibers (forceps minor) carry motor and taste information between the frontal cortices; the central, posterior, and splenial fibers allow the integration of somatosensory, auditory, and visual stimuli by connecting the parietal, temporal, and occipital lobes (94).

These patterns of associations allowed the multidimensional representation of information, thus enabling adaptative coordination of sensory-motor, affective and social responses and facilitating the higher-order cognitive functions (95).

The Cingulate Cortex and the Cingulum Bundle

The Cingulate Cortex is a brain region crucially involved in different functions, with each portion of the CC that subserves a distinct functional specialization, such as emotional homeostasis and reward (pregenual, subgenual, and dorsal anterior cingulate cortices), motivation, executive functions, and social responsiveness (Anterior Cingulate Cortex; ACC), pain processing and motor functions (Anterior and Midcingulate Cortices).

The Cingulum Bundle (CB) is a vast white matter structure that connects subcortical regions to the Cingulate Cortex and interconnects Parietal and Medial Temporal Cortices (96). The Cingulum is a highly environment-sensitive structure with a prolonged development. This reason might explain its crucial role in neurocognitive developmental differences between subjects (97) and its essential involvement in several mental and neurodevelopmental disorders (96). The Anterior and Dorsal CB mediate performance in higher cognitive control and executive function (shifting/inhibition and updating/working memory) (98). The left CB's FA, in particular, was found to be positively associated with verbal and symbolic measures of cognitive control and to general cognitive processing speed (99).

Psychiatric correlates to structural alterations in white matter structures with enhanced integrity in sensation seekers

Regarding the optic radiation, a reduction of FA in bilateral optic radiations is a finding associated with early-stage schizophrenia (100), together with the dysfunctions of the visual dorsal and to the ventral streams (101).

The superior longitudinal and arcuate fasciculi are white matter connections that mainly belonged to the frontoparietal network, and are crucial for sensory processing and cognitive functions, thus subserving several activities linked to daily living, from the use of simple tools up to metacognition and empathy (86). Not surprisingly, these white matter tracts' microstructure alterations are present among severe mental illnesses populations. For example, a recent review of structural brain abnormalities in individuals at ultra-high risk for psychosis includes the set of alterations in the SLF as a "promising neurobiological marker for the risk of psychosis" (102). In particular, a negative correlation emerged between right SLF's FA and positive symptoms severity (102), diagnosis of a brief psychotic disorder (103), the entity of disorganized schizotypy (104), and, together with AF's FA reduction, with schizophrenia with auditory hallucinations (105). Moreover, a meta-analysis of DTI studies on medication-free major depressed subjects reported a robust FA reduction in SLF III (106).

About the anterior thalamic radiation, it is involved in cognitive functions, subserving the executive functions and the complex behaviours planning (107). The ATR is also crucially involved in affective regulation and runs very close the medial forebrain bundle (MFB). Despite their proximity, the two groups of fibers have very different physiological functions: while the ATR mediates feelings of distress, depression, and psychic pain (90,91), the MFB is a pivotal tract of the reward-seeking circuitry (91). Two review articles reported that the decrement of ATR's FA was associated with different mental pathological conditions such as ultra-high-risk psychosis(102) and bipolar disorder (108,109). The FA of ATR in major depressed subjects positively correlated with anhedonia, possibly reflecting early-stage compensation mechanisms (104) and negatively correlated with suicidal behaviours (110). Interestingly, children with sensory processing dysfunction displayed cognitive and visuomotor control impairments linked to reduced FA in ATR and SLF (111).

Concerning the corpus callosum, its structural integrity is associate to resiliency to stress (112) since it displays high plasticity in response to environmental stimuli (113). On the other hand, a reduced integrity of this structure is a common finding among several mental illnesses. In fact, a decrease in FA of the CC was associated with ultra-high-risk psychosis (102), schizophrenia (114), the risk for bipolar disorder (115), bipolar disorder (108,116) major depressive disorder (110), obsessive-compulsive disorder (117), borderline personality disorder (118), ASD and ADHD (119).

Lastly, the left cingulum bundle's integrity is related to conceptual disorganization in untreated first-episode psychosis (120), while the left CB's FA decrease was related to ultra-high-risk psychosis (102), theory of mind abilities in first-episode psychosis (121), bipolar disorder (109), suicidality in depression (110), and bipolar disorder with psychotic features (103).

Gray matter volume and cortical thickness in sensation seekers and major psychiatric disorders

A correlation was found between sensation seeking scores and an increased gray matter (GM) volume in the parahippocampal cortex, precentral gyrus, inferior temporal gyrus, and cuneus.

The parahippocampal cortex (PHC) comprises a vast part of the medial temporal lobe, between the hippocampus and the fusiform cortex. Functionally, it plays an essential role in visuospatial contextual processing and episodic memory (122).

The precentral gyrus is the site of the primary motor cortex, which subserves different crucial functions such as motor activity and learning and consolidation, inhibition of involuntary movement, observation of motor tasks and integration of multiple sensory inputs, and motor imagery (123).

The inferior temporal gyrus has different functions. As part of the ventral visual pathway, it is involved in the visual processing of colours, faces, and shapes (124),moreover, it regulates emotion, language, decision making, and impulsive behaviours (125).

The cuneus covers part of the occipital lobe; it is bounded inferiorly by the calcarine sulcus and the parietooccipital sulcus. The cuneus facilitates the functioning of the dorsal and ventral visual streams, thus allowing basic and higher-order visual processing such as decoding the direction, orientation, and speed of simplex and complex visual stimuli visual imagery processes (126).

Our results resemble those previously reported by Chen and colleagues in a large study (n=11474) on the adolescent brain, sensation seeking dimension, measured through the UPPS-P scale, is associated with volumetric alteration, with increased grey matter volume in several regions, including parietal, temporal, frontal, hippocampal and cingulate cortices (127).

Regarding cortical thickness (CT), a positive correlation was found between sensation seeking scores and inferior frontal gyrus (IFG) and of postcentral gyrus (PCG). The IFG is part of the prefrontal cortex comprises the inferior frontal sulcus superiorly, the

lateral sulcus inferiorly, and the inferior precentral sulcus posteriorly; it is divided into three distinct cortical regions: the pars orbitalis, the pars triangularis, and the pars opercularis (128).

According to available literature, IGF showed functional lateralization (129). In particular, left IGF, which is involved in language processing(130), inhibitory control over motor responses (131), interference suppression (132), tool-use action observation (133), perception, imitation and internal representation of movements, processing of empathy, and working memory (129).

The PCG corresponds to the primary somatosensory cortex, extending on the parietal's lateral surface between the central and postcentral sulci (134). The PCG contains an inverted map of the contralateral body. It is crucially involved in multimodal sensory information processing (135), and its function includes the elaboration of proprioception, mechanical, tactile, thermic, and painful stimuli (136).

Notably, the regions that displayed a correlation between CT and GM volume reduction and the sensation seeking scores are mainly involved in **visuospatial processing and multisensory integration**. Abnormalities in these regions seem to confer an increased risk for major psychiatric disorders. For example, a recent ALE meta-analysis between large sample-size of schizophrenic, bipolar, and depressed subjects reported common evidence of reduced GM volume in the parahippocampal gyrus (137). Furthermore, a more recent systematic review on the topic includes the inferior frontal gyrus, the medial temporal lobe, and the occipital lobe regions that compose the dorsal visual stream between the critical areas associated with the neurobiology of deficient multisensory integration in schizophrenia (138).

Functional connectivity in sensation seekers individuals

According to the present results, none of the AASP subscales had a relationship with functional connectivity at rest. Following the classical approach, when strong a-priori hypotheses are missing, we started to explore the within-network functional connectivity of the default mode network, the main functional brain hub at rest.

According to existing literature that associated the sensation seeking profile to increased motor behaviours, and impulsivity (30) and describe these individuals as constantly researching environmental inputs (9), within network connectivity was also run in sensorimotor, primarily visual, lateral occipital and auditory related RSNs. Consistent with the present literature, these analyses did not produce any results.

Conclusion

Here, we reported that a tendency to sensation seeking in healthy subjects is strongly associated with a higher white matter and grey matter structural integrity in areas mainly involved in visuospatial processing and decision-making functions. Notably, the sensation seeking profile is usually associated with a tendency to actively pursue novel sensory experiences (139) and a tendency to impulsive decision-making processes (140). In this framework, we speculate that the better structural integrity associated with sensation seeking might reflect, at least in part, a possible neurobiological substrate of this sensory profile.

Future neuroradiological investigations comparing healthy subjects with patients with major psychiatric disorders are needed to confirm the possible linkage between sensory profiles and the vulnerability to mental illnesses.

If approved, these hypotheses might lead to a better understanding of the pathophysiology of major psychiatric disorders and the development of specific sensory-based intervention tools to enhance the resilience to mental illnesses.

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